ARCHIVAL REPORT

Maternal-Preterm Skin-to-Skin Contact Enhances Child Physiologic Organization and Cognitive Control Across the First 10 Years of Life

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Background: Maternal-newborn contact enhances organization of the infant's physiological systems, including stress reactivity, autonomic functioning, and sleep patterns, and supports maturation of the prefrontal cortex and its ensuing effects on cognitive and behavioral control. Premature birth disrupts brain development and is associated with maternal separation and disturbances of contact-sensitive systems. However, it is unknown whether the provision of maternal-preterm contact can improve long-term functioning of these systems.

Methods: We used the Kangaroo Care (KC) intervention and provided maternal–newborn skin-to-skin contact to 73 premature infants for 14 consecutive days compared with 73 case-matched control subjects receiving standard incubator care. Children were then followed seven times across the first decade of life and multiple physiologic, cognitive, parental mental health, and mother–child relational measures were assessed.

Results: KC increased autonomic functioning (respiratory sinus arrhythmia, RSA) and maternal attachment behavior in the postpartum period, reduced maternal anxiety, and enhanced child cognitive development and executive functions from 6 months to 10 years. By 10 years of age, children receiving KC showed attenuated stress response, improved RSA, organized sleep, and better cognitive control. RSA and maternal behavior were dynamically interrelated over time, leading to improved physiology, executive functions, and mother–child reciprocity at 10 years.

Conclusions: These findings are the first to demonstrate long-term effects of early touch-based intervention on children's physiologic organization and behavioral control and have salient implications for the care practices of premature infants. Results demonstrate the dynamic cascades of child physiological regulation and parental provisions in shaping developmental outcome and may inform the construction of more targeted early interventions.

Key Words: cortisol, executive functions (EF), Kangaroo Care, mother–infant relationship, longitudinal studies, premature infants, respiratory sinus arrhythmia (RSA)

The close contact between mother and young is a defining feature of mammals. The mother's physical presence and provision of species-typical postpartum behavior supports growth and thriving of mammalian young (1,2). Research in nonhuman mammals, mainly rodents, has shown that early maternal contact is accompanied by biobehavioral processes that promote physiologic and behavioral development and have an impact on the infant's brain systems that manage stress and enhance social adaptation (3,4). Early maternal deprivation, on the other hand, exerts lifelong negative effects on offspring (5). Being a mammal therefore implies that the brain is not fully formed at birth, and maturation of systems that enable adaptive functioning in the world are gradually acquired through close contact with an alert, responsive mother, albeit to varying degrees across species (6).

Not all systems are equally susceptible to maternal contact or deprivation (7). The hypothalamic-pituitary-adrenal (HPA) axis,

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which regulates cortisol production and the body's response to stress, organizes during an early period of neuroplasticity in response to maternal contact. Maternal licking and grooming alters glucocorticoid receptor gene expression in the rat pup's hippocampus, favorably enhancing stress regulation in the adult animal (8). Handled rats taken out of the home cage for several minutes daily display lower cortisol stress response as adults, possibly due to the increase in maternal behavior following return to the home cage (5,9). The autonomic nervous system, which regulates heart rhythms, matures through thermal, tactile, and nutritive stimuli provided by the mother's body (3), and the sleep-wake cycle is shaped by maternal physiologic and behavioral rhythms (10). These systems, which regulate the body's response to changing external demands, provide support to complex cognitive and social skills and moderate the ongoing transactions between the organism and its environment. Such environment-sensitive systems mature in the context of finely tuned synchronous adaptations between the infant's homeostatic states and social signals and the mother's moment-by-moment physiologic and behavioral response (11,12).

Premature birth is a major health care problem worldwide, associated with early and persistent maternal separation. Approximately 12% of infants in industrial societies and substantially more in developing countries are born annually at various degrees of prematurity, leading to increased mortality, morbidity, and measurable developmental delays (13). Although advances in medical technology enable the survival of smaller and sicker infants, many require months of intensive care that preclude full maternal–infant bodily contact (14). Premature birth disrupts brain development, leading to suppressed neurogenesis (15), decreased myelination (16), and white matter disturbances (17),

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and brain anomalies often persist into later childhood and adolescence (18,19). The combination of brain immaturity and maternal separation exerts long-term negative effects on development, particularly on systems sensitive to maternal separation. Prematurely born children exhibit disorganized sleep patterns (20,21), disturbances in HPA reactivity (22,23), and lower baseline respiratory sinus arrhythmia (RSA), indicating less functional autonomic nervous system (24,25). Abilities collectively referred to as executive functions (EF), which tap working memory, cognitive control, and mental flexibility and draw on the postnatal maturation of the prefrontal cortex (26), are also disturbed in premature children (27,28). Finally, premature birth disrupts the mother-infant bonding process, and mothers report greater stress, anxiety, and depression (29,30) and exhibit less optimal mother-infant interactions (31-33). Because development evolves from the cascading interactions of infant biological dispositions and parental provisions, difficulties in physiologic regulation and parenting behavior enhance each other over time, leading to maladaptive outcome (34,35). However, although ecological and multilevel developmental models describe such mutually influencing cascades as causal factors in the consolidation of early risk into childhood psychopathology (36), few studies tested physiological, cognitive, parental mental health, and mother-child relational factors across long epochs beginning at birth in relation to psychopathology and wellness.

Maternal-infant bodily contact may ameliorate some of the difficulties observed in contact-sensitive systems among premature

infants. The Kangaroo Care (KC) intervention, initially developed in Bogota, Columbia, to cope with a lack of incubators, enables premature infants to maintain body heat through skin-to-skin contact with the parent's body (37). Research has demonstrated that KC is safe (37) and contributes to neuromaturation in premature infants during the neonatal period. Newborns receiving KC showed better autonomic maturity (38), electroencephalogram complexity (39), pain response (40), and physiologic stability (41). Similarly, KC improved mother–infant interaction (42,43), maternalinfant bonding (44), and maternal mood (42) in early infancy. Other touch-related interventions, such as massage, yielded similar shortterm improvements, including weight gain, mother–infant interactions, and maternal mood (45–48). However, it is unknown whether any touch-based intervention carries lasting effects on children's development beyond infancy.

