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Handling newborn monkeys alters later exploratory, cognitive, and social behaviors

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ABSTRACT

Touch is one of the first senses to develop and one of the earliest modalities for infant-caregiver communication. While studies have explored the benefits of infant touch in terms of physical health and growth, the effects of social touch on infant behavior are relatively unexplored. Here, we investigated the influence of neonatal handling on a variety of domains, including memory, novelty seeking, and social interest, in infant monkeys (*Macaca mulatta*; $n = 48$) from 2 to 12 weeks of age. Neonates were randomly assigned to receive extra holding, with or without accompanying face-to-face interactions. Extra-handled infants, compared to standard-reared infants, exhibited less stress-related behavior and more locomotion around a novel environment, faster approach of novel objects, better working memory, and less fear towards a novel social partner. In sum, infants who received more tactile stimulation in the neonatal period subsequently demonstrated more advanced motor, social, and cognitive skills—particularly in contexts involving exploration of novelty—in the first three months of life. These data suggest that social touch may support behavioral development, offering promising possibilities for designing future early interventions, particularly for infants who are at heightened risk for social disorders.

1. Introduction

Touch is one of the first senses to develop (Bradley and Mistretta, 1975; Marx and Nagy, 2015). After birth, mothers remain in close proximity to their infants, actively touching them, behaviors that are instinctive and evolutionarily conserved across mammals (Feldman, 2011, 2015). Infants, in turn, seek and develop attachments to providers of contact comfort (Harlow and Zimmermann, 1959), engaging in bi-directional mutually regulated touch interactions (Mantis et al., 2014). Touch is one of the earliest forms of mother-infant communication (Field, 2001), regulating infants' arousal, particularly in distressing contexts (Jahromi et al., 2004) or when facial or vocal communication is disrupted (e.g., still-face paradigm; Bigelow and Power, 2012; Jean et al., 2014). Mothers also use touch to attract and maintain infants' attention (Jean and Stack, 2009). Active maternal touch, including massage and skin-to-skin contact, are critical for the growth and healthy development of immune, endocrine, and nervous systems (Feldman, 2011; Field, 2010; Underdown et al., 2010). Tactile stimulation—compared to auditory and visual stimulation—also elicits more broadly distributed brain activation in newborns, reflecting its primary importance (Shibata et al., 2012).

In addition to supporting healthy physical development, touch is theorized to form the foundation for infants' later high-order functions, social affiliation, and communication (Anisfeld et al., 1990; Feldman, 2011; Hertenstein et al., 2006). Studies report a positive association between maternal touch and early infant sociality. For example, preterm infants who are held for longer durations exhibit higher quality mother-infant interactions at 6 and 12 months of age (Korja et al., 2008). Similarly, 4- to 6-year-olds whose mothers touched them more during a 10-min play session, compared to children touched less, appeared more socially interested (Reece et al., 2016). Furthermore, 5-year-olds' levels of maternal touch were related to brain resting activity and connectivity in regions associated with mentalizing (Brauer et al., 2016).

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While these studies suggest that early tactile contact may be contributing to children's social skills, it is difficult to determine causality. Is maternal touch causing changes in the child, or are children who have more social mothers also more social themselves? Is this commonality shared through genetic, environmental, or epigenetic transmission? Or perhaps mothers are sensitive to whether their child enjoys touch (Mammen et al., 2016) and adjust their behaviors accordingly. In short, it is difficult to establish whether variation in maternal behavior is causing differential developmental outcomes in children, or vice versa, as both partners are known to mutually influence one another. In addition, there may be other factors at play. Mothers who touch their children a lot may also behave differently in other ways towards their children. Thus, isolating the effects of touch specifically can be challenging. In fact, despite the central role of maternal touch in early infant development, the mechanisms remain largely unexplored due to the difficulty of isolating touch from the milieu of other maternal provisions (Fairhurst et al., 2014; Hofer, 2006; Murray et al., 2016; Shibata et al., 2012; Underdown et al., 2010; Weaver et al., 2004).

To begin to address these questions, an experimental design is necessary. Nonhuman primate (NHP) models offer us the opportunity to systematically study the influence of early experiences on development (Bard et al., 2014). Here, we explored whether tactile stimulation, administered to infant macaques throughout the first four postnatal weeks, may have later behavioral effects in the first three months of life. Macaque monkeys, in particular, are an ideal population to test these predictions for a number of reasons. Maternal touch is highly conserved across mammalian species (Feldman, 2011) and macaques are a highly social species with strong mother-infant bonds characterized by complex face-to-face mother-infant interactions in the first weeks of life (Ferrari et al., 2009) and patterns of attachment that are very similar to humans (Suomi, 1999, 2005). As in humans, early physical interactions and contact comfort are important for infant macaque development (Harlow and Zimmermann, 1959). In addition, rhesus mothers, like in humans, show variability in their 'mothering' style, including variability in their tactile contact with infants (Maestripieri, 1994; Maestripieri et al., 2007). Second, studies in macaques allow heightened experimental control that is difficult to achieve in humans (Drury et al., 2016; Gerson et al., 2016). While previous studies in macaques have focused on how maternal behaviors—such as mutual gaze—impact infants' later social development (Dettmer et al., 2016b), here we focused on the influence of social touch on infants' later interactions with a wider variety of environmental stimuli, including both social and non-social interactions.

