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Self-Injurious Behavior in Male Rhesus Macaques: Association with Aggression and Stress as Measured by Salivary Cortisol

Corrine Kay Lutz

A dissertation submitted in partial fulfillment of the requirements for the degree of

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Abstract

Self-Injurious Behavior in Male Rhesus Macaques: Association with Aggression and Stress as Measured by Salivary Cortisol

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Self-injurious behavior (SIB) occurs in populations of socially-reared captive primates and can be a serious problem. The purpose of the first study was to survey a large colony of rhesus macaques for the presence of SIB and to identify potential risk factors. Almost 25% of the subjects were assessed to be self-biters, and over 10% wounded themselves. Subjects with SIB tended to be male and over seven years of age. Environmental risk factors included age when individually housed and the number of blood samples drawn. Although SIB has obvious deleterious effects such as tissue damage, it may also have benefits such as stress reduction. Because of the disruptive nature of obtaining physiological samples, few studies have measured stress concurrent with bouts of SIB. The focus of the second study was to develop new techniques for saliva collection to measure cortisol. These techniques were then used to gauge stress in rhesus subjects at the time of a biting event in comparison to control periods. No differences in cortisol were detected, suggesting that either there was no association between stress and spontaneous biting or the association was not detected due to variability in the data, timing of sample collection, or ameliorated stress by the biting itself. It was then proposed that self-injury is associated with social aggression and occurs in this context when physical contact is prevented. To test this hypothesis, subjects were first presented with videotapes containing either conspecifics or scenery. Levels of cortisol did not increase during the video presentation. Aggression increased during the conspecific videos, but self-biting remained constant, suggesting that the two behaviors were not associated. The subjects were then placed in more stressful situations as determined by cortisol levels: an empty room or a room containing an unfamiliar conspecific. Although these two situations were equally stressful, levels of aggression again increased in the conspecific situation, while levels of self-biting remained constant. SIB is a problem in primate facilities in part due to rearing and housing conditions. Although aggression was not associated with SIB, social settings were, and stressful environments may still play a role.

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CHAPTER I

Introduction to Self-Injurious Behavior

Overview

Self-injurious behaviors (SIB), such as self-biting, are potentially harmful behaviors that have been observed in the human population as well as in populations of captive nonhuman primates. These atypical behaviors may have developed from normal infant or juvenile behavior patterns that matured inappropriately. The cause of this misdirected development is undoubtedly due to an interaction of genetic and environmental factors. Earlier research on such seemingly maladaptive behavior in nonhuman primates focused on isolation rearing, but self-injurious behavior also occurs in less extreme social rearing environments. The focus of Study 1 was to assess the behavior and to survey the historic laboratory records of a large population of socially-reared singly-housed rhesus macaques for the presence of self-biting and self-wounding behaviors and to identify potential risk factors associated with these behaviors.

SIB can have obvious deleterious effects such as tissue damage, but it may also have benefits such as arousal mediation or stress reduction. Previous work, to be reviewed below, describes a number of hypotheses relating to the occurrence of self-injurious behaviors. The possible risk factors discussed range from genetic and physiological to environmental conditions. Because of the number of conditions involved, SIB should be viewed as a symptom of a number of possible disorders rather than a single syndrome. Due to the wide range of hypothesized triggers for self-injurious behavior, the present study focused on two environmental factors, stress and aggression.

One theory of self-injurious behavior is that an individual performs this behavior under stressful conditions and that self-injury aids in reducing stress levels. In support of this theory are human subjects who report that they use self-mutilation as a means to feel relaxed (Favazza and Conterio, 1989). Because self-report is not an option in nonhuman primates, this connection has typically been observed by recording resulting behaviors when an animal is placed in what could be considered a stressful condition. Physiological measures have also been used to determine the effects of self-injurious behavior on levels of stress. However, because of the relatively infrequent occurrences of this behavior as well as the disruptive nature of obtaining physiological samples, few studies have measured indicators of stress concurrent with bouts of self-injurious behavior. The focus of the second and third studies, therefore, was to develop and utilize new techniques for stress measurement and to determine relative levels of stress in rhesus subjects around the time of a biting event in comparison to non-biting episodes.

A second environmental theory addressed in this dissertation was that self-injury is associated with social aggression and that it occurs in aggressive contexts when physical contact is prevented. In support of this hypothesis, self-injury in the human population was associated with both greater lifetime aggression and chronic anger (Simeon et al., 1992; Collacott, Cooper, Branford, and McGrother, 1998). Similarly, in nonhuman primates, isolate rhesus subjects alternated fighting with bouts of self-biting during confrontations with other monkeys (Fittinghoff, Lindburg, Gomber, and Mitchell, 1974). The focus of the remaining two studies in this dissertation was to test whether SIB is associated with social aggression or whether the two behaviors are independent.

Stereotyped and Self-Injurious Behavior

Definitions

Stereotypies are repetitive, seemingly functionless behaviors that often interfere with an animal's typical behavioral repertoire. They are regarded as atypical relative to what is observed in the wild and are habitual in their manifestation (Berkson, 1968). Stereotypies can be categorized into repetitive whole-body or fine motor movements. Whole-body stereotypies may include gross movement patterns such as pacing, back-flipping, and swinging. Alternatively, fine motor stereotypies include more precise and often self-directed movements such as digit-sucking and eye-poking (Berkson, 1968; Bayne et al., 1991). These behaviors have been observed in many species of macaques (*Macaca* sp.) reared or housed in suboptimal captive conditions, often with insufficient social contact (Davenport and Menzel, 1963; McKinney, Kliese, Suomi, and Moran, 1973; Pond and Rush, 1983). Stereotypies may begin as simple reflexes or repetitions, but can become more complex with time (Wolff, 1967). The types of stereotypies, however, appear to be very individualistic and can vary greatly among subjects (Walsh, Bramblett, and Alford, 1982). Although the time devoted to stereotypies may remain constant, the diversity of stereotypies can decrease with age; adults tend to have smaller, more individualized sets of repetitive behaviors than do young (Fittinghoff et al., 1974; Thierry, 1984).

Stereotypies are not generally harmful, however other forms of atypical behavior pose a greater potential for self-injury. *Self-injurious behavior* (SIB) can be defined as a physical attack on or potentially damaging manipulation of one's own body, ranging from self-directed biting and slapping to head-banging and hair pulling, sometimes resulting in injury. Although injury is not a requirement for a behavior to be categorized as SIB, the potential for injury exists. SIB may differ in kind or simply in degree (Cataldo and Harris, 1982) from stereotypies. Like stereotypies, self-injurious behavior tends to be observed in captive-reared animals with a restricted rearing environment (Anderson and Chamove, 1985), and in humans with genetic (Anderson and Ernst, 1994) or personality (Konicki and Schulz, 1989) disorders. Resulting injuries are often ritualized (i.e., same method of execution and same body location) (Konicki and Schulz, 1989).

Incidence of SIB

Self-injurious behavior in humans has been observed in normal children (deLissovoy, 1961; reviewed in Green, 1967), people with mental retardation (Altmeyer et al., 1987), learning disabilities (Collacott et al., 1998), and personality disorders (Konicki and Schulz, 1989), the prison population (Virkkunen 1976; Coid, Wilkins, Coid, and Everitt, 1992), as well as the general population (Briere and Gil, 1998). Age may play a factor in the expression of SIB, with decreased levels observed in older adults (Virkkunen 1976). Although rates of SIB in humans are generally higher in males than in females (Halliday and Mackrell, 1998), not all studies support such gender differences (Pattison and Kahan, 1983; Collacott et al., 1998; Briere and Gil, 1998).

In surveys of institutionalized individuals with mental retardation, 10-14% were reported to engage in SIB (Maisto, Baumeister, and Maisto, 1978; Schroeder, Schroeder, Smith, and Dalldorf, 1978; Griffin, Williams, Stark, Altmeyer, and Mason, 1986; Altmeyer et al., 1987). The rates of SIB were much higher in schizophrenic children (40%; Green, 1967) and psychiatric inpatients (19%; Briere and Gil, 1998) and much lower in non-institutionalized mentally-retarded individuals (1.7-2.6%; Rojahn, 1986; Griffin et al., 1987), the general institutionalized population (4.3%; Phillips and Alkan, 1961), or the general population (4.3%, Briere and Gil, 1998). The incidence of self-injurious behavior in humans can be related to the severity of disability. Between 90 and 96 percent of institutionalized individuals with SIB were rated as profoundly or severely retarded (Maisto et al., 1978; Schroeder et al., 1978; Altmeyer et al., 1987). Maisto et al. (1978) reported that zero percent of mildly retarded, 3.4 percent of the moderately retarded, and 20.7 percent of the profoundly or severely retarded residents exhibited SIB. Head-banging, head hitting, and self-biting were the most frequently reported SIB's in humans (Maisto et al., 1978; Griffin et al., 1986; Griffin et al., 1987).

Self-injurious behavior is not restricted or limited to the human population. In populations of nonhuman primates, SIB is most often reported in captive animals (Bayne, Haines, Dexter, Woodman, and Evans, 1995), particularly those that have experienced social deprivation (Anderson and Chamove, 1985). In two surveys of large primate facilities, approximately 14% of singly-housed male macaques (*Macaca sp.*) were assessed to be self-biters (Jorgensen, Kinsey, and Novak, 1998) and 15.8% of similarly housed macaques at another facility had a record of self-wounding (Bayne et al., 1995).

SIB Correlates

Self-injurious behavior is not usually considered a syndrome in and of itself. Instead, SIB is regarded as a symptom or a characteristic of several different kinds of biobehavioral disorders. In addition to genetic or physiological associations (Lesch and Nyhan, 1964; Simeon et al., 1992), SIB may also be linked to environmental circumstances such as suboptimal rearing or housing conditions (Cross and Harlow, 1965). Few, if any, of the following factors can be said to "cause" SIB. Instead, they should be viewed as correlates which increase the probability of SIB occurrences.

Genetic Influences

Self-injurious behavior is a major feature of several genetic disorders in humans. The Lesch-Nyhan syndrome is an x-linked disorder in which there is a reduction in hypoxanthine-guanine phosphoribosyltransferase (HGPRT), an enzyme that is involved with purine metabolism (Seegmiller, Rosenbloom, and Kelley, 1967). The result is an excess production of uric acid as well as behavioral problems which include self-injury (Lesch and Nyhan, 1964). In this syndrome, aberrant behavior may start in infancy, but more serious problems develop when the teeth first erupt. Self-injury, such as biting of the lips and fingers can then occur (Nyhan, Johnson, Kaufman, and Jones, 1980). Most patients lose a large amount of tissue around the lips, and partial amputations of fingers are not uncommon (Nyhan, 1976). Individuals with this syndrome perceive pain; they do not want to bite themselves and scream or cry when they do (Nyhan, 1976).

The Smith-Magenis syndrome is a rare genetic condition involving a deletion in chromosome 17. Individuals with this condition display symptoms such as learning disabilities, hyperactivity, and sleep disorders (Deb, 1998). They also exhibit self-injurious behaviors such as biting and hitting themselves. Less frequently, they are known to pull out their finger and toenails and insert objects into body orifices (Dykens and Smith, 1998). Individuals with this disorder demonstrate some insensitivity to pain (Deb, 1998).

Self-mutilative behavior has also been reported to be a feature of the Cornelia de Lange syndrome. Individuals with this disorder often scratch themselves to the point of bleeding, and they bite themselves on the thumbs and the lips (Shear, Nyhan, Kirman, and Stern, 1971). Additional features of this disorder include hirsutism, malformed limbs, and below normal intelligence (Jackson, Kline, Barr, and Koch, 1993).

There are several other genetic disorders that result in self-injurious behavior: the Rett syndrome, which involves biting the hands and fingers, head-banging, hair-pulling, and scratching (Coleman, Brubaker, Hunter, and Smith, 1988; Jackson et al., 1993), the Prader-Willi syndrome, a disorder associated with an abnormality in chromosome 15 in which individuals pick at themselves, resulting in persistent sores (Clarke, Waters, and Corbett, 1989), and the Oculocerebrorenal Syndrome of Lowe, an x-linked disorder characterized by cognitive impairment and congenital cataracts as well as self-injurious behavior (Kenworthy, Park, and Charnas, 1993).

There is no direct evidence assessing the genetic basis of SIB in nonhuman primates. Instead, it is inferred indirectly from species differences. For example, stumptailed (*Macaca arctoides*) and rhesus (*Macaca mulatta*) macaques appear to be prone to developing SIB when reared in isolation (Fittinghoff et al., 1974; Anderson and Chamove, 1985), but isolation rearing has a lesser effect on pigtailed (*Macaca nemestrina*) macaques (Sackett, Holm, and Ruppenthal, 1976). Chimpanzees (*Pan troglodytes*) tend to exhibit lower levels of SIB (2-4% of Ss; Walsh et al., 1982; Fritz, Nash, Alford, and Bowen, 1992) than do macaques, although they do exhibit stereotypies and other self-directed behaviors (Anderson and Chamove, 1981).

Neurobiological Factors

In addition to genetic factors, self-injurious behavior often has physiological underpinnings. However, SIB may be a syndrome of diseases that includes more than one biochemical etiology (Herman, 1990; Thompson, Hackenberg, Cerutti, Baker, and Axtell, 1994). Physiological systems associated with stereotypic or self-injurious behavior include the serotonin, the dopamine, the opiate systems, and the hypothalamic-pituitary-adrenal (HPA) axis.

Serotonin

Serotonergic dysfunction may be one physiological mechanism that underlies self-injurious behavior (Simeon, et al., 1992). A strong correlation exists between both outwardly- and inwardly-directed aggression, and serotonin (5-HT) (Coccaro et al., 1989; Van Praag, 1991). Many studies in humans demonstrate that CSF concentrations of 5-HIAA (a major metabolite of serotonin) are inversely related to levels of aggression (Brown, Goodwin, Ballenger, Goyer, and Major, 1979; Brown et al., 1982). For example, offenders who had committed more than one violent crime had a lower 5-HIAA concentration than offenders who committed a single violent crime (Linnoila et al., 1983). Aggression due to reduced serotonin functioning may be more of an irritable-impulsive nature than general physical aggression (Coccaro et al., 1989). For example, reduced central serotonergic function has been associated with a history of impulsive aggression in subjects with personality disorder (Coccaro et al., 1989) and relatively low CSF 5-HIAA levels were found in impulsive violent offenders in comparison to those who premeditated the act (Linnoila et al., 1983). There also tends to be an inverse relationship between serotonin levels and self-injurious behavior (Brown et al., 1982). Reduced concentrations of serotonin and increased concentrations of norepinephrine are associated with self-aggressivity, impulsivity, and parasuicidal behavior, suggesting that in such cases, there is a loss of control over aggressive impulses and that serotonin is associated with more than just aggression (Coccaro and Astill, 1990; Mancini and Brown, 1992; Herpertz, Sass, and Favazza, 1997; New et al., 1997).

In nonhuman primates, self-injurious behavior associated with early social deprivation has been related to changes in the norepinephrine and serotonin systems. In monkeys that self-injure, there may not be adequate linkage between these systems which could help to regulate aggressive behavior (Kraemer and Clarke, 1991). Similarly, in free-ranging rhesus monkeys, there is a significant negative correlation between aggression and CSF 5-HIAA (a major metabolite of serotonin). Monkeys rated high on agonistic scales had lower levels of 5-HIAA (Higley et al., 1992).

Countering low levels of serotonin can help to reduce levels of self-injurious behavior. In humans, one promising treatment has been the use of fluoxetine, a serotonin reuptake inhibitor (Markowitz, 1992). In one study, 10 of 12 individuals with mental retardation showed a significant decrease in SIB after receiving fluoxetine (Singh, Kleynhans, and Barton, 1998). Similar results occurred in subjects with borderline and schizotypal personality disorders (Markovitz, Calabrese, Schulz, and Meltzer, 1991). Treatment with fluoxetine also helped reduce impulsive aggression (Coccaro, Astill, Herbert, and Schut, 1990). Alternatively, providing 5-hydroxytryptophan, a precursor to serotonin, to patients with Lesch-Nyhan syndrome reduced self-mutilative behavior in some subjects (Mizuno and Yugari, 1974; Castells et al., 1979; Nyhan et al., 1980). However, in some cases patients developed tolerance to this treatment (Castells et al., 1979; Nyhan et al., 1980), or the treatment was ineffective (Ciaranello, Anders, Barchas, Berger, and Cann, 1976; Frith, Johnstone, Joseph, Powell, and Watts, 1976).

Serotonin has also been implicated in the treatment of SIB in nonhuman primates. In a study of captive groups of vervet monkeys (*Cercopithecus aethiops*), one of two males in each group was given drugs that enhanced serotonin activity (tryptophan or fluoxetine) or drugs that reduced serotonin activity (fenfluramine or cyproheptadine). Those receiving tryptophan or fluoxetine increased social contact and decreased aggression, while the opposite effect occurred when they received fenfluramine or cyproheptadine (Raleigh, McGuire, Brammer, Pollack, and Yuwiler, 1991). Similarly, the administration of L-tryptophan (a precursor to serotonin) to rhesus monkeys with SIB also resulted in a decrease of SIB and an increase in levels of CSF 5-HIAA concentrations (Weld et al., 1998). However, it remains unclear whether low levels of serotonin are associated specifically with self-injurious behavior or more generally with acts of impulse control and aggression.

Dopamine

There are indications that dysregulation of the dopamine system is also associated with the occurrence of self-injurious behavior. For example, Lesch-Nyhan subjects who self-injured had elevated plasma dopamine β-hydroxylase activity, which was not observed in patients who exhibited only a partial HGPRT deficiency and no SIB (Rockson, Stone, van der Weyden, and Kelley, 1974). However, elevated levels of dopamine are not observed in all subjects. Lloyd et al. (1981) noted a deficit in dopamine-neuron terminals in brains of post-mortem subjects with Lesch-Nyhan syndrome, and using positron emission tomography (PET) imaging, Wong et al. (1996) found a dopaminergic reduction in subjects with Lesch-Nyhan disease when compared to a normal control group. Similarly, Lesch-Nyhan patients had a lower uptake of fluorodopa F18 tracer, suggesting that they had fewer dopaminergic nerve terminals when compared to controls (Ernst et al., 1996). Lake and Zeigler (1977) also found low levels of dopamine β-hydroxylase activity in their subjects with Lesch-Nyhan syndrome, but they hypothesized that this decrease could be related to the subjects' continuously seated posture.

Fluphenazine, a dopamine antagonist at the D_1 and D_2 receptors, reduced SIB in 11 out of 15 severely to profoundly retarded subjects (Gualtieri and Schroeder, 1990). In a case study, risperidone, a serotonin-dopamine antagonist, also reduced self-injurious behavior in one Lesch-Nyhan subject (Allen and Rice, 1996). Similarly, sulpiride, a D2 antagonist, reduced SIB in four subjects with autism (Rothenberger, 1993). In nonhuman primates with ventromedial tegmental (VMT) brainstem lesions, the stimulation of the D_1 dopamine receptors by dopamine agonists elicited self-biting behavior similar to that seen in Lesch-Nyhan syndrome. Pretreatment with dopamine antagonists prevented the occurrence of self-biting (Goldstein et al., 1986; Goldstein, 1989).

Opiate system

An endogenous opioid, β-endorphin, may also underlie the occurrence of self-injurious behavior in some individuals (Herman, 1990). In support of this association are the findings that patients with SIB have higher levels of plasma β-endorphin than controls (Sandman, 1988). Nijman et al. (1999) also reported that psychiatric patients who self-mutilatored had higher dissociation scores on the Dissociative Experiences Scale (DES) than control subjects. In this example, dissociation appeared to follow rather than precede SIB, suggesting the release of β-endorphin might underlie SIB. However, Verhoeven et al. (1999) noted that in mentally-retarded subjects, β-endorphin did not differ between the SIB group and the control group that did not self-injure.

Opiate antagonists such as naltrexone and naloxone have been shown to reduce or eliminate the occurrence of SIB, supporting the theory that the CNS opiate system is associated with SIB (Sandman et al., 1983; Herman et al., 1987; Sandman, 1988; Sandman, Barron, and Colman, 1990; Thompson et al., 1994). For example, treatment with naltrexone decreased self-injury in one autistic and mentally-retarded subject (Barrett, Feinstein, and Hole, 1989). The elimination of SIB appears to last beyond cessation of the treatment in some subjects (Crews, Rhodes, Bonaventura, Rowe, and Goering, 1999). However, not all types of self-injurious behavior are reduced with naloxone or naltrexone, suggesting that this treatment may have behavior- or response-specific effects. For example, in one subject, naltrexone reduced head-slapping under demand conditions, but had no effect on head-banging during other sessions (Garcia and Smith, 1999). Subjects with elevated levels of β-endorphin relative to ACTH showed the largest reduction in SIB when treated with naltrexone. In this subgroup of individuals, the SIB may be associated with endogenous opioids and therefore treatable with naltrexone. The subjects who did not have similar levels of β-endorphin may have had different mechanisms for controlling this behavior (Sandman, Hetrick, Taylor, Marion, and Chicz-DeMet, 2000), further indicating that SIB may have multiple origins.

Two hypotheses relating the opiate system with SIB have been proposed. The "addiction" hypothesis maintains that individuals are addicted to endogenous opioids that are released during SIB (Sandman et al., 1990). In patients with moderate to profound mental retardation and with a history of self-injurious behavior, plasma β-endorphin was elevated after episodes of SIB (Sandman, Hetrick, Taylor, and Chicz-DeMet, 1997). One study compared the effects of two opiate antagonists, naltrexone (with a half-life of 36 hours) and naloxone (with a half-life of 81 minutes) on self-injury of an autistic individual. Naltrexone decreased self-injury, supporting the influence of the CNS opiate system on SIB. However, naloxone, with a shorter half-life, actually increased levels of self-injury in this subject. This increase in SIB upon daily treatment with naloxone may be due to repeated extinction bursts, which occur upon cessation of an addictive substance (Barrett et al., 1989). Extinction bursts commonly occur when the reinforcing element of a behavior such as SIB is removed (Zarcone et al., 1993; Vollmer, Ringdahl, Roane, and Marcus, 1997). Naltrexone, with its longer half-life, may have allowed the initial extinction burst to run its course, but it ultimately caused a decrease in self-injurious behavior (Barrett et al., 1989). The few reported examples of extinction bursts, however, may be evidence to question the addiction hypothesis (King, McCracken, and Poland, 1991; Buitelaar, 1993).

Alternatively, the "analgesia" hypothesis states that individuals who exhibit SIB have an elevated pain threshold brought about by the release of endogenous opioids (Herman, 1990; Sandman et al., 1990). For example, female prisoners who self-injured as well as patients with borderline personality disorder reported that they tended not to feel pain when injuring themselves, suggesting that they were experiencing analgesia (Leibenluft, Gardner, and Cowdry, 1987; Coid et al., 1992). Vietnam veterans with post-traumatic stress disorder (PTSD) reported a decrease in pain ratings after viewing a combat video. This decrease did not occur when the subjects received naloxone, an opiate antagonist, suggesting that exposure to a traumatic stressor (e.g., combat videos) induces opioid-mediated analgesia in people with PTSD (van der Kolk, Greenberg, Orr, and Pitman, 1989). However, subjects with borderline personality disorder (BPD) who self-injured did not report an increase in pain perception during a cold-pressor test after treatment with naloxone (Russ, Roth, Kakuma, Harrison, and Hull, 1994). It is possible that the cold-pressor test was not stressful enough to activate the opiate system; however, these conflicting results suggest that the association between SIB and the endogenous opioid system is not clear. Although both the addiction and the analgesia hypotheses may explain why the self-injurious behavior is not terminated, they do not explain how or why the behavior is initiated in the first place (Carr, 1977; Herman, 1990; Buzan, Thomas, Dubovsky, and Treadway, 1995).

HPA Axis

The HPA (hypothalamic-pituitary-adrenal) axis is typically associated with stress. In general, stress causes an increase in the HPA axis activity, resulting in an increased release of cortisol from the adrenal cortex (Kirschbaum and Hellhammer, 1989, 1994). Cortisol can be used as a measure of stress, because cortisol levels increase with increasing stress levels (Kalin et al., 1985). Environmental stressors that influence the HPA axis can range from novelty to physical pain. Both the anticipation and occurrence of a stressor have been followed by an increase in cortisol (Smyth et al., 1998). For example, cortisol levels are correlated with distress during the heelstick procedure in human infants (Gunnar, Porter, Wolf, Rigatuso, and Larson, 1995). In longtailed macaques (*Macaca fascicularis*), simple room changes produced slight elevations in urinary cortisol on the first day, reflecting some amount of stress in this manipulation (Crockett, Bowers, Sackett, and Bowden, 1993). In contrast to the numerous stress studies which demonstrate increasing levels of cortisol with higher levels of stress, fewer studies have looked at the reverse, the effects of relaxation techniques on the possible lowering of cortisol levels (Gust, Gordon, Hambright, and Wilson, 1993; Kirschbaum and Hellhammer, 1994).

The HPA axis has also been implicated in self-injurious behavior. For example, differences in cortisol output have been observed when comparing individuals with and without self-injurious behavior. Adult mentally retarded subjects rated as having primarily self-injurious aberrant behaviors had a lower plasma cortisol level in comparison with the retarded control group (Verhoeven et al., 1999). Similar results have been obtained with nonhuman primates. Faucheux, Bourliere, and Lemaire (1976) found a negative correlation between the intensity of the auto-aggressive behavior and levels of cortisol in stumptail macaques (*Macaca arctoides*). In addition, those that exhibited self-aggressive behavior showed lower 24-hour urinary cortisol levels than those that did not, and they reacted less to ACTH (a precursor to cortisol) stimulation. Similarly, isolation rearing has been shown to have an effect on cortisol levels in rhesus monkeys. At 19 months, rhesus infants reared in isolation had higher basal cortisol levels than did pair-reared (Sackett, Bowman, Meyer, Tripp, and Grady, 1973). However, this difference was not observed in older animals (Meyer and Bowman, 1972). More recently, Tiefenbacher, Novak, Jorgensen, and Meyer (2000) examined the relationship between self-injurious behavior (defined here as self-wounding requiring veterinary care) and levels of cortisol in rhesus macaques. Monkeys with SIB had consistently lower levels of plasma cortisol, and these levels were negatively correlated with rates of self-biting. The authors conclude that these results indicate a dysregulation of the HPA axis in animals with self-injurious behavior.

Environmental Influences

Physical disorders alone are not the only basis for self-injurious behavior. An individual's rearing history, life experiences, and environmental conditions all help to shape subsequent behavior. Self-injurious behavior may also be a reaction to an inadequate or harmful environment (Fittinghoff et al., 1974). Little is known about the provocation of such behavioral reactions, but the presence of stereotypies or SIB may reflect a past or present environmental deficit (Mason, 1991).

Trauma

The development of self-injurious behavior in humans is often associated with a traumatic experience that occurred during a young age. In the general population, SIB is associated with childhood trauma and sexual abuse (van der Kolk, Perry, and Herman, 1991; Briere and Gil, 1998). For example, female prisoners with SIB are more likely to have experienced cruelty as a child (Coid et al., 1992). In a study of 240 female habitual self-mutilators, 62% of the subjects reported childhood abuse, and the average age of onset was 6-7 years (Favazza and Conterio, 1989). Similar results were obtained in a study of both male and female psychiatric inpatients. Patients who self-mutilated reported more traumatic childhood experiences than did patients who did not self-mutilate (Nijman et al., 1999). The age at which a trauma occurs may influence the severity of self-injurious behavior. In subjects who self-injured by cutting, the earlier the trauma, the more frequently they cut themselves (van der Kolk et al., 1991).