In the current study, we applied the KC intervention to premature infants and followed children seven times across the first decade of life, repeatedly testing physiologic, cognitive, mother–child relational, and parental mental health factors (Figure 1). Consistent with models on the dynamic cascades underpinning normative and pathologic development, we expected that the short-term gains reported for infant neuromaturation and mother–infant bonding following KC would enhance each other over time, leading to lasting gains. We hypothesized that 1) infants receiving KC would show more optimal physiologic functioning in contact-sensitive systems, including autonomic functioning, sleep organization, and HPA reactivity; 2) mother–child interactions would be more optimal following KC; 3) children

Period	Outcomes							
Neonatal								
Term Age	Physiological Processes * Autonomic Functioning * Sleep Organization	Parental Mental Health * Depression	Mother - Child Interaction					
3 Months		* Anxiety * Parenting Stress	Gaze, Affect, Vocalization, Touch					
6 Months								
12 Months				* Mental (MDI)				
24 Months				* Psychomotor (PDI)				
5 Years				- Cognitive Development				
10 Years	Physiological Processes * Cortisol Reactivity * Autonomic Functioning * Sleep Organization	Parental Mental Health * Depression * Anxiety	Mother - Child Interaction Dyadic Reciprocity	* Intelligence (IQ) * Executive Functions				

Figure 1. Overall study design testing the effects of maternal-preterm skin-to-skin contact across the first 10 years of life. MDI, Mental Development Index; PDI, Psychomotor Developmental Index.

who received KC would show improved cognitive skills across childhood, particularly EF that require cognitive flexibility and mental shifting; and 4) individual stability will be observed in each domain (e.g., child physiology, mother–child relationship) over time. Additionally, cross-domain correlations would be found, expressed in both concurrent correlations and long-term associations between early parenting and later child physiology and vice versa. Such withindomain stability and cross-domain associations are hypothesized as the underlying mechanisms through which a birth-related intervention exerts its long-term effects.

Methods and Materials

Participants

Participants included 146 mothers and their premature infants: birth weight: mean = 1270 g (SD = 343.49, range 530-1720 g), gestational age: mean = 30.65 weeks (SD = 2.76, range 25-34 weeks). Of these, 73 infants received skin-to-skin contact (KC), and 73 matched controls received standard incubator care. Mother-infant pairs in the contact and control groups were case-matched for demographic and medical conditions, including gender, birth weight, gestational age, medical risk quantified by the Clinical Risk Index for Babies (49), maternal and paternal age and education, maternal employment, and parity. Only neurologically intact infants raised in two-parent families were included. Medical exclusion criteria included intraventricular hemorrhage grades III or IV, perinatal asphyxia, and metabolic or genetic disease. We also excluded single or teenage mothers and families below poverty cutoff (Table 1). Infants were divided into high- and low-medical risk based on median Clinical Risk Index for Babies scores (Supplement 1).

Recruitment

Because KC is a standardized care option and not considered experimental technique, prospective randomization into intervention and control groups in the same hospital was precluded for ethical reasons. However, at the initiation of the study, KC has not yet been introduced as an intervention option in Israel. This constituted a unique window of opportunity to use a casematched randomization design in two comparable hospitals. We introduced KC sequentially in two medical centers, and this minimized the selection bias that would have occurred if the comparison were between mothers who chose to provide contact and those who did not. The two hospitals were Level 3 referral centers with the same number of admissions, case mix, and nurse-to-patient ratios.

 Table 1. Demographic and Medical Information for Infants and Families

 in the Contact and Control Groups

	Contact (n =	Group 73)	Control (n =	Control Group $(n = 73)$		
	Mean	SD	Mean	SD		
Birth Weight (g)	1245.85	328.21	1289.87	358.08		
CA (weeks)	30.38	2.50	30.82	2.98		
Clinical Risk Index for Babies	2.29	2.98	2.25	2.96		
Mother Age (years)	29.63	4.72	29.07	6.14		
Mother Education (years)	14.70	1.94	14.11	2.32		
Father Age (years)	32.29	5.89	32.46	7.75		
Father Education (years)	14.47	2.27	14.55	3.78		
Primaparous/multiparous	36/	37	36/	37		
Apgar 1	7.21	1.90	7.56	1.30		
Apgar 2	8.67	1.03	8.50	1.14		

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Upon introducing KC in Hospital A, 53 mother-infant dyads were randomly selected to participate in the KC group. For each dyad in the KC group, we randomly selected a matched pair in hospital B where KC has not yet been introduced. During the recruitment period (March 1996-December, 1997), an additional sample of 20 mother-infant dyads were randomly recruited into the control group in hospital B. Following this period (December 1997-September 1998), we introduced KC in hospital B and randomly selected 20 mother-infant pairs into the KC group to case-match the 20 additional dyads in the control group. No differences in birth weight, gestational age, and family demographics were found in the two subgroups of KC infants born in the two hospitals. For each outcome measure that showed significant contact effects in the following analyses, we verified that differences were unrelated to hospital and that both subgroups of infants in the contact group differed from controls (see Supplement 1 for further details and table).

Contact Intervention

Infants were taken out of incubators, undressed, and placed between the mother's breasts. Infants remained attached to cardiorespiratory monitor and were observed by nurses who recorded exact time of contact. Mothers sat in standard rocking chair and used a bedside screen for privacy. KC was provided for 1 hour daily for 14 consecutive days; the remainder of infant care took place in standard incubators.

