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Parentally deprived juvenile Owl monkeys suffer from long-term high infection rates but not from altered hair cortisol concentrations nor from stereotypic behaviours

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Abstract

Background: In captive colonies, owl monkeys' mothers sometimes reject their newborns. To prevent, mortality infants are manually raised by veterinarians. Both parental separation and rejection are stressful experiences, associated with elevated stress, physical, and behavioural disorders. The effect of parental deprivation in IVITA's owl monkeys stress profiles and health is unknown.

Methods: We compared stress biomarkers such as hair cortisol (using cortisol ELISA), stereotypic behaviours (with infrared cameras), and infection histories in juveniles separated from parents soon after birth (n = 14, ~17 months) and controls (n = 11, ~17 months).

Results: Parentally deprived owl monkeys show higher infection rates than controls (p = .001). However, they display no higher incidence of biomarkers of stress: Neither stereotypic behaviour nor cortisol in hair was different between cohorts. Irrespective of deprivation status, rates of infection, and concentration of cortisol in hair were positively associated (R^2 = .29, p = .005).

Conclusion: Early parental deprivation and natural high levels of cortisol secretion are associated with elevated infection levels in the IVITA owl monkey juveniles detectable up to 17 months post separation.

KEYWORDS
cortisol, early life stress, infections, New World monkeys, rejection, stereotypic behaviour

1 | INTRODUCTION

Owl monkeys (*Aotus* spp.) are a genus of New World primates that are bred in captivity as biomedical models for human infectious diseases.[1,2] Although in general efforts have been successful in setting productive colonies, breeding this species in captivity is not without challenge. Owl monkey colonies have suffered from high prevalence abortions and poor reproduction.[2,3] Amongst infants, mortality is also high, with opportunistic infections and maternal rejections as leading causes.[4–6]

The number of maternal rejections at the Nancy ma's owl monkeys (*Aotus nancymaae*) colony in Iquitos Peru has decreased considerably since its establishment (1979),[6] being a successful breeding programme, while maintaining international standards of animal welfare.[1] However, rare rejection events still occur. When this happens, rejected newborns are separated from parents, hand-raised by veterinarians until they recover, and then re-housed with other rejected or orphaned individuals. Whereas separation from parents following rejection (hereby parental

deprivation) has eliminated rejection-related mortality (Sanchez, personal communication) it could represent strong emotional challenge for young primates, leading to an increase risk to suffer mental and physical disease.[7,8]

Experiments where infant primates are temporarily separated from mothers or (hereby 'maternal separation') can cause long-term alteration of the activity of the Hypothalamic Pituitary Adrenal (HPA) axis, the system that regulates the physiological response to stressors,[8] induce abnormal behaviours,[9] and disease estates in primates.[10,11]

The long-term effects of spontaneous rejection and separation on health have not been studied in New World monkeys. However, experimental studies commonly find lower cortisol in maternally separated,[12,13] although some others show the opposite effect.[14] Further reports show that the maternally separated suffer from: altered reactivity to stressors,[14] modified neuronal expression of genes involved in learning and emotion which persist until adolescence,[13] and the display of anxious like behaviours such as distress vocalizations and socialization deficiencies.[12]

We propose that maternal rejection followed by parental separation could be stressful for young owl monkeys as, in nature, groups are territorial, infants (0–8 months) are mainly cared for by their fathers, with mothers remaining as a source of milk through infancy. Juveniles (8 months −3/4 years) of both sexes remain in the natal group until they reach adulthood, at which point they emigrate. Only as juveniles, individuals of different groups come into contact.[15]

Additionally, for primates studied, interruption of mother-infant relationship is also associated with increased risk of gastrointestinal and upper respiratory infections,[10,16] with chronic release of cortisol citing as a likely cause of impaired immune and inflammatory responses.[17] This is relevant for IVITA's parentally deprived infant owl monkeys as they appear to suffer from infections which can become lethal (Sanchez, personal communication). Therefore, we hypothesized that parentally deprived owl monkeys might suffer from lasting dysregulation of the HPA axis and suffer from increased rate of infections. To test this, we compared cortisol deposited in hair; presence of distress behaviours; and rate of medications administered for infections in juveniles which had been rejected and separated in early life and age-matched controls. Our analysis demonstrates that parentally deprived owl monkeys required more treatments for bacterial, fungal and parasitic infections detectable ~17 months after separation. And although there was no statistical difference in stress biomarkers between parentally deprived and controls, the rate of infection treatments was in part explained by high cortisol concentration deposited in hair.