Self-injurious behavior has also been noted in subjects who experienced a traumatic event later in adulthood. In some cases, behavior such as self-cutting becomes part of a post-traumatic stress disorder (PTSD). For example, Greenspan and Samuel (1989) noted self-cutting in three female rape victims. Similarly, Pitman (1990) reported self-cutting and burning in a Vietnam veteran with PTSD. In both reports, the self-injurious behavior followed traumatic experiences.

Rearing Conditions

Trauma in nonhuman primates is most often caused by severe rearing and housing conditions. For example, isolation rearing is an experimental condition that can be considered the most extreme form of deprivation for infant monkeys. In this condition, infant rhesus monkeys were reared in chambers in which they could not see, hear, or touch other animals from birth for up to two years of age (Harlow and Harlow, 1962a). While in isolation, the animals were observed to exhibit a number of self-directed behaviors such as self-manipulation, self-grasping, and self-rubbing (Baysinger, Brandt, and Mitchell, 1972). Upon removal from isolation, the subjects tended to display a pattern of isolate disturbance behaviors which included behaviors such as rocking, crouching, self-orality and self-clasping. For example, when a male and a female infant monkey isolated for two years were removed from isolation and placed in a social situation, they withdrew from conspecifics and huddled in a corner. After being paired together for another two years, the two isolates remained disturbed and did not interact with one another (Harlow and Harlow, 1962a; 1962b). In contrast, when socially-reared monkeys were startled, they tended to pace and piloerect (Mitchell, Raymond, Ruppenthal, and Harlow, 1966). In a later experiment, two males were isolated for a shorter period of time (6 months) and they also exhibited aberrant social behavior. However, two groups of monkeys raised in isolation for an even shorter period (80 days) greatly improved in their social behavior upon removal from isolation (Harlow and Harlow, 1962b).

The effects of isolation continue through adulthood. For example, increases in chewing orality, self-biting, and aggression occurred with an increase in age (Cross and Harlow, 1965) and differences between former isolates and socially-reared control subjects persisted. Moreover, adult rhesus isolates, but not control subjects, displayed stereotypies and bizarre movements when confronted with film segments of monkey threats. Also, when the experimenter rapped on the subject's cage with a metal dowel, isolate subjects self-aggressed or attempted to attack the experimenter, while the control subjects retreated from the stimulus (Fittinghoff et al., 1974)

Partial isolation is considered a less severe form of isolation in which infant monkeys are raised in individual cages from which they can see and hear, but not touch, conspecifics. This condition has been used for both experimental as well as general husbandry conditions such as cases of maternal rejection or nursery rearing with no available partners (Mason and Sponholz, 1963; Bayne and Novak, 1998). Similar to total isolation, partial isolation also results in deleterious behavioral effects for the infants. Abnormal behaviors exhibited by these subjects included repetitive pacing, self-clasping, and self-biting to the point of injury. In addition, none of these subjects showed typical sexual behavior (Harlow and Harlow, 1962a). In a study comparing the behavioral reactions of partial isolate and wild-caught rhesus monkeys to a novel environment, the partial isolates reacted with clasping, crouching, and stereotyped behavior. The wild-caught subjects displayed none of these self-directed behaviors and instead, spent more time locomoting (Mason and Green, 1962). Behavioral differences between wild-caught subjects and partial isolates continue through adulthood. For example, self-injurious behavior, hyperaggression, and stereotypies were more common in adult partial isolates than in controls (Fittinghoff et al., 1974). During a reinforcement and extinction study with lever pressing, more adult partial isolates than controls exhibited self-aggression, and the greatest amount was displayed by male partial isolates. This self-aggression was intensified by extinction, or blocked goal-directed activity (Gluck and Sackett, 1974). Although levels of self-clasp and self-mouth decreased with age, the levels in older adult (10-13 years) partial isolates were still higher than those in similar-aged wild-caught individuals (Suomi, Harlow, and Kimball, 1971).

Social contact and play in infants and juveniles gives monkeys an opportunity to learn appropriate targets and behaviors (Anderson and Chamove, 1980). When monkeys are not socially-housed during this stage of development, they may redirect this aggression onto themselves (Anderson and Chamove, 1980; Gluck and Sackett, 1974). Because the recipient of self-aggression does not "escape," the self-aggressive or self-injurious behaviors may continue (Anderson and Chamove, 1980). When rhesus monkeys were socialized in the dark, they exhibited almost no social aggression when compared to peers socialized in the light, but they exhibited more self-aggression when later individually housed (Anderson and Chamove, 1985). Socialization in the dark may have hindered the development of appropriate targets for aggression. When placed in social situations, the isolates tended to show more hostility than socially-reared control subjects. However, this hostility was comprised more of threats than actual physical aggression (Mitchell et al., 1966). Fewer instances of SIB were observed when the monkeys were socially housed and had an outlet for social aggression (Goosen and Ribbens, 1980; Chamove, Anderson, and Nash, 1984; DeMonte, Anderson, and Charbonnier, 1992).

Self-injury is less likely to occur in monkeys raised in less restrictive environments such as in a group or wild-reared (Fittinghoff et al., 1974; Anderson and Chamove, 1980, 1985). The age when placed in a single cage is important, however. Monkeys singly housed at an earlier age have a greater risk of developing SIB than those housed at a later age (Jorgensen et al., 1998). For example, rhesus monkeys isolated for six weeks before 90 days of age exhibited many self-directed behaviors, but older monkeys (3 years of age) isolated for a longer period of time (80 days) did not display these types of behaviors (McKinney et al., 1973). It would seem, therefore, that younger individuals tend to be more adversely affected by insufficient environments than older ones.

Providing social contact by pairing animals helped to increase species-typical behaviors such as social groom, while at the same time decreased aberrant behaviors such as hair pull, self-oral, and nail bite (Eaton, Kelley, Axthelm, Iliff-Sizemore, and Shiigi, 1994). This decrease in atypical behavior that was seen in social groups did not occur in singly-housed animals with inanimate enrichment (Schapiro, Bloomsmith, Suarez, and Porter, 1996). Allowing for social contact through pair housing also appeared to improve the psychological well-being of female longtailed macaques (*Macaca fascicularis*), however this strategy was not as successful for males (Crockett, Bowers, Bowden, and Sackett, 1994).

Environmental Control

The amount of control an individual has over the environment can also influence levels of abnormal behavior. For example, mentally retarded children who engaged in stereotyped rocking preferred sitting on a rocking chair they could rock themselves over one that was rocked for them (Buyer, Berkson, Winnega, and Morton, 1987). Similarly, a token economy involving rewards for demonstrating self-control, and fines for maladaptive behavior, was used as part of a rehabilitation program for psychiatric inpatients. The result of this social learning program was a reduction in both self-injurious and assaultive behaviors (Bellus, Vergo, Kost, Stewart, and Barkstrom, 1999). Therefore, alternative means for reducing stereotypies and SIB may include providing subjects with more opportunities to effect changes in their environment.

When animals are brought into captivity, such as the laboratory, they lose a large amount of control over their situation. They are restricted as to where they can go, what they can eat, and with which conspecifics they socialize or avoid. As with humans, allowing captive animals some amount of control over their environment may help in reducing frustration, fear, and abnormal behavior. For example, rhesus infants raised in an environment containing manipulanda that allowed them to regulate the delivery of food, water, and treats exhibited fewer fear reactions and more exploratory behavior than the yoked controls that did not have the opportunity for regulation (Mineka, Gunnar, and Champoux, 1986). Similarly, allowing adult rhesus macaques to turn on or off music in the room resulted in an increase in affiliative behavior (Novak and Drewsen, 1989).

The amount of control an individual has over its environment also has an influence on cortisol levels. For example, in humans, both cortisol and heart rate were higher when performing a task during uncontrollable noise than when the subjects had control over the noise (Lundberg and Frankenhaeuser, 1978; Peters et al., 1998). In nonhuman primates, Line, Markowitz, Morgan, and Strong (1991) found a lowered level of cortisol in rhesus monkeys when they could get food or play music by pressing levers on a music/feeder box. Moreover, rhesus monkeys having control over noise had similar levels of cortisol to those not exposed to noise. However, when they subsequently lost control, their cortisol levels increased (Hanson, Larson, and Snowdon, 1976). Baboons (*Papio hamadryas*) lost even more control when they were immobilized and strapped to a table for two hours. Their response was an elevation in cortisol levels which lasted for 24 hours following release (Goncharov et al., 1979). The same increase due to restraint has also occurred in macaques. In a study with three different macaque species (*Macaca mulatta, M. radiata,* and *M. fascicularis*), plasma cortisol levels increased from those of home cage levels when the subjects were placed in novel and in restraint conditions

(Clarke, Mason, and Moberg, 1988). Species differences were also apparent, with longtailed macaques showing the highest levels of cortisol, rhesus showing the lowest, and bonnet macaques showing intermediate levels.

Learning

Learning may also play a role in the development or maintenance of self-injurious behavior via reinforcement through operant conditioning. The association of reinforcement with SIB implies that if self-injury is followed by a reward (positive reinforcement), or if it is followed by the termination of an aversive stimulus (negative reinforcement), it will more likely occur in the future. The evidence for positive reinforcement includes opportunities for individuals to obtain desired objects. For example, a subject used SIB as a means to gain access to preferred objects such as desirable toys (Mace, Shapiro, and Mace, 1998). When another subject was given continuous access to preferred items, SIB was seen to decrease (Roscoe, Iwata, and Goh, 1998). Attention brought about by aberrant behavior can be a reinforcer by itself. When this attention was replaced by a time out period in a separate room, self-injurious behavior decreased (Carr and McDowell, 1980). Positive reinforcement of alternative behaviors such as playing with games or activities such as dressing and feeding, has aided in reducing self-injury in a number of subjects (Measel and Alfieri, 1976; Anderson, Dancis, and Alpert, 1978; Azrin, Besalel, Jamner, and Caputo, 1988). However, there appears to be considerable within- and between-subject variability with respect to responding to types of reinforcement (Iwata, Dorsey, Slifer, Bauman, and Richman, 1994). For example, operant paradigms using mild punishment have not been particularly effective in reducing self-injurious behavior in patients with Lesch-Nyhan disorder (Nyhan, 1976; Libby, Polloway, and Smith, 1983); however extinction helped to reduce SIB in one subject (Duker, 1975).

Evidence for an increase in self-injury via negative reinforcement may include subjects performing SIB to escape demands placed on them by caregivers or other personnel. For example, in a group of 66 individuals diagnosed with mental retardation, SIB was highest during the "demand" condition in which the subjects were required to participate in instructional trials. In contrast, SIB was lower in the alone condition in which the subject was no longer negatively reinforced by the presence of the investigator or the opportunity to avoid demands (Kahng and Iwata, 1998). Task difficulty has also had an influence on negative reinforcement and SIB. Higher rates of problem behaviors were seen during difficult tasks in comparison to easy tasks (Weeks and Gaylord-Ross, 1981). The same was true in subjects who head-banged and self-hit (Carr, Newsom, and Binkoff, 1976; Measel and Alfieri, 1976). However, self-hitting was lower when the demands were placed in a positive context, such as a story (Carr et al., 1976).

Negative reinforcement can be used to reduce SIB by giving the subjects alternative behaviors for avoiding unwanted tasks. For example, two children used self-biting as a means to avoid grooming activities such as tooth brushing and hair combing. They were then presented with a button to press, which resulted in a 10-second break from the unwanted activity. At the same time, self-biting was no longer rewarded with a time out. By having an alternative means of communicating their desire, the negative reinforcement of button-pressing replaced the negative reinforcement of self-biting. The result was a decrease in self-injurious behavior (Steege et al., 1990).

Another means of reducing SIB when it had been acquired or maintained through learning is via extinction techniques. For example, personnel may be instructed to simply ignore unwanted behaviors (Duker, 1975). However, when extinction is used as a means to reduce SIB, extinction bursts (initial increases in the focal behavior) as well as increases in aggression can occur (Lovaas, Freitag, Gold, and Kassorla, 1965; Lerman, Iwata, and Wallace, 1999). In one study, extinction bursts occurred more often when SIB was maintained by negative reinforcement, such as escape from demands, than by positive reinforcement, such as access to attention (Lerman et al., 1999). Because of the potential injury brought about by extinction bursts, alternatives such as fixed-time reinforcement schedules may be more effective in reducing SIB than extinction (Vollmer et al., 1998). With fixed-time schedules, reinforcers are freely available, but the connection between undesirable behavior and its reinforcer is disrupted (Vollmer et al., 1998). Rhesus monkeys reared in isolation have been shown to exhibit extinction deficits (Gluck and Sackett, 1976). In this example, subjects were trained to lever press for a food reward. When a reward was no longer paired with the lever press, isolates made more unrewarded responses and took longer to stop responding. Perhaps SIB is similarly maintained in some animals because they cannot extinguish these behaviors.

Social learning has also been a contributor to SIB. The practice of self-injury, such as wrist-slashing, can be initiated by one subject and communicated to another who later performs the same behavior (Grunebaum and Klerman, 1967). In a psychiatric hospital, self-injurious behaviors can have a contagious quality resulting from imitation among the patients (Offer and Barglow, 1960). For example, in a maximum-security hospital for the criminally insane, one patient self-mutilated by inserting objects into his urethra. Because of the resulting attention from the hospital staff, this behavior was soon copied by other patients in the ward. A policy was then instituted in which the staff refrained from discussing this behavior in front of other patients or staff. As a result of the new policy, no new incidents occurred in units other than the medical unit (Rada and James, 1982). Similarly, in a unit for emotionally disturbed adolescents, an "epidemic" of self-cutting began with one patient, and over a period of seven months spread to 11 children, all of whom had direct or indirect contact with the initial cutter. Included among reasons given for the cutting behavior was "imitation of someone else" (Matthews, 1968). Even though patients seem to learn self-injurious behaviors from one another, this "contagion" does not appear to occur for other behaviors or conditions such as aggression, suicidal talk, substance abuse, or hospitalization (Walsh and Rosen, 1985).

Context of SIB

Arousal

Investigators have questioned whether stereotypies are detrimental, a by-product, neutral, and/or adaptive (Mason, 1991). Behaviors such as self-biting, excessive grooming, or self-sucking can be physically harmful to an animal (Berkson, 1968). On the other hand, some repetitive behaviors may actually improve an animal's wellbeing (Mason, 1991). For example, behaviors such as body rocking may be beneficial in developing motor skills (Berkson, 1983). Alternatively, stereotypies such as eye-covering may simply be a by-product of a stress response to an aversive situation (Thierry, 1984) and have no function in and of itself.

The level of environmental stimulation appropriate for an individual depends not only upon its species and genetic makeup, but also on its experiences and the environment in which it is reared. Individuals reared with a greater amount of stimulation may prefer more complexity, while those reared with less, the extreme being isolation, may prefer less complex stimulation. Environmental stimuli that are slightly more complex than the corresponding developmental level of the animal help to increase its psychological complexity; these stimuli may be referred to as pacers (Sackett, 1965a). A complex environment may act by stimulating the growth of neurons or by reinforcing the connections that are already present (Greenough, 1975). For example, rats reared in an enriched environment had a larger neocortex and hippocampus as well as greater dendritic branching in the visual cortex than those raised under standard conditions such as singly-housed in a wire mesh cage (Volkmar and Greenough, 1972; Greer, Diamond, and Tang, 1982). The result of the environmental effects can then be observed in an animal's behavior. For example, rats reared in a stimulating environment were less excitable than those reared in isolation (Juraska, Greenough, and Conlee, 1983). Those reared in perceptually-impoverished environments also exhibited a lesser exploratory drive than those reared in perceptually-enriched environments (Gardner, Boitano, Mancino, and D'Amico, 1975).

Arousal Increase

Environmental complexity and stimulation can influence the levels of abnormal behavior in an individual. In some situations, stereotypies and SIB may be used as a means for obtaining stimulation to increase arousal in a sterile or non-stimulating environment (Carr, 1977; Berkson, 1983; Pond and Rush, 1983; Buyer et al., 1987; Mason, 1991). An isolated or partially-isolated environment may not provide adequate stimulation to immature individuals. Therefore, to obtain desired stimulation, the subjects may direct their activities towards themselves (Pond and Rush, 1983; Walsh et al., 1982). For example, individuals with a higher IQ exhibited a higher level of atypical behavior in a restricted environment compared to a less restrictive ward setting. However, there was no difference in behavior of individuals with a lower IQ (Forehand and Baumeister, 1971). In nonhuman primates, behaviors such as saluting and eyeball pressing as well as extremes in disposition (apathy or hyper-excitability) are associated with lower levels of arousal (Fittinghoff et al., 1974; Mason, Davenport, and Menzel, 1968) and may be used for stimulation.

Increasing environmental complexity may help to reduce undesirable behavior. For example, human infants receiving the most physical stimulation exhibited the least amount of stereotypies (Thelen, 1980). In addition, visual stimulation resulted in a decrease in stereotyped rocking behavior in mentally retarded individuals. However, in the same study, auditory stimulation actually resulted in an increase in rocking behavior (Forehand and Baumeister, 1970).

A more stimulating environment has also been shown to reduce the amount of aberrant behaviors exhibited by nonhuman primates. For example, infant rhesus macaques raised with a mobile surrogate exhibited fewer stereotypies, more play behavior, and were less fearful than those raised with a stationary surrogate (Mason and Berkson, 1975; Schneider, Kraemer, and Suomi, 1991). Chimpanzees (*Pan troglodytes*) and orangutans (*Pongo pygmaeus*) also displayed less stereotypic behavior when housed in an outdoor compound than when housed in their smaller home cages (Nadler and Braggio, 1974). However, although environmental enrichment has been shown to aid in the reduction of stereotypies, once present in an individual's behavioral repertoire, these behaviors are usually not completely eliminated (Bayne et al., 1991; Schapiro and Bloomsmith, 1994).

Arousal Reduction

Stereotypies can also be observed when individuals are exposed to stressful conditions (Pond and Rush, 1983) and may enable them to cope with a difficult environment that consists of physical restraint, fear or frustration (Mason, 1991). An extended physiological response to stress can actually be harmful to an animal (Cohen et al., 1997; Maier and Watkins, 1998). Therefore, engaging in stereotypies may be used to reduce the impact of stressors. If true, stereotypies may be more cost-effective than the enlistment of either autonomic or neuroendocrine systems (Moberg, 1985).

Stereotypies may be used as a means to reduce arousal. For example, heart rate in school children has been shown to decrease when they swing their legs in a stereotyped fashion (Soussignan and Koch, 1985), and human infants have a lower heart rate and respiration when they are allowed to suck on a pacifier during stressful experiences such as a heelstick (Field, 1990). In addition, infants sucking on a pacifier during sleep are also less responsive to external stimuli than when they are not sucking (Wolff and Simmons, 1967). The sucking behavior may have helped to reduce their arousal level. Similarly, dogs reared in isolation exhibited atypical exploratory and social behavior upon removal from isolation (Fuller, 1967; Fuller and Clark, 1966). Thus, such behaviors may be attributed to emergence trauma, a response to the abrupt increase in environmental stimulation.

Self-injurious behavior may also be used as a coping mechanism to help alleviate stressful situations and reduce arousal (Jones, 1982). Not only stressful, but also disruptive environments can influence levels of SIB. For example, in an inpatient ward setting, self-injurious behavior increased as a result of staff turnover and procedural changes. When the staff started again to work cohesively and with the original rules and regulations, the self-injurious behavior was observed to decrease (Kroll, 1978). Also, mounting tension often precedes SIB (Konicki and Schulz, 1989; Coid et al., 1992) and self-mutilation has been reported to reduce this tension (Grunebaum and Klerman, 1967; Coid et al., 1992; Haines, Williams, Brain, and Wilson, 1995). One subject described feeling emotionally overwhelmed before an incident of self-injury and that the sight of blood seemed to release the tension (Favazza 1989). In a survey of 240 female habitual self-mutilators, 72% reported that they use self-mutilation to control their mind when it is racing, and 65% reported that they use it to feel relaxed (Favazza and Conterio, 1989). Patients with borderline personality disorder exhibited a high incidence of self-injury (Gardner and Cowdry, 1985). Those who reported experiencing no pain during SIB reported an improvement in mood following the cold presser test. Those patients who did feel pain during SIB did not report a mood improvement (Russ et al., 1992). In addition, subjects with a history of self-mutilation experienced a decrease in respiration during an imagery script of SIB. This decrease did not occur during scripts of an accidental injury or an angry interaction (Brain, Haines, and Williams, 1998). This association between SIB and stress reduction was not supported physiologically, however. In one study of institutionalized subjects, blood samples were collected immediately after a bout of self-injurious behavior and on the following day when no SIB occurred. The blood samples were analyzed for ACTH, a physiological measure of stress. No differences were found between samples when the subjects bit and when the subjects did not bite (Sandman et al., 1997).

Associations between stereotypic behavior and arousal may also be observed in nonhuman primates. For example, juvenile chimpanzees increased levels of rocking with an increase in sound level (Berkson and Mason, 1964) and both old world (*M. mulatta*) and new world (*Saimiri sciureus*) monkeys exhibited stereotypies during changes or disruptions of routines (Levison, 1970; McGrogan and King, 1982). However, when monkeys (e.g., *M. mulatta*) were habituated to the testing situation, the frequency of stereotypic behaviors decreased (Fittinghoff et al., 1974).

Self-injurious behavior is also associated with arousal in nonhuman primates. For example, when rhesus monkeys were confronted with an observer wearing black gloves (a threatening stimulus), they exhibited a higher level of self- directed aggression than when no threatening stimuli were present (Cross and Harlow, 1965). Subjects also showed an increase in self-injurious behavior when exposed to an electric shock, or when exposed to a tone (conditioned stimulus) that had previously been paired with shock. In contrast, subjects exposed to the tone alone did not show an increase (Gluck, Otto, and Beauchamp, 1985). Similar increases in self-injurious behaviors were observed with other stimuli, such as a metal pipe striking the cage (Fittinghoff et al., 1974) and threats and cage shaking by the experimenter (Pond and Rush, 1983). Infant macaques (*M. mulatta* and *M. nemestrina*) separated from either their mother or their partner exhibited higher levels of stereotypies and/or self-biting than during pre-separation or upon reunion (Meyer, Novak, Bowman, and Harlow, 1974; Maxim, 1980). Moreover, isolation-reared rhesus monkeys often had difficulty in adapting to new stimuli upon removal from their home cage and reacted with an increase in self- directed behaviors (Sackett, 1972). Heart rate measures show a possible calming influence of self-biting in rhesus monkeys. Subjects vested with heart rate equipment showed an increase in heart rate during the 30 seconds prior to a self-biting episode and a reduction in heart rate following the SIB. This increase and subsequent decrease in heart rate was not observed when the subject bit at the vest containing the heart rate equipment instead of its own body (Marinus, Chase, Rasmussen, Jorgensen, and Novak, 1999). However, the reverse was true in two human subjects with SIB. In this example, heart rate increased after an episode of self-biting (Freeman, Horner, and Reichle, 1999).

Aggression

One theory of self-injurious behavior is that it is the expression of social aggression in animals when contact with the opponent is prevented (Chamove et al., 1984). The aggressive tendencies are then redirected toward the animal's own body. Self-injurious behavior (SIB) could therefore be viewed as continued inappropriate expression of aggressive tendencies or thwarted social aggression (Berkson, 1968; Jones, 1982) as well as aggression inhibited by dominance-submissive relationships (Allyn et al., 1976).

In the human population, there is an association between SIB and aggression. In a study of subjects with personality disorders who self-mutilated, the mutilations were related to an inwardly directed expression of anger (Herpertz et al., 1997). Those that self-mutilated had greater lifetime aggression, and the degree of self-mutilation was correlated with chronic anger (Collacott et al., 1998; Simeon et al., 1992). In the prison population, those who self-injured had more severe disciplinary actions taken against them and had been charged with more assaults while in prison (Jones, 1986). Minnesota Multiphasic Personality Inventory (MMPI) profiles of prison inmates suggest that those who self-injured tended to rely on immature defenses and coping strategies. They also exhibited hostility and aggression, possibly in response to frustration (Shea, 1993). In institutionalized individuals with mental retardation, aggressive behaviors commonly occurred among residents with SIB (Maisto et al., 1978). Also, anger has been reported to be ameliorated by SIB (Kemperman, Russ, and Shearin, 1997).

In nonhuman primates, aggression increases with age and higher levels of SIB are observed in older animals (Anderson and Chamove, 1980, 1985). This increase of SIB with age parallels that of externally-directed threats. The highest increase in levels of SIB in rhesus monkeys occurs around the age of 3 years (Cross and Harlow, 1965; Suomi et al., 1971), which approximately coincides with puberty in the animals. In addition, levels of SIB are higher in males than they are in females (Cross and Harlow, 1965; Gluck and Sackett, 1974; Suomi et al., 1971; Walsh et al., 1982), which parallels the sex differences in aggression observed in the wild (Teas, Richie, Taylor, and Southwick, 1980). Male rhesus monkeys given cyproterone acetate, an antiandrogen, showed a reduction in both testosterone and self-biting (Eaton et al., 1999), supporting the link between aggressive tendencies and self-injurious behavior.

Research Purpose

Although potentially damaging to an individual, self-injurious behavior is exhibited in both human and nonhuman primates under varied conditions. SIB is a complex behavioral phenomenon associated with genetic, physiological, as well as environmental origins. Because the number of factors involved with this behavior is so diverse, the present study will focus on environmentally-related variables, namely, housing conditions, stress, and aggression.

Severe rearing environments such as total and partial isolation have consistently been reported to have devastating effects on an animal's behavior, resulting in such destructive activities as self-biting or self-injury (Harlow and Harlow, 1962a). Today isolation rearing is no longer practiced, but self-injurious behavior persists in primate colonies. Research and husbandry protocols need to be assessed in order to identify environmental variables that are risk factors associated with self-injurious behavior.

SIB and stereotypies also occur in what appears to be a stressful situation. For example, arousal-inducing procedures such as cage-shaking by the experimenter (Pond and Rush, 1983) or electric shock (Gluck et al., 1985) have been shown to elicit behaviors such as self-biting in captive rhesus monkeys. Because of this relationship, SIB has been hypothesized to be utilized for arousal reduction. In support of the arousal reduction hypothesis, humans who self-mutilate report that they injure themselves to feel relaxed (Favazza and Conterio, 1989). However, only a limited number of studies directly link a subject's physiological stress reaction to a self-injurious episode. Sandman et al. (1997) collected blood samples to measure levels of ACTH from humans after an episode of SIB in their home setting. No relationship between SIB and ACTH levels was observed. However, the blood sampling procedures themselves may have affected the subjects' stress levels. In rhesus macaques, Marinus et al. (1999) measured the subjects' heart rates before and after a biting episode and noticed a decrease in heart rate after self-biting. However, because the subjects were not habituated to the vest and heart rate equipment, the research did not allow for the study of spontaneous biting episodes in the subject's home cage.

Finally, because self-injurious behavior often occurs in aggressive contexts, it has been hypothesized that animals self-bite in socially-aggressive situations where contact with their opponent is thwarted. For example, in institutionalized human subjects, those who displayed self-injurious behavior also demonstrated higher rates of aggression (Collacott et al., 1998). Similarly, in nonhuman primates, an isolate rhesus subject alternated fighting with bouts of self-biting during confrontations with other monkeys (Fittinghoff et al., 1974). However, these and other previous studies have not separated the association both behaviors may have with arousal.

Studies of the Present Research

The initial purpose of the present research (Study 1) was to assess the levels of self-biting and self-injury in a large colony of rhesus macaques and to identify possible risk factors associated with these behaviors.

