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Associations between early life experience, chronic HPA axis activity, and adult social rank in rhesus monkeys

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Abstract

Early life experience and socioeconomic status (SES) are well-established predictors of health outcomes in people. Both factors likely influence health outcomes via hypothalamic-pituitary-adrenal (HPA) axis regulation. However, it is unclear how early experience and HPA axis activity influence adult social status. We studied differentially reared female rhesus monkeys (Macaca mulatta, N = 90) as models to test the hypothesis that chronic HPA axis activity assessed via hair cortisol concentrations (HCCs) mediated the relationship between early life experience and adult social rank. We found that mother-peer-reared (MPR) monkeys acquired higher social ranks than either of the two nursery-reared (NR) groups (peer-reared, PR, or surrogate-peer-reared, SPR monkeys) ($\beta = -0.07$, $t_{(89)} = -2.16$, $p = 0.034$). We also found that MPR HCCs were lower during the juvenile period at 18 months ($F(2,25) = 3.49$, $p = 0.047$). Furthermore, for MPR but not NR monkeys, changes in HCCs from 18 to 24 months ($r_{(s)} = -0.627$, $p = 0.039$) and adult HCCs ($r_{(s)} = -0.321$, $p = 0.03$) were negatively correlated with adult social rank. These findings suggest that chronic HPA axis regulation in juvenility, and perhaps in adulthood, may influence adult social status for primates that experience typical early rearing. However, early life adversity may result in dissociation between neuroendocrine stress regulation and adult social competence, which may be risk factors for adverse health outcomes.

Keywords

Early experience; social rank; cortisol; HPA axis; Macaca mulatta

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Introduction

It is well established that early life adversity negatively impacts health outcomes across the lifespan. Major childhood stressors, such as parental divorce, family dissolution, institutionalized care, child abuse and/or neglect, and natural disasters predict morbidity and mortality in adulthood (Miller, Chen, & Parker, 2011; Montez & Hayward, 2014; Power & Hertzman, 1997; Schwartz et al., 1995; Smith, Hart, Blane, Gillis, & Hawthorne, 1997). Another major predictor of adult health disparities is socioeconomic status (SES), which is consistently linked to disability and disease across the lifespan and worldwide (see Bahadori et al., 2015; Hackman, Farah, & Meaney, 2010; Marshall et al., 2015; Miller et al., 2011; National Center for Health Statistics, 2012; Langlois et al., 2015; Smith, 1996; for reviews).

One proposed mechanism for the relations between early life adversity, socioeconomic status (SES), and adult health is the neuroendocrine stress response system. It is known that chronic exposure to circulating glucocorticoids predisposes individuals at risk for developing health problems (McEwen, 2008), and many studies have shown that low SES individuals and those experiencing early life adversity are more prone to heightened and sometimes chronic hypothalamic-pituitary-adrenal (HPA) axis activity (Chen, Cohen, & Miller, 2010; Cohen, Doyle, & Baum, 2006; Gunnar, 2000; Hunter, Minnis, & Wilson, 2011; Li, Power, Kelly, Kirschbaum, & Hertzman, 2007; Luecken & Appelhans, 2006; Lupien, King, Meaney, & McEwen, 2001). In general, individuals exposed to more adversity early in childhood and/or living in low SES families exhibit greater physical and mental health disparities as well as dysregulated HPA axis activity across the lifespan (Browne & Jenkins, 2012; Bush, Obradović, Adler, & Boyce, 2011; Hackman, Betancourt, Brodsky, Hurt, & Farah, 2012; Lovallo, 2013; McLaughlin et al., 2011; Palmer et al., 2013). Importantly, some studies have indicated that, for those exposed to early life adversity, intervention programs can result in normalized cortisol reactivity (Brotman et al., 2007; Dozier, Peloso, Lewis, Laurenceau, & Levine, 2008; Fernald & Gunnar, 2009), and lower cortisol reactivity is associated with an improvement in health problems (Daubenmier et al., 2011; Ebrecht et al., 2004; McKinney, Antoni, Kumar, Tims, & McCabe, 1997).

Studies in animal models produce similar findings to those reported in the human literature. Rodents, non-human primates, and other mammals show similar risks of developing dysregulated HPA axis activity and suboptimal health when exposed to early life adversity (typically in the form of maternal separation; see Conti et al., 2012; Dettmer & Suomi, 2014; Hennessy, Kaiser & Sachser, 2009; McEwen, 2003). A rich body of literature has established the social buffering role that mothers play for their infants (see Hennessy et al., 2009 for a review): mothers mitigate their infants' behavioral and HPA axis responses to disturbances such as temporary separation, novelty, and other threats (Hennessy et al., 2009; Smotherman, Hunt, McGinnis, & Levine, 1979; Wiener, Johnson, & Levine, 1987). Moreover, early life adversity in the form of nursery rearing (NR) reduces monkeys' ability to regulate cortisol and behavioral responses to novelty in adolescence (Winslow, Noble, Lyons, Sterk, & Insel, 2003). Thus, the buffering effect of the mother lasts into adolescence, but it is unclear whether the effects of the lack of a maternal buffer against social stress in infancy continues to exert effects on stress regulation in the adult animal.