Procedure and Measures

Infants and families were seen seven times: at hospital discharge (matched to term age), at 3, 6, 12, and 24 months (age corrected), and at 5 and 10 years. At 10 years, 117 children were seen (55 contact and 62 controls), and attrition was mainly related to inability to locate families or families moving to far locations. The following measures were used and further details on each appear in SM.

Physiologic Processes: Term Age. Autonomic functioning: RSA was quantified from a 10-minute electrocardiogram at term age. RSA was quantified according to Porges (50).

Sleep organization: at four consecutive hours (7–11 pm), trained coders observed infant state in 10-second epochs. Sleep–wake cyclicity was computed by Blackman-Tukey Fourier analysis and the amplitude of the basic cycle, implying the amount of rhythmic oscillations between sleep and wakefulness, was used.

Physiologic Processes: Age 10 Years. Stress reactivity: the Trier Social Stress Test for Children (TSST-C) (51), a validated version of the adult TSST (50), was used. In the TSST-C, children make public speech and compute complex arithmetic before unfamiliar judges. Salivary samples were collected at baseline (after lab arrival), reactivity (15 minutes after the TSST-C), and recovery (15 minutes after the second assessment). Saliva was collected by Salivette (Sarstedt, Rommelsdorft, Germany). Salivettes were kept cooled until thawed before being centrifuged at 4°C at 1000 *g* for 15 minutes, with samples stored at -20° C until assayed. Cortisol was assayed using a commercial enzyme-linked immunosorbent assay kit (Assay Design, Michigan).

Autonomic functioning: RSA was quantified from 1) 3-minute baseline ECG and 2) ECG collected during the arithmetic component of the TSST-C.

Sleep-wake organization, for 5 consecutive nights children wore an actigraph (Mini Motionloger; Ambulatory Monitoring, Ardsley, New York), a wristwatch that monitors movement patterns in 1-minute intervals (52), in conjunction with parental sleep diaries. Two measures reported to differentiate good from poor sleepers at this age were used (52): Sleep Efficacy, the percentage of true sleep out of total time in bed, and Mean Wake Bout Time, the time (minutes) of night waking. Actigraph data were available for 40 KC and 43 control children.

Parental Mental Health. Mothers' depressive symptoms were assessed with the Beck Depression Inventory (53) and anxiety symptoms with the State-Trait Anxiety Inventory (54) at term age, 3 months, 6 months, and 10 years. Measures across the post-partum periods were averaged. Mothers and fathers completed the Parenting Stress Index (55) at 3 months.

Mother–Child Interactions. Postpartum period: Mother– infant interactions were observed at term age, 3 months, and 6 months. Videotapes were microcoded using our reliable computer-based system (33) and assessed the four speciestypical attachment behavior of postpartum human mothers: gaze at infant, "motherese" high-pitched vocalizations, positive affect, and affective touch. Total proportions were summed at each age and averaged across observations into Maternal Attachment Behaviors composite. Interrater reliability averaged 93% (range 87%–99%), kappa = .85 (range = .71–.96).

Age 10 years: Mother and child were videotaped in positive and conflict interactions (56). Interactions were coded with the Coding Interactive Behavior Manual, a well-validated global rating scheme (57). The Dyadic Reciprocity construct, the main index of optimal parent–child relationship at this age, was averaged from the two interactions with interrater reliability, intraclass r = .94.

Cognitive Development Across the First 10 Years of Life. Cognitive development: At 6, 12, and 24 months (corrected) infants were tested with Bayley Scale of Infant Development— 2nd edition (58), which yields two scores: Mental Development Index (MDI) and Psychomotor Developmental Index. At 5 years, children were tested with the Wechsler Preschool and Primary Scale of Intelligence (59) and at 10 years with the Wechsler Intelligence Scale for Children (60).

EFs: At 5 and 10 years children were tested with the NEPSY (61), a standardized test for neuropsychological abilities in children, and the EF score was used. EFs include four subsets summed into a single composite (62).

Tests were conducted by trained psychologists blind to children's group membership. MDI, IQ, and EF from the multiple testing were each averaged into a single composite.

Statistical Analysis

Multivariate analysis of variance (MANOVA) with group (KC, control) and medical risk (high/low) as between-subject factors examined differences in each domain (physiologic processes, parental mental health, mother–child interaction, cognitive development). Pearson correlations tested cross-domain and cross-time associations between variables. Hierarchical multiple regressions were computed to predict developmental outcomes at 10 years from variables measured across the first decade of life.

Results

Differences in Developmental Outcomes Between KC and Controls Across Ten Years

Physiological Processes. MANOVA computed for the two neonatal physiologic measures revealed an overall main effect for group, Wilks's $F_{2,112} = 4.992$, p = .008, Eta² = .082. Neonates receiving KC showed higher baseline RSA and more organized sleep-wake cycle at term age. Overall main effect was found for medical risk, Wilks's $F_{2,112} = 4.891$, p = .009, with sicker neonates showing less organized sleep and autonomic functioning.

MANOVA computed for the three physiologic measures at 10 years: baseline RSA, baseline cortisol (CT), and sleep efficiency, showed main effect for group, Wilks's $F_{3,83} = 3.30$, p = .025, Eta² = .11. KC children showed better autonomic functioning and sleep efficiency. Although no differences emerged in baseline cortisol, repeated-measure analysis of variance of the three CT assessments showed group effect: $F_{1,111} = 4.91$, p = .029, Eta² = .042. KC children scored lower at the reactivity assessment and showed marginally quicker recovery (Table 2). Cortisol stress reactivity (difference between reactivity assessment and baseline) was milder in KC children as was autonomic reactivity to stress (difference of RSA during TSST-C and baseline; Figure 2; Supplement 1).

