Father's brain is sensitive to childcare experiences

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Although contemporary socio-cultural changes dramatically increased fathers' involvement in childrearing, little is known about the brain basis of human fatherhood, its comparability with the maternal brain, and its sensitivity to caregiving experiences. We measured parental brain response to infant stimuli using functional MRI, oxytocin, and parenting behavior in three groups of parents ($n = 89$) raising their firstborn infant: heterosexual primary-caregiving mothers (PC-Mothers), heterosexual secondary-caregiving fathers (SC-Fathers), and primary-caregiving homosexual fathers (PC-Fathers) rearing infants without maternal involvement. Results revealed that parenting implemented a global "parental caregiving" neural network, mainly consistent across parents, which integrated functioning of two systems: the emotional processing network including subcortical and paralimbic structures associated with vigilance, salience, reward, and motivation, and mentalizing network involving frontopolar-medial-prefrontal and temporo-parietal circuits implicated in social understanding and cognitive empathy. These networks work in concert to imbue infant care with emotional salience, attune with the infant state, and plan adequate parenting. PC-Mothers showed greater activation in emotion processing structures, correlated with oxytocin and parent-infant synchrony, whereas SC-Fathers displayed greater activation in cortical circuits, associated with oxytocin and parenting. PC-Fathers exhibited high amygdala activation similar to PC-Mothers, alongside high activation of superior temporal sulcus (STS) comparable to SC-Fathers, and functional connectivity between amygdala and STS. Among all fathers, time spent in direct childcare was linked with the degree of amygdala-STS connectivity. Findings underscore the common neural basis of maternal and paternal care, chart brain–hormone–behavior pathways that support parenthood, and specify mechanisms of brain malleability with caregiving experiences in human fathers.

mothering | parent–infant interaction | alloparental care | transition to parenthood | social brain

Throughout human history and across cultures, women have typically assumed primary caregiving responsibility for infants (1, 2). Although humans are among the few mammalian species where some male parental caregiving is relatively common, father involvement varies considerably within and across cultures, adapting to ecological conditions (1, 3). Involved fathering has been linked with children's long-term physiological and social development and with increases in mothers' caregiving-related hormones such as oxytocin and prolactin (3–6). In addition, animal studies demonstrated structural brain alterations in caregiving fathers (7, 8). It has been suggested that, although maternal caregiving is triggered by neurobiological processes related to pregnancy and labor, the human father's brain, similar to other biparental mammals, adapts to the parental role through active involvement in childcare (1–3). Despite growing childcare involvement of fathers (3, 5, 6), mechanisms for human fathers' brain adaptation to caregiving experiences remain largely unknown, and no study to our knowledge has examined the brain basis of human fatherhood when fathers assume primary responsibility for infant care.

For social species with lengthy periods of dependence, parental caregiving is key to survival and relies on brain structures that maximize survival (2, 9). Animal studies have demonstrated that mammalian mothering is supported by evolutionarily ancient structures implicated in emotional processing, vigilance, motivation, and reward, which are rich in oxytocin receptors, including the amygdala, hypothalamus, nucleus accumbens, and ventral tegmental area (VTA), and that these regions are sensitive to caregiving behavior (9, 10). Imaging studies of human mothers found activation in similar areas, combined with paralimbic insula-cingulate structures that imbue infants with affective salience, ground experience in the present moment and enable maternal simulation of infant states (11–13). These structures implicate a phylogenetically ancient network of emotional processing that rapidly detects motivationally salient and survival-related cues (14) and enables parents to automatically identify and immediately respond to infant distress, thereby maximizing survival. In humans, this emotional processing network is complemented by a cortical mentalizing network of frontopolar-medial-prefrontal-temporo-parietal structures involved in social understanding, theory of mind, and cognitive empathy, including the medial prefrontal cortex (mPFC), frontopolar cortex, superior temporal sulcus (STS), and temporal poles (15). The mentalizing network plays an important role in individuals' ability to infer mental states from behavior, is already activated during the parents' first weeks of parenting, and enables parents to cognitively represent infant states, predict infant needs, and plan future caregiving (11–13).

The few studies examining the human father's brain showed activation in similar areas, including the STS, lateral and medial

Significance

Brain, oxytocin, and parenting behavior were measured in primary-caregiving mothers, secondary-caregiving fathers, and primary-caregiving homosexual fathers raising infants without maternal involvement. Parenting integrated functioning of two neural networks: subcortical-paralimbic structures implicated in emotional processing and cortical circuits involved in social understanding. Mothers showed greater activation in the emotional processing network and fathers in the socio-cognitive circuits, which were differentially linked with oxytocin and behavior. Primary-caregiving fathers exhibited high amygdala activation similar to mothers, alongside high superior temporal sulcus (STS) activation comparable to fathers, and functional connectivity between amygdala and STS. Among all fathers, time spent in childcare correlated with amygdala-STS connectivity. Findings describe mechanisms of brain malleability with caregiving experiences in human fathers.