Animal models also exhibit dysregulated HPA axis activity and poorer health outcomes when occupying lower social ranks (DeVries, Glasper, & Detillion, 2003; Sapolsky, 2004, 2005; Sapolsky, Alberts, & Altmann, 1997). Social rank in animal models, particularly in non-human primates, is arguably a good proxy for SES in humans because in both cases, higher status is related to lower stress hormone expression, greater access to resources, and better health outcomes (see Cummins, 2005, for a review, as well as Kaplan, Manuck, Clarkson, Lusso, & Taub, 1982; Sapolsky, 2004; 2005; Shively, Laber-Laird, & Anton, 1997). An additional benefit to the use of animal models is their faster developmental time course and the ability to collect repeated biological and behavioral samples across the lifespan.

Rhesus macaques (Macaca mulatta) are good models for studying the influences of early life adversity on later social status and HPA axis regulation. In addition to their genetic, physiological, and neuroanatomical similarity to humans (Suomi, 1997), rhesus macaques 1) exhibit clear linear hierarchies (Balasubramaniam et al., 2012); 2) develop strong maternal-infant bonds, the disruption of which leads to behavioral and physiological irregularities across development (Dettmer & Suomi, 2014); and 3) demonstrate variations in maternal investment and care of offspring, ranging from very protective to downright abusive (McCormack, Sanchez, Bardi, & Maestripieri, 2006). These traits make macaques ideal for studying the long-term effects of early social buffering. To date, few macaque studies have examined the link between early life adversity and social rank, but the few that exist indicate that individuals exposed to early adversity occupy lower social ranks as juveniles and young adults (Bastian, Sponberg, Suomi, & Higley, 2003; Stevens, Leckman, Coplan, & Suomi, 2009), presumably because they also exhibit impaired social interactions (Andrews & Rosenblum, 1994; Hol, Van den Berg, Stevens et al., 2009; Van Ree, & Spruijt, 1999). What remains unclear is (1) how long the association between early experience and adult social rank persists, and (2) whether the HPA axis plays a role in this relationship. Elucidating such information may reveal an important relationship between early life adversity and later social status in humans and might also identify a mechanism by which these variables interact. Ultimately, studies answering these questions would add to the body of literature showing the downstream consequences of early social buffering by a competent caregiver.

To begin addressing these questions, we studied differentially reared rhesus monkeys in a cross-sectional study from adolescence through middle age. We tested the hypothesis that early life adversity (in the form of nursery rearing) influences later social rank, and that HPA axis activity relates to social rank differently for mother-peer-reared and nursery-reared monkeys. We also tested the hypothesis that HPA axis regulation in adolescence relates to adult social rank. We relied on hair cortisol concentration (HCCs) to assess HPA axis activity, as they reflect accumulated cortisol concentrations over several months (Meyer & Novak, 2012) and have shown to be a reliable biomarker of chronic stress in human and nonhuman primates (Novak, Hamel, Kelly, Dettmer, & Meyer, 2013; Russell, Koren, Rieder, & Van Uum, 2012). We predicted that mother-peer-reared (MPR) monkeys would occupy higher ranks as adults than nursery-reared monkeys. However, since to our knowledge the relation between early experience, HPA axis activity, and adult social rank has not been explored in nonhuman primates, we did not make specific predictions about the direction of this relationship.

Methods

Subjects, early life history, and housing

Subjects were 90 female rhesus macaques (Macaca mulatta) born and reared at the Laboratory of Comparative Ethology facilities at the NIH Animal Center in Poolesville, MD. Monkeys ranged in age from 3 to 11 years (mean ± SEM: 6.0 ± 0.2). All animals were randomly assigned to one of three rearing conditions according to established, published procedures for our laboratory (Dettmer, Novak, Meyer, & Suomi, 2014; Dettmer, Novak, Suomi, & Meyer, 2012; Shannon, Champoux, & Suomi, 1998): mother-peer-reared (MPR, n = 48), peer-reared (PR, n = 15), or surrogate-peer-reared (SPR, n = 27). Briefly, each birth season (spring), MPR monkeys were reared in social groups containing 1–2 adult males, 8–10 adult females, and 3–5 peers born in the same year. Each year, MPR infants were spread approximately evenly across five different social groups. PR and SPR monkeys were relocated to the nursery on the day of birth and reared by human caregivers for the first 37 days, then assigned to social groups with peers. PR monkeys were placed in a large cage with three other agemates while SPR monkeys lived in single cages with mobile, cloth-covered surrogates (Dettmer, Ruggiero, Novak, Meyer, & Suomi, 2008) and were given daily 2-h play session with three other peers. PR and SPR groups were sex-balanced. Monkeys remained in their rearing conditions until approximately 8 months of age, at which time they were relocated into a single social group comprised of all infants born in the same year (for details on housing specifications, see Dettmer et al., 2012). From 8 months onward, monkeys from each cohort lived together continuously and received identical treatment. At 3 years of age, males and females were separated to avoid unplanned pregnancies. Thus, the female monkeys in this study had all lived together from 8 months onward. Water was provided ad libitum and monkeys were fed Purina Monkey Chow (#5038, St. Louis, MO) and foraging enrichment twice daily.

