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Population density-dependent hair cortisol concentrations in rhesus monkeys (*Macaca mulatta*)

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Summary Population density is known to influence acute measures of hypothalamic-pituitary-adrenal (HPA) axis activity in a variety of species, including fish, deer, birds, and humans. However, the effects of population density on levels of chronic stress are unknown. Given the fact that exposure to chronically elevated levels of circulating glucocorticoids results in a host of health disparities in animals and humans alike, it is important to understand how population density may impact chronic stress. We assessed hair cortisol concentrations (HCCs), which are reliable indicators of chronic HPA axis activity, in rhesus monkeys (*Macaca mulatta*) to determine the influence of population density on these values. In Experiment 1, we compared HCCs of monkeys living in high-density (HD; 1 monkey/0.87 m^2) and low-density (LD; 1 monkey/63.37 m^2) environments ($N = 236$ hair samples) and found that HD monkeys exhibited higher hair cortisol across all age categories (infant, juvenile, young adult, adult, and aged) except infancy and aged ($F_{(5)} = 4.240$, $p = 0.001$), for which differences were nearly significant. HD monkeys also received more severe fight wounds than LD monkeys ($\chi^2 = 26.053$, $p < 0.001$), though no effects of dominance status emerged. In Experiment 2, we examined how HCCs change with fluctuating population levels across 5 years in the adult LD monkeys ($N = 155$ hair samples) and found that increased population density was significantly positively correlated with HCCs in this semi-naturalistic population ($r_{(s)} = 0.975$, $p = 0.005$). These are the first findings to demonstrate that increased population density is associated with increased chronic, endogenous glucocorticoid exposure in a nonhuman primate species. We discuss the implications of these findings with respect to laboratory research, population ecology, and human epidemiology.
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1. Introduction

Population density is known to affect various indices of a population's health. Animal studies have demonstrated that increased population density results in reduced viability in fruit flies (Lewontin, 1955); in reduced growth rates in land snails (Cameron and Carter, 1979), trout (Jenkins et al., 1999), and deer (Pettorelli et al., 2002); and in reduced reproductive success in numerous species including song sparrows (Arcese and Smith, 1988), guppies (Dahlgren, 1979), and red deer (Bonenfant et al., 2002). In humans, increased population density predicts emerging infectious disease events (Jones et al., 2008).

One potential underlying mechanism for these deleterious effects of population density may be exposure to chronically elevated circulating glucocorticoids. Increased population density may act as a stressor due to increased competition for resources including food, mates, and shelter, among others. Evidence for this notion comes from a vast body of literature describing the detrimental effects of long-term exposure to elevated glucocorticoids (i.e., corticosterone and cortisol). Chronic exposure to elevated glucocorticoid levels, whether via persistent environmental stress or repeated administration of glucocorticoids, results in reduced fetal growth (Jobe et al., 1998), growth suppression (Allen, 1996; Emack et al., 2008), suppressed immune function (Dhabhar, 2009), reduced reproductive function (Carragher et al., 1989; Chrousos et al., 1998; Pervanidou and Chrousos, 2012), and is also neurotoxic, particularly to the hippocampus (Bodnoff et al., 1995; Conrad, 2008; Sapolsky et al., 1990). Several animals have demonstrated increased glucocorticoid levels in response to increased population density, including fish (Li et al., 2012; Vijayan and Leatherlan, 1990), voles (Novikov and Moshkin, 1998), chipmunks (Clulow et al., 1969), deer (Li et al., 2007), and primates (Pearson et al., 2007), including humans (Evans and Wener, 2007). One limitation of these studies, however, is that they have relied either on "point" measures of cortisol (i.e., serum/plasma/salivary cortisol) or on indices that reflect less than 1 day of adrenocortical activity (i.e., urinary and fecal cortisol). Thus, while it is likely that population density influences chronic HPA axis activity, this prediction has not been examined outright.

In 2006, our laboratory developed and validated an assay for quantifying cortisol concentrations in the hair of rhesus monkeys (Davenport et al., 2006). This technique has since been applied in studies of chronic HPA axis activity (i.e., accumulation of cortisol into the hair shaft over the past several months, as opposed to minutes or hours as in the point samples mentioned above) in both animals (Bechshøft et al., 2012; Davenport et al., 2008; Malcolm et al., 2012; Meyer and Novak, 2012; Novak et al., 2013) and humans (O'Brien et al., 2012; Vanaelst et al., 2013). Studies utilizing hair cortisol have shown that HCCs decline during the first several years of life in several nonhuman primate species including rhesus monkeys (Dettmer et al., 2012; Feng et al., 2011), vervets (Laudenslager et al., 2012), and baboons (Fourie and Bernstein, 2011), and one study also demonstrated sex differences in HCCs in nonhuman primates during puberty and adulthood (Laudenslager et al., 2012). Moreover, several studies in both human and nonhuman primates have demonstrated increases in HCCs in response to stressful events including relocation (in monkeys; Davenport et al., 2008; Dettmer et al., 2012; Fairbanks et al., 2011), unemployment (in humans; Dettenborn et al., 2010), and chronic health conditions (in humans; Thomson et al., 2010; Van Uum et al., 2008). Thus, we sought to utilize the hair cortisol assay to test the hypothesis that population density affects chronic physiological stress in nonhuman primates. Specifically, we predicted that rhesus monkeys (*Macaca mulatta*) exposed to high-density (HD) housing arrangements would exhibit higher hair cortisol concentrations (HCCs) than those living in low-density (LD) conditions (Experiment 1), and that for monkeys living in the LD (i.e., more naturalistic) environment, changes in population density would predict HCCs (Experiment 2). We further sought to determine whether behavioral indices of stress resulted from increased population density by examining the proportion of individuals in each housing condition that received severe fight wounds, as we predicted that increased population density would result in increased rates of aggression and thus increased fight wounds.

2. Materials and methods

2.1. Experiment 1

Hair samples ($N = 236$) were assayed from 152 rhesus macaques (*M. mulatta*; 30.5% male) born and reared at the Laboratory of Comparative Ethology in Poolesville, MD. Monkeys ranged in age from 0.5 to 18 years (mean $\pm$ SEM = 3.39 ± 0.27 years) during hair sampling, which occurred between 2007 and 2013. Monkeys were housed in one of the two conditions, described in detail below. Table 1 depicts subject characteristics for this experiment.

2.2. High-density (HD) environment

Monkeys ($n = 58$) were housed in one of the two HD enclosures depending on their age. The first type of enclosure, which housed infants (<1 yr) and adults (5+ yrs) used for this study, was an indoor-outdoor enclosure constructed of galvanized steel mesh connected by guillotine doors and wood chips covering the floors. Eight to 10 adult females and one adult male, along with 5–6 infants up to 8 months of age, were housed together in this type of enclosure. Multiple perches, swings, and enrichment devices were provided. The indoor pen measured 2.44 m $\times$ 3.05 m $\times$ 2.21 m, and the outdoor pen measured 2.44 m $\times$ 3.0 m $\times$ 2.44 m. Animals were given free access between indoor and outdoor pens except when

Table 1 Subject characteristics for Experiment 1.

Age category	HD	LD	Total
Infant (<1 yr)	20	17	37
1 yr	19	60	80
2 yr	13	46	61
Young adult (5–9 yr)	19	11	30
Adult (10–14 yr)	14	10	24
Aged (15+ yr)	3	4	6
Total	88	148	236

HD = high density; LD = low density.