This report supports that preventing maternal rejection and/or understanding its effects would be key to improving and refining long-term health management and prevention of common infections in owl monkey colonies.

2 | MATERIALS AND METHODS

2.1 | Humane care guidelines

The work presented was approved by the Ethical committee on animal research of the National Mayor University of San Marcos (UNMSM). Authorization for sampling was granted to Angela Maldonado and Ursula M. Paredes by the Peruvian authority on Fauna and Flora SERFOR (RDG0050-2018-SERFORDGGSPFFS).

2.2 | Sample collection

This study included 25 juvenile owl monkeys housed at the Center for the Reproduction and Conservation of Non-Human Primates (CRCP) of the Veterinary Institute of Tropical and Altitude Research (IVITA) of the Universidad Nacional Mayor de San Marcos (UNMSM), located in the city of Iquitos, Peru. Of these 25, 14 were rejected/separated (5 males and 9 females, mean age 17.7 ± 1.7 months) and 11 were controls (3 males, 8 females, mean age 17.5 ± 2 months). The rejected cohort was composed of juveniles rejected within the 5 months of life (mean age 2.6 ± 1.6 months) and subsequently separated from parents. The criteria for the controls were: age-matched juveniles, reared by parents until weaning age. The weight of these individuals was similar in both groups (rejected/separated and controls 820 ± 16 g; 810 ± 35 g respectively).

2.3 | Family and rearing environment

Primates are housed in large concrete buildings with mesh doors that allow access to natural bio periods throughout the year. In nature this species is territorial, monogamous and lives in small family units. Home ranges are large with juveniles of both sexes mainly coming into contact after dispersal.[18] Therefore at IVITA, breeding pairs or breeding pairs plus immature offspring are housed in a single enclosure (2 m^3, width = 1 m, depth = 1 m height = 2 m). Owl monkeys are fed once a day a diet composed of seasonal fruits, vegetables, IVITA's own dried food, and water *ad libitum*. At 8–9 months, offspring are weaned and juveniles are transferred to a new enclosure and paired with a member of the opposite sex to establish a new breeding pair.

2.4 | Maternal rejection and parental separation

Owl monkey mothers reject attempts of their young to be carried shortly after giving birth (within the first four weeks of life), however, allow offspring to continue suckling. Fathers are the primary caregivers, carrying infants start soon after birth.[18,19] After a period between days and a couple of weeks, mothers occasionally reject suckling, blocking access to the nipples, ignoring calls for help,

offering their back or shielding their nipples. Sometimes mothers gently bite offspring tails and toes to persuade them to stop searching for the nipple (Sanchez, personal communication). Whereas this account of rejection is considered part of the normal weaning process for *Aotus* spp.,[19] complete rejection could lead to starvation, and escalate to aggression to infants, which can be lethal.[4,5] When complete rejection has been observed, maternally rejected infants were removed from parents' enclosure and transferred to incubators under the care of veterinarians. Offspring remained in incubators until recovered from rejection injuries, at which point they were re-housed with other rejected or orphaned infants. For the parentally separated cohort, food consists solely of human infant formula (Nan-Nestlé) until 4 months of age after which formula milk is combined with IVITA's own dry food and fruit.

2.5 | Hair collection and Cortisol measurements

We obtained hair samples for cortisol analysis along a regular IVITA veterinary wellness check- up (one sample/individual ~17 months of age). For these animals were anaesthetized with ketamine hydrochloride (10–20 mg/kg) intramuscularly following established methods.[18] Approximately 1.5 cm of hair (~0.5 g) were cut from the tip of the tail, where hair was long. The hair was stored in the refrigerator at 4°C until processing time. Hair was cut into small sections (~1–2 mm length) with micro scissors and weighed in an electrical microbalance. To isolate and measure cortisol, an Isopropanol precipitation protocol was used, followed by a competitive ELISA salivary cortisol (Salimetrics) validated for hair.[20] Immunoassays were measured as colour change on a plate reader (BMGlabtech) set at 450 nm following kit manufacturer's instructions. The protocol included a standard curve. Absorbance raw values were converted to absolute cortisol concentrations estimations using a reciprocal absorbance method, using the slope constants obtained from fitting a curve to standards' readings. Cortisol concentrations were replicated for 30% of samples by two independent operators.