Seven cohorts were studied, ranging in age from 3 to 9 years (although the 9-year-old cohort also had two 11-year-old females who had been part of the stable social group for many years). Because 3 years represents the transition to sexual maturity in female rhesus monkeys (Rawlins & Kessler, 1986), and because many females give birth to their first infant at 3 years (Blomquist, 2009; Dettmer, 2015), in this study we describe all cohorts as adults (3–9+ years). Table 1 gives a breakdown of each cohort by rearing condition.

Four monkeys from a later cohort (born in 2012) were born to mothers from an earlier cohort (born in 2006). The rearing condition of the mother-infant dyads (mother → infant) was as follows: two MPR → MPR, one MPR → SPR, and one PR → MPR.

Adult social rank

Dominance interactions—Researchers observed each cohort in bi-weekly, 30 min sessions for approximately 2 months. In these sessions, all instances of dominance interactions (i.e., displace, threat, chase, attack, and submissive) were coded ad libitum (Altmann, 1974), along with the individuals involved in the interactions. Each interaction was then entered into a spreadsheet and coded as a win (individual initiated a displacement, threat, chase, or attack, or received submissive behavior) or a loss (individual received a displacement, threat, chase, or attack, or initiated a submissive behavior such as a fear grimace). Inter-rater reliability for this coding was established at ≥85% agreement.

Dominance hierarchies—Dominance hierarchies were constructed from the dominance interactions via Elo-rating, a numerical system that tracks individual rank changes over time by regularly updating values based on wins and losses (Dettmer, Kaburu, et al., 2015; Elo, 1978; Neumann et al., 2011; Wooddell, Kaburu, Dettmer, & Suomi, 2015). Two major advantages of Elo-rating include the ability to track rank changes over time, and accommodating variations in social dynamics. Using the elo. sequence function in R software (v 3.1.2) provided by Neumann et al. (2011), Elo-ratings were generated by setting each animal's initial rating at 1000, and the k factor (a constant weighted based on the probability of winning) at 200. An average Elo-rating was calculated for each individual after approximately 2 months of data collection. For monkeys aged 3–6 years old, Elo-ratings were calculated in April 2015; for all other monkeys Elo-ratings were calculated in September 2014. These times were chosen because all individuals were present in the social groups; after these dates some individuals were permanently removed for colony management reasons. The following interactions were analyzed for Elo-ratings: displace, threat, chase, attack, and fear grimace.

Elo-rating values fluctuate proportionally in relation to the frequency of aggression, which, in turn, can vary between groups (i.e., cohorts), making Elo-rating of monkeys from different cohorts not directly comparable. Therefore, because we aimed to examine predictors of adult rank within the social group, Elo-ratings were then used to calculate a relative rank for each individual within the social group. Within the group, monkeys were assigned ordinal ranks in reverse order from highest to lowest Elo-rating; then, that rank was divided by the total number of animals in the social group at the time of Elo-rating to calculate a relative rank (group size ranged from 12 to 14 individuals). Thus, relative rank within each group ranged from 0.07 (lowest ranking individual) to 1.0 (highest ranking individual). In this way, we could determine predictors of an individual's relative rank within its group.

Hair cortisol collection and assay

Adult hair cortisol—Hair samples were collected in October 2014 and January 2015 according to established protocols (Dettmer et al., 2014; Dettmer, Rosenberg, et al., 2015) during routine health exams by shaving the back of each animal's neck with commercial grooming clippers. These time points were selected as they represented the period of sample collection closest to the assessment of dominance ranks (April 2015 for 3–6 year old monkeys, September 2014 for older monkeys). These samples reflected long-term cortisol accumulation over the previous 3 months, as samples are routinely collected in our colony every 3 months during health exams. Samples were placed into a foil pouch and frozen at −80°C until shipment to the Hormone Assay Core Laboratory at the University of Massachusetts Amherst. Following Dettmer et al. (2014), Dettmer, Rosenberg, et al., (2015), samples were weighed and washed twice with isopropanol and dried for 5–7 days under a fume hood. Samples were then ground to a fine powder with a ball mill grinder (MM200; Retsch, Newtown, PA) and incubated in methanol for 24 h to extract cortisol from the samples. Aliquots of the methanol extract were dried down and reconstituted with assay buffer, then analyzed via enzyme immunoassay (EIA) using a salivary cortisol kit (#1–3002; Salimetrics, State College, PA). Resulting values (μg/dL) were converted to pg/mg for analysis. Inter- and intra-assay coefficients of variation were ≤5% based on aliquots of the same extracted pooled hair sample analyzed repeatedly across assays. Four subjects did not have hair samples; thus the sample size for this data set was n = 86 (out of 90 subjects). Three subjects missing hair samples were MPR and one was PR.