The subsequent purpose of the research (Studies 2 and 3) was to develop and utilize new techniques of saliva collection from adult male rhesus macaques. Cortisol measures obtained from saliva could then be used to measure an animal's stress level without further stressing the subjects with experimental procedures. These techniques of saliva collection were then utilized to physiologically assess the association between spontaneous instances of self-injurious behavior and stress. If SIB were associated with stress, there should then be a relationship between cortisol and self-injurious behavior.

The final purpose of the research (Studies 4 and 5) was to test the association between aggression and self-injurious behavior by placing the subjects in both social and nonsocial situations that could be considered equally arousing. If SIB were associated with social aggression, it should occur more frequently in social contexts than in nonsocial situations where the animal was not faced with a conspecific opponent.

Three central hypotheses involving studies 3, 4, and 5 were tested: a) Cortisol levels, an indicator of stress, are associated with self-biting. b) Self-biting will increase with exposure to social aggression, and c) Self-biting will be higher in social than in non-social contexts. The hypotheses are detailed under the descriptions of these three studies in Chapters IV, V, and VI, respectively.

CHAPTER II

Study 1. Incidence and Risk Factors of SIB

Introduction

Self-injurious behavior, such as self-biting, is well known to have occurred in subjects that were reared in either total or partial isolation (Harlow and Harlow, 1962a). These animals often reacted to stressful or confrontational situations with self-directed activities, such as self-biting, while normally-reared subjects would instead withdraw from the stimulus (Fittinghoff et al., 1974). In part due to the findings of the devastating effects isolation rearing has on an animal's behavior, improvements in animal husbandry have resulted in a virtual elimination of this practice. In spite of these husbandry changes, however, a small percentage of socially-reared animals continue to self-bite, sometimes to the point of self-injury (Bayne et al., 1995; Jorgensen et al., 1998). A number of factors have been proposed to account for the presence of self-injurious behavior in captive primates. These variables range from intrinsic factors such as an animal's age, sex, and health (Jorgensen et al., 1998), to extrinsic factors such as rearing or housing conditions (Bayne and Novak, 1998). Because the frequency of self-injurious behavior is so low, a considerable population of subjects is necessary to observe before any risk factors can be identified. Therefore, the purpose of this study was to examine the incidence of SIB in a large colony of socially-reared rhesus macaques and to identify potential risk factors for self-injurious behavior. This was accomplished by assessing the behavior of individually-housed animals (current data) and utilizing colony records (historic data) to compare intrinsic and extrinsic factors associated with any aberrant behavior.

Methods

Subjects

The subjects were 362 rhesus macaques (*Macaca mulatta*), 163 females and 199 males, housed at the New England Regional Primate Research Center, Southborough, MA. The subjects ranged in age from 2 to 21 years (M = 7 years) and were socially-reared before being placed in individual cages at an average age of 27.5 months (range: 4-132 months).

Housing

The subjects were individually-housed in cages varying in size from the traditional Harford cages measuring approximately 0.73 x 0.62 x 0.36 m to pens measuring 3.1 x 0.95 x 2.5 m. Size of the cage was in part based on the animal's weight; larger animals tended to have larger cages. All subjects had visual and auditory access to conspecifics, and in some cases they were able to touch other animals through the cage bars.

Procedures

Behavioral assessments were conducted by trained observers and lasted approximately five minutes per animal. The observer stood in front of the animal's cage and noted on a check sheet the presence or absence of specific aberrant behaviors, including self-biting, during each five-minute observation. Three assessments were conducted on each animal, and they were separated by a minimum of six months. If an animal was observed to self-bite during any of the three observation periods, it was assessed to be a self-biter.

Past and current colony records of the subjects were then analyzed. Of interest were the age when the subject was individually housed, the number of years the subject was individually housed, the number of times the animal was moved to a new location, the number of blood draws performed on the subject, and whether or not the animal wounded itself, requiring veterinary care.

Data Analyses

The subjects were grouped into two age groups for analysis, less than or equal to six years, and greater than six years. Chi-square analyses were then conducted to compare sex and age with self-biting assessment and wounding incidents.

A logistic regression was subsequently conducted on the data from the colony records to determine the risk factors associated with incidences of self-biting and self-wounding. Variables included in the regression were age, sex, age when individually housed, number of years housed individually, number of times the animal was moved, and number of blood draws.

Results

Almost a quarter of the subjects (24.6%) were assessed to be self-biters, and 11.3 percent of the subjects wounded themselves at least once, requiring veterinary care. Looking at sex differences, more males than females were classified as self-biters (males: 38.7%, females: 7.4%; $X^2 = 47.44$, $p = 0.00$; Figure 1) and more males self-wounded (males: 18.6%, females: 2.5%; $X^2 = 23.24$, $p = 0.00$). With respect to age differences, there was a trend towards more older animals self-biting than younger ones (older: 28.7%, younger: 21%; $X^2 = 2.89$, $p = 0.09$), and significantly more older animals than younger ones wounded themselves (older: 21.6%, younger: 2.6%; $X^2 = 32.31$, $p = 0.00$; Figure 2). In addition, subjects assessed as self-biters were more likely to have wounded themselves (biters: 36%, nonbiters: 3.3%; $X^2 = 71.28$, $p = 0.00$).

Sex and age when individually housed were very strong predictors of self-biting (sex: $\beta = -2.26$, $p = 0.00$; age when individually housed: $\beta = -0.08$, $p = 0.00$). The odds of a female exhibiting self-biting were approximately 1/10 of those for a male (95% confidence interval: 0.04 to 0.25) and for each additional month delay in individual housing, there was an 8% decline in the odds of self-biting (95% confidence interval: 4% to 11%).

There was no significant association between self-biting and age ($\beta = 0.10$, $p = 0.50$; 95% confidence interval: 0.82 to 1.51), number of blood draws ($\beta = 0.00$, $p = 0.98$; 95% confidence interval: 0.98 to 1.02), number of years in individual housing ($\beta = 0.11$, $p = 0.46$; 95% confidence interval: 0.84 to 1.48), or the number of times an animal was moved ($\beta = -0.01$, $p = 0.88$; 95% confidence interval: 0.87 to 1.12).

Because sex and age of individual housing were the only significant predictors for self-biting, the regression was re-run with only these variables to calculate self-biting probabilities. According to the best-fitting logistic regression equation, the probability of self-biting for a male when individually-housed at 6 months was 0.64, at 12 months was 0.57, at 24 months was 0.42, and at 48 months was 0.18. Corresponding probabilities for a female were 0.19, 0.15, 0.09, and 0.03.

Sex and age when individually housed were also very strong predictors of self-wounding (sex: $\beta = -2.97$, $p = 0.00$; age when individually-housed: $\beta = -0.10$, $p = 0.00$).

The odds of a female self-wounding were approximately 1/20 of those for a male (95% confidence interval: 0.01 to 0.23) and for each additional month delay in individual housing, there was a 10% decline in the odds of self-wounding (95% confidence interval: 5% to 15%).

Sex, age, age when individually housed and number of blood draws were included in the regression for calculating self-wounding probabilities. According to the best-fitting logistic regression equation, the probability of self-wounding for a typical male (10 years of age with 15 blood draws) that was individually-housed at 6 months was 0.71, at 12 months was 0.57, at 24 months was 0.28, and at 48 months was 0.03. Corresponding probabilities for a female under the same conditions were 0.12, 0.07, 0.02, and 0.002.

Age was a strong predictor of self-wounding ($\beta = 0.38$, $p = 0.04$). For each additional year of age, there was a 47% increase in the odds of an animal self-wounding. However, the 95% confidence interval was large, extending from a 2% increase to a 112% increase. The probability of a typical male (individually-housed at 24 months and exposed to 15 blood draws) self-wounding at age 5 years was 0.05, at 10 years was 0.28, at 15 years was 0.72, and at 20 years was 0.95.

Number of blood draws was also a good predictor of self-wounding ($\beta = 0.023$, $p = 0.02$). For each additional blood draw, there was a 2% increase in the odds of self-wounding (95% confidence interval: 0.4% to 4.2%). The probability of a typical male (10 years of age, individually housed at 24 months) self-wounding after having received no blood draws was 0.22, after 10 blood draws was 0.26, after 50 blood draws was 0.46, and after 100 blood draws was 0.72.

There was no significant relationship between self-wounding and number of years in individual housing ($\beta = -0.04$, $p = 0.83$; 95% confidence interval: 0.70 to 1.34) or the number of times the animal was moved ($\beta = 0.05$, $p = 0.54$; 95% confidence interval: 0.90 to 1.23).

Conclusions

Assessment results demonstrated that males were more likely than females to exhibit aberrant behavior such as self-biting and wounding. In addition, age also appeared to play a role; older animals were more prone to both self-biting and wounding than were younger subjects. Therefore, only adult males were utilized in subsequent studies.

Husbandry routines, such as singly-housing subjects at an early age and frequent blood draws had a negative impact on the subject's behavior. However, moving an animal from one location to another or individual housing for an extended period of time did not appear to have an impact on these behaviors. Therefore, many factors seemed to influence the development and maintenance of self-injurious behavior in captive rhesus monkeys. Some of these factors were intrinsic to the animal, while others were related to rearing condition, colony management practices, and research protocols.

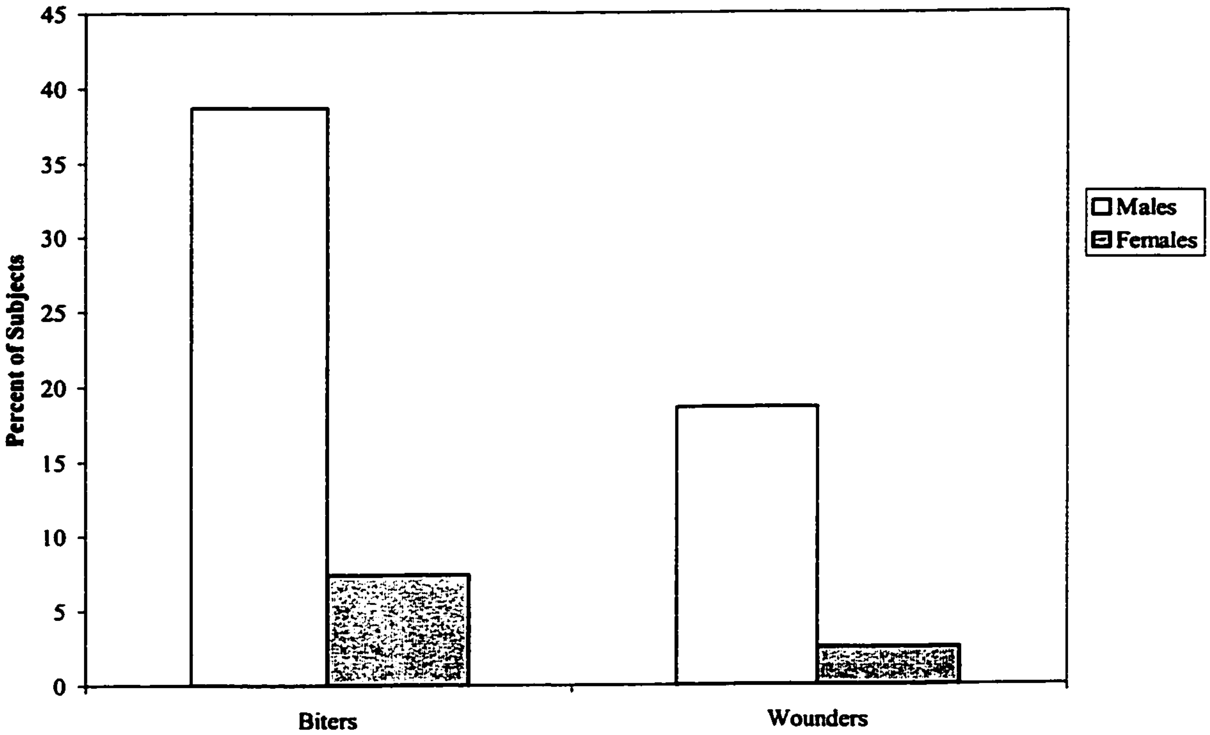


Figure 1. Sex differences in self-biting (p = 0.00) and wounding (p = 0.00).

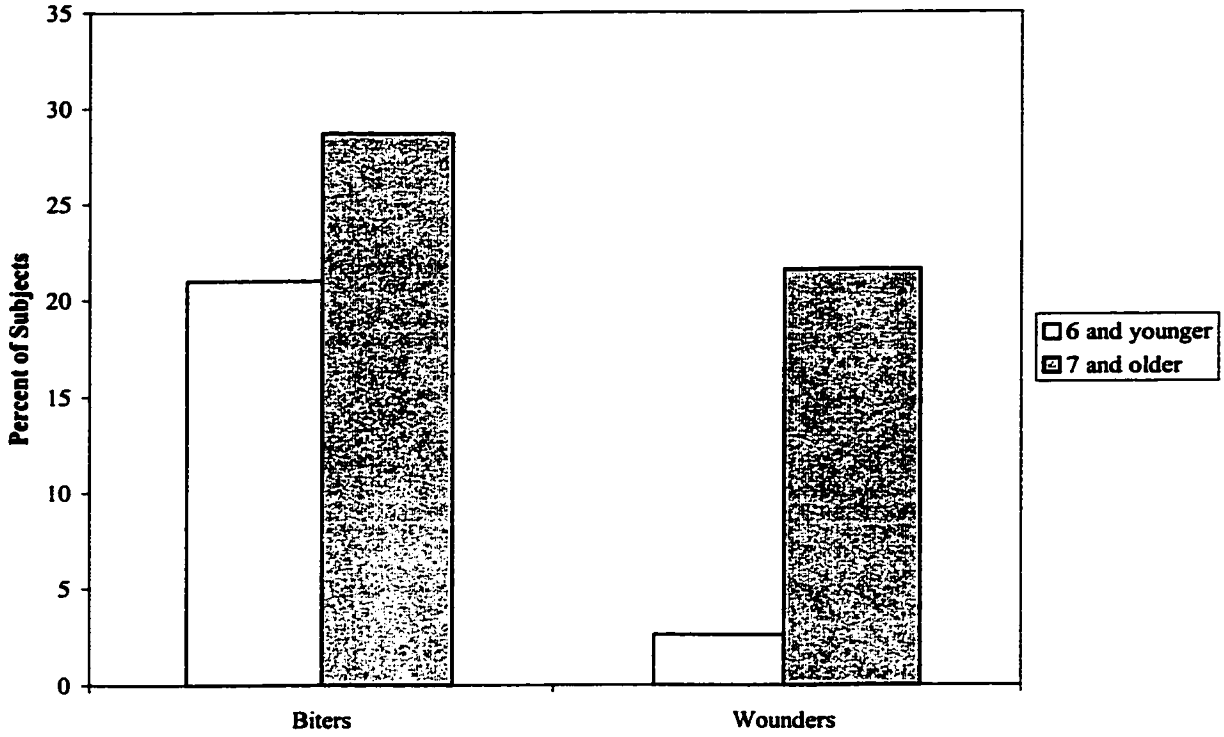


Figure 2. Age differences in biting (p = 0.09) and wounding (p = 0.00).

CHAPTER III

Study 2. Salivary Cortisol Methods

Introduction

To study the relationship between stress and self-injurious behavior, one useful tool is to measure an animal's cortisol level. The measurement of cortisol has been widely used in primate research as an indicator of stress (Hanson et al., 1976; Gunnar, Gonzalez, and Levine, 1980; Bercovitch, Hauser, and Jones, 1995). One way to measure cortisol is to assay blood plasma (Elvidge, Challis, Robinson, Roper, and Thorburn, 1976; Clarke et al., 1988). Measuring cortisol levels in blood is useful for obtaining point samples, or immediate levels. However, blood sampling is inadequate for the present research, because the procedure of drawing blood in itself can be stressful and, in some cases, sedation is required. Urine sampling is less invasive, however it is a measure of the animal's state (Byrne and Suomi, 1991; Crockett et al., 1993) and is inadequate for obtaining instantaneous levels. More recently, cortisol levels have been obtained from saliva (Boyce, Champoux, Suomi, and Gunnar, 1995; Davis and Emory, 1995; Fuchs, Kirschbaum, Benisch, and Bieser, 1997).

Salivary cortisol values are highly correlated with those obtained from plasma (McCracken and Poland, 1989; Harris et al, 1990; Woodside, Winter, and Fisman, 1991; Reid, Intrieri, Susman, and Beard, 1992), but without the problems associated with venipuncture. In addition, after exposure to a stressor, salivary cortisol rises with only a 2-3 minute lag in parallel to that of plasma cortisol (Kirschbaum and Hellhammer, 1994). Unlike urinary cortisol, saliva collection allows for repeated sampling in a relatively short period of time (Fuchs et al., 1997). In addition, because levels of salivary cortisol do not peak until 20-30 minutes after the stressor (Kirschbaum and Hellhammer, 2000), one can record behavioral data on subjects before collecting the saliva sample.

Salivary cortisol has been sampled from humans (Davis and Emory, 1995), squirrel monkeys (Fuchs et al., 1997), and infant rhesus monkeys (Boyce et al., 1995). Unlike the stresses associated with drawing blood, the collection of saliva is non-invasive and relatively stress-free (Kirschbaum and Hellhammer, 1994). However, in each of these cases, saliva collection required that the subject suck or chew on absorbent material which was then retrieved manually by the experimenter. Needless to say, these methods of sampling and retrieval are not suitable for larger, more dangerous animals such as adult rhesus macaques.

The purpose of Study 2 was to develop a method for obtaining saliva samples from adult macaques and to allow the researcher to safely retrieve the samples after they had been collected. Saliva collection would allow for more immediate sampling of cortisol from the subjects without subjecting them to the stresses of venipuncture, and would result in measures that could be directly related to the animal's behavior.

Methods:

Subjects

The subjects were 23 adult male rhesus monkeys (*Macaca mulatta*) ranging in age from 9 to 19 years (mean = 12.4 years). Male subjects were used, because subsequent studies would be conducted on this sex.

Housing

The subjects were all singly-housed in one of two types of cages: The first type of housing consisted of pens measuring 3.1 x 0.94 x 2.5 m. The pens contained perch bars at the far end, and the floors were covered in wood shavings. The pens also contained various manipulable toys. The second type of housing comprised "baboon" cages measuring 0.98 x 0.78 x 1.77 m. These cages also contained perch bars and manipulable toys. The pen room housed a total of 12 monkeys (9 of which were subjects), while the three rooms with the baboon cages housed 5 monkeys each (14 of which were subjects). Each of the rooms had at least one window facing outside. A timer was used to turn on the room lights at 0600 hours and turn them off at 1800 hours daily. The subjects were fed Purina monkey chow *ad libitum*, with fresh fruit given twice a week.

Apparatus

One of two methods was used for collecting saliva, depending on the preference of the monkey. The "screen" method, depicted in Figure 3, involved licking a screen-covered piece of gauze that was sprinkled with dry juice drink crystals. A 3-inch gauze pad (Kendall Curex 12-ply) was cut into a circular shape and placed on a 15 x 15 x 0.6 cm square piece of Plexiglas. A 15 x 15 cm square piece of metal screen (0.16 cm holes) was placed on top of the gauze, which was in turn covered by another square piece of Plexiglas (15 x 15 x 0.6 cm) containing a 6 cm circular hole in the center. The hole was positioned in the center of the Plexiglas, providing access to the mesh and the gauze without allowing the gauze to be pulled out of the apparatus. The whole assembly was screwed together and a Plexiglas rod (2 cm in diameter and 28 cm long) was attached to the back of the apparatus and served as a handle for the experimenter. Dry juice drink crystals were then sprinkled over the mesh and the apparatus was presented to the animal. The animal then licked the drink crystals off the screen and the gauze absorbed the saliva.

The "pole" method, depicted in Figure 4, involved sucking and/or chewing on an attached, flavored, rope. The apparatus consisted of a 50 cm PVC pipe (2 cm diameter) with a screw at the top of the pipe which was secured with a wing nut. A 6-inch braided cotton rope (3/8 inch diameter, Richmond Dental, P.O. Box 34276, Charlotte, NC 28234) flavored with concentrated Kool-Aid® and then dried was looped under the screw and tied in a knot on top. This design allowed for both ends of the rope to protrude from the top of the pipe so as to be presented to the animal. The subject then sucked and/or chewed on the rope, which absorbed the saliva.

Procedures

The subjects were initially habituated to both the screen and the pole apparatus until they reliably came forward and touched the screen and/or the rope. Time to habituation took approximately one to two weeks. After the subjects were habituated to, and interacted with, at least one apparatus, saliva samples were collected in the home cage by giving the animals access to the apparatus for 10 minutes, allowing them to lick or suck on either the gauze or the rope. Subject cooperation did not require prior food deprivation. The amount of time each animal spent licking and/or chewing the gauze was recorded. The apparatus was then removed after 10 minutes, or after the absorbent material became saturated, whichever came first. This procedure was repeated once a day with each apparatus until a trial produced a sample of at least 0.4 ml, or until the animal completed at least five unsuccessful trials. Trials were conducted between 0900 and 1100 hours.

Cortisol Assay

Once the absorbent material was saturated with saliva, it was placed in a Salivette tube (Sarstedt, Inc.; Figure 5) and centrifuged at 2200 RPM for 10 minutes. During centrifugation, the saliva passed from the cotton roll, through the hole at the base of the insert, into the centrifuge tube. Particles were caught in the tip of the centrifuge tube, leaving clear saliva to be decanted. The collected saliva was then aliquotted into eppendorf tubes and frozen at -20° C until assayed. The samples were later thawed and assayed for cortisol using a commercially available radioimmunoassay for plasma cortisol (ICN Biomedicals, Inc., Costa Mesa, CA). To adapt the plasma assay for the analysis of salivary cortisol, the standards (0, 1, 3, 10, 30, and 100 μg/dl) were diluted by placing 25μl of each standard and 200μl of phosphate buffered saline into their respective cortisol antibody-coated tubes. The thawed saliva samples were then vortexed and 200μl of each sample and 25μl of the zero standard were then pipetted into the designated coated tubes. To measure inter-assay variability, a control saliva sample was included in every assay. All tubes, both the standards and the samples, were replicated in duplicate. After the standards and the samples were pipetted, 1.0 ml of ^{125}I cortisol was added to each tube. The tubes were then vortexed to mix each sample. The samples were incubated at 37° C for 45 minutes. After incubation, the tubes were decanted using a foam decanting rack and then struck sharply on absorbent paper to remove all residual droplets. The tubes were then placed in a gamma counter to be counted for 1 minute.

Calculation of Results

To calculate the cortisol values, the counts obtained from the gamma counter were first divided by the average count from the duplicate zero standard. Those values were then log transformed, and a nonlinear regression was used to fit a curve to the standards (which were diluted to: 0.125, 0.375, 1.25, 3.75, 12.5 μg/dl). The values from the sample tubes were calculated from the standard curve. Those values were then transformed using the anti-log to obtain the cortisol values. The coefficient of variance (c.v.) was calculated by dividing the standard deviation of each duplicate sample by the average cortisol value for those two samples. Only samples with a c.v. of less than 20%

were used for data analyses. The inter-assay coefficient of variance was 4.5%, and the minimum detectable dose of cortisol was 0.15 μg/dl.

Effect of Koolaid® on Assay

There has been some concern that acid may interfere with the cortisol assay (Kirschbaum and Hellhammer, 1994) and that flavoring may have an effect on the cortisol level (Schwartz et al., 1998). To determine whether the citric acid in the drink crystals would have an effect on the assay, samples were collected from eight human subjects who sucked on both plain and flavored ropes. The saliva was collected and assayed for cortisol as described above.

Results

Flavoring Effect

The cortisol values obtained from human subjects with the flavored rope ranged from 0.17 to 0.35 μg/dl (mean = 0.26 μg/dl). The values obtained with the plain rope ranged from 0.15 to 0.34 μg/dl (mean = 0.24 μg/dl). These values were not significantly different ($t(7) = 1.15$, $p > 0.28$), and as expected, the values were highly correlated ($r(7) = 0.758$, $p < 0.03$). It was reasonable to expect similar results for nonhuman primate subjects.

Cooperation

Saliva samples were successfully collected from 21 of the 23 monkey subjects using one or both methods. Of the 23 subjects, 21 sucked and/or chewed on the rope, and of those, 16 produced a sample of at least 0.4 ml. Those who did not cooperate with the pole apparatus either did not lick the rope or they bit the ends off the rope, preventing retrieval of the sample. Eighteen of the subjects licked the screen apparatus; however, only 10 of these animals produced a saliva sample of at least 0.4 ml. The subjects who did not produce a sample with this method tended to lose interest before a sufficient volume was collected. Once the subjects became experienced with one of the methods, saliva samples of sufficient volume for cortisol assay were obtained on 88% of subsequent attempts (subject range: 65-100%).

Time to Obtain a Sample

Overall, the screen method required significantly more time to collect an adequate sample than the pole method (screen: 470 seconds, n = 10; pole: 270 seconds, n = 16; $t(24) = 2.843$, $p < 0.01$). The same was true when comparing only the subjects who cooperated with both methods (screen: 487 seconds; pole: 180 seconds, $t(8) = 4.028$, $p < 0.001$).

When comparing SIB subjects with non-biting control subjects, there was no consistent difference in time to collect saliva for either the pole method (SIB: 256 seconds, n = 11; control: 303 seconds, n = 5; $t(14) = 0.53$, $p = 0.60$) or the screen method (SIB: 534 seconds, n = 6; control: 372 seconds, n = 4; $t(8) = 1.36$, $p = 0.21$).

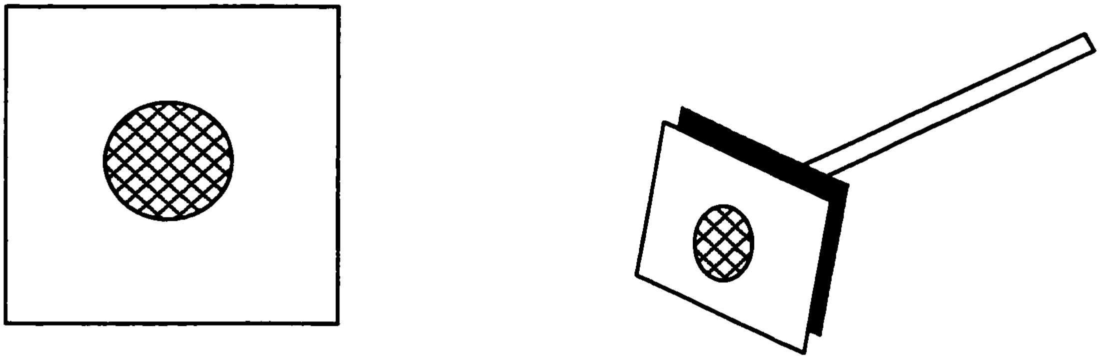
Cortisol

The cortisol values obtained with the pole method ranged from 0.27 to 1.66 µg/dl (mean = 0.73 µg/dl, SE = 0.15, n = 11). Samples were also collected by the screen method from three of the same monkeys used with the pole method along with five additional subjects. In this case, the values ranged from 0.62 to 1.77 µg/dl (mean = 0.99 µg/dl, SE = 0.14, n = 8). The results from the two methods were not significantly different from each other ($t(17) = 1.273$, $p > 0.22$). There was also no statistically significant correlation between the time to obtain a sample and the cortisol concentration ($r = 0.31$, $p > 0.19$).

When comparing SIB subjects with non-biting control subjects, there was no difference in cortisol levels for either the pole method (SIB: 0.76 µg/dl, n = 7; control: 0.67 µg/dl, n = 4; $t(9) = 0.31$, $p = 0.77$) or the screen method (SIB: 1.06 µg/dl, n = 4; control: 0.93 µg/dl, n = 4; $t(6) = 0.39$, $p = 0.71$).