2.6 | Camera recordings and Behaviour analysis

We recorded behaviours 5 weeks post hair collection where arousal cause for sampling procedure would have subsided. Videos were recorded between 5 pm and 6 am as owl monkeys are nocturnal.[15] We set 10 motion-sensitive infrared cameras (Trail Wildlife Camera Trap with Infrared Night Vision, APEMAN 12MP 1080P) placed outside enclosures. Cameras recorded during 5 consecutive nights covering ~60 h/individual (total recorded time for parentally deprived = 17.69 h, controls = 9.11 h). The motion-sensitive cameras were placed 1m from the floor and 1.5 m from the front wall, offering a complete view of the enclosures. In the recordings, we quantified total duration stereotypic behaviours: 'pacing' (locomotion back and forth in the base of the cage), and 'somersaults' (rapid small back flips against the back wall of the enclosure) and number of episodes displayed per individual. Other forms of stereotypic behaviours were not observed in videos. Behaviours were recorded using digital timers, by two independent observers. Interobserver reliability was calculated based on 100% of the video recordings.

2.7 | Analysis of history of treatments for infections

IVITA's individual health records include endoparasite and ectoparasite screenings, injuries and medication administered, age of weaning and rejection events. For infants rejected, monitoring was conducted by veterinarians. After relocation to general colony housing, monkeys suffering from infections or poor health were identified by animal keepers who conducted daily visual checks of all owl monkeys in IVITA facilities. Results of checks were reported back to veterinarian staff, who then assessed animals' health. When animals needed medical care drugs and treatment administered were recorded in individuals' medical histories.

Wide spectrum drugs administered to treat bacterial, fungal and parasitic infections (eg amoxicillin, sulfonamide, cephalosporin, trimethoprim, metronidazole, and ivermectin) were identified medical records and scored. The number of treatments were normalized per number of months lived to the date of collection of hair samples. Multiple administration of the same drug over a few days was scored as one treatment.

2.8 | Statistical analysis

We compared differences in mean cortisol concentrations, time spent in stereotypic behaviours and rate of infection treatment in parentally deprived and controls. Testing of sexual differences was not possible as sample size was too small. We conducted *F*-tests to compare variance of samples and unpaired Welch's *T*-tests (for unequal samples) in GraphPad (PRISM9) to test for statistical differences between means. The null hypotheses were rejected when $p < .05$.

3 | RESULTS

Our study aim was to test if parental deprivation was associated with elevated stress and increased frequency of infections. This study did not identify an association of parental deprivation with elevated rates of stress biomarkers (cortisol concentration Figure 1 and incidence of stereotypia Figure 2). However, our measurements confirmed that owl monkeys that were parentally deprived in early life received significantly more medication to treat infections than controls (Figure 3). As to further explore if stress levels correlated with health outcomes, we identified a correlation between cortisol levels and infection treatment for owl monkeys (Figure 4).

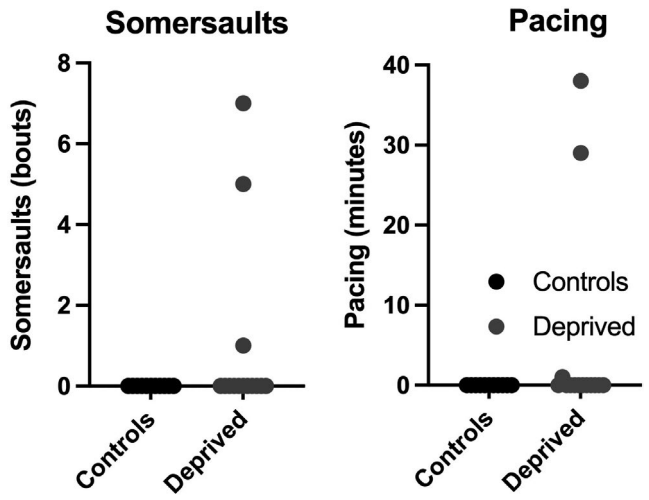

FIGURE 1 Concentration of cortisol in the hair of parentally deprived and control juvenile owl monkeys is not different. Parentally deprived owl monkeys ($n = 14$; grey circles) have similar mean cortisol concentrations as controls ($n = 11$; black circles). Probability $p = .65$ is derived from a Welch's *T*-test (two tailed, $df = 22.22$)