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frontal regions, VTA, inferior frontal gyrus (IFG), and orbitofrontal cortex (OFC) (16, 17). Only one study compared maternal and paternal brain response to infant cues, reporting mothers' greater amygdala activation, fathers' greater superior-temporal and medial-frontal activation, and maternal and paternal oxytocin's different associations with amygdala vs. cortical activation (18). Oxytocin, a nine-amino acid neuropeptide that underpins the formation of affiliative bonds (19), supports the development of human parental caregiving (20). Research has shown that maternal and paternal oxytocin levels are associated with parent–infant synchrony, which is the parent's careful adaptation of caregiving behavior to infant's social signals (21). However, although oxytocin levels are similar in mothers and fathers, oxytocin is differentially linked with the parent-specific repertoire, for instance, with affectionate contact in mothers and stimulatory play in fathers (5, 20).

Ethological perspectives emphasize the importance of studying the neurobiology of parenting in its natural habitat and of using a behavior-based approach to test parents' brain adaptation to ecological pressures (22). Consistent with findings in other mammals (10), studies on brain–behavior associations in human mothers describe links between mother–infant synchrony and brain activation in the mother's subcortical regions, including the amygdala, nucleus accumebens, and hippocampus (11, 13). In contrast, the one study testing human fathers' brain–behavior associations showed correlations with cortical activation (17). Overall, these findings suggest that distinct brain–hormone–behavior pathways may underpin maternal and paternal care; therefore, oxytocin and parenting behavior may be associated with the emotional processing network in mothers but with the socio-cognitive circuit in fathers. Furthermore, animal studies indicate that active caregiving in biparental fathers leads to greater integration of multiple brain networks involved in nurturance, learning, and motivation (7). Hence, active involvement in caregiving may possibly facilitate integration of both parenting-related networks in human fathers, particularly among those who undertake the primary caregiver role.

The present study sought to examine the brain basis of human fatherhood by using a "natural experiment," afforded for the first time in human history, to our knowledge, by contemporary socio-cultural changes. Throughout history, infants without mothers were cared for by other women (2). Current social changes enable the formation of two-father families raising children with no maternal involvement since birth (3). Such a context provides a unique setting to assess changes in the paternal brain on assuming the traditionally maternal role. Moreover, understanding mechanisms of brain adaptation to caregiving experiences in primary-caregiving fathers may shed further light on processes that refine all fathers' responses to childcare activities.

We visited the homes of two-parent families rearing their firstborn child: heterosexual mother-father couples comprising primary-caregiving mothers (PC-Mothers) and secondary-caregiving fathers (SC-Fathers) and homosexual couples comprising two primary-caregiving fathers (PC-Fathers) (*SI Materials and Methods*). We videotaped parent–infant interaction in the natural habitat, measured parental oxytocin, and used the videotaped parent–child interactions as stimuli for functional MRI (fMRI) to test parental brain response to infant-related cues. Five hypotheses were proposed. First, we expected activation in both subcortical areas involved in vigilance and reward and cortical circuits implicated in social understanding in all parents raising a young infant. Second, we expected greater subcortical activation in mothers, particularly in the amygdala, which has been repeatedly linked with mammalian mothering (23, 24), and greater activation in cortical socio-cognitive circuits in fathers. Third, the brain–hormone–behavior constellation underpinning maternal care was expected to center around the emotional-processing network, whereas the brain–hormone–behavior links in fathers were expected to coalesce with the socio-cognitive network. Fourth, consistent with the context-specific evolution of human fathering (1), we expected greater variability in fathers' brain response as mediated by actual caregiving experiences. Such variability would be particularly noted among the primary-caregiving fathers raising infants without mothers and may involve functional integration of the subcortical and cortical networks subserving parenting. Finally, we expected that the pathways leading from the parent's primary caregiving role to greater parent–infant synchrony would be mediated by parental brain activation and oxytocin levels.

Results

Coinciding with ethological perspectives, we first examined differences in parenting behavior. The parent–infant synchrony construct includes eight scales assessing parents' provision of the human parental repertoire (i.e., vocalizations and affective touch) and its coordination with infant signals (*Materials and Methods*). PC-Mothers and PC-Fathers showed significantly greater synchrony than SC-Fathers [$F_{(2,86)} = 10.47$, $P = 0.0001$; Fig. 1]. Next, we assessed differences in oxytocin levels. No differences in oxytocin emerged between the three groups [$F_{(2,79)} = 2.119$, $P > 0.1$; Table S1], consistent with previous research (5, 21). Further analysis showed no differences in oxytocin or parenting behavior between biological and adoptive PC-Fathers (Table S2).