Parental Mental Health. MANOVA for parental mental health across the postpartum indicated overall group effect, Wilks's $F_{4,108} = 2.98$, p = .046, Eta² = .068. Following KC, mothers reported lower anxiety at term, 3 months, and 6 months and less parenting stress, but no group differences were found in maternal depression or father parenting stress (Table 2). No group differences emerged in maternal anxiety or depression at 10 years.

Mother–Child Relationship. Overall group effect emerged for mother–child relationship across the first decade of life, Wilks's $F_{2,112} = 6.71$, p = .002, Eta² = .107. Following KC, mothers provided more attachment behavior across the postpartum period and showed greater mother–child reciprocity at 10 years (Table 2).

Cognitive Development. MANOVA revealed an overall group effect for mental development, Wilks's $F_{3,111} = 4.67$, p = .004, Eta² = .112, significant at 6, 12, and 24 months, but not for psychomotor development. Overall effect also emerged for medical risk, Wilks's $F_{3,111} = 3.17$, p = .027, Eta² = .079. MANOVA conducted for IQ at 5 and 10 years showed no group effect but effect for medical risk, Wilks's $F_{3,111} = 3.17$, p = .027, Eta² = .079. MANOVA conducted for EFs at 5 and 10 years showed overall effects for group, Wilks's $F_{2,111} = 6.83$, p = .002, Eta² = .112, and medical risk, Wilks's $F_{2,111} = 4.56$, p = .013, Eta² = .076. Children who received KC and those born at lower medical risk exhibited better EF (Table 2, Figure 3, and Supplement 1 for subscales).

Cross-Time and Cross-Domain Correlations. Cross-time stability: MDI across infancy correlated with both IQ, r = .32, p = .001, and EF, r = .36, p = .000, in middle childhood, indicating stability in cognitive development across the first decade of life (see Supplement 1 for further details). Neonatal RSA correlated with 10-year RSA, r = .33, p = .001. Maternal attachment behavior correlated with mother-child reciprocity at 10 years, r = .32, p = .001. Maternal anxiety, r = .28, p = .008, and depression, r = .32, p = .001, were each individually stable from newborn to ten years.

Cross-domain same-period correlations: in infancy, maternal attachment behavior correlated with higher RSA, r = .24, p = .009, lower anxiety, r = -.34, p = .000, lower depression, r = -.31, p = .000, and higher infant MDI, r = .22, p = .004. Neonatal RSA correlated with more organized sleep-wake cycle, r = .20, p = .014. At 10 years, physiologic processes were interrelated: cortisol reactivity with lower baseline RSA, r = -.18, p = .049, and longer night wake bouts, r = .37, p = .001. Mother-child reciprocity correlated with higher RSA, r = .20, p = .024, and maternal anxiety with lower sleep efficiency, r = -.25, p = .018.

Cross-domain cross-time correlations: maternal attachment behavior in infancy correlated with lower cortisol at reactivity, r = -19, p = .042, higher baseline RSA, r = .24, p = .009, and lower RSA response to stress at 10 years, r = -.20, p = .024. Neonatal RSA correlated with mother-child reciprocity at 10 years, r = .18, p = .047. Newborns' sleep-wake cyclicity and

Table 2. Study Measures across the First Ten Years of Life in the Contact and Control Groups

	Contact Group		Control	Group		
	Mean	SD	Mean	SD	F	р
Postpartum Period: Birth–6 Months						
Maternal attachment behavior ^a	.53	.23	.44	.21	8.60	.006
Maternal anxiety ^b	31.47	6.22	34.95	8.64	3.96	.048
Maternal depression ^c	6.14	4.44	7.06	4.48	.81	.371
Infancy: 6–24 Months						
6 Months: MDI	96.09	6.75	93.25	8.26	4.04	.047
6 Months: PDI	85.86	13.57	82.79	11.08	1.79	.182
12 Months: MDI	91.33	8.13	84.96	10.59	12.94	.000
12 Months: PDI	86.48	9.93	87.57	10.29	.34	.561
24 Months: MDI	95.62	12.94	89.30	12.29	7.33	.000
24 Months: PDI	87.29	9.59	88.46	10.53	.38	.536
Childhood: 5–10 Years						
Cognitive development						
5 Years: IQ	104.25	15.08	107.82	17.86	1.38	.250
10 Years: IQ	103.91	17.74	100.05	19.69	1.25	.265
5 Years: EFs	102.50	9.24	97.87	14.53	4.06	.046
10 Years: EFs	103.24	12.19	96.18	12.79	9.24	.003
Stress reactivity (nmol/mL)						
Cortisol baseline	6.77	1.30	6.96	.98	.78	.377
Cortisol at reactivity	6.96	1.21	7.75	2.16	5.45	.021
Cortisol at recovery	6.68	1.65	7.27	1.68	3.51	.064
Autonomic regulation						
Baseline RSA	6.98	1.25	6.41	1.15	6.53	.012
Baseline heart period	705.85	78.71	686.68	88.56	1.50	.222
RSA during stress	6.99	1.34	7.07	1.28	.94	.33
Sleep organization						
Sleep efficiency%	87.18	9.53	81.18	16.85	4.75	.032
Mean wake bouttime (min)	1.91	.60	3.11	3.16	5.58	.021
Mother-child relationship						
Mother-child reciprocity ^d	3.67	.61	3.38	.66	5.97	.017

EFs, executive functions; MDI, Mental Development Index, PDI, Psychomotor Development Index; RSA, respiratory sinus arrhythmia.

^aNumbers represents proportion of time mothers provided the species-typical maternal behavior averaged from observations at newborn, 3 months, and 6 months.

^bMeasured with State-Trait Anxiety Inventory (Trait), averaged from assessments at newborn, 3 months, and 6 months.

^cMeasured with Beck Depression Inventory, averaged from assessments at newborn, 3 months, and 6 months.