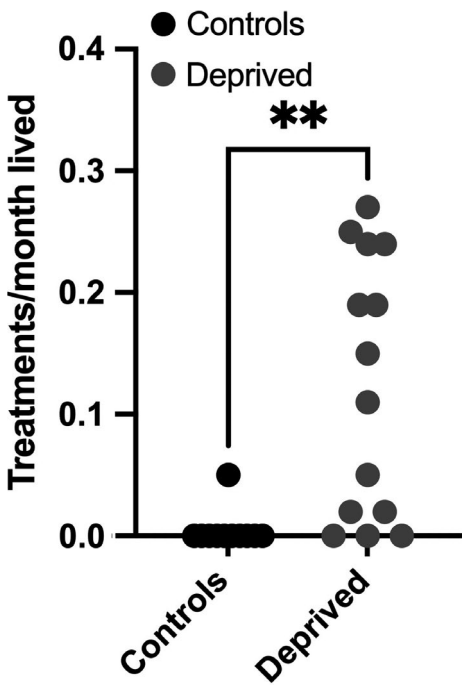

FIGURE 3 Frequency of infection treatments in parentally deprived juveniles is higher than in controls. Parentally deprived owl monkeys ($n = 14$; grey circles) have significantly different rates of treatments for infections than controls ($n = 11$; black circles). Probability $p = .001$ (indicated by **) is derived from a two-sample t-test (Welch) using a T distribution (two tailed, $df = 13.66$)

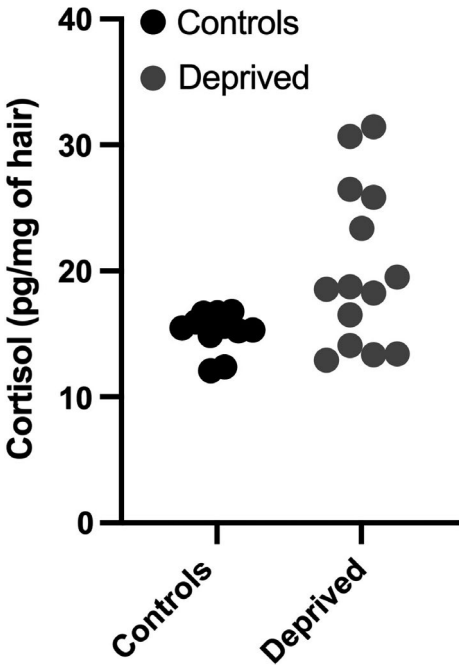

FIGURE 2 Frequency of stereotypic behaviours in parentally deprived and control owl monkeys is not different. Two forms of stereotypia: somersaults and pacing were identified in deprived owl monkeys ($n = 14$; grey circles) but not in controls ($n = 11$; black circles). Behaviours were quantified over 5 consecutive nights (60 h). Number of somersaults bouts and duration of Pacing seen in deprived animals were analysed using a Welch's *T*-test, which showed no significant differences in stereotypic behaviours between groups (Somersaults, $df = 12$, $p = .14$; Pacing $df = 13$, $p = .12$)