To these ends, we investigated in newborn macaques the impact of social touch on a number of behaviors that are representative of different domains in development, such as emotionality, stress-reactivity, memory, novelty seeking, and social interest. We carried out an experiment with macaque infants who were randomly assigned to receive extra handling—which included removing infants from their home cages, holding them, and stroking them in multiple daily 5-min sessions—for the first four weeks of life, hereafter referred to as *handling*. We then recorded infants' behaviors during exposure to a novel environment at 2 weeks of age and exposure to a novel object at 3 weeks of age, common assessments of temperament in human children and NHP species, with individuals who are more reactive (or behaviorally inhibited) less likely to approach novelty (e.g., Clarke and Boinski, 1995; Fox et al., 2015). We also tested infants' working memory for social and nonsocial stimuli at 6 weeks of age (adapted from Noland et al., 2010) and infants' reactions to novel and familiar people at 12 weeks of age (adapted from Gottlieb and Capitanio, 2013). Given that social touch in human children is correlated with decreased arousal (Jean et al., 2014) and increased sociality (Brauer et al., 2016; Reece et al., 2016), we predicted that social touch would regulate infant monkeys' behavioral reactions to unfamiliar social and nonsocial stimuli, improving memory and increasing exploratory behaviors. We also investigated whether adding communicative facial gestures while holding and touching infants would further increase their sociality and reduce fear reactions.

2. Materials and methods

2.1. Subjects

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Animal Care and Use Committee approved the following procedures. The study was conducted in accordance with the Guide for the Care and Use of Laboratory Animals and complied with the Animal Welfare Act.

We tested 48 rhesus macaques (*Macaca mulatta*) from three cohorts of healthy infants, born in 2012 (n = 20), 2013 (n = 18), and 2014 (n = 10). On the day of birth, infants were separated from their mothers and reared in a nursery for unrelated studies. Infants were individually housed in incubators (51 cm × 38 cm × 43 cm) for the first two weeks of life and in larger cages (61 × 61 × 76 cm) thereafter, for the duration of the study (through 12 weeks of age). All housing arrangements contained an inanimate fleece surrogate, loose pieces of fleece fabric, and various plush, plastic, and rubber toys. For the first month, human caretakers were present for 13 h each day, and interacted with infants every two hours for feeding and cleaning. Infants were bottle fed Similac formula. Starting at 16 days of age, infants were additionally offered Purina LabDiet 5045 High Protein Monkey Diet chow. Lights were on from 7:00 to 21:00. For unrelated studies, infants were assigned to one of two rearing conditions when the youngest infant of the group turned 36 days: 28 infants were reared with three to four peers (i.e., peer-reared); 20 infants were reared with their surrogate (i.e., surrogate-reared) and were given 2-h play sessions with three to four peers each weekday (for details: Simpson et al., 2016a).

2.2. Materials and procedures

We videotaped the novel object, novel person, and working memory tasks (Sony Digital Video HDR-CX560V) and scored infants' behaviors offline, frame-by-frame (33 frames per second) using either The Observer XT (Noldus) or VirtualDub software (virtualdub.org). The novel environment task was live-scored via focal animal sampling with JWatcher software (www.jwatcher.ucla.edu).

2.2.1. Intervention

We randomly assigned newborns to either (A) extra exposure to handling and face-to-face interactions, including mutual gaze and lipsmacking (n = 16, 8 females), (B) extra handling without face-to-face interactions (n = 15, 8 females), or (C) standard rearing, with no additional handling (n = 17; 5 females). Infants in groups A and B were removed from their home cages and transported to an adjacent test room by familiar care takers, starting on the first day of life and continuing for the first four weeks (see timing schedule below). For group A, the face-to-face interactions consisted of human caregivers holding and swaddling each infant, gently orienting the infant toward the caregivers' face if the infant turned away, and engaging in communicative exchanges using lipsmacking gestures (LPS)—a natural, affiliative expression involving the rapid opening and closing of the mouth—directed at infants in 5-min sessions. In each session, a human caregiver directed LPS gestures at the infant for 5 s, followed by 10 s of eye contact, then a 15 s break period in which the human would look away from the infants. This sequence was repeated 10 times in the 5-min session, and was designed to allow infants to imitate the gesture, as they have been shown to do (Ferrari et al., 2006; Simpson et al., 2014), following natural mother-infant facial interactions (e.g., Dettmer et al., 2016a; Ferrari et al., 2009). Infants in group B (extra handling only) were held at the same times and for the same durations as the face-exposure group, but did not receive the face-to-face interactions. For this group, caretakers' faces were covered so infants could not see them.