Juvenile hair cortisol—Some of these subjects (n = 26) were part of a larger study examining the influences of early life experience on chronic HPA axis activity across development. As such, hair samples were taken following procedures described above at months 6, 12, 18, and 24, representing HPA axis activity from infancy through the juvenile period. We previously found that early rearing experience results in differential HCCs at months 12 and 18 (Dettmer et al., 2012), the period during which the young monkeys are adapting to the mixed-group formation that occurred at 8 months, and that by 24 months of age HCCs were the same across rearing groups. For this study, we examined HCCs taken at 12 (n = 25; MPR/PR/SPR samples = 11/5/9, respectively), 18 (n = 26; MPR/PR/SPR samples = 11/6/9, respectively), and 24 (n = 26; MPR/PR/SPR samples = 11/6/9, respectively) months. Thirteen of these 26 subjects were part of the Dettmer et al. (2012) study.

Hair samples were analyzed for cortisol content according to the methods described above. Inter- and intra-assay coefficients of variation were <10%.

Data analysis

Regression analysis was used to examine whether early rearing experience (MPR, PR, or SPR) predicted adult rank, with relative rank as the dependent variable and cohort as a control variable. ANOVA was used to test for rearing effects on adult HCCs. To assess HPA axis regulation across the juvenile period, independent samples t-tests were used to test for rearing effects on HCCs at 12, 18, and 24 months, and for changes in HCCs from months 12 to 18 and 18 to 24 (calculated as percentage differences). This analysis was conducted for MPR vs. PR/SPR together (i.e., MPR vs. nursery-reared, or NR) owing to small samples sizes in the two NR groups.

To examine the extent to which individual HPA axis activity and/or regulation influences adult rank, owing to small samples sizes Spearman correlations were run for each rearing group separately to determine whether individuals with higher HCC values in adulthood or juvenility (to assess HPA axis activity), or with higher increases in HCCs across juvenility (to assess HPA axis reactivity), were associated with relative rank. A Bonferroni correction for multiple comparisons was made, resulting in an adjusted $p \leq 0.01$.

IBM SPSS v.22 was used for all analyses, and an $\alpha < 0.05$ was considered statistically significant.

Results

Early life history and adult social rank

Regression analysis revealed that early rearing experience predicted adult social rank, such that MPR monkeys outranked PR and SPR monkeys, and PR monkeys outranked SPR monkeys ($\beta = -0.067$, $t_{(89)} = -2.03$, $p = 0.046$; Figure 1). Early rearing also explained a significant proportion of variance in adult social rank ($R^2 = 0.05$, F(1,85) = 4.11, $p = 0.046$).

Early life history and hair cortisol concentrations

Results from the t-tests revealed that the rearing groups (MPR and NR) differed in HCCs taken at 18 months ($t_{(24)} = -2.99$, $p = 0.008$). No rearing group differences were revealed at any other time point in juvenility or adulthood. The t-tests did not reveal any rearing group differences (MPR vs. NR) for changes in HCCs across the juvenile period.

Adult hair cortisol and adult social rank

Spearman correlations revealed that, for MPR monkeys only, adult HCCs were negatively correlated with adult social rank ($r_{(s)} = -0.327$, $p = 0.03$, $n = 43$; Figure 2). No such relation was evident for PR ($r_{(s)} = 0.288$, $p = 0.30$, $n = 15$) or SPR monkeys ($r_{(s)} = -0.156$, $p = 0.45$, $n = 26$).

Juvenile hair cortisol and adult social rank

For MPR monkeys only, the change in HCCs from 18 to 24 months was significantly negatively correlated with adult social rank ($r_{(s)} = -0.627$, $p = 0.039$, $n = 11$; Figure 3; Table 2). However, when Bonferroni corrections for multiple comparisons were made, these results did not reach significance with the adjusted $p \le 0.01$. No other significant correlations were found with any other changes in HCCs, or with any HCCs taken at specific time points (i.e., 12, 18, and 24 months).

No significant correlations were evident between HCCs, or changes in HCCs, at any time in the juvenile period and adult social rank for NR monkeys (all $r_{(s)}$ values ranged between −0.34 and 0.20; all p-values ranged between 0.23 and 0.98; NR n = 15). The same was true when PR/SPR were examined separately (PR $n = 6$, SPR $n = 9$; Figure 3).

Discussion

To our knowledge, this is the first study in any primate linking early life adversity, chronic HPA axis activity, and adult social rank. Relying on nonhuman primate models of development, we studied female rhesus monkeys in a cross-sectional design across the lifespan and found that exposure to early life adversity in the form of nursery-rearing resulted in lower social status well into adulthood. Importantly, this is also the first study to show that early rearing predicts adult social rank from sexual maturity (3 years) through middle age (9–11 years), extending previous findings linking early rearing with juvenile and young adult social rank (Bastian et al., 2003). These findings indicate that early life experiences exert lifelong impacts on one’s social standing, which may have important implications for social status-related health outcomes.

