

Project Number:	3R24RR011122-13S1	Contact Principal Investigator:	NOVAK, MELINDA ANN
Title:	SELF-INJURIOUS BEHAVIOR AND PRIMATE WELL-BEING	Awardee Organization:	HARVARD UNIVERSITY (MEDICAL SCHOOL)

Abstract Text:

Rhesus monkeys are a crucial research resource, and major scientific advances in medicine, biology, and neuroscience can be attributed to their use. Despite recent strides in controlling colony diseases and enhancing the environment of captively housed primates, some monkeys develop a syndrome of self- injurious behavior (SIB). The occurrence of SIB compromises the goal of promoting psychological well-being as mandated by the Animal Welfare Act (Revised, 1991) and threatens the quality of the monkey research resource. During the previous grant period, we made significant strides in determining the underlying causes of SIB, in identifying factors that trigger episodes of SIB, in explaining why SIB persists, and in evaluating possible treatments. As a result of this effort, we have formulated an integrated developmental- neurochemical hypothesis in which SIB arises from adverse life events, is maintained by dysregulations of several neurochemical and physiological systems (e.g., the stress response system and the opioid system), and serves to reduce anxiety. Our goals during this next grant period are to test the generality of this hypothesis, develop screening procedures for identifying precursors to SIB in young primates, explore the influence of various candidate genes in the expression of SIB, and test efficacy of various therapies based directly on our research findings. In our first aim, we will test the hypothesis that SIB is associated with increased behavioral and physiological indices of anxiety. Specific Aim 2 will investigate the relationship between SIB and the endogenous opioid system and determine whether monkeys with SIB exhibit opioid receptor supersensitivity. The third specific aim will focus on a longitudinal prospective study of large cohort of monkeys to identify genetic, behavioral, and physiological markers of SIB. In Specific Aim 4, we will establish effective pharmacological treatments for SIB in monkeys and evaluate individual differences in treatment efficacy.

3R24RR011122-13S1	SELF-INJURIOUS BEHAVIOR AND PRIMATE WELL-BEING	NOVAK, MELINDA ANN	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2010	NCRR	NCRR	\$192,784
5R24RR011122-13	SELF-INJURIOUS BEHAVIOR AND PRIMATE WELL-BEING	NOVAK, MELINDA ANN	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2009	NCRR	NCRR	\$371,437
5R24RR011122-12	SELF-INJURIOUS BEHAVIOR AND PRIMATE WELL-BEING	NOVAK, MELINDA ANN	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2008	NCRR	NCRR	\$371,437
5R24RR011122-11	SELF-INJURIOUS BEHAVIOR AND PRIMATE WELL-BEING	NOVAK, MELINDA ANN	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2007	NCRR	NCRR	\$379,018
5R24RR011122-10	SELF-INJURIOUS BEHAVIOR AND PRIMATE WELL-BEING	NOVAK, MELINDA ANN	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2006	NCRR	NCRR	\$390,338
2R24RR011122-09	SELF-INJURIOUS BEHAVIOR AND PRIMATE WELL-BEING	NOVAK, MELINDA ANN	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2005	NCRR	NCRR	\$416,980
5R24RR011122-08	SELF INJURIOUS BEHAVIOR AND PRIMATE WELL BEING	NOVAK, MELINDA ANN	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2004	NCRR	NCRR	\$365,010
5R24RR011122-07	SELF INJURIOUS BEHAVIOR AND PRIMATE WELL BEING	NOVAK, MELINDA A	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2003	NCRR	NCRR	\$365,010
5R24RR011122-06	SELF INJURIOUS	NOVAK, MELINDA	HARVARD UNIVERSITY	2002	NCRR	NCRR	\$365,010

	BEHAVIOR AND PRIMATE WELL BEING	A	(MEDICAL SCHOOL)				
5R24RR011122-05	SELF INJURIOUS BEHAVIOR AND PRIMATE WELL BEING	NOVAK, MELINDA A	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2001	NCRR	NCRR	\$365,010
2R24RR011122-04	SELF INJURIOUS BEHAVIOR AND PRIMATE WELL BEING	NOVAK, MELINDA A	HARVARD UNIVERSITY (MEDICAL SCHOOL)	2000	NCRR	NCRR	\$378,260
5R24RR011122-03	SELF INJURIOUS BEHAVIOR AND PRIMATE WELL BEING	NOVAK, MELINDA A	HARVARD UNIVERSITY (MEDICAL SCHOOL)	1999	NCRR		
5R24RR011122-02	SELF INJURIOUS BEHAVIOR AND PRIMATE WELL BEING	NOVAK, MELINDA A	HARVARD UNIVERSITY (MEDICAL SCHOOL)	1998	NCRR		
1R24RR011122-01	SELF INJURIOUS BEHAVIOR AND PRIMATE WELL BEING	NOVAK, MELINDA A	HARVARD UNIVERSITY (MEDICAL SCHOOL)	1996	NCRR		

A rhesus monkey model of self-injury: effects of relocation stress on behavior and neuroendocrine function.

[Davenport MD](#), [Lutz CK](#), [Tiefenbacher S](#), [Novak MA](#), [Meyer JS](#).

[Biol Psychiatry](#). 2008 May 15;63(10):990-6. Epub 2008 Feb 27.

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Abstract

BACKGROUND: Self-injurious behavior (SIB), a disorder that afflicts many individuals within both clinical and nonclinical populations, has been linked to states of heightened stress and arousal. However, there are no published longitudinal data on the relationship between increases in stress and changes in the incidence of SIB. This study investigated the short- and long-term behavioral and neuroendocrine responses of SIB and control monkeys to the stress of relocation.

METHODS: Twenty adult male rhesus macaques were exposed to the stress of relocation to a new housing arrangement in a newly constructed facility. Daytime behavior, sleep, and multiple measures of hypothalamic-pituitary-adrenocortical (HPA) axis function were investigated before and after the move.

RESULTS: Relocation induced a complex pattern of short- and long-term effects in the animals. The SIB animals showed a long-lasting increase in self-biting behavior, as well as evidence of sleep disturbance. Both groups exhibited elevated cortisol levels in saliva, serum, and hair, and also an unexpected delayed increase in circulating concentrations of corticosteroid binding globulin (CBG).

CONCLUSIONS: Our results indicate that relocation is a significant stressor for rhesus macaques and that this stressor triggers an increase in self-biting behavior as well as sleep disturbance in monkeys previously identified as suffering from SIB. These findings suggest that life stresses may similarly exacerbate SIB in humans with this disorder. The HPA axis results underscore the potential role of CBG in regulating long-term neuroendocrine responses to major stressors.