Infants in the standard-rearing group did not see facial gestures and did not receive any handling beyond basic care and other unrelated experimental procedures. We balanced the number of infants from each rearing group in each of our intervention groups: Extra handling groups (A and B) had 18 peer-reared (58%) and 13 surrogate-reared infants (42%); Standard-reared group (C) had 10 peer-reared (59%) and 7 surrogate-reared infants (41%).

We intentionally decreased the intervention rates gradually rather than having an abrupt end for two reasons. We wanted to approximate natural mother-infant interactions and to minimize potential infant distress that may be caused by an abrupt end to handling. Groups A and B received interventions on the following schedule, always following feeding. In the first 2 weeks of life: 4 times per day on weekdays (~10 a.m., 12 p.m., 2 p.m., 6 p.m.), twice per day on weekends (~10 a.m., 12 p.m.); in the third week of life: 3 times per day on weekdays (~10 a.m., 12 p.m., 2 p.m.), once per day on weekends (~10 a.m.); in the fourth week: twice per day on weekdays (~10 a.m., 2 p.m.), once per day on weekends (~10 a.m.).

2.2.2. Novel environment task

At 2 weeks of age (M = 14 days, SD = 1, range = 13-17 days) infants were re-housed from their home incubator to a larger home cage. A trained observer live scored the infant's behaviors twice, for 5 min each, once immediately upon placement into the large cage, then a second time 3 h later. Since we detected no differences among the intervention conditions between these time points (i.e., no interactions between intervention group and time; see Table S1), we combined both times into an overall score for the first day in the novel cage.

We scored four behaviors: locomotion, exploration, self-mouthing, and sleeping. Exploration was defined as any manual, pedal, or oral examination, exploration, or manipulation of the physical environment, such as foraging through the floor grate or on the foraging board. Locomotion was defined as any self-induced change in location of the self, including changes in location through walking, running, dropping from ceiling to floor, rolling, hopping on all fours, and bouncing around the cage. Self-mouthing was defined as sucking (not biting) at any bodily appendage or own fur, including the thumb. Sleep was defined as the infant had his or her eyes closed and was not active. Inter-rater reliabilities were assessed between new and established coders until inter-rater agreement was 80% or higher for 5 consecutive sessions (5-min each). Reliability was calculated via JWatcher software (http://www.jwatcher.ucla.edu/). Training occurred prior to the actual assessments. Data were not collected on two infants, both in group B, due to technical malfunctions.

2.2.3. Novel object reach-grasp task

We measured infants' reach-grasp motor behavior in a novel object task. At 3 weeks of age (M = 22 days, SD = 1; range = 21–27 days), infants participated in a novel ball reach-grasp task (adapted from Sclafani et al., 2015). Infants were removed from their home cage and taken to a testing room in which they were positioned with their feet on a platform, with a caregiver supporting their chest. Small, unfamiliar balls were presented to infants at eye-level (see Fig. 1 in Sclafani et al., 2015), and we measured infants' latency to approach and make physical contact with them. The balls were attached to sticks and presented through a small window to infants by one experimenter (out of view) while the second experimenter held the infant in position on a platform. There were four types of trials: (1) small ball in near space, (2) small ball in far space, (3) large ball in near space, and (4) large ball in far space. Balls of two sizes (7 mm and 21 mm diameters) were presented in peripersonal/near (within arm's reach) and extrapersonal/far space (just outside of arm's reach). Infants could locomote to reach balls that were outside of their immediate reach. Each type of trial was presented twice per session, in a predetermined counter-balanced order, so that infants were presented with a total of 8 trials, each lasting 20 s. If the infant interacted with the ball, the experimenter let the infant manipulate the ball for few seconds, after which the ball was removed. If the infant made no interaction attempt within 20 s, the trial ended and the ball was removed. Trials without tactile contact were excluded from the reaction time analysis.

Our three measures were latency, number of attempts, and accuracy (proportion of error-free reach-grasps). Latency and number of attempts capture infants' interest in the novel objects. Accuracy captures infants' motor skill in reaching for the novel object. Latency was computed from the time the infant first looked at the object to the time of first physical contact between the infant and the ball (usually with the hand, but sometimes with the arm or mouth). An attempt was defined as an infant moving towards the ball with any appendage (hand or mouth), and grasping for it, including unsuccessful attempts. A grasp was considered successful when infants contacted the ball either with the mouth or the fingers flexed around the target. Attempts that did not result in contact were typically due to reach-grasp errors, which included misjudging the height of the ball (i.e., reaching above or below the actual ball location), and misjudging the distance of the ball (i.e., reaching not far enough or too far beyond the ball). Two observers analyzed all videos frame-by-frame offline; there were no cases of disagreement during coding (for details, see Sclafani et al., 2015).