We also identified a first link between chronic HPA axis activity, measured via HCCs, and adult social rank, but this relationship differed for MPR and PR/SPR monkeys. Only MPR monkeys showed a negative correlation between adult HCCs and contemporaneous social rank. They also tended to show negative correlations between changes in HCCs in the juvenile period (18–24 months) and adult social rank. However, these results should be interpreted with caution given the small sample size in these analyses, and future studies should aim to replicate these findings with larger cohorts. These results suggest that HPA axis activity/regulation beginning in adolescence, and possibly persisting into adulthood, may influence social rank later in life. As a consequence of their normative early experience, MPR monkeys likely experienced social buffering during a critical window of development that established HPA axis set points for this group that differ for those of NR monkeys (Gunnar, 2003). It is also possible that stress sensitivity conferred by nursery-rearing results in both hyperactivity of the HPA axis and behavioral responsivity to novelty or stress during adolescence that later influence adult rank. This notion is supported by the literature in numerous mammals (see Hennessy et al., 2009 for a review), and is especially supported by findings from Winslow et al. (2003) demonstrating that MPR monkeys exhibit more appropriate behavioral and neuroendocrine responses to novelty than NR monkeys. Future studies examining HPA axis reactivity, social behavior, and rank changes in the same individuals continually from infancy to adulthood are warranted to test this hypothesis directly.

Why might HPA axis regulation during the juvenile period in particular play such an important role in later social competence? It is possible that since the period of 18–24 months is a time of increasing agonistic behavior, particularly amongst juvenile females (Bernstein & Ehardt, 1985, 1986), NR monkeys—who have not witnessed typical adult social interactions—may take longer than MPR monkeys to figure out both the social dynamics and the regulation of stress during formation of dominance hierarchies. It is also possible that individual temperament, which may influence later social rank, influences HPA axis activity and regulation. However, the current study does not have the data to explore this hypothesis; such studies would add important information to current knowledge in the field. Another explanation is that the brain expression of receptors to which glucocorticoids bind during baseline and stressful conditions has been altered by early life experience (Hostinar, Sullivan, & Gunnar, 2014; Oitzl, Champagne, van der Veen, & de Kloet, 2010). Thus, by the time they are juveniles, NR monkeys exhibit an imbalance in glucocorticoid (GR) and mineralocorticoid receptors (MR) that put them at risk for ineffective regulation of stress responses, including behavioral responses (Oitzl et al., 2010). It is well established that epigenetic changes in the expression of MR:GR are induced by early life experiences in rodents (Meaney & Szyf, 2005; Oitzl et al., 2010), but future studies are necessary to elucidate similar mechanisms in macaques.

Our findings are consistent with studies of stable social groups of adult macaques showing that subordinate individuals exhibit higher short-term cortisol levels (i.e., plasma or urinary cortisol), especially when subjected to higher rates of social stressors (Abbott et al., 2003; Gust, Gordon, Hambright, & Wilson, 1993), such as the increased aggression recorded for low-ranking monkeys in the present study. That no relationship between HCCs and adult social rank was found for any NR monkeys indicates a dissociation between neuroendocrine stress regulation and adult social competence that appears to be present in MPR monkeys. However, the small sample sizes for the juvenile HCCs warrant further investigation of this potential mechanism. It is possible that, if housed in an iso-rearing group after relocation, NR monkeys may have exhibited a relationship between HCCs and social rank in the adult group, absent MR monkeys being present. The current study could not address this possibility, but future work will be important in elucidating the influences that MR monkeys exert on juvenile and adult social ranks.

Our current results showing increased HCCs in SPR monkeys at 18 months of age partially replicate our previous findings of higher HCCs in both SPR and PR monkeys, compared to MPR monkeys, at this age (Dettmer et al., 2012). The fact that in the present study, PR monkeys exhibited intermediary HCC values between SPR and MPR monkeys underscores the necessity of studying individual differences in stress responsivity (particularly as it relates to later behavior). It is possible that subtle individual variations in HCCs across puberty are present for different rearing groups across different cohorts, although the sample size in the present study was too small to test this hypothesis directly. Nevertheless, our collective findings (the present study and those of Dettmer et al., 2012) suggest not only early maternal contact, but the amount of exposure to peers early in life, may be a key factor in the regulation of long-term HPA axis activity.

One limitation of our study is that we only examined female rhesus monkeys, and our results may not be applicable to male primates. Clearly, research with larger, mixed-sex social groups is needed, though most primate research programs that employ nursery rearing do not maintain male monkeys beyond adolescence due to the high demand for these animals in biomedical research. Another limitation is the small sample sizes for the juvenile hair cortisol data. We are currently adding to this data set and will be able to determine whether the findings here are replicable in the near future, although it is equally important for these findings to be replicated in other primate facilities that house larger, mixed-sex social groups. Thus, an intriguing opportunity exists for researchers who study naturally occurring variations in maternal care (i.e., neglect, rejection, abuse; see Maestripieri, Hoffman, Anderson, Carter, & Higley, 2009) in large social settings to study chronic HPA axis activity as it relates to later social rank.