^dCoded from mother-child interactions on a scale of 1 to 5, averaged of positive and conflict interactions at 10 years.

infant MDI correlated with lower maternal anxiety at 10 years, r = -.22, p = .038, r = -.19, p = .046, respectively.

Predicting Outcomes at 10 Years

Five hierarchical regressions were computed predicting outcomes at 10 years: EF, baseline RSA, cortisol production (average of three assessments), sleep efficiency, and mother–child reciprocity. Variables were entered in eight theoretically ordered blocks: The first two blocks included intervention (KC, control) and medical risk (high, low), to partial their effects. The next four blocks included infancy measures: neonatal RSA, maternal attachment behavior, maternal mental health (average of standardized anxiety and depression), and infant MDI. The final blocks included two interaction terms: neonatal RSA by intervention and maternal behavior by intervention (Table 3).

Models predicting CT and sleep efficiency were not significant, and the three significant models appear in Table 3. EF was independently predicted by provision of KC, low medical risk, higher neonatal RSA, infant MDI, and the interaction of RSA and intervention. Among preterm with high neonatal RSA, those receiving KC exhibited significantly better EF (mean = 103.21, SD = 11.4) than control children (mean = 95.48, SD = 12.13), $t_{1,55} = -2.47$, p = .017. However, among preterm with low

neonatal RSA, no difference emerged between those receiving KC (mean = 101.43, SD = 8.12) and controls (mean = 97.48, SD = 11.57), $t_{1,59}$ = 1.04, nonsignificant. Mother–child reciprocity was independently predicted by provision of KC, neonatal RSA, and maternal attachment behavior. Ten-year RSA was uniquely predicted by KC, neonatal RSA, and maternal attachment behavior.

Discussion

Touch is the most basic mammalian maternal behavior and the first social experience mammalian young partake immediately after birth (11). Maternal–infant contact is also deeply rooted in human cultural heritage; throughout human history and across cultural communities, images of maternal–infant contact serve as the primary symbol of the human capacity to love (11,52). Such evolutionarily conserved behavior must bear important consequences for survival, growth, and adaptation (2,52). In this prospective longitudinal study, we used a low-cost touch intervention and confirmed that maternal–infant bodily contact during the postpartum period bears long-term benefits for child development. Specifically, by 10 years of age, premature infants who received skin-to-skin contact as neonates showed attenuated stress response, more mature autonomic functioning, organized



Figure 2. Cortisol reactivity, autonomic functioning, and sleep organization in infants receiving skin-to-skin contact and case-matched control infants. Cortisol reactivity was computed as the difference between cortisol following stress and baseline cortisol. Respiratory sinus arrhythmia (RSA) change was computed as the difference between RSA during challenge and baseline RSA. Sleep efficacy is the proportion of true sleep out of total time in bed measured by actigraphs across 5 consecutive nights. $^+p = .064$; $^*p < .05$; $^{**}p < .01$.



sleep, better cognitive control, and more reciprocal mother-child relationship. These results are the first to demonstrate that augmenting maternal-infant contact in the neonatal period has a favorable impact on stress physiology and behavioral control across long developmental epochs in humans and may have salient implications for the care practices of preterm infants.

What are the mechanisms through which KC exerts its effects? We suggest that for any early intervention to succeed, it must contain three elements: 1) specificity: because any intervention affects certain processes and leaves others untouched, interventions must target specific processes on the basis of research that linked ingredients of the intervention with the expected improvements. 2) Sensitive periods: models applying dynamic systems theory to developmental psychopathology (25,34) suggest that during sensitive periods in the maturation certain skills, even small inputs have a major effect. Applying an intervention during the sensitive period of impaired processes would thus be the most parsimonious way to utilize an intervention. 3) Individually stable components: once intervention improves a function known to be stable, it would likely exert long-term effects by building on the natural process of development of this function.

The 10-year improvements found here were likely mediated by these processes and accord with the mechanism of continuity in small steps, adapted from dynamic systems' theory to describe iterative effects on developmental continuity and change (63,64). Our results noted that functioning in each domain was individually stable across the 10-year span: children's RSA was stable from termage to 10 years, cognitive development showed continuity between MDI across infancy and both IQ and EF in middle childhood, and mother-child relationship was continuous across infancy and from infancy to 10 years, as was maternal emotional distress. Premature neonates show lower RSA, which predicts later cognitive and behavior difficulties (65,66). We have previously shown that KC improves infants' RSA from pre-KC (32 weeks' gestation) to term age (38). The maturation of heart rhythms and the vagal tone normally occur in utero at 33 weeks' gestation, a developmental milestone missed by most of our infants (24,67). The postpartum extra utero KC intervention, applied during this sensitive period, targeted maturation of the parasympathetic arm of the autonomic nervous

Figure 3. Cognitive development and executive functions in infants receiving skin-to-skin contact in the neonatal period and case-matched controls. Mental Development Index assessed with the Bayley Scales of Infant Development. *p < .05; **p < .01; ***p < .001.