2.2.4. Working memory task

At 6 weeks of age (M = 42 days, SD = 2, range = 39–49 days), infants participated in a modified peek-a-boo game (for details see Simpson et al., 2017; adapted from Noland et al., 2010). Our testing apparatus consisted of a black cloth screen (75-cm-wide × 120-cm-tall) draped to the floor, creating three target-zones in which stimuli could appear. In the middle of the screen, at eye-level for the infant (90 cm from the ground) a video camera filmed the infant through a 10-cm circular opening. A manually operated central distractor—a metal cup filled with colorful plastic beads, with the end secured with plastic wrap and a rubber band, which produced a rattle noise when shaken—was positioned above the camera. A nonsocial stimulus—an array of reflective bows with rattling beads attached, covered in clear plastic—was rotated, producing both sound and movement. An experimenter served as the social stimulus, LPS at the infant, therefore producing both sound and movement. The social stimulus was always the same person and the nonsocial stimulus was always the same object. All infant groups (A–C) were equally familiar with both stimuli.

At the start of a session, an experimenter held the infant in a comfortable position (i.e., swaddled in a pad or clinging to a fleece surrogate), seated in front of a black curtain, approximately 65 cm away. A second experimenter (the model) served as the source of the stimuli. First, a target appeared in one of three locations: at the top, right, or left of the screen. It produced a "call" to the infant (LPS or rattle). The call continued until the infant oriented to it. When the infant oriented to the target, the infant was rewarded with either LPS or by getting to watch the toy continue rattling for approximately 2 s. After that, the target disappeared behind the curtain. At that time, the distractor jingled to orient the infant toward the center of the screen (manually operated by the experimenter behind the curtain), then stopped once the infant looked for approximately 1 s. Nothing happened in the following 5 s, during which time the infant was videotaped to measure the infant's gaze toward the three target locations. After 5 s, the next trial began.

Working memory was measured by examining the proportion of times the first-look was to the correct location (the location where the target most recently appeared prior to the delay), out of the total number of valid trials. A trial was considered valid if the infant looked to the target, then to the distracter, then oriented to one of the three locations. If the infant did not look to one of the three target locations, the trial was not considered valid, and was not included in the analysis. A session was only included if infants completed at least 3 trials in that session. Infants participated in two test sessions with 12 trials each. Within each session, one of two targets appeared in each of the three locations, in a randomized predetermined order, such that no more than