The precise mechanisms by which early social experience might influence juvenile and adult HPA axis activity, and adult social rank, are unclear. It is possible that early social experience results in higher chronic cortisol levels for some NR monkeys (Dettmer et al., 2012) owing to these monkeys' lack of appropriate social behaviors as has been documented previously (Stevens et al., 2009; Suomi, 1997). However, it is also possible that altered HPA axis activity, especially in the juvenile period, makes certain individuals more likely to be hyper-fearful and less likely to be socially competent, and thus more likely to receive aggressive interactions, across development and into adulthood. It is also likely that differences in early caregiving experience are resulting in differential expression of receptors in the brain that bind glucocorticoids (Meaney & Szyf, 2005; Oitzl et al., 2010), thus resulting in differences in physiological and behavioral responses to stress. Future work should increase study population sizes, assess hair samples across the entire developmental period, and examine receptor expression to begin to elucidate these relationships.

Taken together, our findings suggest an intriguing association between early life experience, long-term HPA axis activity/regulation, and adult social status. Each of these variables is known to predict adult health outcomes. Our findings lay the groundwork for future studies examining how the association between these traits puts individuals at risk for physical and mental health disparities later in life, and suggest that nonhuman primates are an important translational model for such studies in humans.

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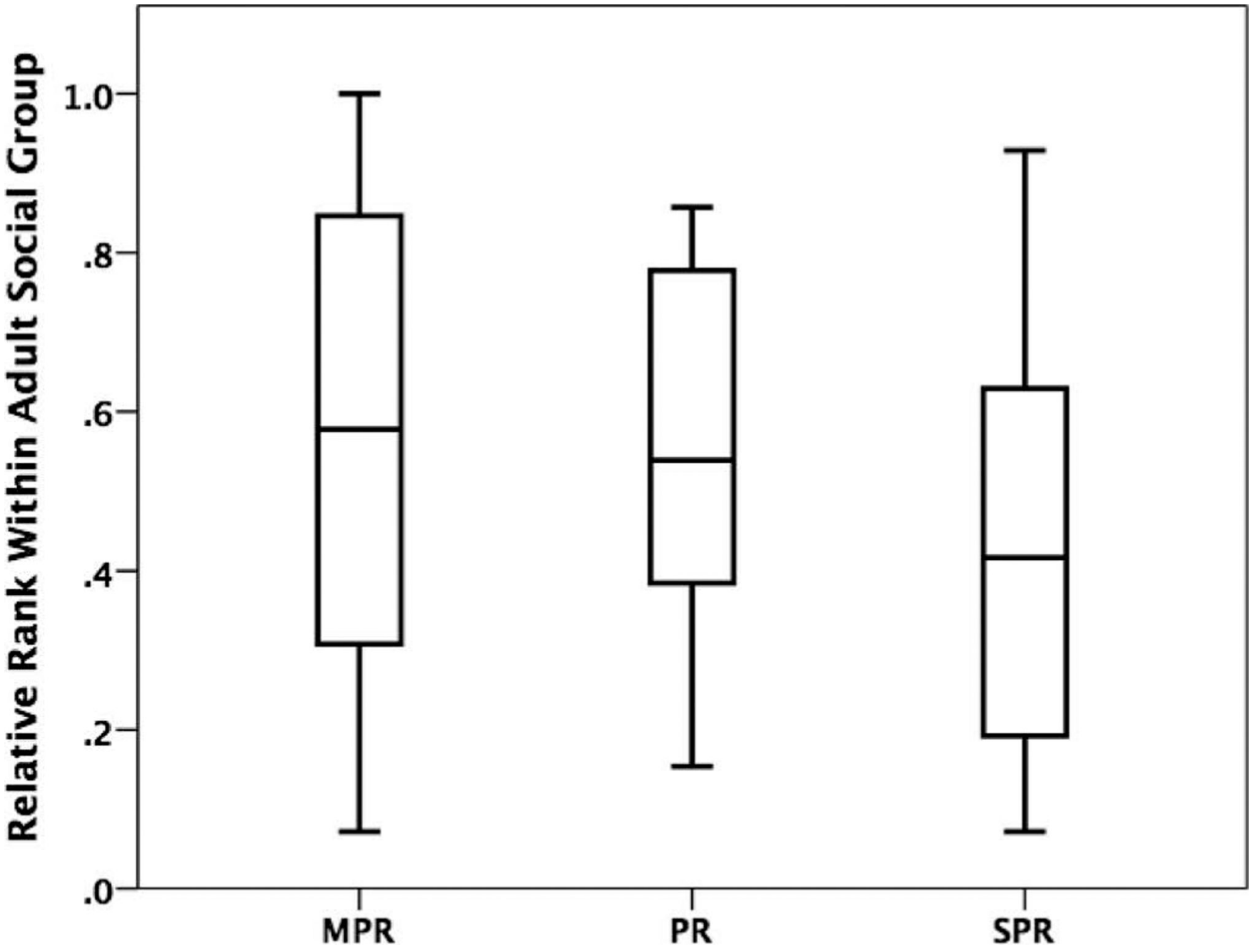

Figure 1.