Conclusions

Salivary cortisol can be safely collected and used as an indicator of stress in adult macaques. In addition, the Koolaid flavoring does not appear to influence cortisol levels in the assay. Cooperation is better and the time required to obtain a sample is faster with the pole method. However, choice of technique depends on both the subject's behavior and the experimenter's preference.



Front View

Side View

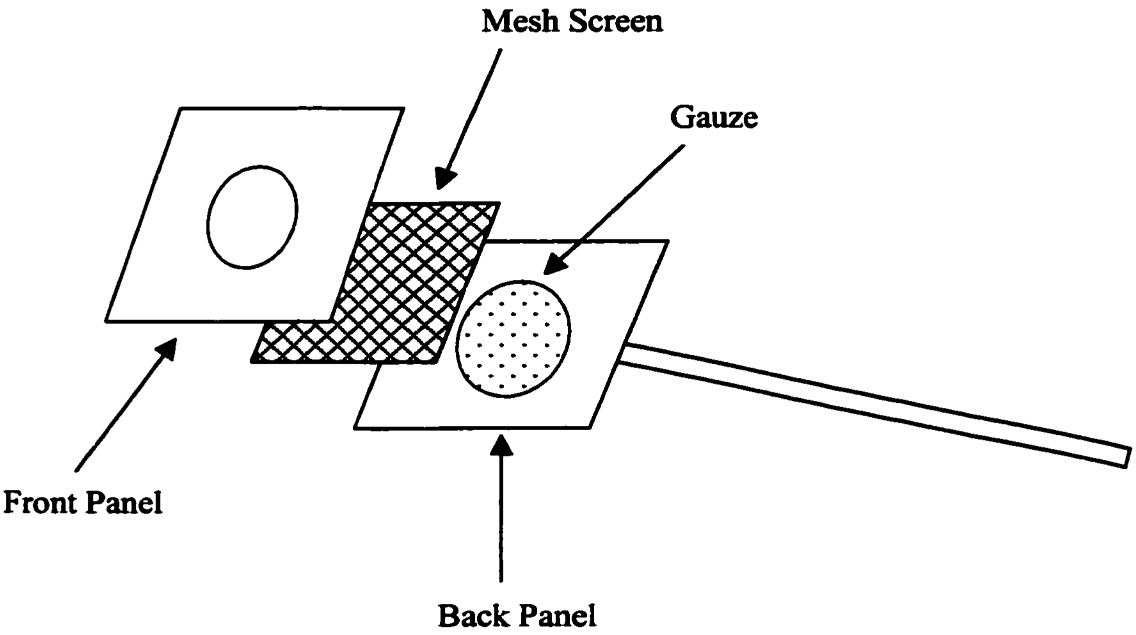


Figure 3. Diagram of the screen apparatus for saliva collection. See text for details.

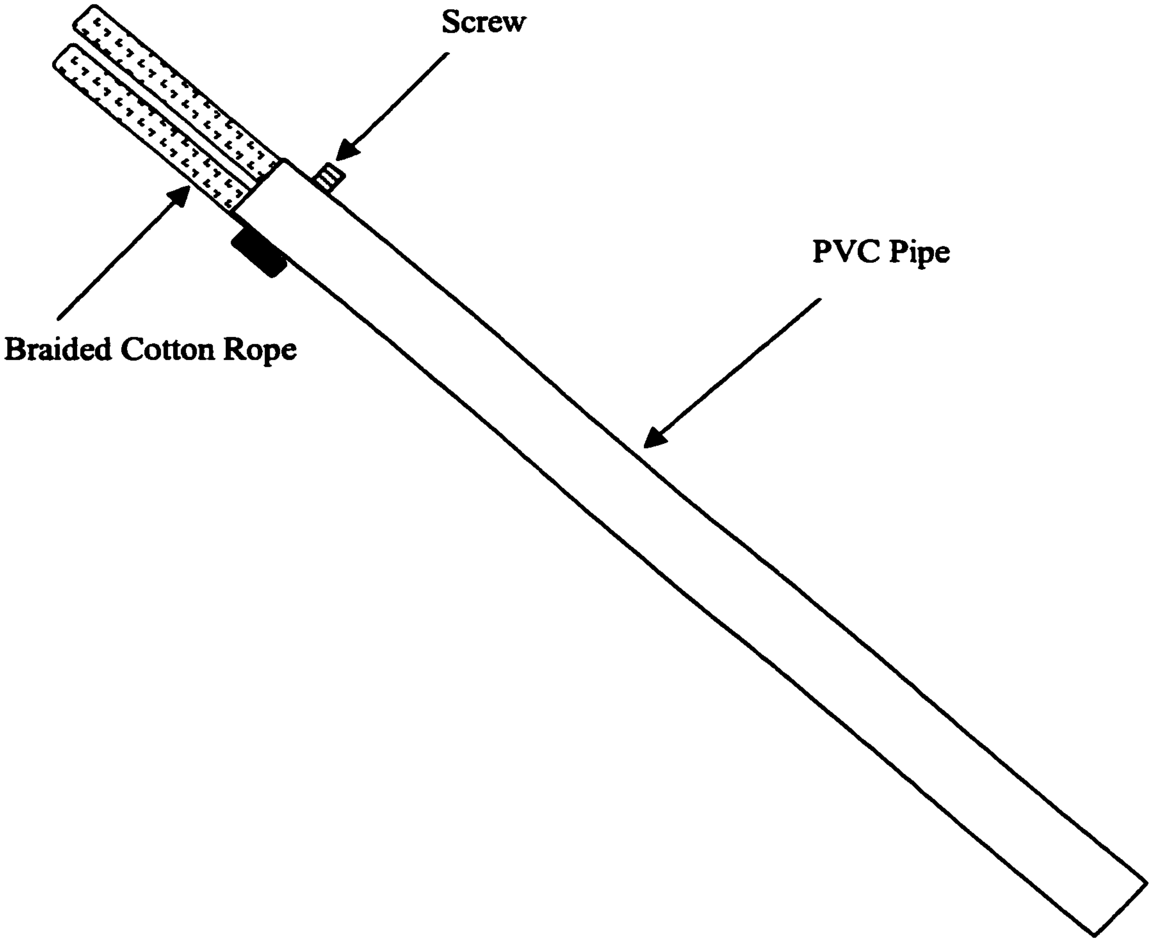


Figure 4. Diagram of the pole apparatus for saliva collection. See text for details.

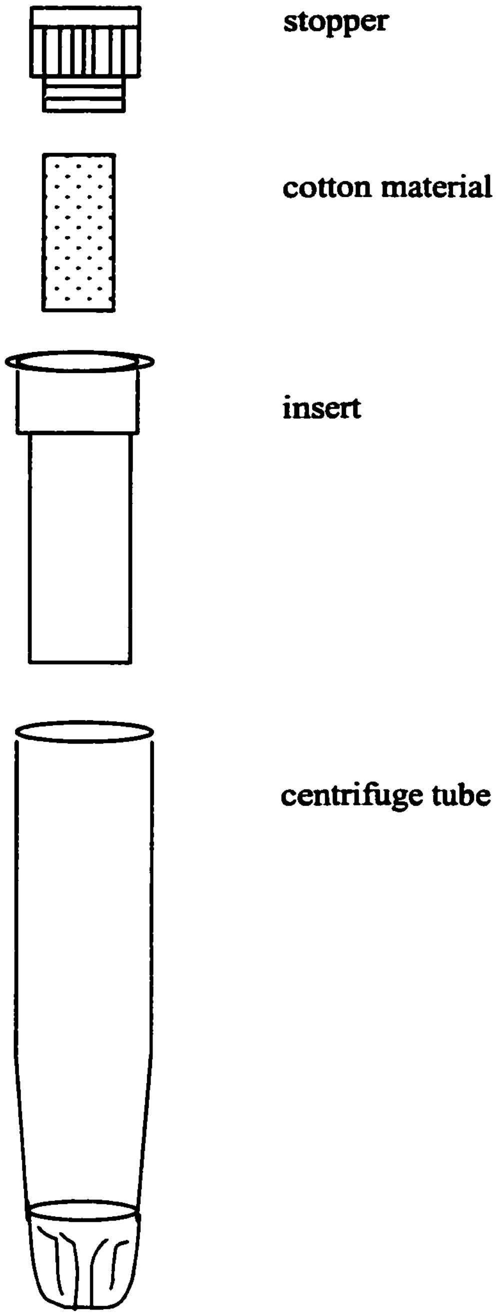


Figure 5. Salivette tube (Sarstedt, Inc., Rt. 2, St. James Church Rd., Newton, NC 28658) for saliva collection. See text for details.

CHAPTER IV

Study 3. SIB and Stress Measured by Salivary Cortisol

Introduction

Self-biting behavior is not uncommon in captively-housed rhesus macaques. As described in Study 1, approximately 39 percent of 199 singly-housed male rhesus macaques exhibited some form of self-biting. Although the potential for serious wounding does exist, not all animals who self-bite injure themselves. Of the 199 individually-housed rhesus males, 18.6 percent were treated by a veterinarian for self-inflicted wounding at least once during their lifetime. Because of the potential cost of this behavior in terms of injury, it is hypothesized that such behavior must have some benefit to the animal.

One possible benefit of self-biting may be a reduction of stress. Humans with a record of self-injurious behavior often report that self-injury helps to reduce anxiety (Coid et al., 1992). For some individuals, the sight of the blood is what helps to reduce this tension (Favazza, 1989). Simply an imagery script of SIB is enough to reduce respiration in some subjects with a history of self-mutilation (Brain et al., 1998). Therefore, in humans, self-injury has been demonstrated through self-report and through physiological measures (e.g., respiration; Brain et al., 1998) to reduce stress.

Because self-report is not an option for nonhuman primates, indirect behavioral evidence has been used to demonstrate the connection between stress and self-injurious behavior. For example, increases in self-biting have been observed in situations that may be considered stressful. Examples of these situations include the administration of a shock, or a tone previously paired with a shock (Gluck et al., 1985), a metal pipe striking the cage (Fittinghoff et al, 1974), and threats and cage shaking by the experimenter (Pond and Rush, 1983).

Few studies have utilized direct physiological evidence to associate levels of spontaneous biting with an animal's level of stress. Sandman et al. (1997) collected blood samples from institutionalized subjects after episodes of SIB. Results did not reveal a difference in levels of ACTH, a precursor to cortisol, between samples collected after SIB episodes and on control days. However, although blood sampling was a routine procedure for these subjects, it may still have been stressful enough to artificially inflate the ACTH levels. Heart rate was also utilized to test the association between self-biting and arousal in rhesus macaques (Marinus et al. 1999). In this example, heart rate increased prior to a self-biting episode and decreased afterwards. However, the subjects were not adapted to the heart rate equipment and they were placed in a stressful situation that may have elicited self-biting.

The purpose of study 3 in the present research project was to test the theory that spontaneous instances of self-injurious behavior are a manifestation of an animal's stress. Saliva collection and cortisol measurement techniques were utilized to measure stress levels without inducing additional stress via the experimental procedure.

Methods

Subjects

The subjects were nine adult male rhesus monkeys (aged 8-17 years, M=10.8 years) with a history of self-biting. Eight of the nine subjects had at least one veterinary record of self-injury. One subject was nursery-reared, then placed with peers before individual housing, five subjects were mother/peer reared before individual housing, one was mother-reared, then placed with peers before individual housing, and two had unknown rearing histories. All were subjects in the previous saliva collection study (see Chapter III).

Housing

The subjects were all singly-housed in one of two types of cages: Two subjects were housed in pens measuring 3.1 x 0.94 x 2.5 m. The pens contained perch bars at the far end, and the floors were covered in wood shavings. The pens also contained various manipulable toys. Seven of the subjects were housed in "baboon" cages measuring 0.98 x 0.78 x 1.77 m. These cages also contained perch bars and manipulable toys. The pen room housed a total of 12 monkeys (2 of which were subjects), while the three rooms with the baboon cages housed 5 monkeys each (7 of which were subjects). Each of the rooms had at least one window facing outside. Timers turned on the lights at 0600 hours and turned them off at 1800 hours daily. The subjects were all fed Purina monkey chow *ad libitum*, with fresh fruit given twice a week.

Procedures

Two subjects were housed in each of three animal rooms and were considered to be yoked pairs. The remaining three subjects were housed in the fourth room and were ranked according to biting rates (e.g., low, medium, and high). The subject with the medium biting rate was yoked with each of the other two subjects (low and high).

Two observers watched each yoked pair for 10 minutes per observation. Observations of each pair lasted a total of 6 to 15 hours (Mean = 8 hours, 30 minutes). Each observer watched one of the two subjects. If a subject self-bit during the observation, a saliva sample was collected using the pole (n = 7) or the screen (n = 2) method five minutes after the bout of self-biting from both the monkey that bit and the yoked control, with the criterion that the yoked control did not self-bite at any time during the observation. A second saliva sample was collected from both animals 20 minutes after the first sample, provided that neither animal self-bit in the interim. In humans, saliva collected 20 minutes after a report of a current problem or future stressor showed an increase in cortisol levels (Smyth et al., 1998). Because salivary cortisol levels do not peak until 20-30 minutes after the stressor (Kirschbaum, Wust, and Hellhammer, 1992; Kirschbaum et al., 1995; Kirschbaum, Kudielka, Gaab, Schommer, and Hellhammer, 1999; Kirschbaum and Hellhammer, 2000), the first sample should reflect pre-SIB cortisol, while the second sample should reflect post-SIB cortisol levels.

For a control measure, two more samples were collected from each monkey at the same times on the following day. Both the subject and the yoked control were observed for 20 minutes prior to these final control samples to ensure that self-biting did not occur at the respective time on the second day. If self-biting did occur, saliva collection was postponed to the following day until samples could be collected when the subjects did not bite prior to sampling.

Cortisol Assay

Once the absorbent material was saturated with saliva, it was collected and stored as described in Study 1. The samples were later thawed and assayed for cortisol using a radioimmunoassay for plasma cortisol (Diagnostic Products Co., Los Angeles, CA) different from that of Study 1. This kit has a lower range for the standard curve. To adapt this plasma assay for the analysis of salivary cortisol, the standards (0, 1, 5, 10, 20, and 50 µg/dl) were diluted by placing 100µl of each standard and 900µl of distilled water into labeled eppendorf tubes. The diluted standards and the thawed saliva samples were then vortexed and 100µl of each sample was then pipetted into the designated cortisol antibody-coated tubes. To measure inter-assay variability, a control saliva sample was included in every assay. All tubes, both the standards and the samples, were replicated in triplicate. After the standards and the samples were pipetted, 500µl of ^{125}I cortisol were added to each tube. The tubes were then vortexed to mix each sample. The samples were incubated at room temperature for 3 hours. After incubation, the tubes were decanted using a foam decanting rack and then struck sharply on absorbent paper to remove all residual droplets. The tubes were then placed in a gamma counter to be counted for 1 minute.

Calculation of Results

The cortisol levels were calculated from the gamma counter results as described in Study 1. However, with the Diagnostics Product Company assay, the standards were diluted to: 0.1, 0.5, 1.0, 2.0, and 5.0 µg/dl and the tubes were run in triplicate rather than duplicate as before. If the coefficient of variance (c.v.) in a triplicate was greater than 15%, the outlier was deleted and the average cortisol and c.v. were recalculated with the remaining two samples. Only samples with a final c.v. of less than 20% were used for data analyses. Control samples were also run in triplicate in each assay to obtain a measure of inter-assay variability. The inter-assay coefficient of variance was 10.2%.

Data Analyses

Cases in which subjects were missing more than one out of the four data points were deleted from the sample. For the subjects missing a single data point on the biting day and/or on the following non-biting day, a value was calculated for that point using the best least squares estimate. Means were then calculated from the remaining values for each subject and yoked control.

A repeated measures analysis of variance was conducted on the data with day (1,2) and time (1,2) as within subject variables and condition (subject vs. yoked control) as between subject variables.

Hypotheses

If self-biting is a marker for stress, the subject's cortisol levels on the first day, particularly at time 2, should be higher than the levels on the following day. The two samples collected the following day should not be different from one another. The cortisol levels for the yoked control monkey should not change from day 1 to day 2 or time 1 to time 2. If self-biting is not associated with stress, or if it is somehow used to dampen down stress levels, there should be no consistent difference between the time 1 and time 2 levels for either day 1 or day 2 for either the subject monkey or the yoked control. If both the subject and the yoked control experience higher levels of cortisol on day 1 than on day 2, SIB will be considered an inconsistent marker for stress.

Results

Between two and six sets of samples were collected for each of eight subjects. No samples were obtained from the ninth subject due to a lack of cooperation. Three of the subject sets and four of the yoked control sets had two or more missing data points and were subsequently deleted from the data set. Single data points missing for a given subject were then filled using the best least squares estimate. This procedure was conducted on four of the subjects' data and on three of the yoked controls' data.

There was no consistent cortisol difference between the biting subjects and the non-biting yoked controls ($F(1) = 0.299$, $p > 0.59$). There was also no statistically significant difference from day 1 to day 2 ($F(1) = 0.68$, $p > 0.42$), but there was a trend from time 1 to time 2 ($F(1) = 4.13$, $p > 0.06$; Figure 6) with time 2 levels higher. There was no interaction ($F(1) = 0.273$, $p > 0.60$). A post hoc power analysis for an alpha of 0.05 resulted in a power of 0.044. In other words, to get a power of 0.80 or greater, the number of subjects needed would be greater than 250.

Because there was no consistent difference in cortisol levels between biting and non-biting episodes, a post hoc time course study was conducted to confirm that the salivary cortisol response parallels that of humans. This study involved stressing the animal at a given time and measuring changes in cortisol across time due to the stressor.

Methods of Post-hoc Time Course Study

Subjects

The subjects were eight singly-housed adult male rhesus macaques with a consistent record of cooperation during saliva collection in Study 2. Four of the animals were also subjects in the spontaneous biting study (Study 3).

Procedures

A saliva sample was initially collected from the subjects by the investigator for the pre-stress baseline measurement. The animals were then stressed by a second investigator. The stressor consisted of squeezing the subject in its cage using the squeeze-back mechanism and injecting it with a saline solution. This stressor lasted approximately one minute. Additional saliva samples were then collected by the first investigator at 5, 15, and 25 minutes after the saline injection. The procedures were conducted between 0810 and 1015 hours and on only one subject per room on a given test day. Saliva samples were later assayed for cortisol as described above.

Data Analyses

A repeated measures analysis of variance was conducted with time (pre, 5, 15, 25 minutes) as the dependent variable. Post-hoc contrasts compared the pre-stress sample with each of the following samples (5, 15, and 25 minutes).

Results of Post-hoc Study

There was a significant change in cortisol across time ($F(3) = 3.27$, $p = 0.041$). Post hoc contrasts showed that the pre-stress sample was significantly lower than the five minute ($F(1) = 8.52$, $p= 0.022$) and the 15 minute ($F(1) = 5.92$, $p = 0.045$) samples. However, there was no statistically significant difference between the pre-stress sample and the 25 minute sample ($F(1) = 1.70$, $p = 0.234$; Figure 7). These results contradict previous reports of a peak in salivary cortisol closer to 20-30 minutes after the stressor (Kirschbaum and Hellhammer, 2000; Lehnert et al., 1989).

Conclusions

Because there was no associated rise in cortisol along with biting events, results suggest that spontaneous episodes of self-biting may not be associated with stress. In addition, the post-hoc time course study suggests that peak salivary cortisol levels after a brief stressor may occur closer to 5 minutes rather than 20-30.

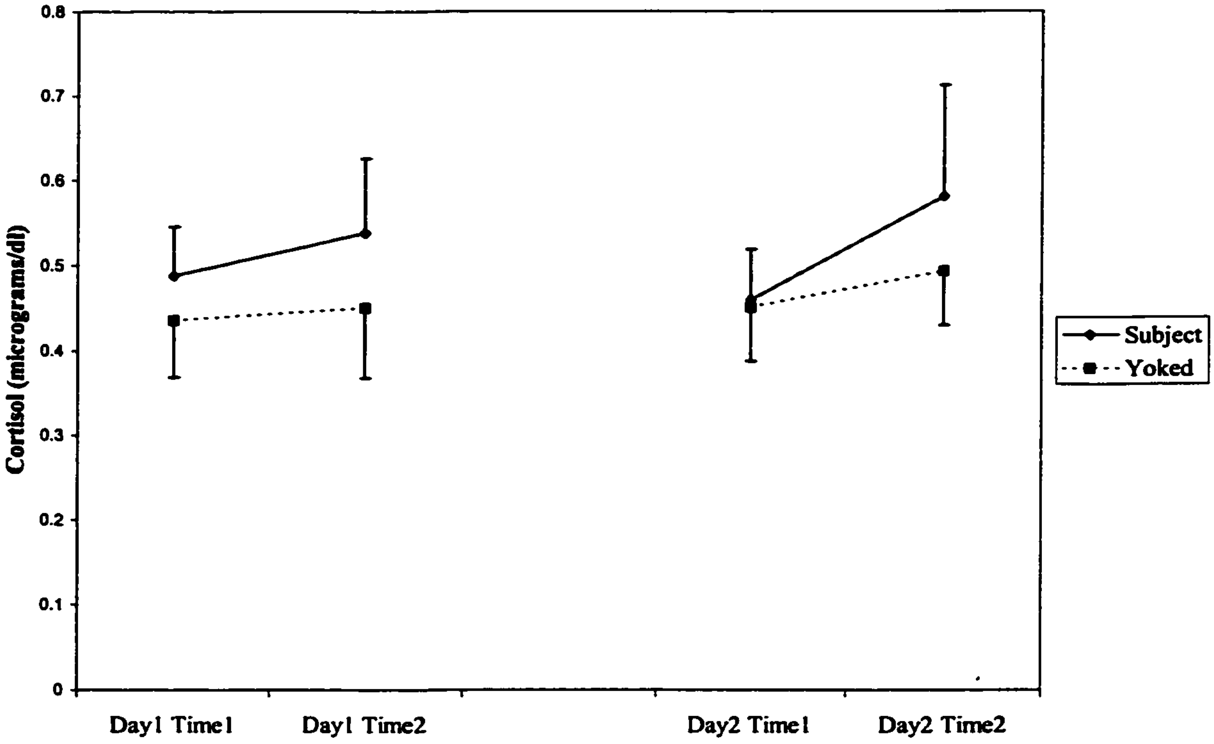


Figure 6. Comparing cortisol levels (mean and SE) between subjects who self-bit and yoked controls who did not self-bite ($p > 0.59$).

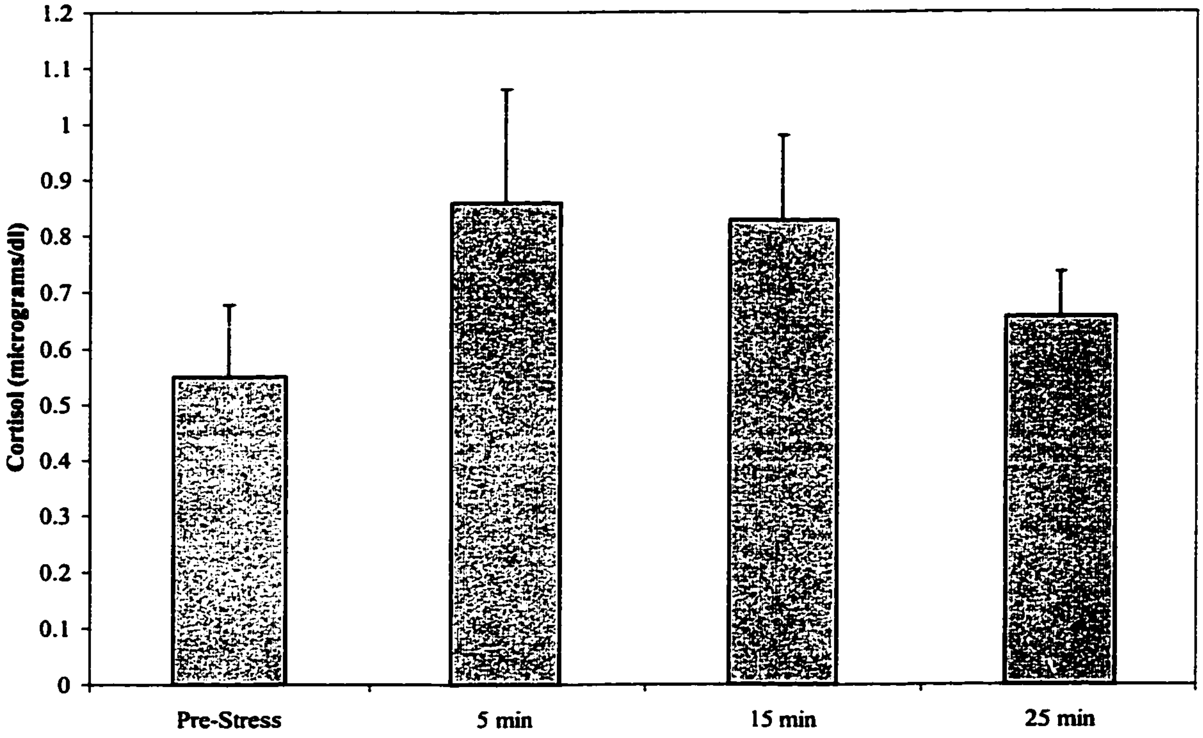


Figure 7. Cortisol levels (mean ± SE) across time after a brief stressor (pre vs. 5 min.: p = 0.022; 15 min.: p = 0.045; 25 min. p = 0.234).

CHAPTER V

Study 4. SIB and Aggression: Videotape Condition

Introduction

One possible explanation of self-injurious behavior is that it is the expression of social aggression when contact with the opponent is prevented (Chamove et al., 1984). The aggressive tendencies are then redirected onto the animal's own body. If self-injurious behavior is simply thwarted social aggression, then SIB should primarily be exhibited in a social context in which physical contact is prevented. To test this theory, videotapes of aggressive and nonaggressive situations were utilized.

Visual exploration has been shown to be rewarding to monkeys, and they have worked on discrimination learning tasks for the opportunity to view the environment (Butler 1953). However, what is presented to the animal for observation is important. For example, juvenile rhesus monkeys preferred looking at another monkey or a moving train to that of an empty chamber (Butler, 1954; 1958; Haude, Kruper, and Patton, 1966). One method that allows subjects to visually observe live animals and make a preference choice based on that observation is the self-selection circus. This apparatus allows for testing the effects of variables such as age and rearing condition on social choice (Sackett, Griffin, Pratt, Joslyn, and Ruppenthal, 1967). However, one limitation of this procedure is that the test subjects can visually interact with the stimulus animals through the observation window separating them. Therefore, preference could be affected by differential behavior of the stimulus animal.

To avoid the inherent problems of live stimulus animals, alternate means of testing have been utilized. Sackett (1965b) demonstrated that monkeys respond to colored slides, and this response can vary with the animal's age and/or rearing condition. For example, subjects reared in the laboratory showed submission and withdrawal to threat pictures, while wild-caught subjects showed threat behavior. Infant rhesus monkeys have also responded appropriately to slides of monkeys, even when they were isolation-reared (Sackett, 1966). In this example, threat pictures elicited the highest level of disturbance and vocalization. Content of the slides also influences frequency of attending. For example, slides of unfamiliar animals were observed more frequently than slides of familiar animals (Haude and Detwiler, 1976). The face appeared to be the most attractive and salient feature for primate visual exploration (Kyes and Candland, 1987), and even infant monkeys preferred looking at drawings of normal, as opposed to distorted, adult macaque faces (Lutz, Lockard, Gunderson, and Grant, 1998). These slide studies demonstrate that monkeys do pay attention to pictures and that pictures of conspecifics are differentiated and have some meaning to them (Humphrey, 1974).