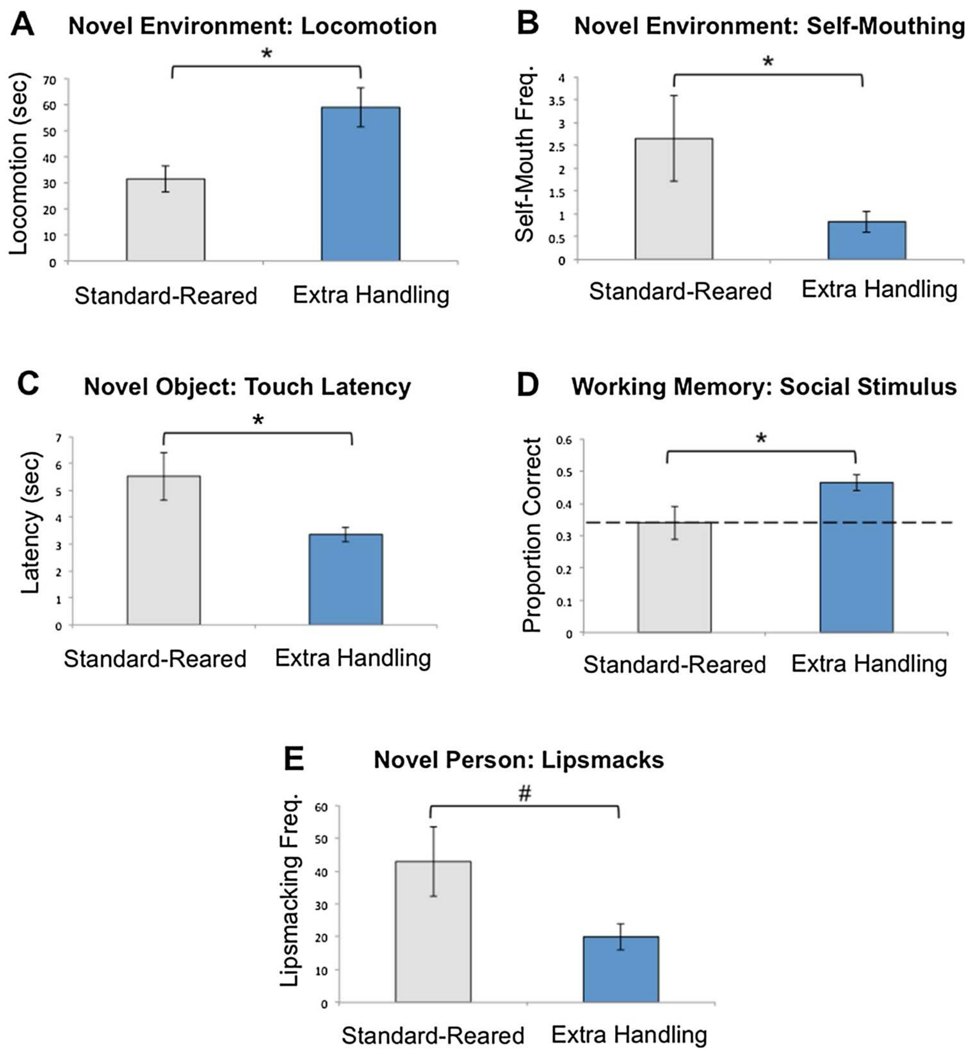

Fig. 1. The four tasks revealed effects of extra handling, with the extra handled infants exhibiting: (A) greater locomotion and (B) less self-mouthing in a novel environment at 2 weeks, (C) faster latencies to touch novel objects at 3 weeks, (D) better working memory at 6 weeks, and (E) less lipsmacking in response to a novel person at 12 weeks. Light gray bars reflect infants who received no additional handling (standard-reared). Blue bars reflect infants who received additional handling (handling only and face-to-face + handling groups combined). Across all tasks, standard-reared infants differed from each group of handled infants, $^{*}ps < 0.05$, $^{\#}p = 0.056$. Error bars reflect standard error of the mean. Dashed line indicates chance (graph D). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

two trials in a row were in the same location. Two additional infants (one group A, one group C) were tested but excluded due to failure to complete at least 10 test trials (i.e., inattention). Out of 24 total trials, infants completed 10–24 trials ($M = 17$, $SD = 4$). The number of trials excluded did not differ between conditions (social, nonsocial) or our groups (handled, standard-reared), $ps > 0.05$. Inter-observer reliability was computed with Cohen's Kappa (κ) between two coders, on a random selection of 20% of the videos and agreement was high: first anticipatory looks left (κ = 0.91), right (κ = 0.90), and up (κ = 1.0) (details: Simpson et al., 2017).

2.2.5. Social interaction task

At 12 weeks of age ($M = 87$ days, $SD = 3$; range = 83–100 days), infants participated in a human interaction task across two days, once with a familiar human and once with a novel human (Simpson et al., 2016b). As part of this task, the human model was seated in front of the infant's home cage, 30 cm from the cage front, and made eye contact with the infant. During the first 2 min of the test, the human model only looked at the infant. During the second 2 min of the test the human placed a hand on the infant's feeder box, located just outside of the infant's home cage, while continuing to maintain eye contact. Sessions were videotaped with only the infant in view. In total, each session was 4 min.

We were interested in two social behaviors: LPS frequencies, which outside of mother-infant interactions can indicate uncertainty, anxiety, or submissive behavior (Bethea et al., 2004), and social attention (total time looking at the person). We were unable to collect data from one infant (group C) for this task. Inter-observer reliability was computed between two independent observers who scored frame-by-frame from videos offline. Reliability was high for both behaviors, $r > 0.90$, $p < 0.001$ (for details, see Simpson et al., 2016b).

3. Results

Preliminary analyses revealed no differences between the face-to-face and handling-only groups across any of these tasks (see Table S2 for details); therefore, to increase statistical power, we combined groups A and B and compared them to the standard-reared group (C) who did not receive extra handling. We also confirmed there were no effects of peer-rearing groups: peer-reared vs. surrogate-peer-reared ($ps > 0.05$). Independent samples t tests compared handled infants to standard-reared infants for all behaviors within each task (Table 1). All analyses were two-tailed. We checked for violations of the homogeneity of variance assumption with Levene's test and report adjusted degrees of freedom where appropriate.

3.1. Nonsocial interactions: novel environment and novel object

First, we explored whether infants' exploratory and anxious behaviors in the novel environment task—locomotion and self-mouthing—were correlated with their exploratory and approach behaviors in the novel object task—number of touch attempts and touch latency.

Table 1
Presents the four tasks and the behaviors of interest in each task, comparing standard-reared and extra handled infants.

Task	Behavior	Operational Definition	Standard-Reared *M (SD)*	Extra Handled *M (SD)*	*t*	*df*	*p*	*d*
Novel Environment	Exploration	Duration (sec) exploring environment	94 (80)	144 (87)	1.17	44	0.250	0.36
	Locomotion	Duration (sec) moving around environment	31 (21)	59 (36)	2.95	44[a]	0.005*	0.78
	Self-Mouthing	Frequency of self-mouthing (e.g., thumb sucking)	2.65 (3.84)	0.77 (1.17)	2.35	44	0.023*	0.72
	Sleeping	Duration (sec) eyes closed, inactive	115 (133)	22 (80)	1.82	44	0.076[a]	0.55
Novel Object	Touch Latency	Latency to touch object (sec)	5.53 (3.70)	3.36 (1.57)	2.31	19[a]	0.032*	0.86
	Number of Attempts	Total Frequency of Reach-Grasp Attempts	7.35 (1.27)	7.81 (0.54)	1.40	19[a]	0.177	0.52
	Accuracy	Proportion of error-free grasps out of total attempts	0.72 (0.20)	0.76 (0.17)	0.74	46	0.463	0.22
Working Memory	Accuracy for Social	Proportion of correct anticipatory looks to person	0.34 (0.20)	0.47 (0.14)	2.41	44	0.020*	0.76
	Accuracy for Nonsocial	Proportion of correct anticipatory looks to object	0.49 (0.16)	0.47 (0.16)	0.44	44	0.664	0.14
Social Interaction	Attention to novel person	Duration (sec) looking at novel person	50 (36)	45 (26)	0.47	45	0.638	0.75
	LPS to novel person	Frequency of Lipsmacking to novel person	43 (42)	20 (22)	2.44	45	0.019*	0.15
	Attention to familiar person	Duration (sec) looking at familiar person	42 (21)	42 (29)	0.024	45	0.981	0.007
	LPS to familiar person	Frequency of Lipsmacking to familiar person	11 (13)	6 (8)	1.589	45	0.119	0.489

Note. Means (*M*), standard deviations (*SD*), independent samples *t* tests, degrees of freedom (*df*), and Cohen's *d*, comparing standard-reared infants (Group C) to extra handled infants (Groups A and B combined) within all four tasks.