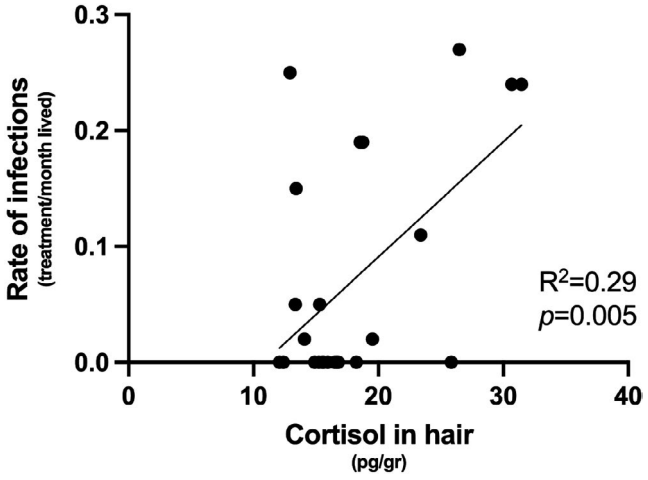

FIGURE 4 Correlation between treatment/month lived and hair cortisol concentration in all owl monkeys. Linear regression of cortisol and rate of infection treatments revealed a positive correlation between cortisol and rate of infections in parentally deprived monkeys ($n = 25$, $p = .005$; $R^2 = 0.295$; $F = 9.601$)

Cortisol concentration deposited in hair rejected/separated and controls was compared using an ELISA immunoassay (Figure 1). The mean cortisol of each cohort was different (deprived = 20.22 ± 6.1 pg/g, controls = 15.2 ± 1.5 pg/g). However, an unpaired Welch's *T*-test demonstrated that cortisol concentration in hair measured in hair up to 17 months post parental deprivation was not significantly different from the found in controls (two tailed, $df = 22.22$, $p = .65$).

Our camera recordings demonstrated the presence of whole body stereotypic behaviours amongst IVITA's owl monkeys, specifically,

we identified pacing and somersaults (Figure 2). Interobserver reliability was measured, with the scores being 93% and 85% for somersaults bouts and pacing duration respectively. The incidence of both stereotypic behaviours was higher for the parentally deprived (in 3 of 14) than for controls (in 0 of 11), where these or other stereotypic behaviours were not recorded. However, statistical analysis of pacing duration and somersaults bouts demonstrated no significant differences between cohorts (Welch's *T*-test, Somersaults, $df = 12$, $p = .14$; Pacing $df = 13$, $p = .12$). The total amount of time (duration) and number of times (frequency) the three parentally deprived individuals engaged in these behaviours varied significantly. Two of the three individuals lived in the same enclosure and displayed pacing and somersaults in four out of five days of recording. Whereas the pair engaged in multiple somersaults and pacing for 30–40 min (in total), the third individual only engaged in pacing for one minute and did one somersault. Consequently, the standard deviation of these behaviours in the parentally deprived sample were large (Somersault bouts in parentally deprived mean = 2 ± 2.8, controls = 0; Pacing mean parentally deprived = 9 ± 15.6 min controls = 0 min).

To determine the association between parental deprivation history and infection rates, we analysed the frequency of administration of drugs to treat parasitic, bacterial and fungal infections as recorded in medical histories. The results are shown in Figure 3. Our analysis showed that the number of treatments for infections per month lived was higher in parentally deprived (mean = 0.12 ± 0.10) than in controls (mean = 0.0 ± 0.01). Furthermore, a two-tailed Welch's *T*-test showed that this difference was statistically significant ($df = 13.66$, $p = .001$). Furthermore, it was noticed that juvenile control owl monkeys were almost never treated for infections.

We had hypothesized elevated cortisol secretion induced by a history of parental deprivation could be a contributing factor to increased rates of infections in these owl monkeys. As there was no difference in cortisol concentration between our stressed and control cohorts, we used a simple linear regression analysis to explore if cortisol concentration alone, irrespective of rearing history, correlated with frequency of treatments for infection (Figure 4). This analysis showed a significant correlation between cortisol and infection treatment rates ($p = .005$), explaining a small portion of the variance of infection treatment rates ($R^2 = 0.29$, $F = 9.601$).

4 | DISCUSSION

Experiencing parental separation in early life can permanently modify stress reactivity, health outcomes and behaviour.[21,22] In our study we tested whether parental deprivation, a more severe form of separation, would be associated with stress and poor health in parentally deprived owl monkeys. Our study confirmed that parental deprivation is associated with greater frequency of infection treatment detectable (up to) ~17 months post-parental separation. Furthermore, we confirmed that infection prevalence is linked to elevated cortisol accumulation in hair, although the source of this elevated physiological stress marker is not explained by rearing history. Altogether, the study suggests that early adverse experiences and naturally elevated physiological stress levels could predispose juvenile owl monkeys to poor health.