When subjects were presented with a series of slides, visual exploration increased with rate of slide changes (Haude and Ray, 1967), however static slide images did not elicit as much interest as moving videotapes (Butler, 1961; Swartz and Rosenblum, 1980). As with slides, videotapes have also elicited socially appropriate behavior in macaques (Plimpton, Swartz, and Rosenblum, 1981; Capitanio, Boccia, and Colaiannia, 1985). For example, juvenile bonnet macaques (*Macaca radiata*) showed the highest scores of lipsmack and contact with the mother when they were presented with videos of a threatening male, and they approached the stimulus more when it was a passive female (Plimpton et al., 1981). In addition, pigtailed macaques (*Macaca nemestrina*) threatened more to a video of a submissive animal, and they displayed more submissive signals when they were exposed to a video of aggressive behavior (Capitanio et al., 1985). Therefore, the use of videotapes is another useful method of staging social interactions. Videotaped social encounters presented to the subjects allow the investigator to control what each monkey observes while maintaining relevance to the animal.

The purpose of Study 4 was to investigate social aspects of SIB and to test the hypothesis that self-injurious behavior is redirected social aggression in situations where physical contact is prevented. Videotapes of aggressive and nonaggressive behavior were utilized to present the subjects with different social and non-social contexts to determine whether or not SIB could be viewed as redirected social aggression.

Methods

Subjects

The subjects were 11 adult male rhesus monkeys (aged 8-17 years, M=10.5 years) with a history of self-biting. Nine of the subjects were used in Study 3, and all of the subjects were used in Study 2. Ten of the 11 subjects had at least one veterinary record of self-injury. One subject was nursery-reared then placed with peers before individual housing, one subject was placed in single caging after nursery-rearing, five subjects were mother/peer reared before individual housing, one was mother-reared then placed with peers before individual housing, and three had unknown rearing histories.

Housing

All of the subjects were individually housed in "baboon" cages measuring 0.98 x 0.78 x 1.77 m. These cages also contained perch bars and manipulable toys. They were housed in four rooms. One room housed a total of 12 monkeys (two of which were subjects), while the other three rooms housed five monkeys each (nine of which were subjects). Each of the rooms had at least one window facing outside. Timers turned the lights on at 0600 hours and turned them off at 1800 hours daily. The subjects were all fed Purina monkey chow *ad libitum*, with fresh fruit given twice a week.

Procedures

The videotape stimuli consisted of the following conditions: aggressive social, non-aggressive social, nonsocial, and blank screen. Because older rhesus prefer watching unfamiliar monkeys over familiar ones (Platt and Novak, 1997), all of the tapes showing monkeys contained animals that were unfamiliar to the subjects. The aggressive social condition consisted of a video containing segments of monkeys aggressing toward the camera or toward other animals. The non-aggressive social condition consisted of segments showing monkeys interacting in a non-aggressive fashion, such as grooming or visual exploratory behavior. Because background and contrast may differ considerably between laboratory and wild video clips, a total of four social videos were used, one aggressive and one non-aggressive videotape of conspecifics in the wild, and one aggressive and one non-aggressive videotape of conspecifics in a laboratory. The nonsocial conditions consisted of a scenery video and a video touring a laboratory with no animals visible. The blank screen condition was conducted to test the effect of the equipment alone on the animals' behavior.

Each videotape condition lasted 20 minutes. Because monkeys' interest in visual stimuli decreases rapidly after constant exposure (Humphrey, 1974), and because the mean duration of each look can be as short as 14 seconds (Swartz and Rosenblum, 1980), the videos consisted of twenty 30-second clips (Capitanio et al., 1985) with 30 seconds of blank screen in-between each clip.

The subjects were presented with the videos while they remained in their home cage. An observer watched the animal and recorded the amount of time the subject watched the 20-minute video. In addition, the subject was videotaped at this time for later behavioral scoring. A saliva sample was collected using the pole method immediately before and 10 minutes after the 20-minute exposure to each condition for later cortisol assay. The study took place on Tuesdays and Thursdays. The days of presentation were counterbalanced among the subjects using a Latin square design.

Two observers scored each subject's videotape using the Observer ™ program. Duration of the behaviors, with interest focusing on externally-directed aggression and self-biting (Table 1), were recorded using a percent agreement criterion of 90% for duration and 80% for frequency. In the cases where the two observers were not reliable, a third observer scored the tape to reach reliability with at least one of the first two observers. Overall reliability averaged 97.5% for duration and 91.0% for frequency.

Data Analyses

The percent viewing times for wild and laboratory videos were averaged for each of the four conditions: aggressive, nonaggressive, scenery, and blank videos. A repeated measures analysis of variance was then conducted on the viewing data to determine differences in viewing time under the four conditions. The following contrasts were run on significant results: 1) "action" videos (aggressive, nonaggressive, scenery) vs. blank videos, 2) aggressive vs. nonaggressive videos, 3) conspecific videos (aggressive and nonaggressive) vs. scenery videos.

For the cortisol measures, two subjects that had missing data due to lack of cooperation or insufficient volume were removed from the data set. A repeated measures analysis of variance was conducted on the data from the remaining nine subjects with video type (aggressive, nonaggressive, scenery, blank) and sample time (pre, post) as within subject variables.

Parametric repeated measures analyses of variance were conducted on the behavioral data for "*yawn*," "*locomote*," and "*other*." Due to inequality of variance and non-normal distributions, nonparametric Friedman repeated measures analyses of variance were then conducted on the remaining behaviors (*aggression, self-biting, stereotypic, fear grimace, cage shake, pace, self-sex,* and *social*). The following

Wilcoxan contrasts were run on significant results: 1) "action" videos (aggressive, nonaggressive, scenery) vs. blank videos, 2) aggressive vs. nonaggressive videos, 3) monkey videos (aggressive and nonaggressive) vs. scenery videos. Correlations were also conducted comparing levels of aggression, self-biting, and change in cortisol.

Hypotheses

If self-injurious behavior is a form of re-directed social aggression, levels of self-biting should be higher when the animal is presented with videos containing conspecifics (aggressive and nonaggressive videos) than when it is presented with nonsocial videos (scenery and blank videos). Alternatively, if SIB is independent of aggression, self-biting should not be higher in the social condition. If self-biting is associated with stress, self-biting should correlate with a rise in cortisol regardless of the social or nonsocial condition.

Results

Percent viewing time averaged 43 ± 5, 41 ± 5, 37 ± 5, and 15 ± 3 (mean ± SE) seconds for the aggressive, nonaggressive, scenery, and blank videos, respectively (Figure 8). The overall repeated measures ANOVA showed a significant difference in viewing time ($F(3) = 22.65$, $p = 0.000$). The contrast results were as follows: 1) "Action videos" (aggressive, non-aggressive, scenery) vs. Blank videos $F(1) = 71.08$, $p = 0.000$, 2) Aggressive vs. Nonaggressive videos $F(1) = 0.66$, $p = 0.44$, 3) Conspecific videos (aggressive and nonaggressive) vs. Scenery videos $F(1) = 1.36$, $p = 0.27$. Percent viewing time was significantly less for the Blank videos than the other three video conditions.

A repeated measures analysis of variance demonstrated that there was no effect of video type on cortisol ($F(3) = 1.37$, $p = 0.28$) and no consistent difference between the pre-video and the post-video samples ($F(1) = 2.96$, $p = 0.12$). There was also no interaction ($F(3) = 1.66$, $p > 0.20$; Figure 9).

A nonparametric Friedman repeated measures analysis of variance revealed a significant effect of videotape on *aggressive* behavior ($F(3) = 12.08$, $p = 0.007$). Post-hoc contrasts demonstrated that videos containing conspecifics elicited significantly more *aggression* than scenery videos ($p = 0.008$). There was also a trend towards decreased *aggression* during the blank videos in comparison to the other videos ($p = 0.086$) and there was a trend towards increased *aggression* during the aggressive videotapes in comparison to the nonaggressive videotapes ($p = 0.066$; Figure 10).

There was no effect of videotape type on *self-biting* behavior ($F(3) = 1.445$, $p = 0.695$; Figure 11), *stereotypic* behavior ($F(3) = 0.518$, $p = 0.915$; Figure 12), or the remaining behaviors (*yawn*: $F(3) = 0.841$, $p = 0.48$; *fear grimace*: $F(3) = 0.90$, $p = 0.82$; *cage shake*: $F(3) = 1.47$, $p = 0.69$; *locomote*: $F(3) = 2.16$, $p = 0.11$; *pace*: $F(3) = 1.74$, $p = 0.63$; *self-sex*: $F(3) = 4.44$, $p = 0.22$; *social*: $F(3) = 2.21$, $p = 0.53$; *other*: $F(3) = 1.71$, $p = 0.19$; Figure 13).

There was no correlation between *aggression* and *self-biting* ($p > 0.05$ for all videotape conditions). There was no correlation between *self-biting* behavior and change in cortisol levels for any of the video conditions ($p > 0.50$ for all conditions). However, there was a positive correlation between *aggressive* behavior and cortisol change ($r = 0.644$, $p = 0.045$; Figure 14) during the nonaggressive video condition.

Conclusion

Self-biting did not increase with aggression during videotapes of conspecifics. These results suggest that self-biting may not be associated with aggression.

Table 1

Ethogram for recording behavioral data

AGONISTIC	
aggression	threats, which include a complex behavioral signal involving open mouth stare, eyebrows lifted, ears flattened, rigid body posture and piloerection, and agonism, which includes attack or attempted attack of another animal or object such as the cage or a toy
yawn	an involuntary opening of the mouth, exposing the teeth
fear grimace	a grin-like facial expression
cage shake	any vigorous rocking of the cage
STEREOTYPY/SIB	
self-bite	closure of mouth around one's own body-may or may not break skin
stereotypy	nonlocomotive ritualized, repetitive behaviors which include self-grasp, eye poke, digit suck, hair pull and self-slap, and locomotive stereotypies, which include bounce, rock, body flip and swing
pace	a repetitive circling of the cage that consists of at least two complete cycles
OTHER BEHAVIORS	
self sex	any oral or tactile manipulation of the genitals not involved in grooming
social	includes presents, which consist of a posture involving exposing the flank, belly, rump, or neck, and lipsmack, which consists of pursing the lips together and moving them to produce a smacking sound
locomotion	any two directed steps in the horizontal or vertical plane, or when at least half of the animal's body is moved from one quadrant of the cage to the other
other	tactile/oral explore, visual explore, sleep, self-groom

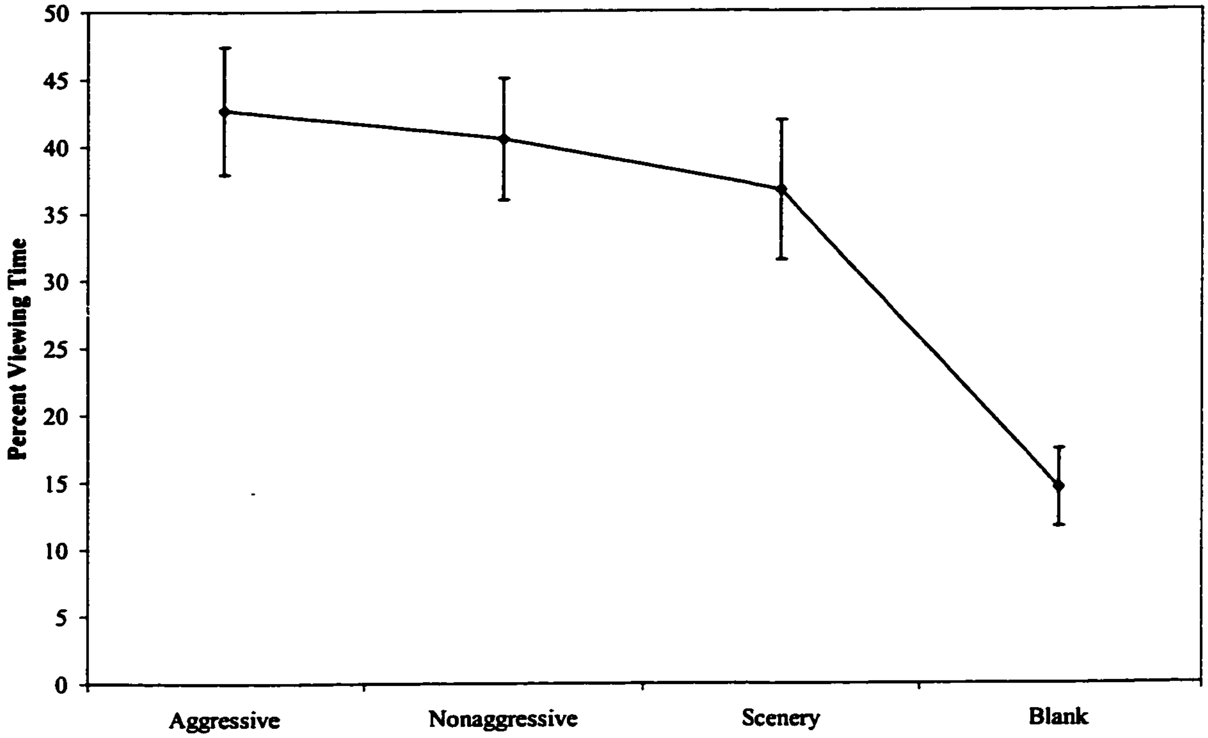


Figure 8. Mean (± SE) percent viewing time by video. Blank video vs. other three, p = 0.00. See text for details.

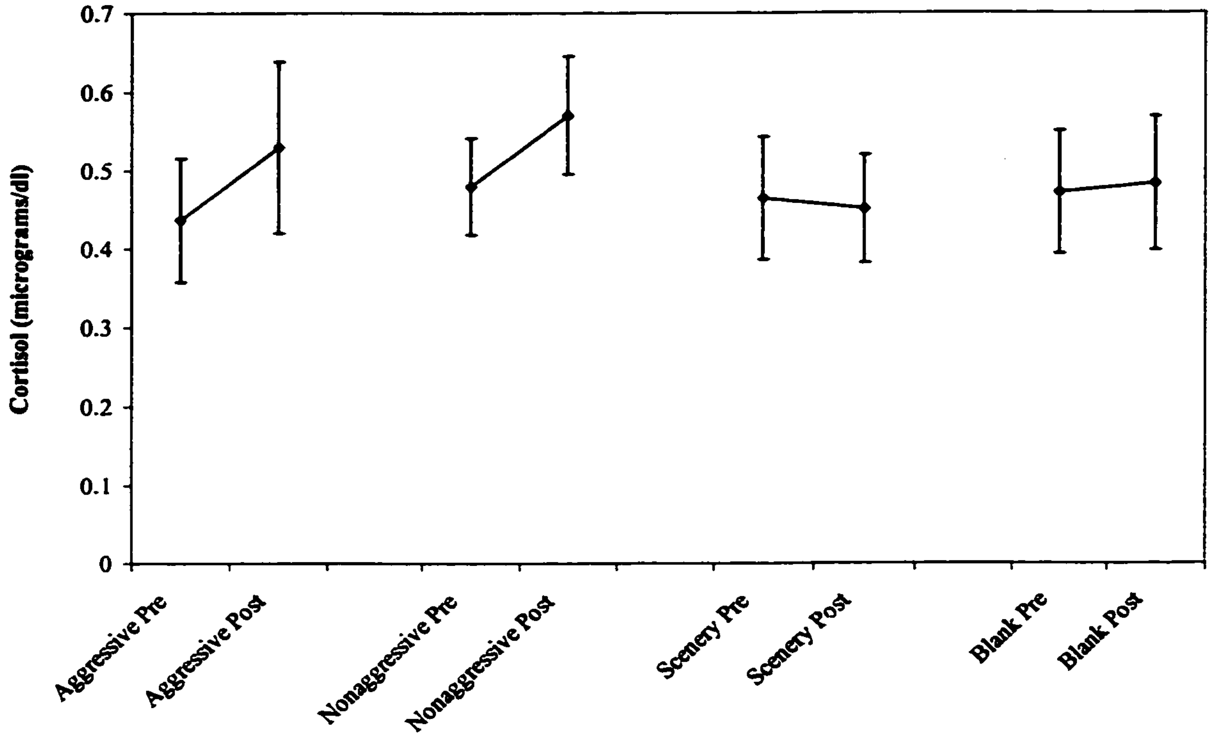


Figure 9. Mean (± SE) change in cortisol in μg/dl during video conditions (p's > 0.12 for all conditions). See text for details.

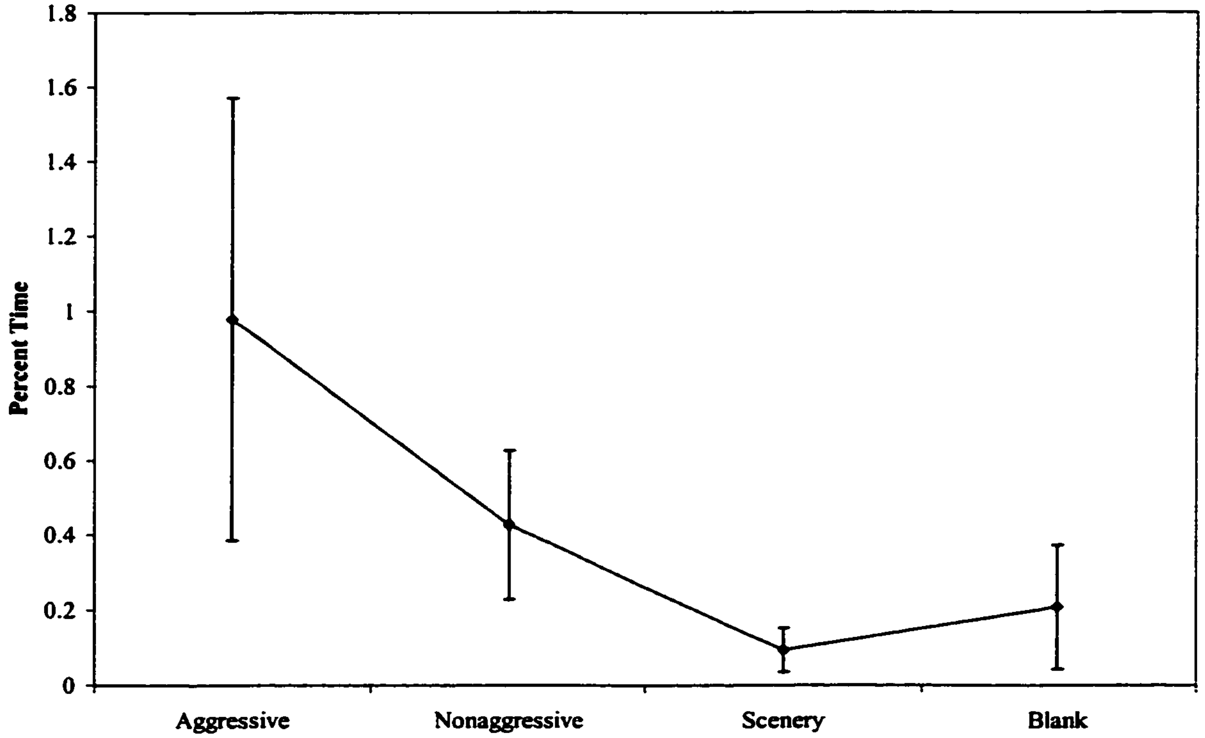


Figure 10. Mean percent time (±SE) in aggressive behavior during the four video Conditions. Conspecific (Aggressive + Nonaggressive) vs. Scenery videos (p = 0.008); Aggressive vs. Nonaggressive videos (p = 0.066).

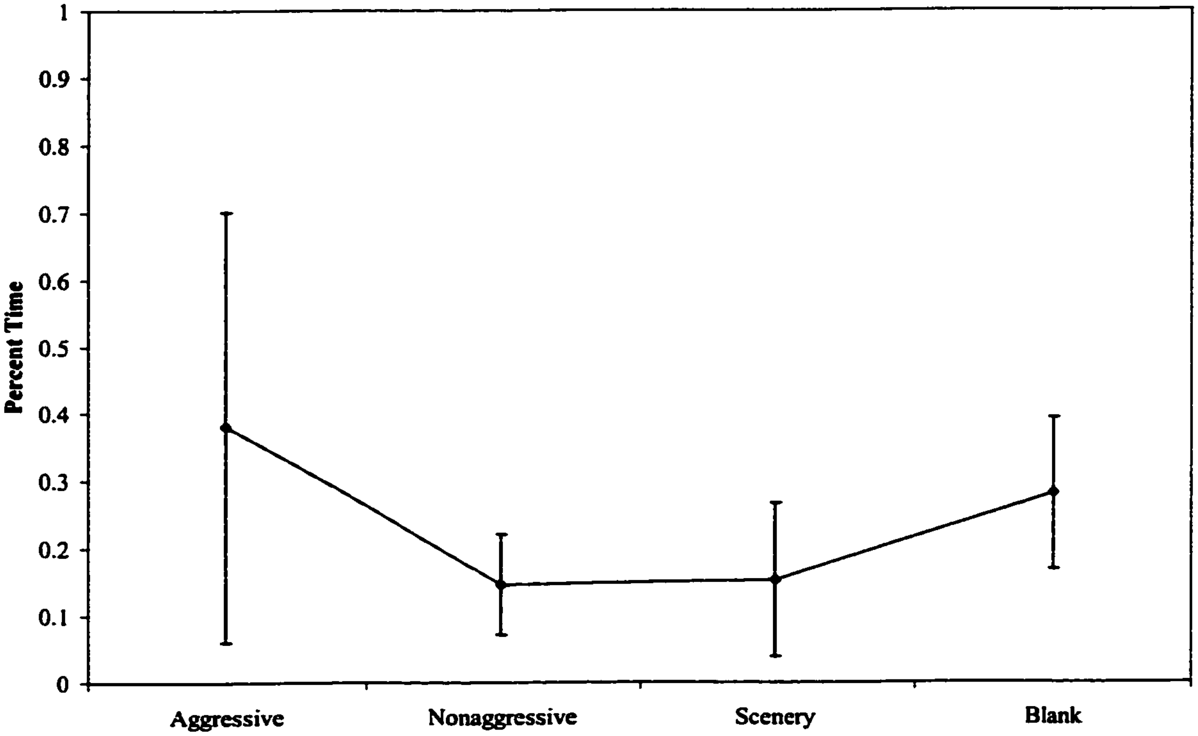


Figure 11. Mean percent time (±SE) spent self-biting during the four video conditions ($p = 0.695$).

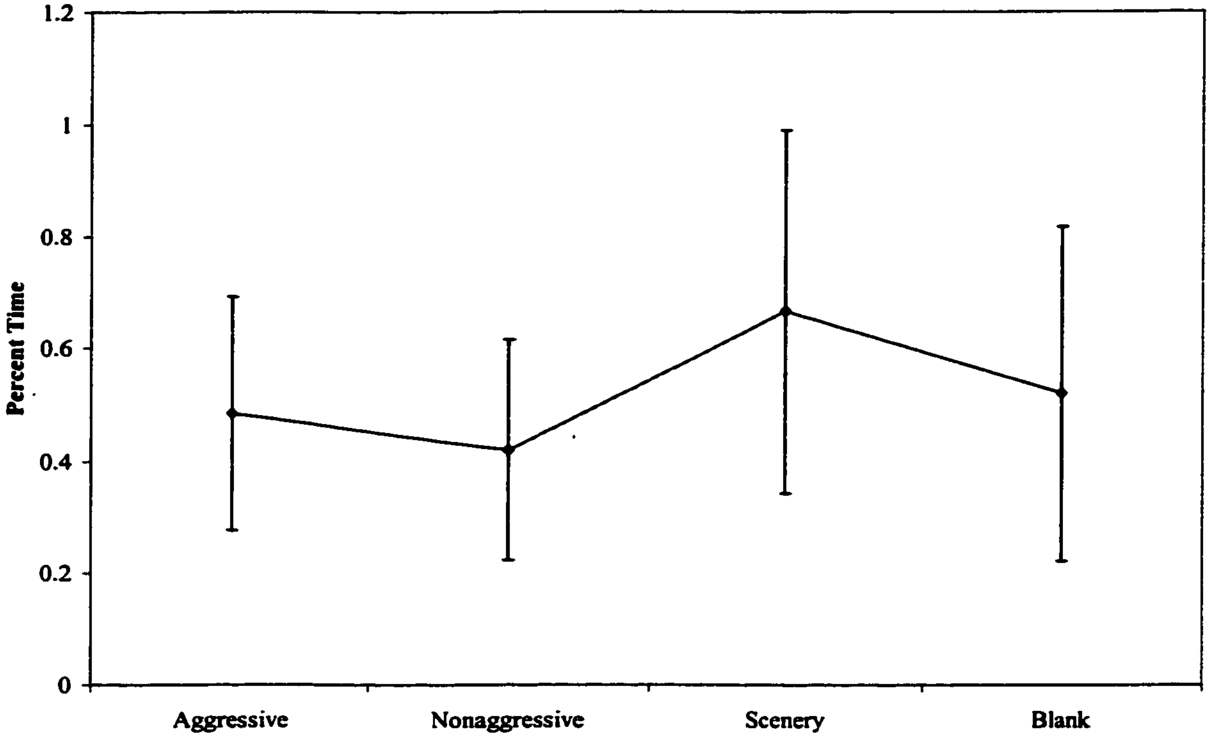


Figure 12. Mean percent time (±SE) in stereotypic behavior during the four video conditions (p = 0.915).

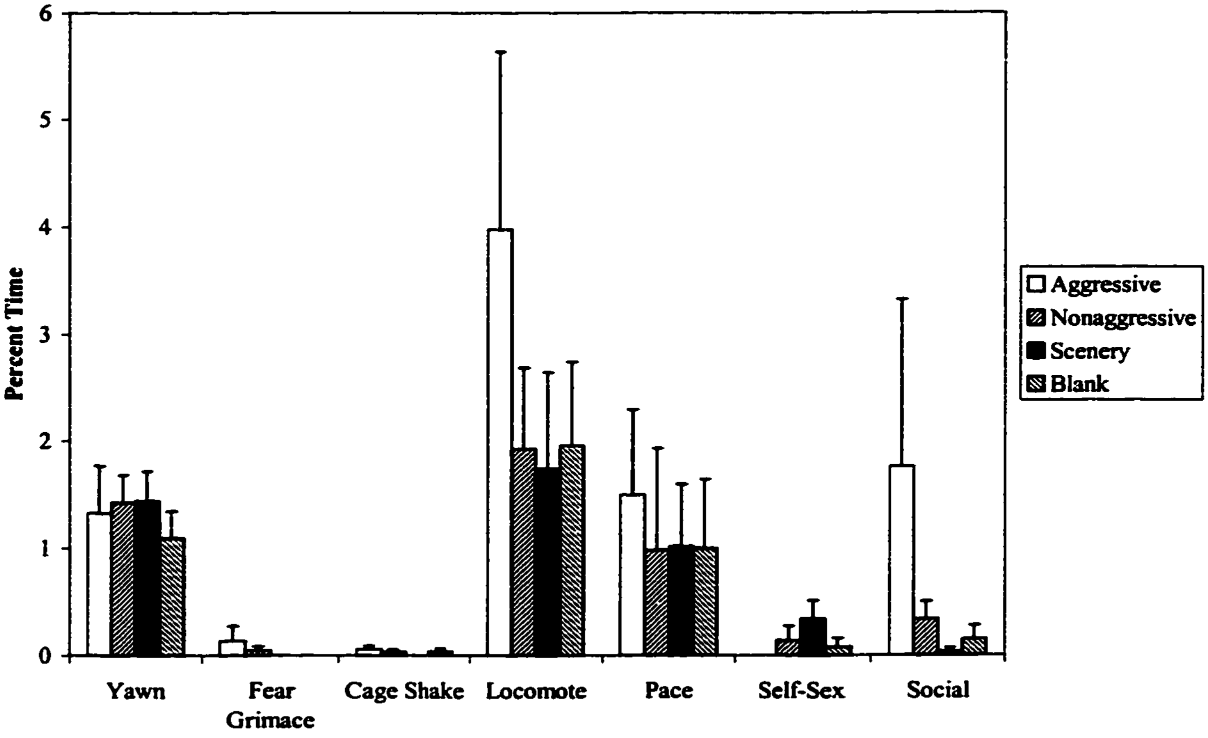


Figure 13. Mean percent time (±SE) for yawn (p = 0.48), fear grimace (p = 0.82), cage shake (p = 0.69), locomote (p = 0.11), pace (p = 0.63), self-sex (p = 0.22), social (p = 0.53).