Next, conjunction analysis was conducted to establish a neural parental caregiving network across all parents raising young infants, regardless of group (hypothesis 1). This analysis attempted to pinpoint parents' attachment-specific fMRI brain activations stimulated specifically by watching themselves interact with their infant while controlling for a familiarity response to the presented videos and for activation in response to watching their own solitary activity (*SI Materials and Methods*). Thus, two contrasts were used: Self–Infant Interaction > Self and Self–Infant Interaction > Unfamiliar Parent–Infant Interaction. Results revealed a rich set of activations in subcortical, paralimbic, and cortical regions, which mapped onto the two expected networks: emotional processing network [bilateral amygdala, ventral anterior cingulate cortex (vACC), left IFG/insular cortex, and VTA] and mentalizing network (bilateral STS, ventromedial prefrontal cortex, temporal poles, and lateral frontopolar cortex) (Fig. 2*A* and Table S3).

We next conducted region of interest (ROI) analysis to test group differences for the Self–Infant Interaction > Unfamiliar Parent–Infant Interaction contrast (hypothesis 2). Although activity in most brain areas was comparable across parents, two areas showed group differences. PC-Mothers showed greater amygdala activation than SC-Fathers, who exhibited greater STS activation than PC-Mothers. Intriguingly, PC-Fathers showed high amygdala activation similar to PC-Mothers [$F_{(2,84)} = 4.775$, $P < 0.02$], alongside high STS activation similar to SC-Fathers [$F_{(2,84)} = 4.433$, $P < 0.02$; Fig. 2*B* and Table S4]. No differences emerged between biological and adoptive PC-Fathers in any brain area (Table S2).

To tap brain–hormone–behavior constellations (hypothesis 3), we examined each group's correlations between brain activation to Self–Infant Interaction, oxytocin levels, and parent–infant

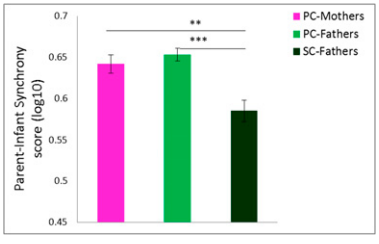

Fig. 1. Bars present mean log-transformed levels of parent–infant synchrony scores as indicated by pink (PC-Mothers, $n = 20$), bright green (PC-Fathers, $n = 48$), and dark green (SC-Fathers, $n = 21$) bars. PC-Mother and PC-Father groups showed higher synchrony than SC-Fathers (Tukey post hoc comparisons; $^{**}P < 0.01$; $^{***}P < 0.001$).

synchrony. Based on findings from ROI analysis (Fig. 2), we tested each network's associations with parenting behaviors and oxytocin. Parent–infant synchrony correlated with activity in bilateral amygdala only for PC-Mothers ($r = 0.579$, $P < 0.01$; Fig. 3*A*, *Left*), but not for SC-Fathers or PC-Fathers. Maternal oxytocin did not correlate with the amygdala but did with the vACC ($r = 0.477$, $P < 0.05$; Fig. 3*B*, *Left*), another component of the emotional processing network. Among fathers, parent–infant synchrony correlated with STS activation in both paternal groups (SC-Fathers, $r = 0.667$, $P = 0.001$; PC-Fathers, $r = 0.4$, $P = 0.005$; Fig. 3*A*, *Right*). Similarly, oxytocin correlated with STS activation in both paternal groups (SC-Fathers, $r = 0.603$, $P < 0.01$; PC-Fathers, $r = 0.337$, $P < 0.05$; Fig. 3*B*, *Right*). No correlations emerged between amygdala or emotional processing network area activation with oxytocin or behavior in SC-Fathers or PC-Fathers or between mentalizing network area activation with oxytocin or behavior in PC-Mothers.

Inasmuch as only PC-Fathers showed high activation in both amygdala and STS, we postulated that for optimal caregiving in a two-father context, both networks must be recruited to enable the entire range of parenting behavior (hypothesis 4). We examined functional connectivity between the amygdala and STS in each group (*SI Materials and Methods*). For only PC-Fathers, this analysis revealed significant connectivity between amygdala and STS in the Self–Infant Interaction compared with baseline ($t = 3.117$ for left amygdala-STS connectivity; $t = 2.806$ for right amygdala-STS connectivity; $P < 0.05$, Bonferroni-corrected), but not for PC-Mothers or SC-Fathers ($P > 0.05$, uncorrected; Fig. 4*A*). Next, we examined whether this mechanism of amygdala-STS connectivity operates in all fathers in relation to childcare experiences as assessed by the interview (*SI Materials and Methods*). For all fathers, time spent alone with the child, in direct responsibility for infant care, correlated with amygdala-STS connectivity during Self–Infant Interaction, indicating the overlap of the two networks ($r = 0.330$, $P = 0.005$; Fig. 4*B*).