* $ps < 0.05$.

[a] Adjusted due to significant Levene's Test.

Bivariate correlations revealed there was consistency in how infants performed, with positive correlations between self-mouthing and touch latency, $r = 0.313$, $p = 0.034$, $n = 46$, and a trend of a correlation between locomotion and number of touch attempts, $r = 0.272$, $p = 0.067$, $n = 46$. However, there were no other relations ($ps > 0.05$), suggesting these tasks may be tapping different proclivities, so we decided to analyze these tasks separately.

In the novel environment task, extra handled infants exhibited higher rates of locomotion compared to standard-reared infants, $t(44) = 2.95$, $p = 0.005$, $d = 0.78$, (Fig. 1A), and less self-mouthing, $t(44) = 2.35$, $p = 0.023$, $d = 0.72$ (Fig. 1B). Extra handled infants also exhibited a non-significant trend of sleeping less than compared to standard-reared infants, $t(44) = 1.82$, $p = 0.076$, $d = 0.55$. There were no differences between infants with extra handling and standard-reared infants for exploration, $t(44) = 1.17$, $p = 0.25$.

In the novel object task, extra handled infants and standard-reared infants were equally likely to attempt to reach-grasp the objects, $t(19) = 1.40$, $p = 0.177$ (Table 1). However, standard-reared infants were slower to touch the novel objects compared to extra handled infants, $t(19) = 2.31$, $p = 0.032$, $d = 0.34$, Fig. 1C. The extra handling group and the standard-reared group did not differ in their accuracy (proportion of error-free reach-grasps), $t(46) = 0.74$, $p = 0.463$.

3.2. Social interactions: working memory and novel person

First, we explored whether infants' working memory for the social stimulus and social behaviors in the novel person task—social attention and LPS—were associated. However, there were no associations between infants' working memory and their behaviors directed at novel or familiar people, $ps > 0.05$; therefore, we analyzed each of these tasks separately.

In the working memory task, infants who were handled exhibited more correct anticipatory looks for the social stimulus, compared to standard-reared infants, $t(44) = 2.41$, $p = 0.020$, $d = 0.76$, Fig. 1D. However, there were no differences across rearing groups for the nonsocial stimulus, $t(44) = 0.44$, $p = 0.664$ (Table 1). One sample *t* tests compared each infant group's performance to chance, which revealed that both groups were above-chance for the nonsocial stimulus (standard-reared: $t(14) = 3.98$, $p = 0.001$, $d = 1.03$; handled: $t(30) = 4.79$, $p < 0.001$, $d = 0.86$), but only handled infants were above chance for the social stimulus, $t(30) = 5.07$, $p < 0.001$, $d = 0.91$, Fig. 1E.

In the social interaction task, when the person was familiar, there were no differences in social attention between extra handling and standard-reared infants, $t(45) = 0.024$, $p = 0.981$ (Table 1). Extra handled infants also did not differ from standard-reared infants in their LPS to the familiar person, $t(45) = 1.60$, $p = 0.119$. When the person was novel, however, infants who were handled showed a non-significant trend of LPS less compared to standard-reared infants, $t(20) = 2.03$, $p = 0.056$, $d = 2.44$, Fig. 1E. There were no differences in attention to the novel person between extra handling and standard-reared infants, $t(45) = 0.47$, $p = 0.638$.

4. Discussion

We used an animal model to experimentally test the hypothesis that social touch supports infants' emotional, cognitive, and social behaviors in the first months of life. We found that neonatal handling altered infant macaque behavior across four tasks involving interactions with both social and nonsocial stimuli. Monkey infants who received extra handling in the neonatal period subsequently demonstrated more advanced motor, social, and cognitive skills—particularly in contexts involving novelty—in the first three months of life. While replications with larger samples are clearly needed to confirm these findings, we think this study provides important preliminary evidence to suggest the critical role of social touch in the first postnatal period as a moderator of early infant behavior.