Table 3. Predicting Ten-Year Outcomes from Measures across the Infancy Period

	Executive Functions			Mother-Child Reciprocity			Autonomic Functioning (RSA)			
	Beta	R ² Change	F Change	Beta	R ² Change	F Change	Beta	R ² Change	F Change	df
Intervention	.26 ^a	.06	7.69 ^b	.25ª	.05	5.97 ^a	.27 ^a	.05	6.53 ^a	1, 115
Medical Risk	20	.05	7.52 ^b	12	.02	2.33	.02	.00	.54	2, 114
Neonatal RSA	.17	.01	1.35	.19	.04	3.85 [°]	.35 ^b	.09	11.69 ^b	3, 113
Maternal Attachment Behavior (Infancy)	.18	.00	.12	.29 ^a	.06	7.81 ⁶	.22	.03	3.68 ^a	4, 112
Maternal Emotional Distress (Infancy)	16	.02	1.93	07	.00	.28	.06	.00	.37	5, 111
Infant MDI (6, 12, 24 months)	.27 ^a	.05	7.58 ^b	.11	.00	.73	.15	.00	.45	6, 110
Neonatal RSA*Intervention	.29 ^a	.03	3.96 ^a	19	.00	.21	.02	.00	.64	7, 109
Maternal Behavior*Intervention	.19	.00	.45	.04	.00	.06	01	.00	.02	8, 108
R^2 Total =	.23, F	_{8,108} = 3.81,	v < .001.	.17, <i>I</i>	F _{8,108} = 2.69,	p = .01	.17,	$F_{8,108} = 2.71,$	р = .009	

RSA, respiratory sinus arrhythmia; MDI, Mental Development Index.

system, which provides brainstem-mediated support for flexible interaction with the world and underpins the subsequent capacities for social engagement and focused attention (68). The improvement in RSA during its sensitive period, consistent with animal research linking autonomic maturation with maternal contact, initiated a cascade of favorable outcomes. Neonatal RSA predicted more maternal attachment behavior across infancy and greater mother-child reciprocity at 10 years, moderated the effects of KC on child EF across childhood, and predicted better autonomic functioning at 10 years. In parallel, the maternal postpartum repertoire, presumably triggered by maternal-newborn contact and oxytocin release (4,69,70), was enhanced by KC. This improvement in maternal behavior during its sensitive period carried long-term benefits for children's cognitive growth and maternal mood. Thus, the KC intervention provides an example for the three principles outlined here: it is a birth-related intervention that targets empirically informed processes, it is applied during the sensitive period for these processes, and builds on individually stable dimensions. As KC improved both child physiologic organization and maternal behavior, the two may have dynamically reinforced each other over time, leading to sustained improvements.

Another important aspect of the KC intervention is its accessibility. The findings that such low-cost intervention carries lasting gains for infants and families can have salient implications for public health policy and the care practices of premature infants. KC was initially introduced in a society with little resources, and its current application in developing countries may be easy once care professionals become aware of its evidence-based benefits. KC also highlights the provisions afforded by the natural ecology of the maternal body. As a social mammalian species, humans are ushered into social participation through experiences afforded by the mother's body that support adaptation to the ecosocial niche (2,41,42). As seen, maternal contact was especially beneficial for systems that monitor online response to external fluctuations and operate by oscillations between excitation and inhibition: in hours (sleep-wake cyclicity), moments (cortisol reactivity and recovery), or milliseconds (heart rhythms). Such systems are particularly responsive to synchronous exchanges between maternal and child's physiologic and behavioral signals and showed both immediate and long-term improvements. Future research is required to test whether these gains are unique to mothers or whether KC by fathers, grandparents, or trained volunteers can lead to similar improvements. Research on massage, for instance, has shown that massage provided by mothers and trained professionals led to similar increases in weight gain, but the effects on mother-infant interactions were unique to the

mother-massage group (48,71). As such, the differential effects of maternal versus nonmaternal KC should be carefully studied.

Several study limitations should be remembered. First, the lack of father data is an important drawback. Another limitation involves the lack of true randomization due to ethical reasons. Still, much care was taken to carefully match the two groups and only neurologically intact infants of low social risk were recruited to eliminate the confounding effects of factors that independently affect infant development. It is also possible that an unknown factor (e.g., genetic) is implicated in both premature birth and RSA and cortisol dysregulation. Because we did not include a full-term group, no direct comparisons with normative controls are available for physiological data. Regarding the cognitive tests, normed to mean = 100, SD = 15, the findings show that controls scored at the low end of the norm and KC enhanced performance, typically by third to half SD. Finally, KC mothers expressed substantially more breast milk than control mothers. However, because no further information on breastfeeding was collected, effects of breastfeeding on development could not be assessed, and this remains a study limitation.

Future studies should focus on the effects of KC in cases of potential disruptions to maternal–infant bonding, including maternal postpartum depression, infants at risk for autism, or newborns hospitalized for medical conditions. Finally, it would be important to test whether for any human infant—premature or born at term—if enhancing the mother's uninterrupted presence and full bodily contact during the neonatal period may help reduce the high levels of unregulated stress, sleep disturbances, and cognitive difficulties observed in so many of today's children.

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- 1. Harlow HF (1958): The nature of love. Am Psychologist 13:673-685.
- **2.** Bowlby J (1969): *Attachment and Loss: Attachment*. London: The Hogarth Press and the Institute of Psychoanalysis.