Relative rank within adult social groups for mother-peer-reared (MPR), peer-reared (PR), and surrogate-peer-reared (SPR) female rhesus monkeys ($\beta = -0.067$, $t_{(89)} = -2.03$, $p = 0.046$).

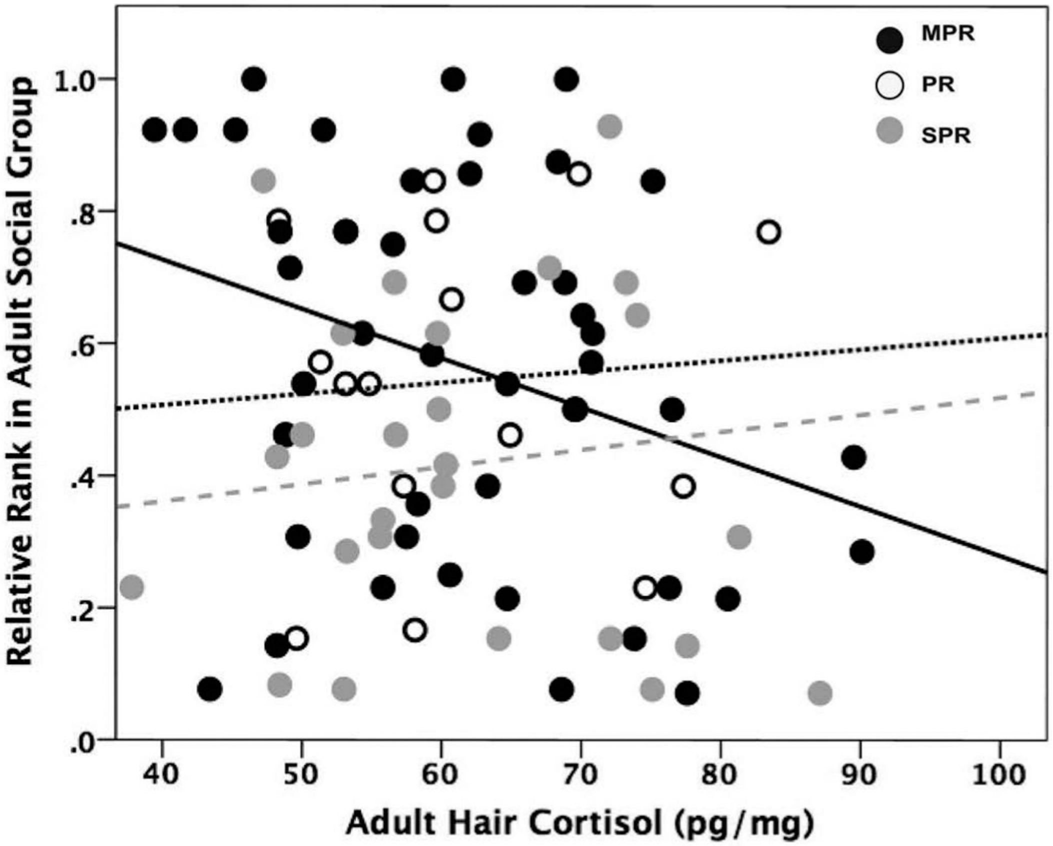

Figure 2.

For mother-peer-reared (MPR) monkeys only (black circles), adult hair cortisol concentrations (HCCs) were negatively correlated with contemporaneous social rank ($r_{(s)} = -0.327$, $p = 0.03$). Adult HCCs were not associated with rank in peer-reared (PR, white circles), or surrogate-peer-reared (SPR, gray circles) monkeys.