Extra neonatal handing increased infants' locomotion and decreased stress-related behaviors (self-mouthing—e.g., thumb or finger sucking—a self-comforting behavior), in a novel environment at 2 weeks of age. Infants who had extra handling were faster to approach and touch a novel object at 3 weeks of age, compared to infants without extra handling. These results are consistent with previous studies in animals. For example, piglets that received extra handling showing higher rates of locomotion and exploration compared to a control group (Zupan et al., 2016). The present results are also consistent with previous studies that suggest that early mother-infant interactions may regulate infants' anxiety, fear, and exploratory behavior. For example, in humans, maternal attentiveness and stimulation predicted exploratory behavior in infants (Belsky et al., 1980; Rubenstein, 1967). These reports suggest that maternal sensitivity in general may regulate infant exploration; however, previous studies did not determine to what extent touch specifically played a role. While the present findings need to be replicated across other species—including humans—they nonetheless suggest that neonatal touch may decrease stress-related behaviors in response to novelty.

We also found that social touch influenced infants' later social behaviors and cognition, influencing infants' working memory for a social (but not a nonsocial) stimulus, at 6 weeks of age. In this task, all infants performed relatively well, with the exception of standard-reared infants in the social condition. It seems that there is something about the social stimulus that was more difficult for infants to remember when they did not receive extra handling. Extra handled infants also exhibited lower rates of LPS in the presence of a novel (but not a familiar) person at 12 weeks of age, suggesting they may have been less fearful or less anxious compared to standard-reared infants. There were no other differences in social behavior, as infants in both groups were equally socially attentive.

A similar study in chimpanzees compared two types of early rearing in a controlled experiment, with one group receiving "responsive care" and another receiving "standard-care" (Bard et al., 2014). The responsive care group had a greater number and more time with caregivers who were trained to interact in species-typical ways. In contrast, in the standard-care group, caregivers met infants' basic needs but did not provide additional interactions, and infants therefore had to learn from their peers to develop species-typical behaviors. In the first year of life, social cognitive skills were more advanced in the responsive care group, particularly for joint attention and cooperation. These findings are consistent with those of the present study that suggest experimental manipulations to early social environments can have a profound influence on infant social and cognitive development and highlight the importance of considering early postnatal social experiences in models of primate social cognition (Bard et al., 2014).

The present findings are also consistent with those in human adults, suggesting that social touch can have wide-ranging positive effects on social behavior. For example, in adults, even brief, unintentional touches (e.g., hand-to-hand) can increase how much we like that person and increase positive social behaviors towards that person (for a review: Hertenstein et al., 2006). The present findings are also consistent with studies in human children. For example, children who are touched more by their mothers later appear more socially attentive (Reece et al., 2016) and exhibit differences in brain resting activity and connectivity in regions associated with mentalizing (Brauer et al., 2016). Moreover, preterm infants who are held for longer durations exhibit higher quality mother-infant interactions in the first year of life (Korja et al., 2008). However, across all of these human studies, it is difficult to determine causality; to what extent did the infants contribute to the maternal behavioral interaction and to what extent did the mothers drive the interactions? The present study highlights the importance of true experiments with animal models to tease apart these contributions and suggests that the handling itself may be, to some extent, causing individual differences in infant social behavior.

Compatible with the above mentioned interpretation is the hypothesis that extra-handling is beneficial for infants because it could provide extra stimulation through low threshold mechanoreceptive C tactile afferents (CT). CT fibers—activated through slow stroking—seem to mediate the affective components of touch (Vallbo et al., 1999) and to produce several positive effects in rodent models, including analgesia and reduced anxiety (Menard et al., 2004; Olausson et al., 2010). In humans, mothers often use this type of touch, gently caressing their infants with affectionate, slow, gentle strokes (Ferber et al., 2008). One study reported that 9-month-old human infants, like adults, appear particularly fond of CT-targeted touch, based on their behavioral and physiological responses (Fairurst et al., 2014). Another study of younger babies—1.5 to 3.5 months old—reported that, during a face-to-face interaction, when infants were touched, compared to when they were not touched, infants made more eye contact, smiles, and vocalizations, and spent less time crying (Peláez-Nogueras et al., 1996). While we did not specifically test the influence of this form of social touch here, we think such studies are an important future direction, given that different types of touch may have different behavioral effects on infants. In addition, parents touch some infants more than others; for example, male infants are touched more than female infants (Lewis, 1972). The types of caregiver touch, and the consequences of this differential treatment are currently unclear.

A recent study observed wild rhesus macaque infants in the first 14 weeks after birth and found that, in addition to mothers, an average of 13 other group members handled infants (Dunayer and Berman, under review). They also reported that infants bonded more strongly with individuals who handled them more often. While it is likely that infants reared by their mothers receive greater amounts of handling than those provided in the present study, the present study nonetheless has a number of advantages that complement naturalistic observations. A notable strength of the present study is that it is experimental and we were therefore able to single out specific aspects of the early rearing environment while controlling all other variables, which cannot be teased apart in naturalistic studies of mother-infant interactions.

A limitation of the present study is that handling necessarily included multiple forms of stimulation—including both touch and proprioception—so it is difficult to know if one in particular (or their combination) contributed to the behavioral effects observed here. Future research should tease apart specific types of touch, such as to specific body parts, or specific types of stroking (e.g., massage compared to gentle stroking). As mentioned above, some of the effects we found in the present study could be mediated by the activation of these CT fibers. However, unlike other touch receptors, these are located all over the body and especially in places with hair—concentrated on top of the head, upper torso, arms and thighs—but not glabrous (hairless) skin, e.g., lips, palms of the hands, and soles of the feet (e.g., Olausson et al., 2002). It is therefore likely that gentle touch activates differently CT fibers depending on the pattern of body that is stimulated.