 $^{^{}a}p < .05.$

 $^{^{}b}p < .01.$

- 3. Hofer MA (1987): Early social relationships: A psychobiologist's view. *Child Dev* 58:633–647.
- Meaney MJ (2001): Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. *Annu Rev Neurosci* 24:1161–1192.
- 5. Levine S (2005): Developmental determinants of sensitivity and resistance to stress. *Psychoneuroendocrinology* 30:939–946.
- Carter, CS, Lieselotte, A, Grossmann, KE, Hrdy, SB, Lamb, ME, Porges, SW, Sachser, N editors (2005): Attachment and Bonding: A New Synthesis. Cambridge, MA: The MIT Press: Cambridge, MA: The MIT Press, 2005.
- 7. Pryce CR, *et al.* (2005): Long-term effects of early-life environmental manipulations in rodents and primates: Potential animal models in depression research. *Neurosci Biobehav Rev* 29:649–674.
- 8. Liu D, Diorio J, Tannenbaum B, Caldji C, Francis D, Freedman A, et al. (1997): Maternal care, hippocampal glucocorticoid receptors, and hypothalamic-pituitary-adrenal responses to stress. *Science* 277: 1659–1662.
- 9. Pfeifer W, Rotundo R, Myers M, Denenberg VH (1976): Stimulation in infancy: Unique effects of handling. *Physiol Behav* 17:781–784.
- Hofer MA, Shair H (1982): Control of sleep-wake states in the infant rat by features of the mother-infant relationship. *Dev Psychobiol* 15:229–243.
- 11. Feldman R (2012): Oxytocin and social affiliation in humans. *Horm Behav* 61:380–391.
- 12. Rosenblatt JS (1965): The basis of synchrony in the behavioral interaction between the mother and her off spring in the laboratory rat. In: Foss BM, editor. *Determinants of Infant Behaviour*. London: Methuen, 3–45.
- March of Dimes (n.d.) Peristats. Available at: http://www.marchof dimes.com/peristats/Peristats.aspx. Accessed August 2012.
- 14. Beck S, et al. (2010): The worldwide incidence of preterm birth: A systematic review of maternal mortality and morbidity. Bull World Health Organ 88:31–38.
- Malik S, et al. (2013): Neurogenesis continues in the third trimester of pregnancy and is suppressed by premature birth. J Neurosci 33:411–423.
- Woodward LJ, Anderson PJ, Austin NC, Howard K, Inder TE (2006): Neonatal MRI to predict neurodevelopmental outcomes in preterm infants. N Engl J Med 355:685–694.
- Mewes AUJ, et al. (2006): Regional brain development in serial magnetic resonance imaging of low-risk preterm infants. *Pediatrics* 118:23–33.
- 18. Nagy Z, et al. (2003): Preterm children have disturbances of white matter at 11 years of age as shown by diffusion tensor imaging. *Pediatr Res* 54:672–679.
- 19. Peterson BS (2003): Brain imaging studies of the anatomical and functional consequences of preterm birth for human brain development. *Ann N Y Acad Sci* 1008:219–237.
- Hibbs AM, et al. (2008): Prenatal and neonatal risk factors for sleep disordered breathing in school-aged children born preterm. J Pediatr 153:176–182.
- Wolke D, Meyer R, Ohrt B, Riegel K (1995): The incidence of sleeping problems in preterm and fullterm infants discharged from neonatal special care units: an epidemiological longitudinal study. J Child Psychol Psychiatry 36:203–223.
- 22. Bagner DM, Sheinkopf SJ, Vohr BR, Lester BM (2010): A preliminary study of cortisol reactivity and behavior problems in young children born premature. *Dev Psychobiol* 52:574–582.
- 23. Haley DW, Weinberg J, Grunau RE (2006): Cortisol, contingency learning, and memory in preterm and full-term infants. *Psychoneuroendocrinology* 31:108–117.
- 24. Feldman R (2006): From biological rhythms to social rhythms: Physiological precursors of mother-infant synchrony. *Dev Psychol* 42: 175–188.
- 25. Doussard-Rossevelt J, Porges SW, McClenny BD (1996): Behavioral sleep states in very low birth weight preterm neonates: Relation to neonatal health and vagal maturation. J Pediatr Psychol 21:785–802.
- Mento G, Bisiacchi PS (2012): Neurocognitive development in preterm infants: Insights from different approaches. *Neurosci Biobehav Rev* 36: 536–555.
- Aarnoudse-Moens CSH, Duivenvoorden HJ, Weisglas-Kuperus N, Van Goudoever JB, Oosterlaan J (2012): The profile of executive function in very preterm children at 4 to 12 years. *Dev Med Child Neurol* 54:247–253.
- Luu TM, Ment L, Allan W, Schneider K, Vohr BR (2011): Executive and Memory Function in Adolescents Born Very Preterm. *Pediatrics* 127: e639–e646.