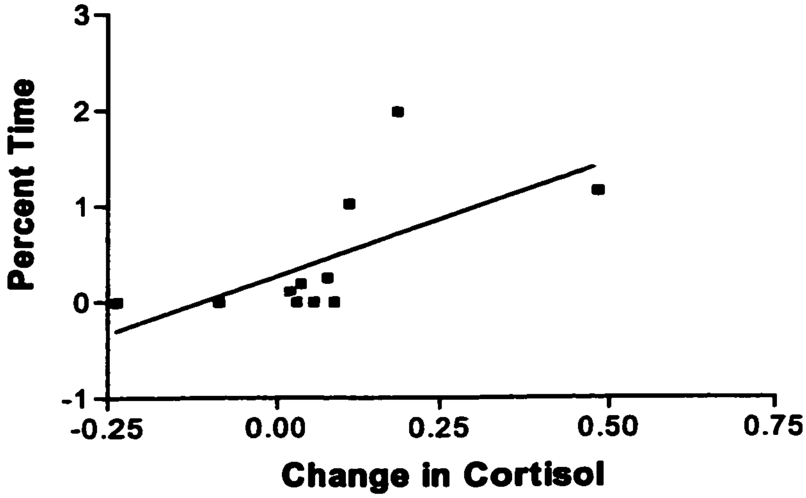


Figure 14. Correlation between aggressive behavior and change in cortisol during the nonaggressive video condition (r = 0.644, p = 0.045). Line is the least square fit of the data.

CHAPTER VI

Study 5. SIB and Aggression: Live Conspecific Condition

Introduction

The purpose of this study was to further explore the social and stress-related aspects of self-injurious behavior and to give the subjects a more natural social experience. The previous study had a measure of control over what each animal experienced, but a video may not be a realistic-enough social stimulus for aggressive interactions. Social pairing of strangers has been demonstrated to be a stressful procedure as measured by plasma cortisol (Kimura, Shimizu, Hayashi, Ishikawa, and Ago, 2000), and it reliably elicited both anxiety-related and aggressive behaviors in adult male rhesus macaques (Habib et al., 2000). Therefore, the present study used a live animal stimulus to create a more realistic social interaction. This study further explores the relationship between aggression and self-injurious behavior and tests the hypothesis that self-biting occurs more in social situations when aggressive physical contact is prevented than in nonsocial conditions.

Methods

Subjects

The subjects were 10 adult male rhesus monkeys (aged 8-17 years, M=10.6 years) with a history of self-biting. All of the subjects in this study were also used in Studies 2 and 4, and 9 of the subjects in the present study were used in Study 3. Nine of the 10 subjects had at least one veterinary record of self-injury. One subject was nursery-reared then placed with peers before individual housing, one subject was placed in single caging after nursery-rearing, five subjects were mother/peer reared before individual housing, one was mother-reared then placed with peers before individual housing, and two had unknown rearing histories.

Five adult male rhesus monkeys served as additional stimulus animals. These animals had low to no self-biting rates, and no veterinary record of self-injury. They ranged in age from 14 to 18 years (Mean = 15.2 years). One subject was nursery-reared before individual housing, three subjects were nursery-reared then placed with peers before individual housing, and one subject had an unknown rearing condition.

Housing

All of the animals were individually housed in "baboon" cages measuring 0.98 x 0.78 x 1.77 m. These cages also contained perch bars and manipulable toys. They were housed in four rooms. One room housed a total of 12 monkeys (two of which were subjects, and two were stimulus animals), while the other three rooms housed five monkeys each (eight of which were subjects, and three were stimulus animals). Each of the rooms had at least one window facing outside. Timers turned on the lights at 0600 hours and turned them off at 1800 hours daily. The animals were all fed Purina monkey chow *ad libitum*, with fresh fruit given twice a week.

Procedures

The subjects were each assigned two “strangers” for social testing based on the criteria that the strangers were not currently housed in the same room and had not been housed in the same room for the past year. The two strangers consisted of one of the other nine subjects and one of the five additional stimulus animals. Therefore, the subjects each served as a stranger for one other subject, and each stimulus animal served as a stranger for two subjects.

Saliva samples were initially collected from the subjects using the pole method as the baseline measure (pre). Following the first sample, the subjects, housed individually in baboon cages, were wheeled into the test room. Either the animal was placed into the room next to an empty cage (control condition), or the animal was placed in the room with one of the two assigned stranger animals (stranger condition). In the stranger condition, the cages were placed close together, but far enough apart to prevent physical contact. Both the subject and the stranger were videotaped with separate cameras for 20 minutes during the interaction for later behavioral scoring. Of interest were the subject's aggressive and self-injurious behaviors. After videotaping, the subjects were wheeled back into their home room and allowed to settle down for 10 minutes. A second saliva sample was then collected (post). The procedures were conducted on Tuesday and Thursday over a period of two weeks per subject, with the control session being conducted on one day and the stranger session being conducted on the other day. The control and stranger days were counterbalanced among the subjects.

In addition to the test conditions, two 20-minute videos were recorded from each subject while in its home cage. This taping was conducted on non-experimental days between 0900 and 1100 hours.

The test condition and home cage videotapes of both the subjects and the stimulus animals were scored as described in Study 3. Overall inter-observer scoring reliability for these tapes were 90.2% for frequency and 95.3% for duration.

Data Analyses

Friedman two-way analyses of variance by ranks tests were conducted on the behavioral data (*aggression*, *self-bite*, and *stereotypy*) to compare the three stranger conditions (SIB animal as subject, SIB animal as stranger, and stimulus animal as stranger). There was no consistent difference in behavior (*aggression*: $F(2) = 0.284$, $p = 0.756$, *self-bite*: $F(2) = 1.243$, $p = 0.312$, *stereotypy*: $F(2) = 0.382$, $p = 0.688$) between the three conditions. A repeated measures analysis of variance was then conducted on the cortisol data for the six subjects who produced adequate saliva samples. Test condition and time (pre vs. post) were within subject variables. Not surprisingly, there was an effect of time ($F(1) = 11.94$, $p = 0.018$). However, there was no difference between conditions ($F(2) = 0.29$, $p = 0.75$), and there was no interaction ($F(2) = 0.57$, $p = 0.58$). Therefore, the three stranger conditions were combined into a single category (Stranger) for further analysis.

Wilcoxon signed ranks tests were conducted to compare behavior (*aggression*, *self-bite*, *stereotypy*) between the two empty cage conditions. There was no significant behavioral difference between the two conditions with the exception of a trend for *stereotypy* (*aggression*: $t(9) = 0.15$, $p = 0.88$, *self-bite*: $t(9) = 0.92$, $p = 0.38$, *stereotypy*: $t(9) = 2.08$, $p = 0.07$). A repeated measures analysis of variance was then conducted on the cortisol data for the seven subjects who produced adequate samples. Empty cage condition (first day vs. second day) and time (pre vs. post) were the within subject variables. There was no difference between conditions ($F(1) = 0.18$, $p = 0.69$) and there was no interaction ($F(1) = 0.235$, $p = 0.645$). Therefore, the two empty cage conditions were also combined into a single category (Empty) for further analyses.

A repeated measures analysis of variance was then run on the cortisol data, with condition (Stranger, Empty Room) and sample time (pre, post) as within subject variables. To compare the test room conditions with home cage, cortisol measurements collected from eight yoked control subjects in Study 3 that were the same subjects as in the present study were used for the home cage data. A repeated measures analysis of variance was again conducted on the cortisol data from these eight subjects, with condition (Stranger, Empty Room, Home Cage) and sample time (pre, post) as within subject variables.

Repeated measures analyses of variance were conducted on the behavioral data for *pace*, *locomote* and "*other*" to compare behaviors in the stranger, the empty room, and the home cage situations. Due to inequality of variance and non-normal distributions, a Friedman two-way analysis of variance was conducted on the remaining behaviors: *aggression*, *stereotypy*, *self-bite*, *yawn*, and *cage shake*. The following contrasts were conducted on significant results: 1) Test room (Stranger and Empty Room) vs. Home Cage, and 2) Stranger vs. Empty Room. These procedures were also conducted separately for the four subjects that consistently self-bit during this study.

Correlations were then computed between *aggressive* and *self-injurious* behavior and change in cortisol level.

Hypotheses

If SIB is a form of re-directed *social aggression*, levels of self-biting should be higher when the animal is in a social context than when it is in a non-social condition. There should also be a positive correlation between the amount of time the animal exhibited *aggressive* and *self-biting* behavior. Alternatively, if SIB is independent of *aggression*, *self-biting* would not be higher in the social condition. If SIB is associated with stress, *self-biting* should correlate with a rise in cortisol regardless of the social or nonsocial condition.

Results

Cortisol

The repeated measures analysis of variance on nine subjects reported no cortisol difference between the two test conditions (Empty Room vs. Stranger; F(1) = 0.928, p = 0.364). However, there was a difference in time (pre vs. post; F(1) = 11.51, p = 0.009), but no interaction (F(1) = 0.40, p = 0.544). The repeated measures analysis of variance on the eight subjects with samples from all three conditions (Stranger, Empty Room, Home Cage data from Study 3) demonstrated that there was an effect of condition (Stranger, Empty Room, Home Cage; F(2) = 10.88, p = 0.001) and an effect of time (pre-test, post-test; F(1) = 17.22, p = 0.004) on cortisol levels. There was also an interaction between condition and time (F(2) = 20.94, $p > 0.001$). Post-hoc contrasts demonstrated that cortisol levels were lower in the home cage condition in comparison to the two test conditions combined (pre-test: F(1) = 7.09, p = 0.032; post-test: F(1) = 20.65, p = 0.003). However, the two test conditions were not different from each other (pre-test: F(1) = 0.00, p = 0.99; post-test F(1) = 1.83, p = 0.22; Figure 15).

To assess any interaction effect, a repeated measures analysis of variance on the change in cortisol demonstrated that there was an effect of condition on cortisol change (F(2) = 8.15, p = 0.004). Contrasts showed that there was a greater cortisol increase in the two test conditions in comparison with the home cage condition (F(1) = 19.96, p = 0.003), but there was no consistent difference between the two test conditions (F(1) = 1.17, p = 0.32; Figure 15).

Behavior

There was no significant effect of condition on *self-biting* behavior (F(2) = 0.45, p = 0.80; Figure 16). However, there was a significant overall effect of condition on *aggression, pace, locomote* and "*other*" behaviors (*aggression*: F(2) = 10.40, p = 0.006; *pace*: F(2) = 3.89, p = 0.04; *locomote*: F(2) = 20.55, p = 0.000; *other*: F(2) = 11.75, p = 0.001). Contrasts showed that levels of *aggression* were higher in the Stranger condition than in the Empty Room condition (p = 0.005; Figure 17), *pace* and *locomote* were greater in the test conditions than in the Home Cage (pace: p = 0.036; locomote: p = 0.001; Figure 18) and that "*other*" was greater in the Home Cage condition than in the test conditions (p = 0.003; Figure 18). There was no effect of condition on the remaining behaviors (*yawn*: F(2) = 3.05, p = 0.22; *cage shake*: F(2) = 1.85, p = 0.40; *stereotypy*: F(2) = 1.95, p = 0.38; Figure 19).

There was no correlation between *aggression* and *self-biting* in any of the conditions ($p>0.10$ for all conditions).

Behavior and Cortisol

There was a trend towards a correlation between cortisol and *aggression* in the Stranger condition (r = 0.599, p = 0.089). However, there was no correlation in the

Empty Room condition ($r = -0.225$, $p = 0.560$) and there was no correlation between cortisol and *self biting* (Stranger: $r = 0.01$, $p = 0.98$; Empty Room: $r = -0.075$, $p = 0.85$).

Biters Only

When analyzing data from only the four subjects that consistently self-bit during this study, there was an overall effect of condition on *self-biting* behavior ($F(2) = 8.0$, $p = 0.018$). Contrasts showed that there was a trend towards higher levels of *self-biting* in the Empty Room condition in comparison to the Stranger condition ($p = 0.068$) and that there was a trend towards higher levels of *self-biting* in the test rooms (Stranger and Empty Room) in comparison to the Home Cage ($p = 0.068$; Figure 20).

There was no consistent effect of condition on duration of *social aggression* ($F(2) = 3.50$, $p = 0.174$; Figure 21). However, there was an effect of condition on frequency of *aggression* ($F(2) = 6.00$, $p = 0.05$; Figure 22). Contrasts showed a trend towards a greater frequency of *aggression* in the Stranger condition in comparison to the Empty Room condition ($p = 0.068$), but no consistent difference when comparing the Test conditions (Stranger and Empty Room) with the Home Cage condition ($p = 0.144$). In addition, there was a significant overall effect of condition on *locomote* and "*other*" behaviors (*locomote*: $F(2) = 29.075$, $p = 0.001$; *other*: $F(2) = 9.821$, $p = 0.013$; Figure 23). Contrasts showed that *locomotion* was greater in the Test Room (Stranger and Empty Room) in comparison to the Home Cage ($p = 0.012$) and "*other*" was greater in the Home Cage in comparison to the Test Room ($p = 0.026$).

There was no correlation between *aggressive* and *self-injurious* behavior in the subjects that self-bit ($p > 0.30$ for all conditions).

Comparing three subjects that *self-bit* (the fourth was omitted due to prednisone medication that affects the cortisol results) with the six subjects that did not *self-bite* during this study, there was no difference in cortisol increase in either of the Test Room conditions (Empty Room: $t(7) = 0.224$, $p = 0.829$; Stranger condition: $t(7) = 0.007$, $p = 0.995$).

Further comparing the four subjects that bit with the six subjects that did not bite, nonparametric Kruskal-Wallis one-way analysis of variance revealed no significant difference in *aggressive* behavior ($p > 0.25$ for all conditions; Figure 24). However, the biters had overall higher levels of *stereotypy* for the Empty Room ($F(1) = 4.57$, $p =$

0.032) and Home Cage conditions (F(1) = 3.92, p = 0.048), but not the Stranger condition (F(1) = 1.68, p = 0.195.; Figure 25). In addition, the biters had higher levels of *locomotion* in the Stranger condition (F(1) = 4.54, p = 0.033) but no difference in the Empty Room condition (F(1) = 1.14, p = 0.286) or the Home Cage condition (F(1) = 1.14, p = 0.286; Figure 26). A parametric ANOVA showed that biters had lower levels of "*other*" behavior in the Stranger condition (F(1) = 7.512, p = 0.025) and a trend towards lower levels in the Empty Room condition (F(1) = 4.49, p = 0.067), but not the Home Cage condition (F(1) = 1.731, p = 0.225; Figure 27).

Comparing the live test room conditions (Study 5) with the video conditions from the previous study (Study 4), Wilcoxon Signed Ranks test showed that there was a trend towards greater levels of self-biting in the Test Room conditions (Stranger and Empty Room) than during the Video conditions (t(9) = 1.86, p = 0.06). However, there was no consistent difference between the two studies with respect to aggressive behavior (t(9) = 0.28, p = 0.78).

Conclusions

Self-biting does not appear to be linked to aggression. Instead, it may occur in response to the arousal caused by the aggression.

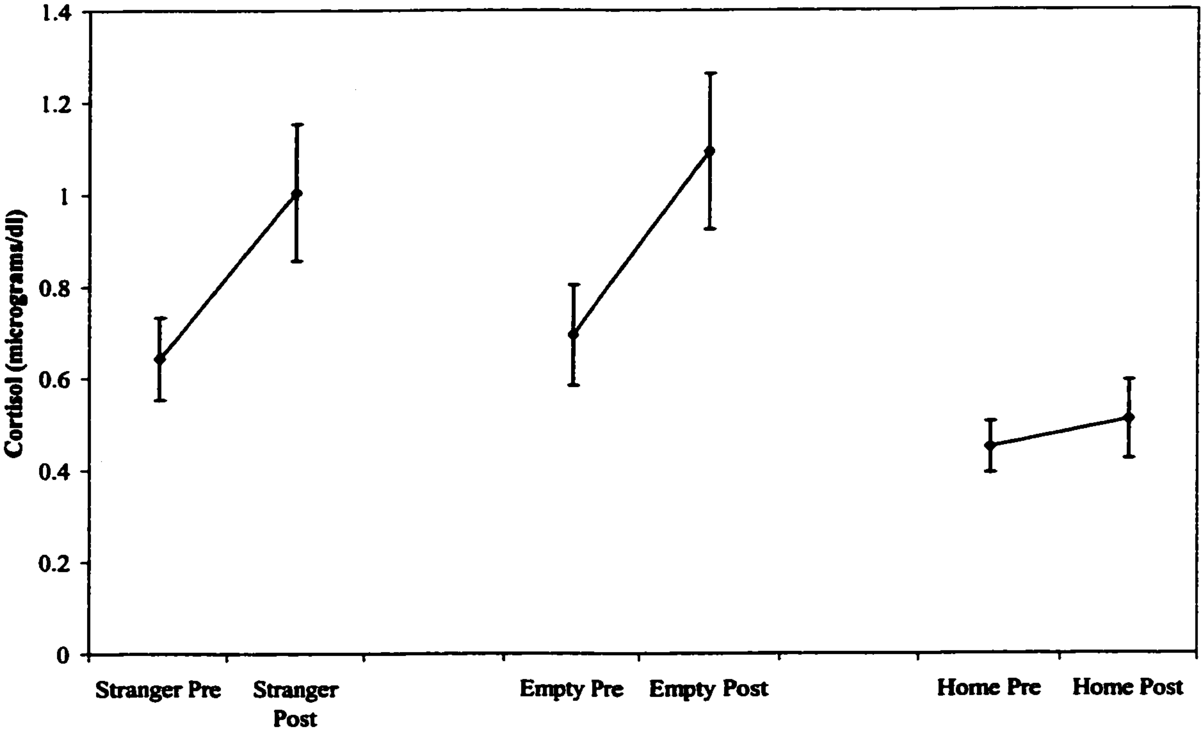


Figure 15. Change in cortisol (μg/dl, Mean ± SE) during the stranger (N =9), the empty room (N = 9), and the home cage (N = 8; Study 3) conditions. Cortisol levels were lower in the home cage (pre: $p = 0.032$; post: $p = 0.003$). Post cortisol levels were higher than pre in the test conditions (stranger and empty room, $p = 0.009$).

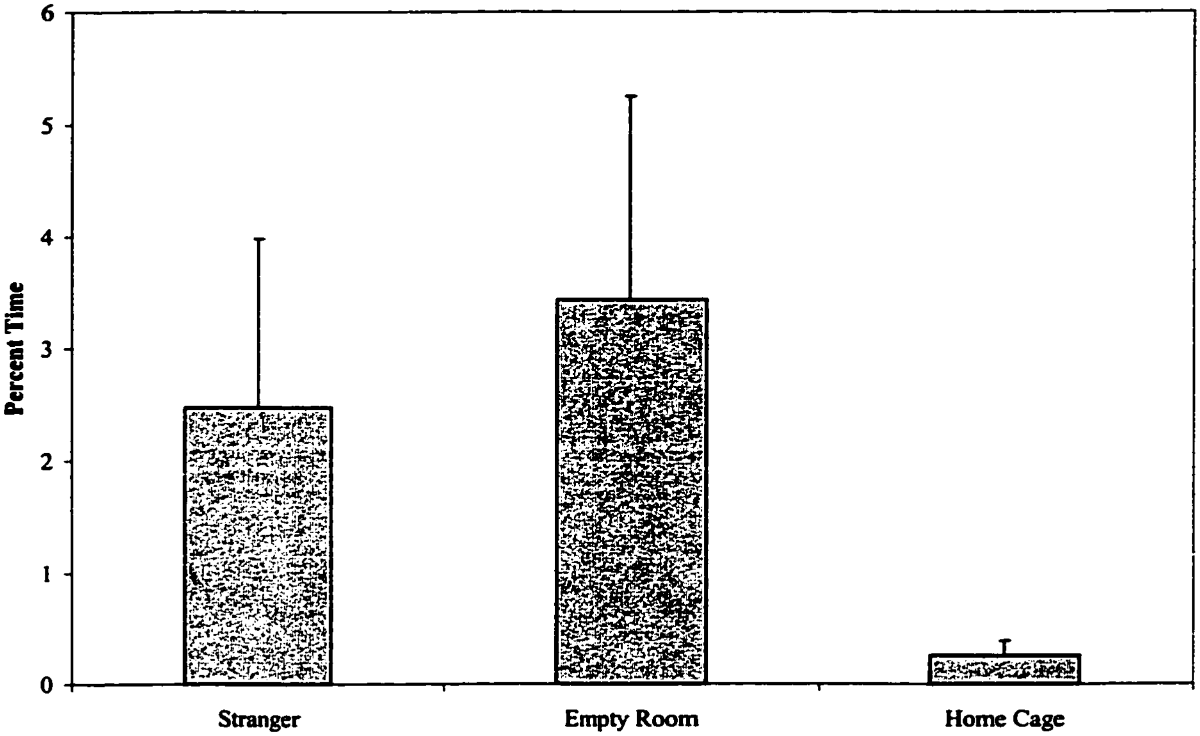


Figure 16. Self-biting behavior in the Stranger, Empty Room, and Home Cage conditions (p = 0.80).

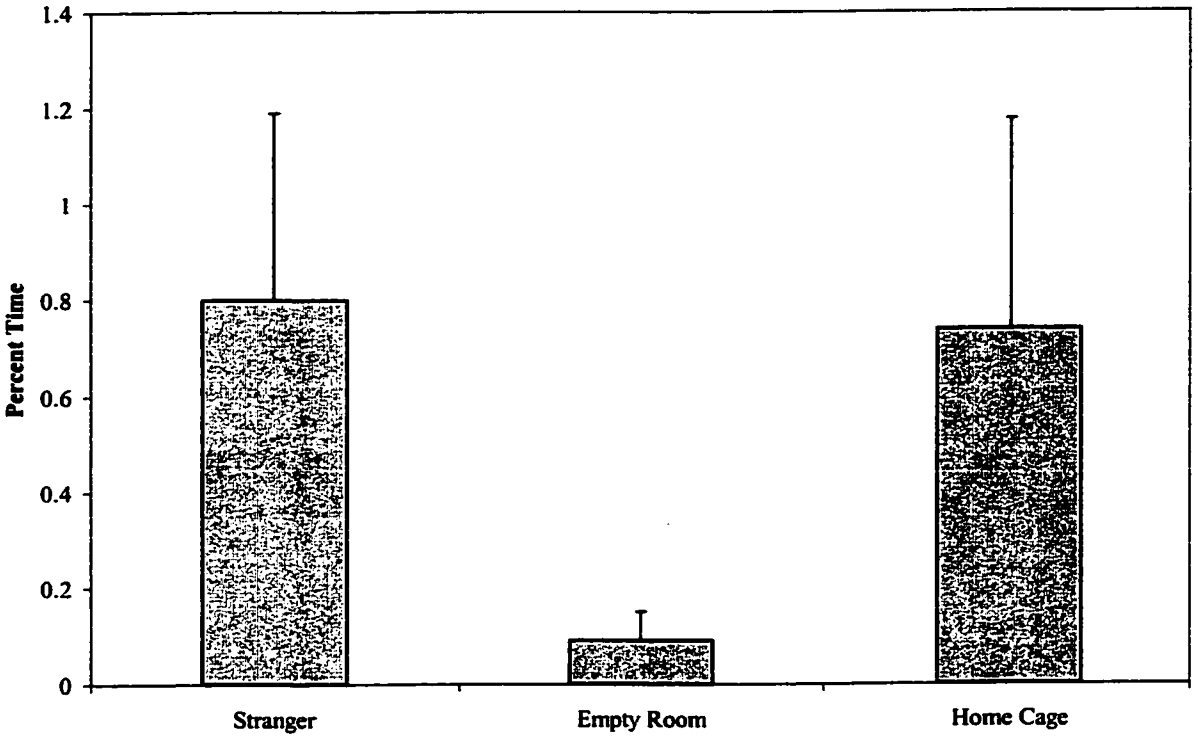


Figure 17. Aggressive behavior (Mean ± SE) in the Stranger, Empty Room, and Home Cage conditions (Stranger vs. Empty Room, p = 0.005; Test Rooms (Stranger and Empty Room) vs. Home Cage, p = 0.33).

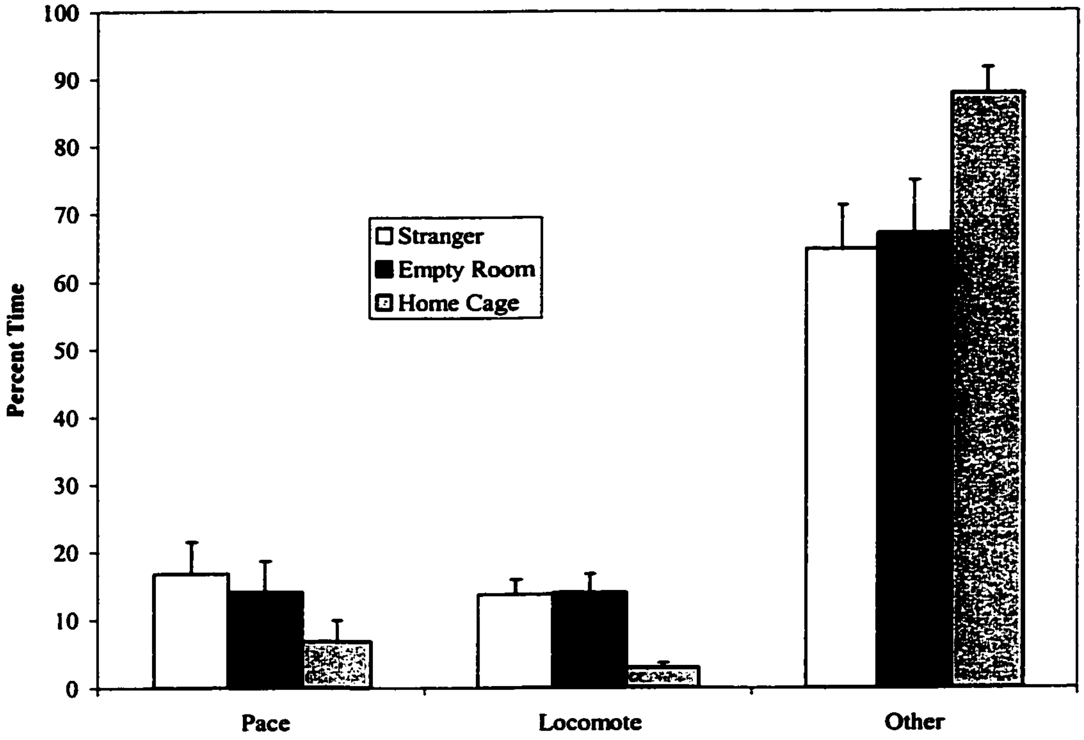


Figure 18. Percent time (Mean ± SE) in behaviors "pace" ($p = 0.04$), "locomote" ($p < 0.001$), and "other" ($p = 0.001$) during Stranger, Empty Room, and Home Cage conditions. Significant contrasts: Test Rooms (Stranger and Empty Room) vs. Home Cage (pace: $p = 0.036$; locomote: $p = 0.001$; "other": $p = 0.003$).