We hypothesized that our parentally deprived cohort would suffer from chronic stress, and that cortisol secretion would be dysregulated as a result. Our calculations do not support our hypothesis, the mean hair cortisol concentration detected was no different between parentally deprived owl monkeys and controls (Figure 1). This would suggest that exposure to this stressor does not lead to alteration in cortisol concentrations in captive owl monkeys which can be detected ~17 months after separation. At a first glance, it would appear that our study disagrees with larger literature which shows long-term alterations in cortisol release to milder forms of parental separation.[8,12–15] However, there are several reasons which might explain this discrepancy. Comparisons of our study with previous reports suffers from important differences in study design, which affect release and measurement of cortisol.[8] Whereas we studied spontaneous rejection and parental separation in hair ~17 months after stressor, studies in other New World monkeys describe experimental maternal or familial separation, in plasma measured after days,[14] or in cerebrospinal fluid twelve months post separation.[13] Closer study designs are found in studies describing maternal separation experiments in rhesus macaques, were cortisol was measured in hair within a similar time frame as ours (~15–17 months post separation). However, even when only considering studies within these parameters, the effect of separation in cortisol deposited in hair is not always the same. Sometimes effects of separation are lasting, with lower cortisol detected in separated and peer reared macaques,[23] whereas sometimes cortisol dysregulation is not observed beyond 6 months.[24]

Another way on how we addressed whether parental deprivation affected stress phenotypes was measuring the prevalence and frequency of stereotypic behaviours (Figure 2). We proposed that, given the severity of the emotional trauma, behavioural abnormalities could occur in owl monkeys. As there are no accounts for such behaviours in juveniles of this species, we searched for commonly recorded stereotypies. Analysis of our camera recordings confirm the prevalence of pacing and somersaults in the parentally deprived cohort, whereas these were absent in controls. However, amongst parentally deprived only three of fourteen display these behaviours. Statistical analysis comparing frequency of these behaviours does not reveal significant differences between groups. This result would suggest that the frequency at which owl monkeys display these behaviours (parentally deprived or not) are not different. It is noteworthy that a number of studies show that in any given human population, not all individuals exposed to a stressor display behavioural abnormalities, those sensitive or reactive to environmental conditions at risk.[25] Whether this might also be the case for IVITA's Owl monkeys is unknown, however, future studies to assess the proportion of stress reactive individuals in IVITA's owl monkeys to test these interactions.

Furthermore, whether pacing and somersaulting are direct indicators of stress in owl monkeys is not clear. Some authors even

suggest stereotypia could also reflect boredom, or the need to walk.[26] Notwithstanding, pacing and somersaults have been widely associated with externalization of stress, observed primarily in captive primates, commonly identified in those which have suffered disruption of their relationship with their mothers.[8,27] Therefore, when considering cortisol and behavioural data together, our study would suggest that ~17 months post-separation, parentally deprived owl monkeys do not display deregulation of behavioural or hormonal stress biomarkers.

Our analysis of medical histories suggests that parental deprivation is associated with increased frequency of medication for infections in owl monkeys (Figure 3). Our findings agree with research conducted on Old World monkeys and apes. Conti and colleagues[10] conducted a retrospective study of health outcomes in rhesus macaques (*Macaca mulatta*) separated from their mothers, and these primates were shown to have a lifetime higher incidence of treatment for gastrointestinal infections. Similarly, Clay et al,[16] described a lifetime elevated risk for developing upper respiratory infections in nursery reared chimpanzees (*Pan troglodytes*).

Since cortisol was not elevated in our parentally deprived cohort, long-term dysregulation of this hormone may not be a mechanism for higher infection risk in owl monkeys. However, the relationship between cortisol and long-term consequences of stressful experiences is far from clear. It has been proposed that stressful experience itself, modifies inflammatory and immunological responses to infections which is independent from alterations in cortisol secretion.[17]