Next, we constructed a path model (Fig. 5) leading from the parent's caregiving role to parent–infant synchrony as mediated by brain activation and oxytocin (hypothesis 5). The model was analyzed with AMOS20 and provided a good fit for the data [$\chi^2_{(10)} = 10.66$, $P = 0.385$; comparative fit index (CFI) = 0.99; normed fit index (NFI) = 0.89; root-mean-square error of approximation (RMSEA) = 0.03, and Tucker-Lewis index (TLI) = 0.97; *SI Materials and Methods*]. The caregiving role had a direct path to synchrony, with primary caregivers exhibiting greater synchrony. Additionally, the caregiving role had a significant indirect effect on synchrony via amygdala activation, as moderated by sex (moderated mediation). The significance of the mediated-moderated paths was tested with 95% CI based on 5,000 bootstrapped samples (25). Results indicated that the indirect effects of the primary-caregiving role on synchrony through increased amygdala activation were significant for females (mediated $\beta = 0.13$, $P < 0.05$, $b = 0.18$, SE = 0.08, 95% CI = 0.05, 0.39) but not for males (mediated $\beta = -0.02$, not significant, $b = -0.03$, SE = 0.04, 95% CI = –0.13, 0.05). Amygdala and STS activity were bidirectionally correlated. STS had a significant direct effect on synchrony. Moreover, STS was associated with oxytocin, which, in turn, impacted on synchrony, indicating that STS indirectly affected synchrony via increases in oxytocin (mediated $\beta = 0.08$, $P < 0.05$, $b = 0.10$, SE = 0.05, 95% CI = 0.03, 0.25).

Finally, we examined differences in masculinity and femininity between the two father groups using the Bem Sex Role Inventory (26). No differences in masculinity and femininity were found between homosexual and heterosexual fathers, suggesting that the current findings can be attributed to the fathers' primary-caregiving role (Table S5).

Discussion

The current study provides compelling evidence for brain malleability with caregiving experiences in human fathers and describes one mechanism underpinning this malleability. Several previously unidentified aspects of our findings should be noted. First, this is the first period in human history when fathers are raising infants within a partnered relationship with no maternal involvement since birth, and ours is the first, to our knowledge, empirical investigation on parental brain patterns in such a novel family setting. Second, the current findings are, to our knowledge,