Another potential interpretation of these results is that handling infants in the intervention may have prepared them for tasks in which they were handled later in development. While this interpretation is consistent with the novel object and working memory tasks, both of which included familiar caregivers holding infants, it cannot account for the results of the novel environment or novel person tasks, which took place in infants' home cages, without any handling. Therefore, we think it is unlikely that the general pattern of results can be attributed to simply becoming more comfortable to being held. Moreover, all infants were held daily, as part of routine infant care, therefore all infants were relatively comfortable with coming out of their home cages and being held by familiar caregivers.

We found no evidence that face-to-face interactions—including mutual gaze and LPS—influenced infants' sociality, cognition, or reactions to novelty. At first, this seems surprising, given that our previous work demonstrated that infant monkeys who received more face-to-face interactions, compared to infants who did not receive these additional interactions, were more likely to imitate facial gestures at one week of age (Simpson et al., 2014) and were more socially attentive and engaged at 2–5 months of age (Dettmer et al., 2016b). There are a few reasons why we may not have found effects of facial interactions in the present study. One possibility is that the effects of facial interaction were small, and therefore the present study was insensitive for detecting these effects. Another possibility is that, for face-to-face interactions to support development in a meaningful and lasting way, they need to be ongoing, beyond the newborn period. Natural face-to-face interactions between macaque mothers and infants continue well beyond the first month of life (Dettmer et al., 2016a). In contrast, in the present study the intervention only lasted for the first 4 weeks, so it is possible that continuing the intervention for longer may have resulted in more lasting effects. A third possibility is that face-to-face interactions and touch might support infant development in different ways, with facial interaction more important for social competence and engagement, whereas touch may be more involved in emotional regulation as it appeared to reduces arousal/anxiety, thereby promoting infant approach of novelty more generally (social and non-social).

The apparent lack of effects of face-to-face interactions may also be due to natural changes in the modalities with which infants interact with caregivers, as they get older. In natural mother-infant interactions there is a shift with age, in the extent to which mothers interact with their infants through tactile vs. facial modalities. For example, in chimpanzees, time spent cradling infants is inversely related to the amount of mutual gaze (Bard et al., 2005; Okamoto-Barth et al., 2007). Similarly, in human infants, there is greater mutual gaze with mothers when not in tactile contact (Lavelli and Fogel, 2002). Similarly, as macaque infants develop, after the first month of life they spend less time in tactile contact with their mothers (Hinde et al., 1964), but continue to engage in facial interactions when not in tactile contact (Dettmer et al., 2016a; Ferrari et al., 2009). In sum, it is not that facial interactions do not support development—indeed they are of utmost importance—but rather, being held appears to have larger or more long-lasting effects beyond the newborn period, even when these touch interactions cease.

Another intriguing future direction is to explore individual differences in infants' reactions to touch, as they may be indicative of different developmental trajectories (Kaiser et al., 2016; Scheele et al., 2014). There are also individual differences in the extent to which infants appear to enjoy social touch (Schaffer and Emerson, 1964), and infants who like to be touched also tend to have primary caregivers who like to be touched (Fairhurst et al., 2014). It is unclear, however, whether this association is due to infants' experiences with touch or the heritability of this sensitivity (Morrison et al., 2011).

5. Conclusions

The present study highlights the importance of studying the behavioral effects of caregivers' physical closeness with infants in the first weeks of life. Maternal touch is not a uniform construct; there are different types that serve different functions (Jean et al., 2009). While future studies are necessary to determine whether there may be similar effects of social touch in human and other NHP neonates, as well as the precise developmental timing in which these experiences are most important, these data suggest that there is early plasticity in these systems, which may be supported by social touch. Such findings offer promising possibilities for designing early interventions for high-risk infants, including those who are premature (Maitre et al., 2017), born to underage mothers (Williams, 2017), or at heightened risk for developing disorders (e.g., autism; Field et al., 1997; Voos et al., 2013). Experimental studies in NHP are important for understanding human infant social and cognitive development and the environments that best help infants to meet their full potential (Gerson et al., 2016; Weiss and Santos, 2006). Further research is warranted to examine infants' behavioral and physiological changes during and following different types of touching, including short-term and long-term effects of acute and chronic touch, as well as the extent to which infants play active roles in mutual touch interactions.

Author contributions

E.A. Simpson, A. Paukner, V. Sclafani, and P.F. Ferrari designed the studies. E.A. Simpson, V. Sclafani, and A. Paukner carried out the intervention. E.A. Simpson, S.S.K. Kaburu, and V. Sclafani collected the data. E.A. Simpson and V. Sclafani coded the videos. E.A. Simpson analyzed the data and drafted the manuscript. All authors approved the final version of the manuscript for submission.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.dcn.2017.07.010.

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