- 29. Barratt MS, Roach MA, Leavitt LA (1992): Early channels of motherinfant communication: preterm and term infants. *J Child Psychol Psychiatry* 33:1193–1204.
- 30. Brooten D, et al. (1988): Anxiety, depression, and hostility in mothers of preterm infants. Nurs Res 37:213–216.
- Crnic KA, Ragozin AS, Greenberg MT, Robinson NM, Basham RB (1983): Social interaction and developmental competence of preterm and full-term infants during the first year of life. *Child Dev* 54:1199–1210.
- **32.** Greene JG, Fox NA, Lewis M (1983): The relationship between neonatal characteristics and three-month mother–infant interaction in high-risk infants. *Child Dev* 54:1286–1296.
- **33.** Feldman R, Eidelman AI (2007): Maternal postpartum behavior and the emergence of infant–mother and infant–father synchrony in preterm and full-term infants: The role of neonatal vagal tone. *Dev Psychobiol* 49:290–302.
- 34. Sameroff AJ (1997): Understanding the social context of early psychopathology. In: Noshpitz J, editor. *Handbook of Child and Adolescent Psychiarty*. New York: Wiley, 224–235.
- Fogel A, Thelen E (1987): Development of early expressive and communicative action: Reinterpreting the evidence from a dynamic systems perspective. *Dev Psychol* 23:747–761.
- **36.** Cicchetti D, Blender JA (2006): A multiple-levels-of-analysis perspective on resilience: Implications for the developing brain, neural plasticity, and preventive interventions. *Ann N Y Acad Sci* 1094:248–258.
- 37. Charpak N, Figueroa Z, Ruiz JG (1998): Kangaroo mother care. *Lancet* 351:914.
- Feldman R, Eidelman AI (2003): Skin-to-skin contact (Kangaroo Care) accelerates autonomic and neurobehavioural maturation in preterm infants. *Dev Med Child Neurol* 45:274–281.
- Kaffashi F, Scher MS, Ludington-Hoe SM, Loparo KA (2013): An analysis of the kangaroo care intervention using neonatal EEG complexity: A preliminary study. *Clin Neurophysiol* 124:238–246.
- 40. Cong X, Cusson RM, Hussain N, Zhang D, Kelly SP (2012): Kangaroo care and behavioral and physiologic pain responses in very-low-birth-weight twins: A case study. *Pain Manag Nurs* 13:127–138.
- Bergman NJ, Linley LL, Fawcus SR (2004): Randomized controlled trial of skin-to-skin contact from birth versus conventional incubator for physiological stabilization in 1200- to 2199-gram newborns. *Acta Paediatr* 93:779–785.
- Bigelow A, Power M, MacLellan-Peters J, Alex M, McDonald C (2012): Effect of mother/infant skin-to-skin contact on postpartum depressive symptoms and maternal physiological stress. J Obstet Gynecol Neonatal Nurs 41:369–382.
- **43.** Feldman R, Weller A, Sirota L, Eidelman AI (2003): Testing a family intervention hypothesis: The contribution of mother-infant skin-to-skin contact (Kangaroo Care) to family interaction, proximity, and touch. *J Fam Psychol* 17:94–107.
- 44. Tessier R, et al. (1998): Kangaroo mother care and the bonding hypothesis. Pediatrics 102:e17–e17.
- 45. Field T, Diego M, Hernandez-Reif M (2011): Potential underlying mechanisms for greater weight gain in massaged preterm infants. *Infant Behav Dev* 34:383–389.
- **46.** Field T (1995): Massage therapy for infants and children. *J Dev Behav Pediatr* 16:105–111.
- Field T, Diego M, Hernandez-Reif M (2010): Prenatal depression effects and interventions: A review. *Infant Behav Dev* 33:409–418.
- 48. Ferber SG, *et al.* (2005): Massage therapy facilitates mother–infant interaction in premature infants. *Infant Behav Dev* 28:74–81.
- 49. The International Neonatal Network (1993): The CRIB (Clinical Risk Index for Babies) score: A tool for assessing initial neonatal risk and comparing performance of neonatal intensive care units. *Lancet* 342:193–198.
- 50. Porges SW (1985): Method and apparatus for evaluating rhythmic oscillations in aperiodic physiological response systems.
- Buske-Kirschbaum A, et al. (1997): Attenuated free cortisol response to psychosocial stress in children with atopic dermatitis. *Psychosom Med* 59:419–426.
- Carter CS (1998): Neuroendocrine perspectives on social attachment and love. Psychoneuroendocrinology 23:779–818.
- Beck AT (1978): Beck Depression Inventory. San Antonio, TX: Harcourt Brace Jovanovich.
- 54. Spielberger CD, Gorsuch RL, Lushene R (1983): *Manual for the State-Trait Anxiety Inventory.* Palo Alto, CA: Consulting Psychologists Press.

- Abidin RR (1983): Parenting Stress Index. Charlottesville, VA: Pediatric Psychology Press. Available at: http://www.eric.ed.gov/ERICWebPortal/ detail?accno=ED238896. Accessed June 23, 2013.
- 56. Feldman R, Bamberger E, Kanat-Maymon Y (2013): Parentspecific reciprocity from infancy to adolescence shapes children's social competence and dialogical skills. *Attach Hum Dev* 15: 407–423.
- 57. Feldman R (2012): Parenting behavior as the environment where children grow. In: Mayes LC, Lewis M, editors. *The Cambridge Handbook of Environment in Human Development*. New York: Cambridge University Press, 535–567.
- 58. Bayley N (1993): *Baley Scales of Infant Development, 2nd ed.* New York: The Psychological Corporation.
- Wechsler D (1967): Manual for Wechsler Preschool and Primary Scale of Intelligence. San Antonio, TX: The Psychological Corporation.
- **60.** Wechsler D (1974): Wechsler Intelligence Scale for Children. New York: Psychological Corporation.
- 61. Korkman M, Kemp S, Kirk U (1998): *NEPSY: A Developmental Neuropsychological Assessment; Manual.* New York: The Psychological Corporation.
- 62. Diamond A, Barnett WS, Thomas J, Munro S (2007): Preschool program improves cognitive control. *Science* 318:1387–1388.
- 63. Thelen ES (1996): A Dynamic Systems Approach to the Development of Cognition and Action. Cambridge, MA: MIT Press.

- 64. Feldman R (2007): Mother–infant synchrony and the development of moral orientation in childhood and adolescence: Direct and indirect mechanisms of developmental continuity. *Am J Orthopsychiatry* 77: 582–597.
- **65.** Doussard-Roosevelt JA, McClenny BD, Porges SW (2001): Neonatal cardiac vagal tone and school-age developmental outcome in very low birth weight infants. *Dev Psychobiol* 38:56–66.
- 66. Doussard-Roosevelt JA, Porges SW, Scanlon JW, Alemi B, Scanlon KB (1997): Vagal regulation of heart rate in the prediction of developmental outcome for very low birth weight preterm infants. *Child Dev* 68:173–186.
- 67. Groome LJ, Loizou PC, Holland SB, Smith LA, Hoff C (1999): High vagal tone is associated with more efficient regulation of homeostasis in low-risk human fetuses. *Dev Psychobiol* 35:25–34.
- 68. Porges SW (2003): Social engagement and attachment: A phylogenetic perspective. Ann N Y Acad Sci 1008:31–47.
- 69. Keverne EB, Kendrick KM (1992): Oxytocin facilitation of maternal behavior in sheep. Ann N Y Acad Sci 652:83–101.
- 70. Insel TR (1992): Oxytocin—a neuropeptide for affiliation: evidence from behavioral, receptor autoradiographic, and comparative studies. *Psychoneuroendocrinology* 17:3–35.
 71. Ferber SG, *et al.* (2002): Massage therapy by mothers and trained
- 71. Ferber SG, *et al.* (2002): Massage therapy by mothers and trained professionals enhances weight gain in preterm infants. *Early Hum Dev* 67:37–45.