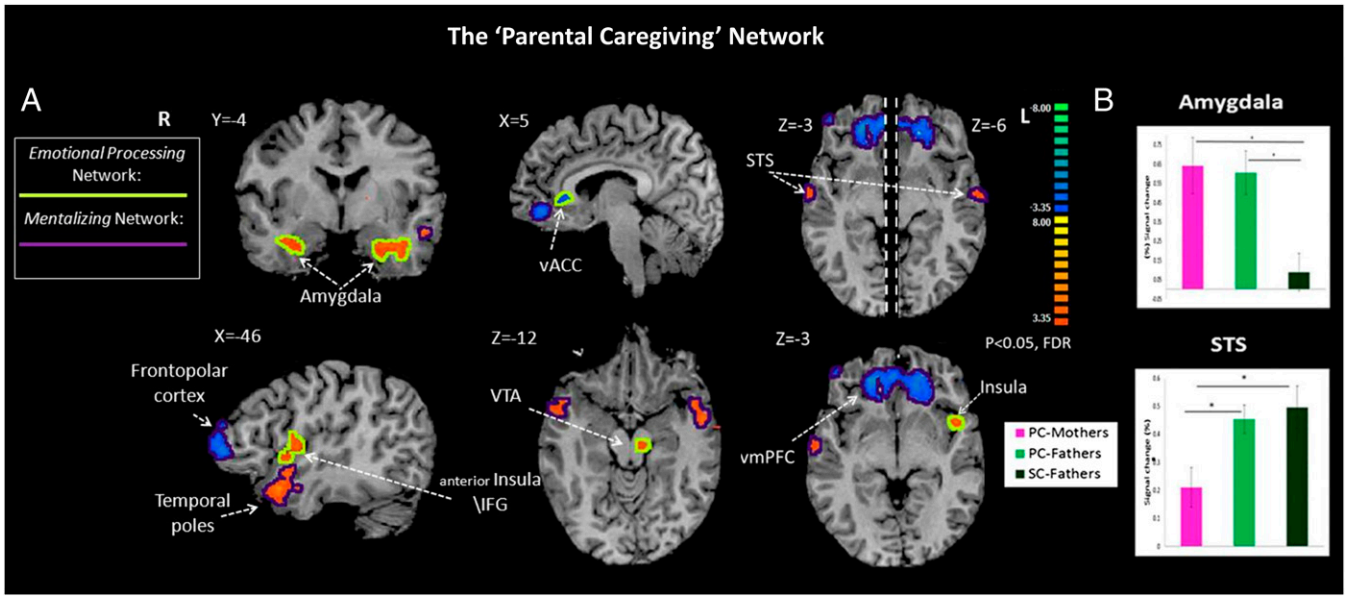

Fig. 2. (*A*) Whole-brain conjunction analysis (Self–Infant Interaction > Self ∩ Self–Infant Interaction > Unfamiliar Parent–Infant Interaction) revealed two brain systems: the emotional processing network (yellow line around activation) included bilateral amygdala, vACC, left insular cortex and IFG, and VTA, and the mentalizing network (purple line around activation) included bilateral STS, lateral frontopolar cortex, vmPFC, and temporal poles. Random, $n = 87$, $P < 0.05$ FDR-corrected, cluster size > 3×3^3. (*B*) Bar plots present averaged percent signal change for Self–Infant Interaction minus Unfamiliar parent–infant interaction contrast for PC-Mothers (pink, $n = 20$), PC-Fathers (bright green, $n = 47$), and SC-Fathers (dark green, $n = 20$). (Tukey post hoc comparisons; $^*P < 0.05$). vmPFC, ventromedial prefrontal cortex; vACC, ventral anterior cingulate cortex; IFG, inferior frontal gyrus; VTA, ventral tegmental area; L, left; R, right.

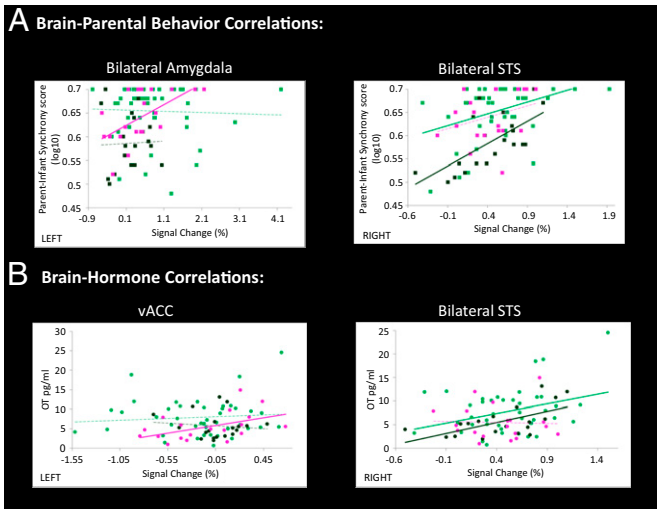

Fig. 3. Regression lines indicated by pink (PC-Mothers, $n = 20$), bright green (PC-Fathers, $n = 47$), and dark green (SC-Fathers, $n = 20$) lines. Solid lines indicate significant correlations and broken lines nonsignificant correlations. (*A*) Scatter plots show significant correlations between brain activity and parent–infant synchrony scores for PC-Mothers in bilateral amygdala (*A*, *Left*, $r = 0.579$, $P < 0.01$), but not for PC-Fathers and SC-Fathers (*A*, *Left*, $r = -0.043$, $P > 0.7$; and $r = 0.057$, $P > 0.8$, respectively). For both PC-Fathers and SC-Fathers, significant correlation was found in the bilateral STS (*A*, *Right*, $r = 0.400$, $P = 0.005$; and $r = 0.667$, $P = 0.001$, respectively), but not for PC-Mothers (*A*, *Right*, $r = 0.30$, $P = 0.2$). (*B*) Scatter plots show correlations between brain and oxytocin levels for PC-Mothers in vACC (*B*, *Left*, $r = 0.477$, $P < 0.05$), but not for PC-Fathers and SC-Fathers (*B*, *Left*, $r = 0.09$, $P > 0.5$; and $r = -0.119$, $P > 0.6$, respectively), and for PC-Fathers and SC-Fathers in bilateral STS (*B*, *Right*, $r = 0.337$, $P < 0.05$; and $r = 0.603$, $P < 0.01$, respectively), but not for PC-Mothers (*B*, *Right*, $r = -0.039$, $P > 0.8$).

the first to compare brain patterns, affiliation hormones, and concrete parenting behavior in the natural habitat in first-time mothers and fathers, describing the parent's neurobiological adaptation to the transition to parenthood. Finally, our study is, to our knowledge, the first to chart an overall model of brain, hormones, and parenting behavior leading from the parent's role in caregiving to parent–child synchrony as mediated by neural activation, oxytocin levels, and parents' sex. Overall, our results describe a global parental caregiving brain network that was mainly consistent across parents and involved brain structures implicated in vigilance, salience, reward, motivation, social understanding, and cognitive empathy. These brain structures were linked with oxytocin, the hormone implicated in human and mammalian bond formation (19, 20), and with the human-specific repertoire of parental behavior, indicating that assuming the role of a committed parent and engaging in active care of the young may trigger this global parental caregiving network in both women and men, in biological parents, and in those genetically unrelated to the child. Such findings are consistent with the hypothesis that human parenting may have evolved from an evolutionarily ancient alloparenting substrate that exists in all adult members of the species and can flexibly activate through responsive caregiving and commitment to children's well-being (2). Such an alloparental caregiving system, observed throughout the animal kingdom, may have contributed to the extreme variability and flexibility of paternal care observed throughout the evolution of our species.