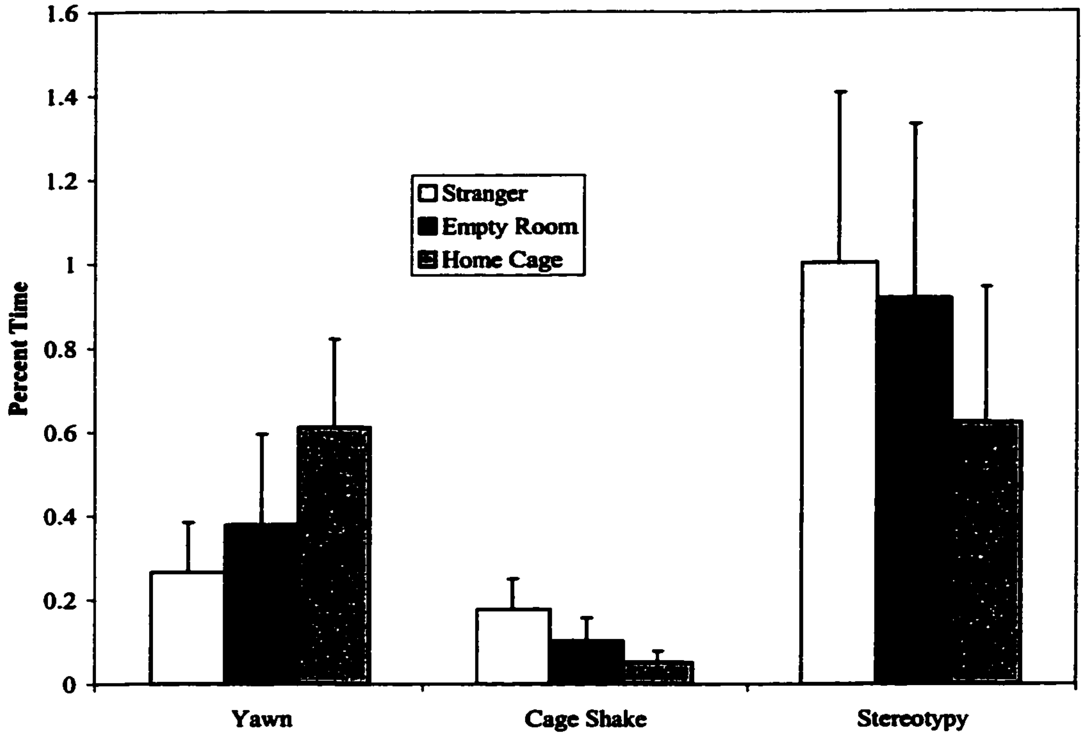


Figure 19. Percent time (Mean ± SE) in behaviors "yawn" (p = 0.22), "cage shake" (p = 0.40), and "stereotypy" (p = 0.38).

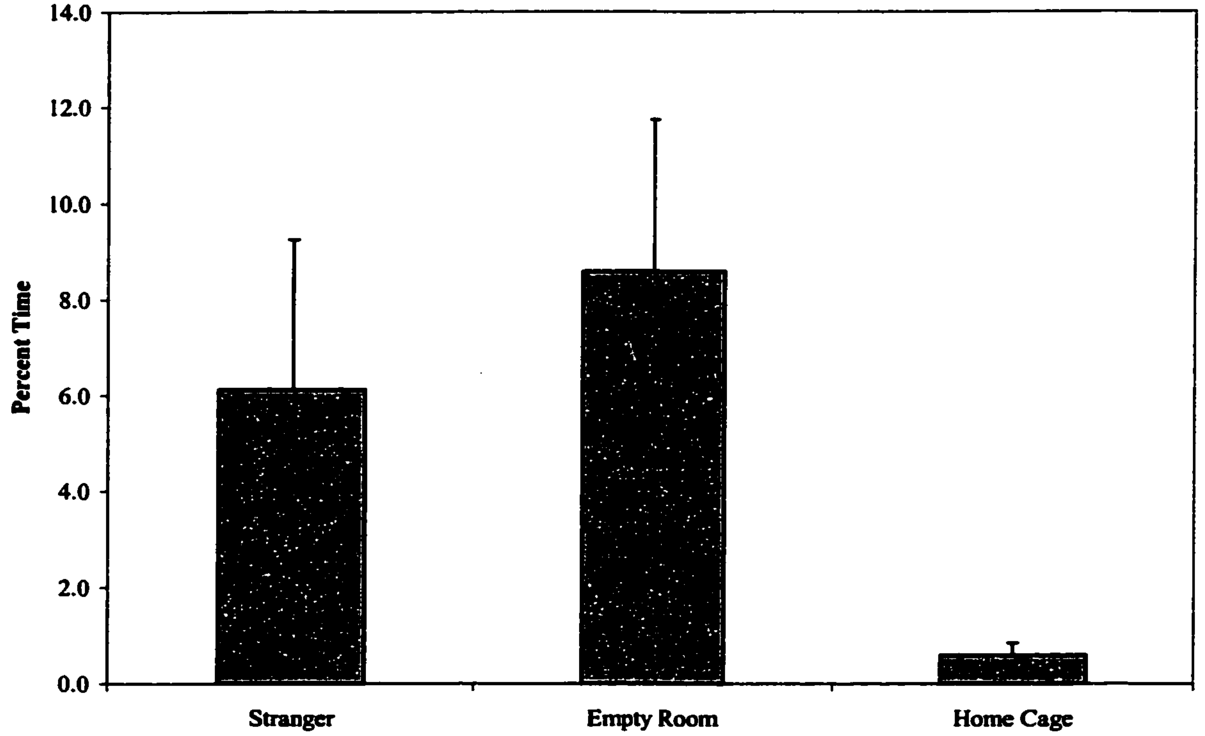


Figure 20. Self-biting behavior by condition (M ± SE; only Ss that self-bit). Stranger vs. Empty Room, p = 0.068; Test conditions (Stranger and Empty Room) vs. Home Cage, p = 0.068.

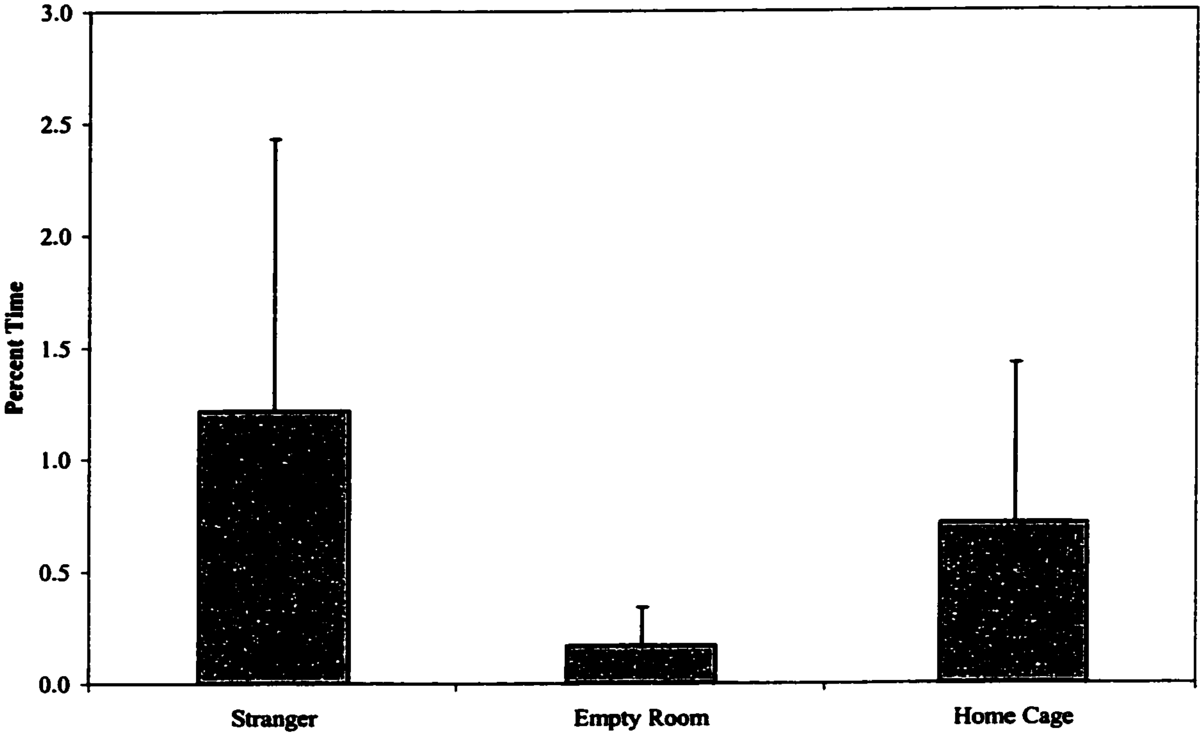


Figure 21. Social Aggression by condition (M ± SE; only Ss that self-bit), p = 0.174.

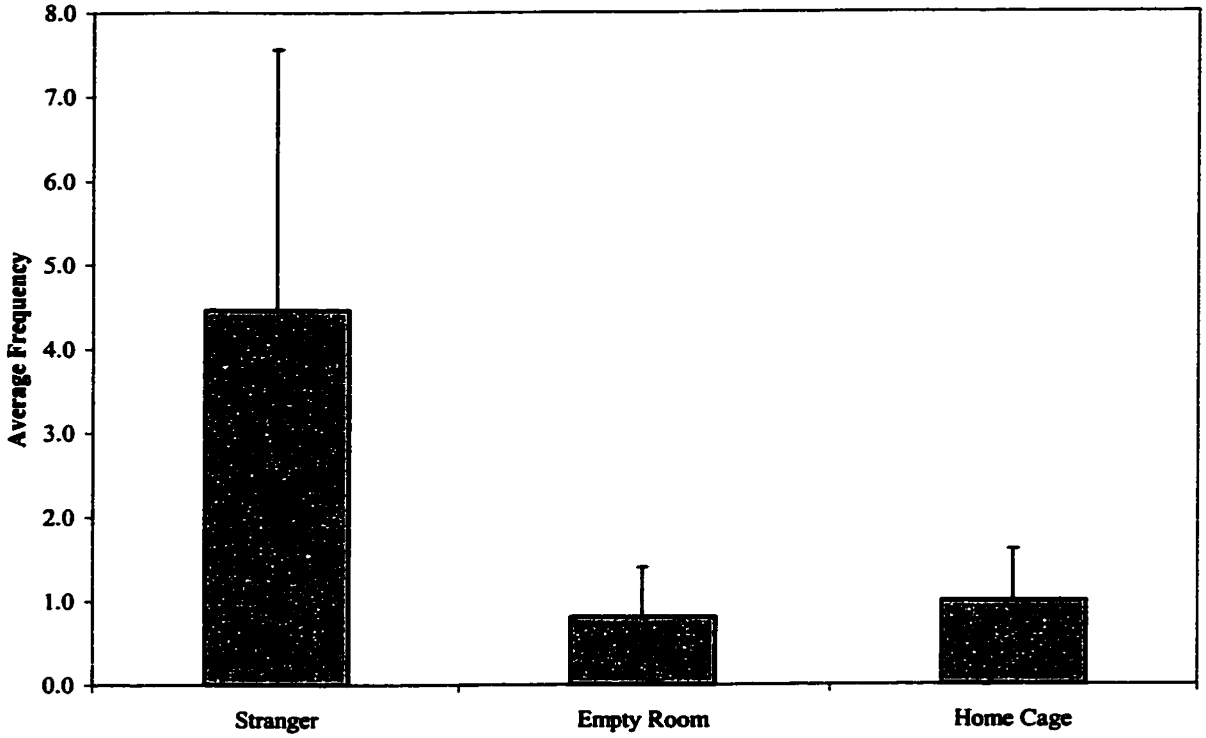


Figure 22. Frequency of Social Aggression (M ± SE; only Ss that self-bit), $p = 0.05$. Stranger vs. Empty Room, $p = 0.068$; Test Rooms (Stranger and Empty Room) vs. Home Cage, $p > 0.10$.

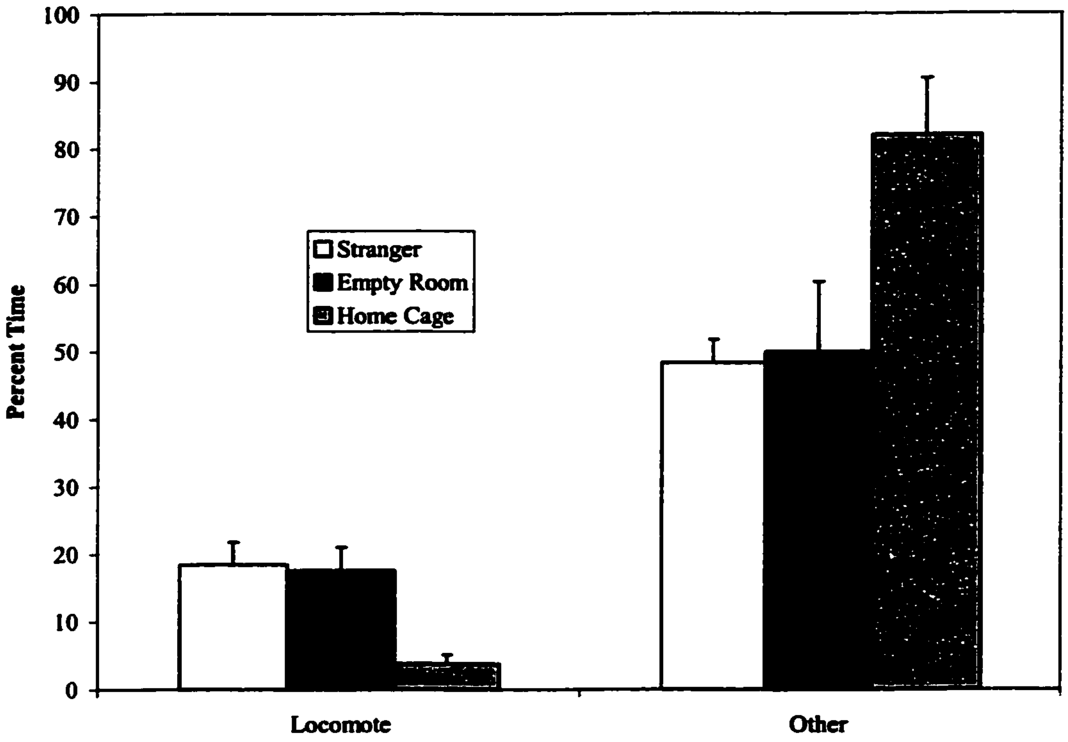


Figure 23. Percent time (M ± SE; only Ss that self-bit) in behaviors "locomote" (p = 0.001) and "other" (p = 0.013) during Stranger, Empty Room, and Home Cage conditions. Significant contrasts: Test Rooms (Stranger and Empty Room) vs. Home Cage ("locomote": p = 0.012; "other": p = 0.026).

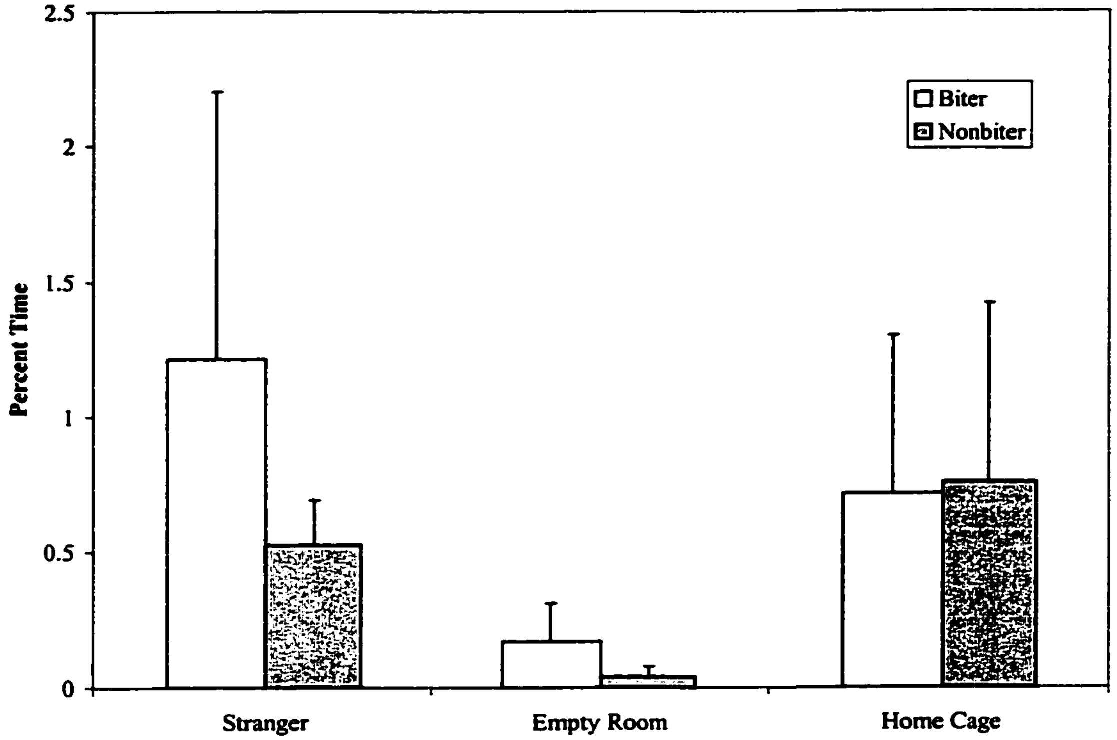


Figure 24. Levels of social aggression: biters vs. nonbiters (Mean ± SE; $p > 0.25$ for all conditions)

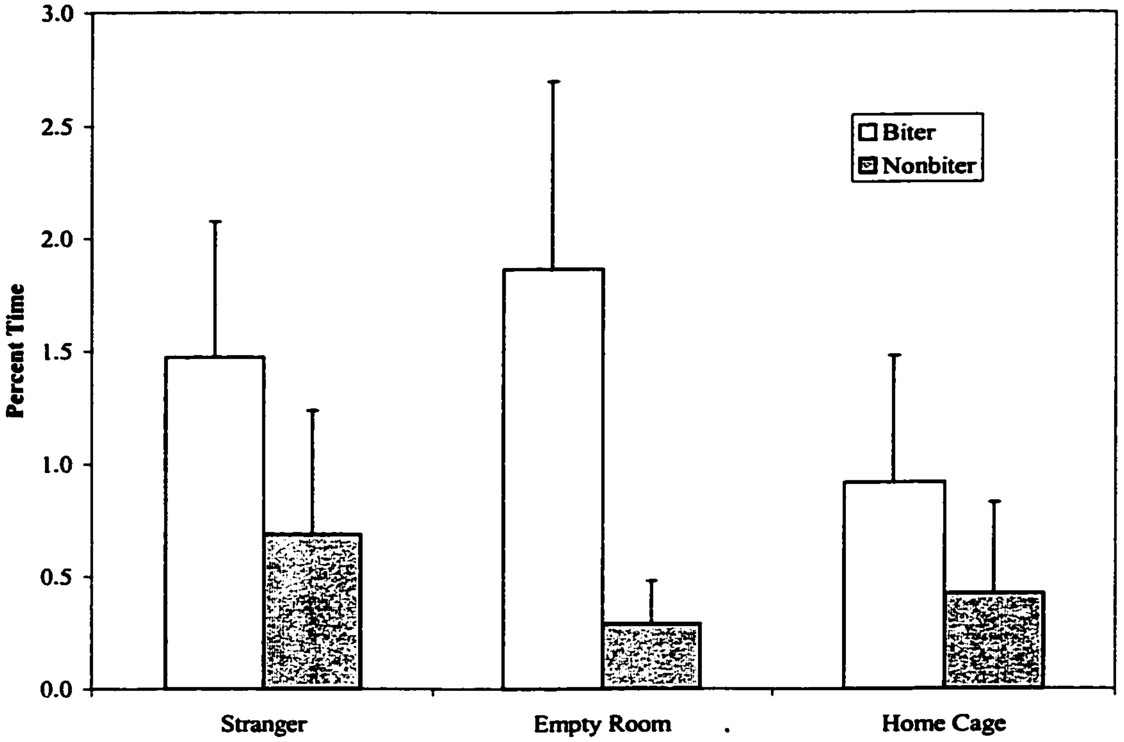


Figure 25. Levels of stereotypy: biters vs. nonbiters (Mean ± SE): Stranger, p = 0.195; Empty Room, p = 0.032; Home Cage, p = 0.048.

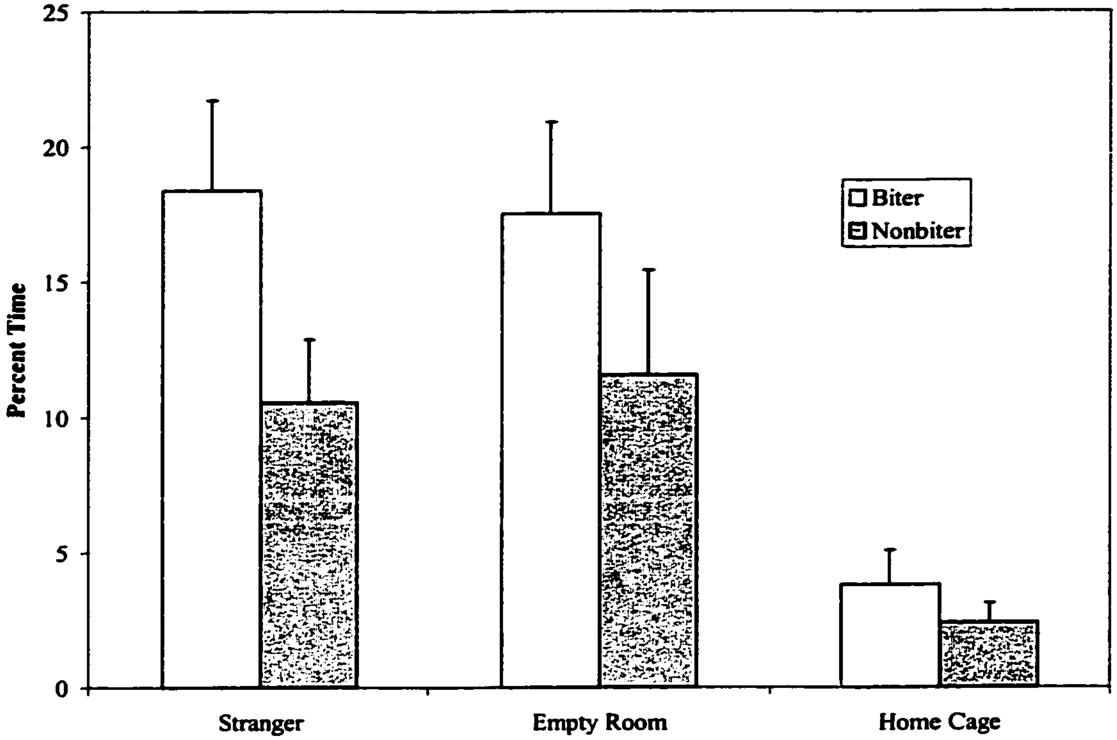


Figure 26. Levels of locomotion for biters and. nonbiters (Mean ± SE): Stranger, p = 0.033; Empty Room, p = 0.286; Home Cage, p = 0.286.

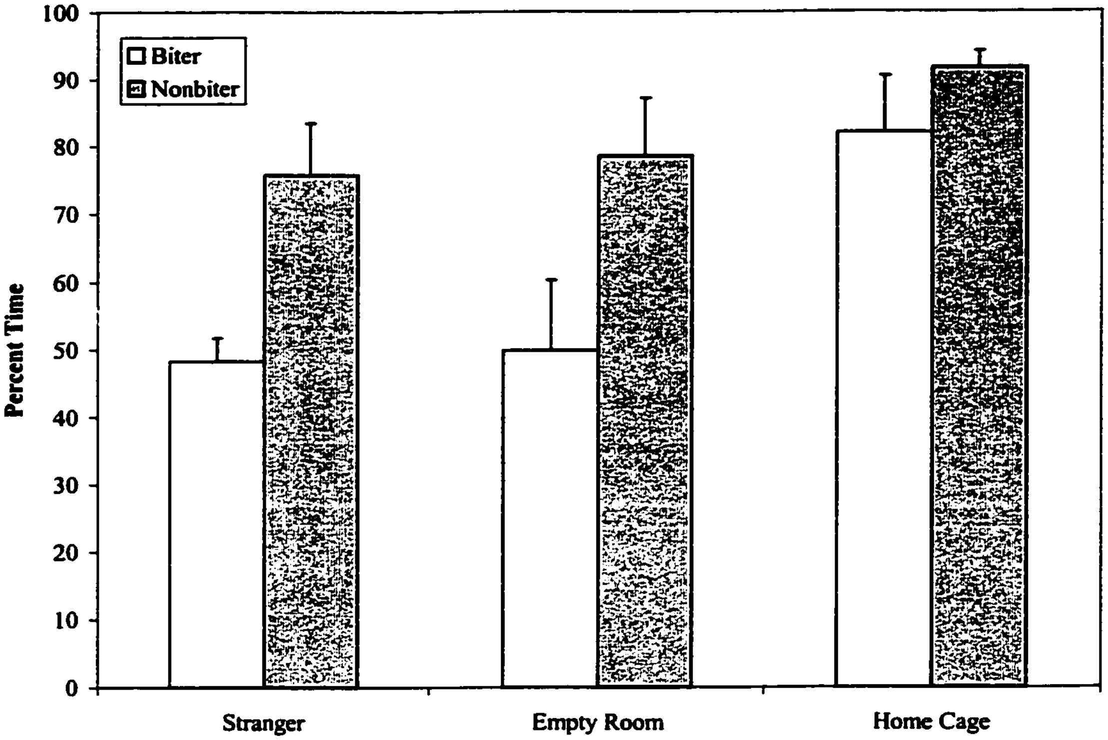


Figure 27. Levels of "other" for biters and. nonbiters (Mean ± SE): Stranger, p = 0.025; Empty Room, p = 0.067; Home Cage, p = 0.225.

CHAPTER VII

General Discussion and Conclusions

Self-injurious behavior is a phenomenon that is difficult to understand. On the surface, it is a behavior that can be damaging and counterproductive to an individual. For example, repeated self-biting can result in severe tissue damage requiring medical care. However, a small percentage of the population, both human and nonhuman, continue to self-injure. The objectives of this dissertation were 1) to examine the incidence of SIB in a large colony of rhesus macaques, 2) to identify risk factors of SIB, 3) to develop and utilize a noninvasive technique for measuring an animal's response to stress, 4) to examine actual episodes of SIB and determine the relationship to stress, and 5) to determine the association between SIB and aggression. The results of this research contributed new technology (non-invasive devices for collecting saliva) and new findings that SIB may not be a function of social aggression, but a function of early separation from the social group, housing conditions, and/or arousal.

