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# Altered hypothalamic–pituitary–adrenocortical function in rhesus monkeys (*Macaca mulatta*) with self-injurious behavior

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## Abstract

Individually housed rhesus monkeys sometimes spontaneously develop self-injurious behavior (SIB) in the form of self-directed biting that, on occasion, results in severe tissue damage and mutilation. We previously demonstrated lower levels of plasma cortisol in rhesus monkeys with a history of self-wounding (SW) when compared to non-wounders (NW). Furthermore, cortisol levels were negatively correlated with rates of self-directed biting. The present study was designed to further characterize the relationships between hypothalamic–pituitary–adrenocortical (HPA) activity, self-wounding, and self-directed biting. Basal 24-h urinary free cortisol excretion, the urinary free cortisol response to a low dose of dexamethasone, and the plasma cortisol response to ACTH were examined in 24 individually housed rhesus monkeys, based on wounding history, i.e. the presence/absence of a veterinary record of self-wounding, and current rates of self-directed biting, i.e. the median split of self-directed biting frequency (independent of wounding status). There were no reliable group differences on any of the physiological measures when analyzed by wounding history. However, the plasma cortisol response 30 min post-ACTH stimulation was significantly correlated with wounding recency, such that lower responsiveness was associated with more recent wounding episodes. When the results were analyzed on the basis of biting frequency, high frequency biters (HFB) compared to low frequency biters (LFB) showed decreased HPA negative feed-

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back sensitivity to dexamethasone and a trend towards an attenuated plasma cortisol response to ACTH stimulation. These findings suggest that SIB in socially reared monkeys is associated with complex changes in HPA axis function that are related to the expression of the pathology, i.e. self-directed biting, and to the recency of a wounding episode. It remains to be determined whether humans who exhibit SIB show similar alterations in HPA function.

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*Keywords:* Self-injurious behavior; Self-bite; Cortisol; Dexamethasone challenge; ACTH challenge; Rhesus macaque

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## 1. Introduction

Self-injurious behavior (SIB) is a devastating phenomenon that affects a diverse group of clinical and nonclinical populations (Johnson and Day, 1992; Favazza, 1998). The etiology and physiology of this disturbing pathology in humans is not well understood, and despite great efforts, successful interventions for SIB remain elusive (Luiselli et al., 1992). Most studies concerning the pathophysiology of SIB have focused on various neurotransmitter or neuropeptide systems (Herman, 1990; Sivam, 1996; Oquendo and Mann, 2000). However, endocrine dysfunction might also be present in individuals with SIB, with recent findings suggesting altered hypothalamic–pituitary–adrenocortical (HPA) activity in both developmentally disabled patients and psychiatric patients who show self-injury (Verhoeven et al., 1999; Sachsse et al., 2002).

Animal models may be useful in elucidating the physiological correlates of SIB. One such model involves the spontaneous development of SIB that occurs in approximately 5–13% of captive, individually housed macaques (Bayne et al., 1995; Bayne and Novak, 1998). In socially reared rhesus monkeys, this pathology usually takes the form of repetitive self-directed biting that on occasion can result in severe tissue damage and mutilation (Bayne et al., 1995; Bayne and Novak, 1998). Presently, however, the relationship between an animal's history of self-injury and the expression of the pathology (i.e. current rates of self-directed biting) are not well understood. Data derived from colony records at the New England Regional Primate Research Center (NERPRC) suggest that males are more likely to develop the syndrome than females (Jorgensen et al., 1998; Lutz et al., 2000; Novak et al., 2002). Furthermore, age at which animals were individually housed and duration of individual cage housing appear to be significant risk factors for the development of SIB in monkeys (Jorgensen et al., 1998; Lutz et al., 2000; Novak et al., 2002). Despite a few reports of differences between socially reared monkeys with SIB and controls (Faucheux et al., 1976; Weld et al., 1998; Eaton et al., 1999), the physiological correlates of this syndrome remain poorly characterized. Increasing our understanding of the underlying pathophysiology of SIB in monkeys will not only help us to identify possible etiologies, but more importantly it may allow us to develop more effective pharmacological interventions for the syndrome in humans.

Previous studies in our laboratory identified a persistent HPA dysregulation in

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