In addition to consistency, substantial malleability was found in the human paternal brain, which resembles the plasticity observed in other biparental mammals (1, 7, 8). Whereas primary-caregiving mothers showed higher subcortical activation and secondary-caregiving fathers exhibited greater activation in cortical socio-cognitive circuits, brain malleability with caregiving experience in primary-caregiving fathers involved the coactivation of these two networks. Consistent with ethological models, our findings highlight the central role of actual caregiving behavior as an important pathway to the parental brain. As shown, mothers and primary-caregiving fathers exhibited greater parent–infant synchrony, a style marked by provision of the human parental repertoire in accordance with the infant's social signals that parallels the licking-and-grooming behavior of rat dams (20). However, the brain–hormone–behavior constellation underpinning motherhood implicated the emotion processing network, whereas the brain–hormone–behavior associations in primary- and secondary-caregiving fathers were supported by the socio-cognitive network. Thus, the phylogenetically ancient role of maternal care, which has remained relatively uniform across time and culture, appears to be underpinned by evolutionarily ancient structures, whereas the facultatively expressed paternal care (1) that has shown great variability throughout human evolution appears to be underpinned by later-developing prefrontal temporo-pariatel circuits supporting social understanding. The functional connectivity between the two networks in primary-caregiving fathers suggests that, although only mothers experience pregnancy, birth, and lactation, and these provide powerful primers for the expression of maternal care via amygdala sensitization, evolution created other pathways for adaptation to the parental role in human fathers, and these alternative pathways come with practice, attunement, and day-by-day caregiving.

The amygdala has been repeatedly shown as the central node of mammalian mothering. It undergoes structural alterations during pregnancy and childbirth (24); amygdala lesions reduce maternal behavior (23); and significant amygdala c-fos changes are observed following the mother–pup interaction (27). In contrast, the STS is a central region of the mentalizing network, playing a vital role in social cognition, biological motion, social goal interpretation, prediction making, and updating regarding others' behavior (28, 29). Thus, in addition to much commonality, somewhat different pathways seem to underpin maternal and paternal caregiving. The first, an evolutionary ancient path, operates via immediate fight-or-flight responses, danger signals, and motivational salience; the latter relies on later-evolving

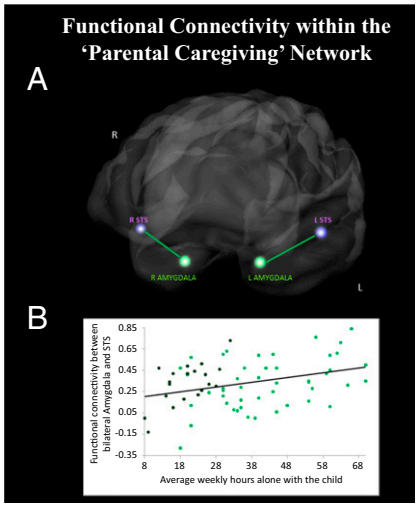

Fig. 4. Presented are correlation lines as indicated by bright green (PC-Fathers, $n = 47$) and black (all fathers, $n = 67$) lines and dots. Solid lines indicate significant correlations. (*A*) Functional connectivity between amygdala and STS. Amygdala and STS are significantly more interconnected during Self–Infant Interaction compared with baseline only among PC-Fathers ($P < 0.05$, Bonferroni-corrected), but not for PC-Mothers or SC-Fathers ($P > 0.05$, uncorrected). (*B*) Scatter plot shows that functional connectivity between amygdala and STS, measured by the correlation between blood-oxygen–level dependent (BOLD) signal in bilateral amygdala and STS during Self–Infant Interaction condition, is predicted by father's average weekly hours alone with the infant for both fathers' groups ($r = 0.330$, $P = 0.005$).

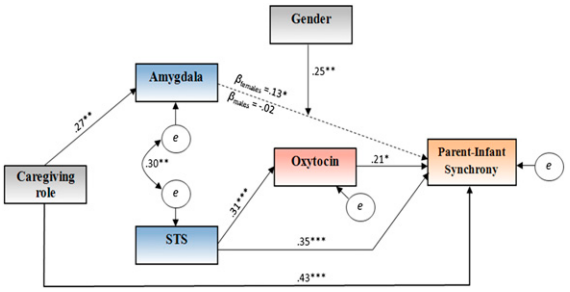

Fig. 5. Path model leading from the parents' role in caregiving to parent–infant synchrony as mediated by brain activation and oxytocin levels. *P < 0.05; **P < 0.01; ***P < 0.001.

structures and implements circuits affording third person perspective and future planning (14, 15). These different pathways were demonstrated by the structural model, which showed that STS in all fathers had a direct path to parent–infant synchrony, as well as a mediated path via increases in oxytocin. The comparable amygdala response in mothers and primary-caregiving fathers indicates the potential to activate the evolutionary ancient pathway when fathers raise infants without mothers, demonstrating amygdala sensitivity to the primary-caregiving role. These findings are consistent with animal studies showing influences on c-fos expressions in the amygdala in sexually naive male prairie voles following pup exposure (30).