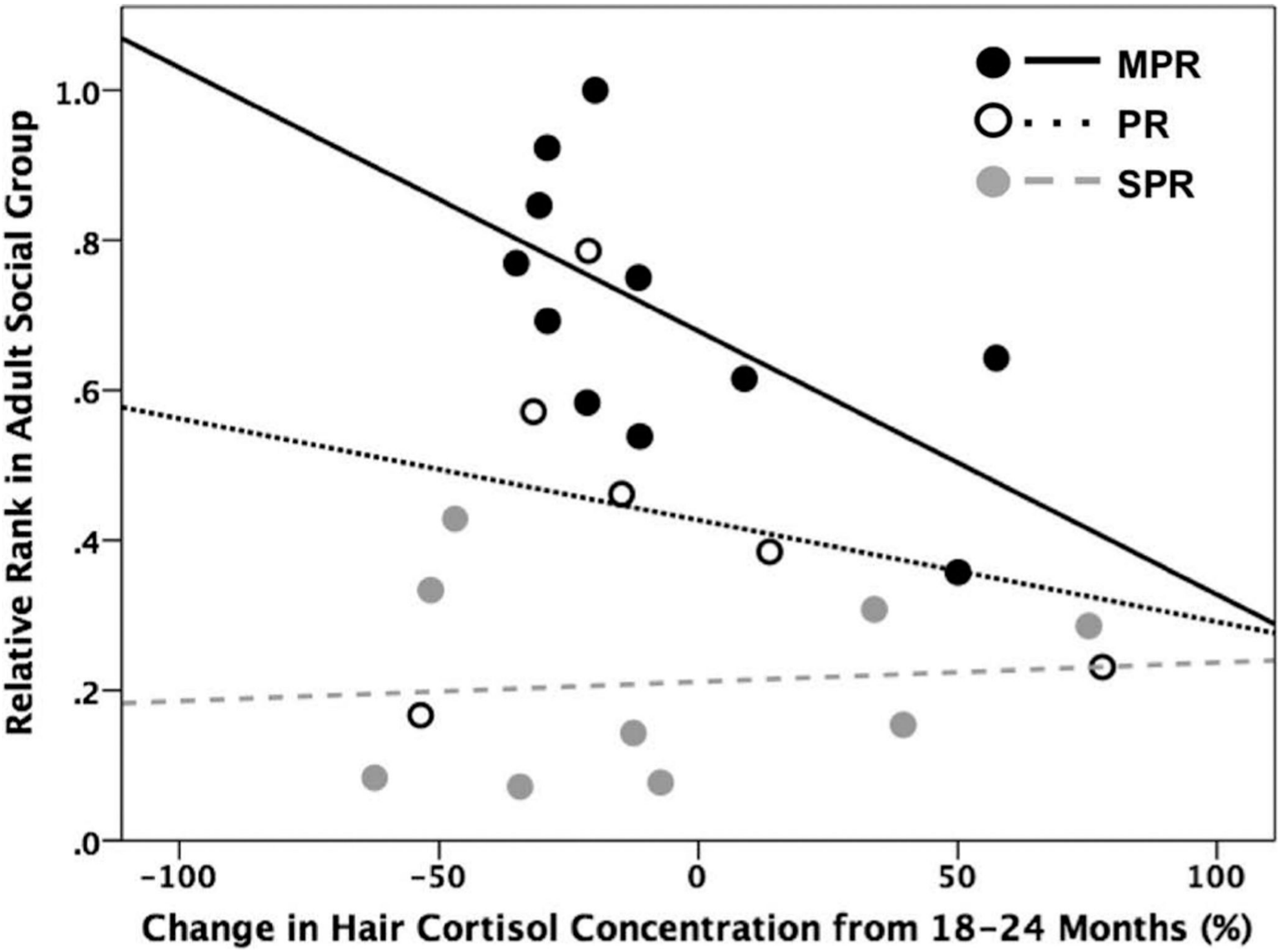

Figure 3.

For mother-peer-reared (MPR) monkeys only, changes in hair cortisol concentrations (HCCs) in the juvenile period (18–24 months) tended to negatively correlated with adult social rank ($r_{(s)} = -0.627$, $p = 0.039$). A subset of individuals ($n = 26$) had hair samples available during the juvenile period.

Table 1.

Sample sizes for cohorts based on rearing condition.

	Rearing condition			
Cohort (year)	**MPR**	**PR**	**SPR**	**Total**
3	7	3	3	13
4	8	2	4	14
5	6	3	4	13
6	4	3	5	12
7	9	0	3	12
8	8	2	4	14
9+	6	2	4	12
Total	48	15	27	90

Table 2.

Correlations between hair cortisol concentrations (HCCs) and adult rank for mother-peer-reared (MPR) and nursery-reared (NR) monkeys.

Rearing condition	Adult rank (*n*[a])	p-value
MPR		
Adult HCCs	−0.327 (43)	0.037
Juvenile HCCs		
12 months	−0.518 (11)	0.102
18 months	−0.227 (11)	0.502
24 months	−0.573 (11)	0.06
Δ Juvenile HCCs		
12–18 months	0.545 (11)	0.08
18–24 months	−0.627 (11)	0.039 *
NR		
Adult HCCs[b]	PR: 0.288 (15)	0.30
	SPR: −0.156 (26)	0.45
Juvenile HCCs		
12 months	0.204 (14)	0.483
18 months	0.011 (15)	0.970
24 months	0.05 (15)	0.860
Δ Juvenile HCCs		
12–18 months	−0.341 (14)	0.233
18–24 months	−0.007 (15)	0.980

[a] n = sample size for each correlation.

[b] For adult HCCs, NR rearing conditions were examined separately:PR = peer-reared; SPR = surrogate-peer-reared.

* After Bonferroni correction for multiple corrections, the correlation was not significant (p ≤ 0.01).