Incidence of self-injurious behavior was assessed in a large colony of rhesus monkeys in two ways. First, health records were analyzed for incidents of self-inflicted wounding requiring veterinary care. Some 11% of the singly-housed rhesus macaques had a veterinary record of self-injury. Significantly more males than females had such a record, and older subjects wounded themselves more than younger subjects. These numbers are slightly lower than those reported by Bayne et al. (1995: 15.8% as derived from the data) and may be due to a larger sample size in the present study and differences in colony management and/or record keeping. Second, the subjects of this dissertation were observed during three separate behavioral assessments, and episodes of self-biting were recorded. Assessment results showed that almost a quarter of the subjects exhibited self-biting behavior, demonstrating that not all self-biters are wounders. Significantly more males than females self-bit, and older subjects tended to self-bite more than younger individuals. In comparison to other assessments, these numbers are larger than those reported by Jorgensen et al. (1998: 14%). This difference may be again due to a larger sample size or differences in collecting assessment data. Jorgensen et al. relied on caretaker interviews, whereas the present study utilized direct observations of the subjects, which may be more reliable. Comparing the above results to human subjects, these percentages are most similar to those found in institutionalized psychiatric inpatients (Briere and Gil, 1998) or severely retarded human subjects (Maisto et al., 1978).

Similar sex differences in self-biting and self-wounding have been observed in rhesus monkeys reared in partial or total isolation (Cross and Harlow, 1965; Gluck and Sackett, 1974). However, age differences reported in previous studies suggested that subjects aged 3-7 years tended to have higher levels of self-biting than those younger or older in age (Cross and Harlow, 1965; Suomi et al., 1971). The age ranges reported for these two studies was 0-7 years and 0-13 years, respectively. The present study observed subjects ranging in age from 2- 21 years. The trend towards higher levels of biting in older individuals in the present study suggests that a large age range is necessary to draw any such conclusions. In the present study, the greatest amount of wounding occurred in older males, which may be in part due to higher biting rates as well as large canine teeth that make serious wounding more easily accomplished. In severe cases, self-injury may require euthanization of the animal. Because of this possible danger and because self-biting and self-injury are correlated, both behaviors can be considered significant problems for colony managers.

Potential environmental risk factors for SIB in nonhuman primates were assessed by comparing the presence/absence of self-biting and self-injury with records of the rearing, husbandry, and medical procedures for each of the subjects. Environmental variables that appear to be risk factors for SIB include individual housing at a young age and increased number of blood draws. The rhesus subjects in Study 1 were not known to have a physical disorder that would predispose them to self-biting or self-injury. Instead, the results most likely reflect such environmental factors. Early separation from social contact was significantly associated with both self-biting and self-injury. Although all of the subjects were reared socially, animals were moved to individual cage housing at a mean age of 27.5 months (range: 4-132 months). Previous research had demonstrated that rearing rhesus infants in total or partial isolation has devastating effects on their behavior, resulting in self-biting and self-injury (Cross and Harlow, 1965). Similarly, rhesus infants chambered prior to one year of age exhibited self-directed behaviors that were not observed in subjects chambered at a later age (3 years; McKinney et al., 1973).

Separation from social contact in the present study, although delayed, may also have contributed to the development of self-biting and self-wounding. Although number of blood draws was associated with self-wounding, this result may require caution in interpretation. The blood draws themselves may play a role in SIB, but they may also be associated with research protocols and/or additional treatments that have an influence over this behavior.

The above assessment results are interesting and indicate increased vulnerability under certain environmental conditions. Because SIB can result in serious wounding, preventative measures should be taken. Although experimental research is required to determine cause and effect, recommendations can still be made. In primate facilities today, infants are no longer reared in partial isolation as a common husbandry procedure. However, they are still removed from their social groups at various ages for specific research protocols. Assessment results suggest that even in socialized infants, the age at which they are removed from their social groups is important and should be delayed as long as possible.

The third objective of this study was to develop and utilize a method to noninvasively assess stress response in adult rhesus macaques by obtaining measures of salivary cortisol. Prior to this study, measurements of salivary cortisol were limited to infant subjects due to the inherent difficulties and dangers of sample retrieval. Cortisol measures in adult macaques were limited to blood (of which sampling in itself causes stress) and urine (which is a state measurement and not adequate as an indicator of acute stressors).

The research demonstrated that either the pole or the screen method can be utilized to safely and effectively collect saliva from unrestrained adult macaque monkeys for cortisol assay. The cortisol values obtained were comparable to those previously reported for infant rhesus macaques (Boyce et al., 1995). In addition, as shown in human subjects, there was no significant effect of flavoring on the cortisol assay. Unlike blood sampling, this saliva technique allows for cortisol sampling without restraint, anesthesia, or additional stress. In addition, saliva sampling allows for a more immediate point measure than what is obtained with urine collection.

There was no consistent difference with respect to type of saliva-gathering apparatus used in the levels of cortisol obtained. However, there are advantages and disadvantages to each method. The pole apparatus collected the greatest amount of saliva in the least amount of time, but some subjects tended to bite off the rope, preventing retrieval of the sample. Alternatively, the screen method allowed for easy retrieval of the sample; however, more time was required to obtain a sample of sufficient volume. This additional time requirement can result in the animal losing interest. Therefore, choice of method depends on the subject's behavior and the experimenter's preference.

The persistence of self-injurious behavior in spite of its potential for wounding suggests that there may be a reinforcing and/or a beneficial aspect to this potentially harmful behavior. In support of this hypothesis, human subjects who self-injure often report increasing tension prior to an injurious behavior such as cutting, and a release of tension after the injury (Coid et al., 1992; Haines et al., 1995). Because self-report is not possible for research with nonhuman primates, indirect measures need to be utilized. The fourth objective of the present research was to utilize the saliva collection techniques developed in Study 2 to further explore aspects of self-injurious behavior and add to the limited number of studies addressing direct physiological measurements of stress during an SIB episode.

Few studies have utilized physiological indices as direct measures of stress when that behavior occurred. Sandman et al. (1997) collected blood samples from institutionalized subjects with self-injurious behaviors (e.g., self-hitting, head-banging, and self-biting) so as to measure levels of ACTH. In this example, results did not reveal a difference between samples collected after SIB episodes and on the following day when SIB did not occur. However, the three behavior types were combined for that study, so self-biting alone was not tested. In addition, although blood sampling was a routine procedure for these subjects, it may still have been stressful enough to artificially inflate the ACTH levels.

As an alternative to blood sampling, Marinus et al. (1999) and Freeman et al. (1999) utilized heart rate to test the association between self-injurious behavior and arousal. The benefit of this technique is that an immediate response in heart rate (within seconds) can be detected and it is an ideal method to use when the animal is placed in short-term situations that may elicit biting. Marinus et al. (1999) demonstrated that heart rate increased prior to a self-biting episode and decreased afterwards in rhesus monkeys under induced stress conditions. This increase and subsequent decrease did not occur when the animal bit the vest containing the heart rate equipment as opposed to his own body. Alternatively, Freeman et al. (1999) noted an increase in heart rate after episodes of self-biting in two mentally-retarded humans. However, the sample size was small, and unlike the rhesus subjects in Marinus et al. (1999), the human subjects in Freeman et al. (1999) were not placed in a stressful situation. Although differences in timing of heart rate changes may reflect species or research protocol differences, both Marinus et al. (1999) and Freeman et al. (1999) suggest a physiological association between self-biting and stress.

For the present study, the subjects were observed in their home cage specifically for unprovoked self-biting episodes. When an episode of self-biting was observed, saliva samples were collected after the biting episode, at the same time on the following day when the subject did not bite, as well as from subjects housed in the same room who did not bite. Unlike Marinus et al. (1999), the subjects were observed in their home cage and were not already under a stressed condition. This allowed for the study of spontaneous episodes of biting not induced by the experimental procedures. In addition, unlike Sandman et al (1997), cortisol levels were measured from saliva samples instead of blood plasma. Results did not reveal a difference in cortisol between biting days and non-biting days for the subjects, and there was no difference between subjects who bit and those housed in the same room who did not bite. These results support the findings of Sandman et al. (1997), but are inconsistent with cardiac measures of arousal (Freeman et al., 1999; Marinus et al., 1999). However, the power of the present study was very low (0.044), indicating that there was too much variability in the data to draw a strong conclusion. Therefore, these results can have two possible interpretations: spontaneous episodes of self-biting are not associated with stress, or self-biting is associated with stress, but it was not detected by the procedures used.

If SIB is not associated with stress, the question remains as to why the animals continue to perform this potentially harmful behavior. One possibility is that the subjects began the self-biting behavior when they were younger, and at the time, the behavior was associated with a particular environmental event or experience. Environmental conditions such as individual housing may have predisposed an animal to developing SIB, but specific triggers or experiences may have initiated the actual behavior. With repetition, this behavior could have become ritualized, i.e., less variable, more automatic, and more difficult to stop. Characteristics of automatized behavior include such factors as a stereotyped performance, little cognitive effort, lack of awareness, and an association with specific stimuli (Tiffany and Carter, 1998). Automatized behavior also becomes highly stimulus bound (Tiffany and Carter, 1998), which means that even a simple presentation of the stimulus could result in the performance of the behavior. Rhesus monkeys reared in isolation have been shown to exhibit extinction deficits (Gluck and Sackett, 1976). Perhaps the subjects in the current study were singly-housed early enough to have similar problems with inhibiting self-injurious behaviors. With time, SIB may have become automatic, although still cued by particular stimuli.

Alternatively, self-biting behavior is associated with stress, but the association was not detected by the procedures used here. One possibility is that self-biting helps to reduce stress levels quickly, before the stress can be reflected by elevated cortisol. The rhesus monkey heart rate data (Marinus et al., 1999) suggest that this may be the case. Heart rate was high during the 30-seconds prior to a biting episode and then decreased during the 30 seconds after the animal self-bit. If this pattern of stress reduction occurred in the present study, the biting behavior could have caused a reduction in stress levels at 30 seconds, before the cortisol had a chance to rise, or before it could be detected in the saliva samples collected at 5 and 25 minutes.

Another possible reason for the difference in heart rate and cortisol results is a blunted HPA response with respect to self-biting. For example, human subjects with war-related PTSD showed an increase in heart rate when presented with combat sounds in comparison to control subjects. Their cortisol levels, however, did not change during this time, but their baseline levels were elevated in comparison to controls (Liberzon, Abelson, Flagel, Raz, and Young, 1999). Perhaps as in humans with PTSD, the sympathetic heart rate and the HPA systems may be dysregulated in self-biting monkeys. Therefore, what may precipitate an increase in heart rate in these animals, may not result in a parallel increase in cortisol.

However, even if the stress influenced the HPA axis, the cortisol measurements may be too variable to detect a significant change. Power analysis suggests that a sample size of 250 would be needed to obtain significant results in this study. Given the labor-intensive procedures as well as the fact that one of the largest populations of monkeys with SIB was already utilized here, the required sample size would not be possible.

Finally, the time course results suggest that the time interval based on the literature may have been inaccurate. Previous reports estimated a peak in salivary cortisol to be 20-30 minutes after a stressor (Kirschbaum and Hellhammer, 2000). The procedures for Study 3 were based on these times reported in the literature. However, the time course results later tested and reported in Study 3 suggest that the peak salivary cortisol levels post-stressor in rhesus macaques may be much sooner (5-15 minutes after a stressor). If the time course study is correct and a peak does occur at five minutes instead of 20-30 minutes, a difference at 5 minutes for the spontaneous biting study would still be expected. However, there was no difference between day 1 and day 2 at 5 minutes, suggesting once again that either the animal was not stressed, biting reduced the stress, or there was too much variability in the cortisol measures to detect a difference.

Given the problems with both timing and variability for utilizing salivary cortisol in spontaneous biting studies, a better alternative may be heart rate data. Both Freeman et al. (1999) and Marinus et al. (1999) demonstrated that changes in heart rate occur within 30 seconds of a biting episode. Because of the apparently transient effects biting has on an animal's physiology, waiting 25 minutes after a biting event may be too long. Although collecting heart rate data over long-term observations may not be practical, it may be a more precise method for measuring stress at the time of biting episodes during short-term stressful events.

The redirected aggression hypothesis takes a different approach with respect to self-injurious behavior. One prediction is that SIB is redirected social aggression in situations where physical contact with an opponent is prevented. Research in support of this prediction generally show a comparison between levels of self-injury and overall levels of aggression in an individual. (Cross and Harlow, 1965; Suomi et al., 1971; Simeon et al., 1992; Collacott et al., 1998). Similarly, chemically reducing levels of aggression by injecting male rhesus macaques with an antiandrogen also reduced SIB in the subjects (Eaton et al., 1999). Therefore, if self-injurious behavior and aggression are linked, further manipulating aggression should lead to parallel changes in SIB.

Both self-injurious behavior and aggression have been associated with stress. In human subjects, for example, cortisol significantly increased during experimentally-induced aggression (Gerra et al., 1997). Similarly, heart rate in a socially-housed pigtailed macaque increased significantly during agonistic behavior (Boccia, Reite, and Laudenslager, 1989). Stress has also been associated with self-injurious behavior. For example, rhesus macaques responded to stressful laboratory conditions (e.g., threatening observer or shock) with increased self-directed biting (Cross and Harlow, 1965; Pond and Rush, 1983; Gluck et al., 1985) and they also showed an increase in heart rate prior to a self-biting episode (Marinus et al., 1999). Therefore, because both SIB and aggression are associated with stress, levels of arousal need to be kept constant while comparing the two behaviors in contrasting situations.

The fifth objective of the present study, therefore, was to test the redirected aggression hypothesis of self-injurious behavior and to determine whether self-injurious behavior is directly associated with social aggression or whether the two behaviors are independent. Instead of comparing SIB with an animal's general levels of aggression, the subjects were placed specifically in socially aggressive situations where physical contact was prevented. This was accomplished in two ways. First, subjects were presented with videotapes containing either scenery or conspecifics exhibiting aggressive or neutral behavior (Study 4), and secondly, they were presented with live, unfamiliar conspecifics (Study 5). More importantly, these procedures placed the subjects in both social and nonsocial situations that were equally arousing as determined by salivary cortisol.

For the video study, subjects were presented with videotapes of conspecifics in aggressive and neutral contexts, scenery videos, and blank videos. Viewing time data showed that the subjects watched the videos significantly more than the blank screen, demonstrating that they do pay attention to what is on the television and not just the television itself. Behavioral data indicate that levels of aggression were significantly higher when a conspecific was in the video in comparison to scenery videos containing no human or nonhuman primate subjects. In addition, there was a trend towards increased aggression during the aggressive conspecific videotapes in comparison to the nonaggressive conspecifics. However, there was no effect of videotape on either self-biting, stereotypy, or any of the other recorded behaviors. In addition, there was no correlation between aggressive behavior and SIB or stereotypy.

Previous studies connecting self-biting with aggression did not separate out the effects of stress (Fittinghoff et al., 1974). In these examples, self-biting and aggression may have occurred together, because of the stress induced by the situation. In contrast, during the video study (Study 4), the levels of cortisol remained constant, suggesting that stress did not significantly increase during any of the four video conditions. However, levels of aggression increased during videos containing conspecifics while self-biting remained constant. These results suggest that self-biting and aggression are not associated and that self-biting is not a form of redirected social aggression. Instead, aggression appeared to be associated with the presence or absence of unfamiliar conspecifics, while self-biting continued at a steady rate and may instead be associated with situations that elicit comparable levels of arousal.

If the redirected aggression hypothesis is correct, perhaps the videotapes were not realistic or stressful enough to increase self-biting along with the aggressive behavior. One benefit of the videotapes is that each subject can be presented with identical stimuli. However, the lack of a cortisol rise during the videotapes may lead one to question the realism of the stimuli presented to the subjects. To increase realism, as well as relevance, for the subjects, Study 5 utilized live conspecifics, instead of videotapes, as stimulus animals. These animals were strangers to the subjects and such an encounter may have served as a more realistic and arousing stimulus to the subjects than videotapes.

For Study 5, the subjects were placed either in an empty room or in a room with an unfamiliar animal. Unlike the videotape study, both conditions (Stranger vs. Empty Room) resulted in a significant increase in cortisol. In addition, there was no difference in the cortisol rises between the two conditions, suggesting that they were equally stressful. In comparison, no cortisol rise was observed when samples were collected from the subjects in their home room (Study 3).

Behaviorally there were differences between the two test conditions (Stranger vs. Empty Room). Levels of aggression were significantly higher when a stranger was present than when the animal was alone in the room. However, both levels of stress (as measured by salivary cortisol) and levels of self-biting were consistent between the two test conditions. In other words, aggression rose in the presence of a conspecific, but levels of self-biting remained relatively constant. These results further contradict the hypothesis that SIB is associated with social aggression.

The home cage data in comparison with the test room conditions are not as clear-cut. Because saliva samples were collected in the home cage for Study 3, these procedures were not repeated in Study 5. Not surprisingly, cortisol levels did not significantly rise when samples were collected from subjects in their home cage. However, although levels of self-biting were lower in the home cage condition in comparison to the test conditions, they were not significantly lower. In addition, although levels of aggression in the home cage were similar to those in the Stranger condition, they were not statistically higher than those in the Empty Room condition.

Part of the problem with the present comparisons is variability. There were a number of subjects who did not self-bite and/or aggress, while other subjects repeatedly self-bit during the Stranger and Empty Room conditions. For example, during the two test room conditions (Stranger vs. Empty Room), only four subjects consistently self-bit. The remaining six subjects bit very infrequently or not at all. Repeating the data analyses on the four biting subjects alone, similar results were obtained. There was a trend towards higher levels of self-biting in the test room conditions in comparison to the home cage condition. However, there was also a trend towards higher levels of self-biting in the *Empty Room* condition in comparison to the Stranger condition. These results more strongly contradict the social aggression hypothesis, which would predict a trend in the opposite direction. In addition, due in part to the small sample size, there was no effect of condition on percent time in aggressive behavior. However, looking at frequency, instead of duration, of aggression, there was a trend towards higher levels of aggression in the Stranger condition in comparison to the Empty Room condition.

Self-biting was not significantly correlated with cortisol in any of the studies. Nevertheless, the results from Studies 4 and 5 suggest that there may still be a relationship between self-biting and stress. Levels of both cortisol and self-biting were relatively low while the subject was in its home room, either with or without the videos. However, both self-biting and stress, as measured by salivary cortisol, increased during the test room conditions (Stranger and Empty Room). Perhaps the variability in both the cortisol data and the biting rates interfered with a clear correlation. The simultaneous increase in both cortisol and self-biting during the two test room conditions suggest that there may be a relationship between self-biting and stress.

The findings of this dissertation are useful in three respects (for a summary of the conclusions, see Table 2). First, assessment data reiterate that self-biting and self-injury continue to be a problem in primate facilities. Previous research on SIB tended to utilize subjects that were reared in total (McKinney et al., 1973) or partial (Cross and Harlow, 1965) isolation. The present study demonstrated that self-injurious behavior can occur even in subjects that were socially-reared, but the age at which the animal was housed individually continues to be a risk factor in the development of SIB. Sex differences reported here were consistent with previous data on self-injurious behavior in that males are more likely than females to manifest SIB (Cross and Harlow, 1965; Gluck and Sackett, 1974). However, age differences contradict previous research. In the present study, older animals manifested SIB more than did younger. Earlier studies reported SIB in subjects from 3-7 years (Cross and Harlow, 1965; Suomi et al., 1971), but the age ranges tested were limited (up to 13 1/2 years). Given that the subjects in the present study included ages up to 21 years, the current findings allowed for a better picture of the association between age and SIB.

Secondly, salivary cortisol has been shown to be a viable method for measuring stress response in adult macaques. Previous studies have utilized plasma (Gunnar et al., 1980) or urinary (Crockett et al., 1993) cortisol for measuring stress. Although plasma cortisol is a good measure of an animal's immediate stress response, the process of collecting the blood sample itself may alter the response. Urinary cortisol can be collected in a way that is stress-free for an animal, but it is a long-term (e.g., 24 hour) stress measure. The new process of saliva collection described in Chapter 3 allows an investigator to obtain an immediate measure of an animal's stress without inducing additional stress. This process was utilized in Chapter 4 to measure an animal's stress levels during an episode of biting. For the first time, cortisol samples were collected before and after spontaneous instances of biting without inducing stress or additional biting.

Finally, Studies 4 and 5 have demonstrated that aggressive behavior does not appear to play a direct role in SIB. This result contradicts virtually all research that compares both self-injurious behavior and aggression in both humans (Jones, 1986; Collacott et al., 1998) and nonhuman primates (Fittinghoff et al., 1974; Eaton et al., 1999). Although the connection between SIB and aggression appears reasonable (for example, subjects with SIB are often more aggressive), none of the previous studies looked at the relationship while keeping arousal constant. The present study tested the effects of aggressive and nonaggressive situations on the subjects' behavior while keeping the situations equally stressful (or stress-free) as measured by cortisol levels. Because stress was kept constant, it was possible to determine that SIB was not associated with aggression, but may instead be associated with arousal, as levels of SIB were higher in the more stressful test conditions.

Self-injurious behavior is a complex phenomenon that cannot be understood in just a few studies on a single population of animals. The causes and effects of SIB vary greatly by species, environment, and physiology. However, it is important to make inroads and test hypotheses to start fitting pieces to the puzzle. The present research helped in this regard by suggesting that aggression is not the most salient avenue to pursue. Moreover, the association SIB seems to have with stress and arousal appears to be a more fruitful direction. Although Study 3 did not find an association between spontaneous episodes of self-biting and stress, the results were inconclusive. For example, in studies 4 and 5, levels of self-biting were higher in the more stressful situations, suggesting that stress may very well be associated with SIB. Because heart rate data are more immediate than even salivary cortisol, that may be the more decisive route to take in exploring the acute conditions surrounding episodes of self-biting. However, this will require electrode implants and telemetry. For charting a longer time course of action, however, salivary cortisol as advanced here will allow research without the contamination of uncontrolled stress that arises via other techniques employed (e.g. plasma cortisol samples).

Table 2

Summary of the Conclusions

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1. Risk factors for self-injurious behavior in rhesus macaques include:
    a. Sex
    b. Age
    c. Age when individually housed
    d. Number of blood draws experienced

2. Salivary cortisol can be safely collected and used as an indicator of stress in adult macaques.

3. Peak salivary cortisol levels after a brief stressor may occur closer to 5 minutes rather than 20-30.

4. Spontaneous episodes of self-biting may not be associated with stress.

5. Self-biting does not appear to be linked to aggression. Instead, it may occur in response to the arousal caused by the aggression.

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CURRICULUM VITAE

Corrine Kay Lutz

Education

PhD (Psychology)	University of Washington, Seattle, WA Major Area: Animal Behavior Minor Area: Zoology	2001
MS (Zoology)	University of Massachusetts, Amherst, MA Thesis title: The use of foraging racks as enrichment tools for social groups of rhesus monkeys (*Macaca mulatta)*	1991
BA (Biology)	Illinois Wesleyan University, Bloomington, IL Cum Laude Minor: German	1988

Selected Scholarships, Fellowships, and Awards

Dissertation Award, 2000
Department of Psychology, University of Washington, Seattle, WA

Travel Award, 1997
Department of Psychology, University of Washington, Seattle, WA
Funding for travel to the Animal Behavior Society Conference, College Park, MD

Travel Award, 1996
Department of Psychology, University of Washington, Seattle, WA
Funding for travel to the American Society of Primatologists Conference, Madison, WI

Research Fellowship, 1989
Willowbrook Wildlife Haven, Glen Ellyn, IL

Research Intern Stipend, 1988
Smithsonian Museum of Natural History, Washington, DC

Alumni Award Scholarship, 1984
Illinois Wesleyan University, Bloomington, IL

Memberships

American Society of Primatologists
Awards and Recognition Committee member

American Zoo and Aquarium Association

Animal Behavior Society

Tri-Beta, Biology Honor Society

Professional Experience

New England Regional Primate Research Center, Harvard Medical School, Southborough, MA
Dissertation research, 1998-2001
Conducted behavioral research on self-injurious behavior in nonhuman primates, developed new techniques for saliva collection, and conducted radioimmunoassays for salivary cortisol measurement

Behavioral Assessment and Intervention Program Coordinator, 1998-2001
Coordinated the Behavioral Assessment Program for individually-housed animals and the Intervention Program for animals with behavioral problems

Committee membership, 1998-2001
Environmental Enrichment Committee
Breeding Colony Management Committee

Ecotarium, Worcester, MA
Independent Research, 1999
Developed and implemented methods of saliva collection from awake, unrestrained polar bears and bobcats for cortisol assay.

University of Washington, Seattle, WA
Independent Research, 1996-1998
Utilized remote heart rate transmitter system for simultaneous heart rate and behavioral recordings of unrestrained infant pigtailed macaques.

Brookfield Zoo, Chicago, IL
Independent Research, 1995
Collected behavioral data for study on vigilance behavior in captive meerkat groups.

Woodland Park Zoo, Seattle, WA
Independent Research, 1994-1995
Developed ethogram and collected behavioral data for study on vigilance behavior in captive meerkat groups.

National Institutes of Health, Poolesville, MD
Biologist 1991-1993
Operantly conditioned rhesus monkeys to perform cognitive tasks, assisted in surgery, managed small primate colony and provided environmental enrichment.

National Zoo, Washington, DC
Volunteer Research Assistant, 1992-1993
Collected behavioral data on exhibit interaction by the public and on flamingo mating displays.

Willowbrook Wildlife Haven, Glen Ellyn, IL
Research Fellow, 1989
Analyzed and reformulated nutritional content of infant and permanent display animal diets. Recorded weights and developed infant animal growth curves.

Smithsonian Museum of Natural History, Washington, DC
Research Intern, 1988
Prepared, measured, and analyzed research specimens of spiny rats, *Proechimys semispinosus*. Curated the 1988 Panama mammal collection.

Teaching Experience

Instructor "Primate Behavior" Museum of Science, Boston, MA, 2000
Developed and taught a course on primate behavior and behavioral data collection.

Invited Talk "Behavioral Pathology in Monkeys" Brookfield Zoo, Chicago, IL, 1999

Teaching Assistant for "Animal Behavior," University of Washington, Seattle, WA
1993-1998 Taught discussion sections on current topics in animal behavior.

Guest Lecturer for "Introductory Psychology," University of Washington, Seattle, WA, 1998

Guest Lecturer for "Animal Behavior," University of Washington, Seattle, WA, 1995

Volunteer Public Educator, National Zoo, Washington, DC, 1992-1993
Gave talks and answered questions concerning the cheetah conservation program

Teaching Assistant for "Human Anatomy and Physiology," University of Massachusetts, Amherst, MA, 1990-1991
Instructed laboratory sections on human anatomy and physiology for pre-med and nursing students.

Teaching Assistant for "Research Methods in Psychology," University of Massachusetts, Amherst, MA, 1990
Instructed psychology majors on methods used in psychological research.

Teaching Assistant for "General Biology" and "General Zoology," University of Massachusetts, Amherst, MA, 1988-1989
Instructed laboratory sessions in introductory biology and zoology courses.

Publications

Lutz, C., Tiefenbacher, S., Jorgensen, M., Meyer, J., and Novak, M. 2000. Techniques for collecting saliva from awake, unrestrained, adult macaque monkeys for cortisol assay. American Journal of Primatology 52:93-99.

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Lutz, C. and Farrow, R. 1996. Foraging device for singly housed longtailed macaques does not reduce stereotypies. Contemporary Topics in Laboratory Animal Science 35:75-78.

Lutz, C. and Novak, M. 1995. Use of foraging racks and shavings as enrichment tools for groups of rhesus monkeys (*Macaca mulatta*). Zoo Biology 14:463-474.

Published Abstracts

Lutz, C., Marinus, L., Chase, W., Meyer, J., and Novak, M. 2001. Self-injurious behavior in male rhesus macaques: Association with aggression and stress. American Journal of Primatology Supplement 54:76.

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