Although functional amygdala–STS connectivity was observed only in primary-caregiving fathers, among all fathers, the overlap between the two structures correlated with the father's direct caregiving experiences. These findings coincide with biparental animals' greater integration of multiple brain networks (7). Both the amygdala and STS are key structures of the social brain circuitry (15, 31, 32). The STS plays a key role in social perception (33), and STS projections to the amygdala determine its role in mentalizing and social perception processes (28, 29). The STS sends feed-forward projections to the amygdala and receives feedback projections from it (29), with the amygdala fine-tuning neural response to affect-laden stimuli (34). Stronger amygdala–STS connectivity has been linked with better social cue detection (32), and amygdala-damaged patients revealed lower STS response to affective facial expressions (35). Individuals with larger, more complex social networks showed stronger amygdala–STS connectivity, suggesting greater adeptness at initiating and maintaining social bonds (32). Our findings suggest that this interconnected social perception network, indexed by amygdala–STS connectivity, may underpin a flexible and generalized form of nurturance that is not dependent on pregnancy and childbirth but on caregiving experiences. Such human nurturance, whether related to parenting or other forms of committed caregiving, may support the ancient and widespread practice of "alloparental caregiving." Our results are also consistent with animal research suggesting that caregiving experiences, exposure to offspring, and accompanying hormonal changes involve structural and functional changes in the father's brain (4, 7, 8).

Results of the current structural model indicate that the primary-caregiving role directly affected amygdala response in mothers and fathers, but amygdala effects on behavior were observed only in mothers. In contrast, the STS, which activated all fathers' responses to infant cues, had both a direct effect on synchrony and mediated effects via oxytocin, which has been repeatedly shown to support the development of synchronous parenting (5, 20, 21). Oxytocin administration has been shown to increase STS response to tasks that require mentalizing (36). Thus, our model charts two pathways of brain–hormone–behavior in first-time parents: one mediated by the amygdala for mothers and the other by the STS for fathers. In addition, the model charts both direct and oxytocin-mediated paths between STS and synchrony in fathers. The interconnectedness between the amygdala and STS suggests that these two paths are interrelated and open to bidirectional effects.

Finally, in this study, we assumed no inherent differences in the parental caregiving network as a function of the parent's sexual orientation. This assumption is consistent with recent imaging studies, which showed no differences in response to the attachment target between homosexual and heterosexual men (37), and with our finding that homosexual and heterosexual fathers did not differ in their masculinity and femininity scores. Findings for all fathers that degree of amygdala–STS connectivity was associated with the amount of direct childcare responsibility further supports the hypothesis that our results describe human fathers' brain adaptation to caregiving activities. However, it must be remembered that only a handful of studies examined the brain basis of human fatherhood, and research in this area requires much further investment. Future research should continue to explore similarities and differences in the maternal and paternal brain; describe how mothers' and fathers' brains evolved to complement each other in the joint effort of raising young infants; and test how the forces that redefine the human family function to reorganize the human social brain. Current sociocultural and technological advances are already assembling new families, workplaces, and social networks. Such novel social bonds will likely create a new interplay between the consistencies of the human social brain and the malleabilities resulting from unique contextual requirements, role definitions, cultural beliefs, and individual life histories. Much further research and conceptual effort is required to understand how these profound and rapid social changes shape brain, behavior, social relationships, the capacity for nurturance, and the larger social climate in which we live.

Materials and Methods

Participants. A total of 89 first-time parents raising their infant within partnered relationships participated [mean age, 36.1 ± 4.34 y (SD)]: 41 heterosexual biological parents comprising 20 PC-Mothers [mean age, 34.05 ± 4.54 y (SD)] and 21 SC-Fathers [mean age, 35.0 ± 2.58 y (SD)], and 48 primary-caregiving homosexual fathers who were living within a committed two-parent family, had a child through surrogacy, and were raising the infant without maternal involvement since birth [PC-Fathers; mean age, 37.4 ± 4.47 y (SD)] (Table S6). In each fathers couple, one father was the biological father [n = 23; mean age, 38.5 ± 3.17 y (SD)] and the other was the adoptive father [n = 23; mean age, 36.52 ± 5.47 y (SD)] (Table S7). Infants [mean age, 11 ± 6.67 mo (SD)] were all born at term and were healthy since birth (Tables S8 and S9). Data of two fathers (one in SC-Fathers and one in PC-Fathers group) were excluded from brain analyses due to strong movement artifacts. Participants were compensated for their time and gave written informed consent. The study was approved by the Ethics Committee of the Tel Aviv Sourasky Medical Center.