It is well accepted that intrinsic (eg genetic) factors could contribute to heightened reactivity to stressors irrespective of rearing history. For example, genetic variation in loci associated to stress reactivity (eg in Serotonin transporter gene promoter) is associated with deficiencies in immune response to certain viruses.[28] To address this possibility we conducted a regression analysis between cortisol and rates of infections across the whole sample (Figure 4), which confirmed a weak association but significant association. Furthermore, we observed that this correlation is largely driven by those who experienced parental deprivation (Figure 4, deprived black circles, controls grey circles), which may suggest that a combination of genetic and historical factors contribute to poor health outcomes in this species. This finding agrees with previous literature showing that epigenetic changes -in the same genetic loci linked with stress reactivity- is associated with outcomes parentally stressed rhesus macaques.[29]

A caveat of our study is that we did not consider the effect of breast milk as a nutritional stressor in our parentally deprived samples, which were not breastfed for as long as controls. This is relevant and rarely considered as it is widely recognized that breast milk confers immune protection against pathogens in infants through transmission of maternal immunoglobulins (secretory IgA)[30] and through the establishment of gut microbial communities, which promotes healthy immune profiles in primates.[31] However, previous maternal separation experiments in cross fostered rhesus macaques, where breastfeeding regimes were not interrupted, showed long-term dysregulation of immune profiles[11] suggesting the lack of breastmilk alone would not be responsible for effects on immunity in owl monkeys. Altogether, our study suggests that infection rates in parentally deprived owl monkeys might be the result of deficiencies experienced during critical developmental periods (emotional and perhaps nutritional), and intrinsic factors (genetic risk variants to stress reactivity) which result in long lasting effects on health profiles.

5 | CONCLUSION

In conclusion, parental deprivation is associated with increased rates of treatment for infections in juvenile owl monkeys. Furthermore, considering the individual history of parental deprivation together with cortisol concentrations in hair could help veterinarians to identify owl monkeys most likely to develop clinical symptoms of infection and improve the management of this species in captivity.

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CONFLICT OF INTEREST

The authors of this manuscript have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Center for the Breeding and Conservation of Primates of the Peruvian Primatology Project. National Research Council (US) Institute for Laboratory Animal Research. International Perspectives: The Future of Nonhuman Primate Resources. National Academies Press (US); 2003. https://www.ncbi.nlm.nih.gov/books/NBK221782/ Accessed February 10, 2021
2. Málaga CA, Weller RE, Buschbom RL, Baer JF, Kimsey BB. Reproduction of the owl monkey (*Aotus* spp.) in captivity. *J Med Primatol*. 1997;26(3):147-152.
3. Rouse R, Bronson R, Sehgal PK. A retrospective study of etiological factors of abortion in the owl monkey, *Aotus trivirgatus*. *J Med Primatol*. 1981;10:199-204.
4. Gozalo A, Montoya E. Reproduction of the owl monkey (*Aotus nancymai*)(Primates: Cebidae) in captivity. *J Med Primatol*. 1990;21(1):61-68.
5. Sánchez N, Gálvez H, Montoya E, Gozalo A. Mortalidad en crías de Aotus sp. (Primates:Cebidae) en cautiverio: una limitante para