Procedure. The study included two sessions with each family. In the first session, families were visited at home between 4:00 and 8:00 PM (to control for diurnal variability in oxytocin). After familiarization, salivary samples were collected for oxytocin, and each parent was interviewed and completed self-report measures. Next, each parent was videotaped interacting with the infant. Experimenters ascertained that infants were calm during videotaping; when infants were fussy, visits were rescheduled. The experimenter stood ∼1.2 m from parent and child and videotaped their faces and upper bodies. Finally, we videotaped a 2-min segment of each parent alone and the infant alone during solitary activity in the same natural ecology. Parent–infant interaction videos were coded offline for parent–infant synchrony. In the second session, several days after the home visit, each parent underwent functional brain scanning.

Collection of Saliva Samples and Determination of Salivary Oxytocin. Saliva samples were collected twice—at baseline and following parent–infant interactions—by sallivette (Sarstedt). Salivettes were immediately stored at −20 °C to be centrifuged twice at 4 °C at 1,500 × g for 15 min in the next weeks. Samples were then stored at −80 °C until further processed and then transferred to −20 °C. Recent studies across several laboratories showed that salivary oxytocin measured by immunoassay is a reliable biomarker, stable over time, and correlates with oxytocin-related processes like breastfeeding. Consistent with our research and other's research (20), samples were concentrated by four (lyophilized) and then measured using a commercial ELISA kit (Enzo Life Sciences). Measurements were performed in duplicate and calculated using

MatLab-7 according to relevant standard curves. The intra-assay coefficient of variability (cv%) was less than 15.4%. The average of the two assessments was used.

Parenting Behavior. Parent–infant interactions were coded using the Coding Interactive Behavior (CIB) Manual (38). This global rating system for adult–child interactions includes 42 scales, which aggregate into theoretically meaningful constructs. The CIB is well-validated showing good psychometric properties (39). We used the eight-scale CIB parent–infant synchrony construct to index the central behavioral expression of attuned human caregiving. Codes describe (*i*) parents' behavioral repertoire such as expression of warm and positive affect, gaze at infant, provision of affective touch, and high-pitched "motherese" vocalizations, and (*ii*) these behaviors' coordination with infant signals like parents' adaptation to changing infant states, resourcefulness in handling various infant communications, and provision of supportive presence for infant play and exploration. Coding was conducted by trained raters who were blind to parent group. Interrater reliability, measured on 20% of the sample, was, intraclass $r = 0.95$ (range = 0.87–0.99).

fMRI Data Acquisition and Analyses. Imaging was performed on a GE-3T Sigma Horizon echo-speed scanner with a resonant gradient echoplanar imaging system. Functional T2*-weighted images were obtained using field of view = 220 mm, matrix size = 96 × 96, repetition time = 3,000 ms, echo time = 35 ms, flip angle = 90°, acquisition orientation of the fourth ventricle plane, 39 axial slices of 3-mm thickness, and gap = 0. In addition, each functional scan was accompanied by a 3D anatomical scan using anatomical 3D sequence spoiled gradient echo sequences that were obtained with high-resolution of 1 × 1 × 1 mm. The fMRI data were analyzed with the BrainVoyager analysis package (version 2.1; Brain Innovation). After standard preprocessing (*SI Materials and Methods*), statistical maps were prepared for each participant using a general linear model (GLM), in which the various blocks were defined as district predictors. Single-participant analysis was followed by multiparticipant analysis computed with random effects using a gray matter mask. To account for hemodynamic responses, predictors were convolved with a 6-s hemodynamic response filter for all participants. A statistical threshold of $P < 0.05$ was used, with a false discovery rate (FDR) correction for multiple comparisons and minimal cluster size of 3 × 33 voxels. ROI analysis was conducted on the brain areas identified by the whole-brain GLM conjunction analysis and previous research as components of the parental caregiving neural network (Table S4). ROIs were defined functionally and anatomically using the WFU Pick Atlas Tool (40). Specifically, for each region, a box-shaped volume of five voxel diameter was placed around the peak of activation (*SI Materials and Methods*). Associations between ROI activation and parental behavioral and hormonal data were assessed using Pearson correlation and reported at $P < 0.05$.

Interregional Functional Connectivity Analysis. To analyze functional connectivity between amygdala and STS, we defined ROIs functionally and anatomically using the WFU Pick Atlas Tool (40), placing a box-shaped volume of five voxel diameter around the activation peak. The signal was extracted from all ROIs, and a set of all pairwise Pearson correlation values was calculated for each participant and condition, incorporating a hemodynamic delay of two repetition times. After Fisher Z transformation, two-tailed *t* statistics were computed to compare conditions. All pairwise ROIs with connections that were significant at the $P < 0.05$ level using Bonferroni correction were reported (*SI Materials and Methods*).

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