estudios biomédicos con modelos animales. *Revista Peruana De Medicina Experimental Y Salud Publica*. 2006;23(3):221-224.
6. Gozalo A, Montoya E. Reproduction of the Owl Monkey (*Aotus nancymai*) (Primates: Cebidae) in Captivity. 1994; Primate Report 40.
7. Harlow HF, Dodsworth RO, Harlow MK. Total social isolation in monkeys. *Proc Natl Acad Sci USA*. 1965;54(1):90.
8. Sanchez MM. The impact of early adverse care on HPA axis development: nonhuman primate models. *Horm Behav*. 2006;50(4):623-631.
9. Latham NR, Mason GJ. Maternal deprivation and the development of stereotypic behaviour. *Appl Anim Behav Sci*. 2008;110(1–2):84-108.
10. Conti G, Hansman C, Heckman JJ, Novak MF, Ruggiero A, Suomi SJ. Primate evidence on the late health effects of early-life adversity. *Proc Natl Acad Sci USA*. 2012;109(23):8866-8871.
11. Kinnally EL, Martinez SJ, Chun K, Capitanio JP, Ceniceros LC. Early social stress promotes Inflammation and Disease Risk in Rhesus Monkeys. *Sci Rep*. 2019;9(1):1-8.
12. Dettling AC, Schnell CR, Maier C, Feldon J, Pryce CR. Behavioral and physiological effects of an infant-neglect manipulation in a biparental, twinning primate: impact is dependent on familial factors. *Psychoneuroendocrinology*. 2007;32(4):331-349.
13. Law AJ, Pei Q, Walker M, et al. Early parental deprivation in the marmoset monkey produces long-term changes in hippocampal expression of genes involved in synaptic plasticity and implicated in mood disorder. *Neuropsychopharmacology*. 2009;34(6):1381-1394.
14. Levine S, Wiener SG, Coe CL. Temporal and social factors influencing behavioral and hormonal responses to separation in mother and infant squirrel monkeys. *Psychoneuroendocrinology*. 1993;18(4):297-306.
15. Fernandez-Duque E. Social monogamy in the only nocturnal haplorhines. *Primates Perspect*. 2007;139-154.
16. Clay AW, Bloomsmith MA, Bard KA, Maple TL, Marr MJ. Long-term effects of infant attachment organization on adult behavior and health in nursery-reared, captive chimpanzees (*Pan troglodytes*). *J Comp Psychol*. 2015;129(2):145.
17. Cohen S, Janicki-Deverts D, Doyle WJ, et al. Chronic stress, glucocorticoid receptor resistance, inflammation, and disease risk. *Proc Natl Acad Sci USA*. 2012;109(16):5995-5999.
18. Baer JF, Weller RE, Kakoma I. Aotus: the owl monkey. *Academic Press*. 2012;152-153.
19. Dixson AF. Some observations on the reproductive physiology and behaviour of the Owl monkey in captivity. *Int Zoo Yearb*. 1982;22(1):115-119.
20. Meyer J, Novak M, Hamel A, Rosenberg K. Extraction and analysis of cortisol from human and monkey hair. *J Visual Exp*. 2014;83:e50882.
21. McEwen BS. The neurobiology of stress: from serendipity to clinical relevance. *Brain Res*. 2000;886(1–2):172-189.
22. Gluckman PD, Hanson MA, Cooper C, Thornburg KL. Effect of in utero and early-life conditions on adult health and disease. *N Engl J Med*. 2008;359(1):61-73.
23. Feng X, Wang L, Yang S, et al. Maternal separation produces lasting changes in cortisol and behavior in rhesus monkeys. *Proc Natl Acad Sci USA*. 2011;108(34):14312-14317.
24. Dettmer AM, Novak MA, Suomi SJ, Meyer JS. Physiological and behavioral adaptation to relocation stress in differentially reared rhesus monkeys: hair cortisol as a biomarker for anxiety-related responses. *Psychoneuroendocrinology*. 2012;37(2):191-199.
25. Lionetti F, Aron A, Aron EN, Burns GL, Jagiellowicz J, Pluess M. Dandelions, tulips and orchids: Evidence for the existence of low-sensitive, medium-sensitive and high-sensitive individuals. *Transl Psychiat*. 2018;8(1):1.
26. Poirier C, Bateson M. Pacing stereotypies in laboratory rhesus macaques: Implications for animal welfare and the validity of neuroscientific findings. *Neurosci Biobehav Rev*. 2017;83:508-515.
27. Novak MA, Hamel AF, Kelly BJ, Dettmer AM, Meyer JS. Stress, the HPA axis, and nonhuman primate well-being: a review. *Appl Anim Behav Sci*. 2013;143(2–4):135-149.
28. Capitanio JP, Abel K, Mendoza SP, et al. Personality and serotonin transporter genotype interact with social context to affect immunity and viral set-point in simian immunodeficiency virus disease. *Brain Behav Immun*. 2008;22(5):676-689.
29. Kinnally EL. Epigenetic plasticity following early stress predicts long-term health outcomes in rhesus macaques. *Am J Phys Anthropol*. 2014;155(2):192-199.
30. Hanson LA, Winberg J. Breast milk and defence against infection in the newborn. *Arch Dis Child*. 1972;47(256):845.
31. Ardeshir A, Narayan NR, Méndez-Lagares G, et al. Breast-fed and bottle-fed infant rhesus macaques develop distinct gut microbiotas and immune systems. *Science Transl Med*. 2014;6(252):252ra120.

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