

Neurobiology of culturally common maternal responses to infant cry

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This report coordinates assessments of five types of behavioral responses in new mothers to their own infants' cries with neurobiological responses in new mothers to their own infants' cries and in experienced mothers and inexperienced nonmothers to infant cries and other emotional and control sounds. We found that 684 new primipara mothers in 11 countries (Argentina, Belgium, Brazil, Cameroon, France, Kenya, Israel, Italy, Japan, South Korea, and the United States) preferentially responded to their infants' vocalizing distress by picking up and holding and by talking to their infants, as opposed to displaying affection, distracting, or nurturing. Complementary functional magnetic resonance imaging (fMRI) analyses of brain responses to their own infants' cries in 43 new primipara US mothers revealed enhanced activity in concordant brain territories linked to the intention to move and to speak, to process auditory stimulation, and to caregive [supplementary motor area (SMA), inferior frontal regions, superior temporal regions, midbrain, and striatum]. Further, fMRI brain responses to infant cries in 50 Chinese and Italian mothers replicated, extended, and, through parcellation, refined the results. Brains of inexperienced nonmothers activated differently. Culturally common responses to own infant cry coupled with corresponding fMRI findings to own infant and to generic infant cries identified specific, common, and automatic caregiving reactions in mothers to infant vocal expressions of distress and point to their putative neurobiological bases. Candidate behaviors embedded in the nervous systems of human caregivers lie at the intersection of evolutionary biology and developmental cultural psychology.

maternal responsiveness | neurobiology | culture | infant cry | fMRI

When Charles Darwin had his firstborn son, William Erasmus ("Doddy"), he made extensive notes and eventually wrote in his "Biographical Sketch of an Infant" that "during the first 7 days... of course sucking and screaming, were well performed by my infant" (1). Human infants command precious few means of agency, and so their faces and voices serve signaling functions essential to their survival (2–4). The acoustic structure of infant distress vocalizations (cries) and caregiver responses appear to be conserved among mammals, including humans (2, 5). Infant cries reflect the coevolution of displays of progeny physiological state and caregiver psychobiological mechanisms designed to optimize strategic patterns of investment (6). From the moment of birth, certain signals from babies effectively influence parenting: Infant cries motivate adults to approach and to act (7, 8). That is, infant cries and caregiver responses to them constitute an integrated dyadic system that encompasses the infant production of cries as well as the adult anatomy (9–12), physiology (5, 13), and perception, processing, and response apparatus to cries (2, 4, 5, 14–17). Cries put both infant and caregiver in states of strong mutual nervous system activation and increase the probability of behavioral attunement (18).

How and why do caregivers respond to their infants' cries? Here, we report a confluence of results from two previously divergent approaches to understanding this fundamental and necessary act

of human caregiving. We hypothesize that, where evolutionary biology and developmental cultural psychology intersect, we might pinpoint universal behaviors and the structures that subserve them likely embedded in the nervous systems of human caregivers. The essential challenge of systems neuroscience is to identify and quantify brain activity underlying behavior. Specifically, human infants' altricial dependence on adult caregiving suggests that mechanisms associated with prompt and appropriate caregiver responsiveness ought to be automatic and deeply ingrained in the caregiver nervous system. From the perspective of evolutionary biology, the human brain evolved adaptive mechanisms to optimize decisions that enhance reproductive success (19), such as responding to the infant cry to sustain life. To test our general hypothesis, we undertook a series of interlocked complementary studies. In observations of maternal behavior in situ in 11 countries, we hypothesized preferred and common patterns of new mothers' responses to their own infants' cries. In three independent companion fMRI experiments in three countries, we sought to identify neurobiological underpinnings of the same behavioral responses in new mothers in the United States to their own young infants' cries, in experienced mothers in China to infant cries in comparison with noninfant cry emotional sounds, and in experienced mothers and inexperienced nonmothers in Italy to generic infant cries.

Care-soliciting vocalizations are common in the young of many species (2, 6, 16, 20, 21) and constitute a signal system that has been conserved throughout mammalian evolution (2, 22). Human infants effectively elicit parental attention, proximity, and solicitude by crying (23–29); in times of famine, for example, crying

Significance

We undertook an interdisciplinary exploration that unites evolutionary biology, neuroscience, and developmental cultural psychology. Based on extensive and detailed behavioral analyses of 684 new mothers in 11 countries and complementary functional magnetic resonance imaging (fMRI) analyses of brain responses in 43 first-time new US mothers to their own infants' cries, 44 experienced Chinese mothers to infant cries and control emotional sounds, and 12 Italian mothers and nonmothers to generic infant cries, we identified specific behavior repertoires and specific corresponding activated brain regions in human caregivers that constitute primary responses to infant distress. This study set will appeal to scientific and general audiences because it elucidates the foundations of core parenting practices in response to infant vocal distress.

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infants are more properly cared for, enhancing their chances of survival (30, 31). Indeed, mothers react neurobiologically (32–39), autonomically (28, 39, 40), and hormonally (41–44), as well as behaviorally (45–48), to their babies' cries.

No study of a single society can reveal universals of childcare in our species. However, similarities in parenting practices across diverse cultural groups would supply unique evidence that responses to crying constitute culturally common, species-general, fundamental processes (49, 50). A central limitation of research in infancy and parenting to date is that it has described constructs, structures, functions, and processes largely deriving from Western, educated, industrialized, rich, and democratic societies (50, 51). Reviews of the literature consistently show that upwards of 80 to 90% of published psychological and developmental studies have been conducted in North America and Western Europe (the minority developed world) whereas only 10 to 20% of the world's literature represents the majority (developing) world (51). This limitation has impeded a comprehensive understanding of caregiving and child mental health (52), led to critiques of monocultural perspectives, and motivated consistent calls for enlarged multicultural study. Cross-cultural comparisons are especially valuable because they expose and deepen understanding of processes that likely generalize across disparate populations. Identifying what is culturally common biologically and psychologically is theoretically significant in social, behavioral, and neural science. For our behavioral observation, therefore, we recruited mother–infant dyads from one country in North America, two in South America, three in Western Europe, two in sub-Saharan Africa, one in the Middle East, and two in East Asia (see [Table S1](#)). For our companion neurobiological experiments, we recruited mothers (and nonmothers) from one country in North America, one in Western Europe, and one in East Asia.

What do new mothers naturally do when their infants cry and why? Mothers may display affection to the infant, distract the infant, nurture the infant, pick up and hold the infant, or talk to the infant (3, 5, 7, 18) (see [Fig. 1A](#) and [Supporting Information](#)). When infants cry, caregivers must balance empathy and approach motivations with the potential to cause harm (46). That is, infant cries draw a caregiver's attention and solicitude but sometimes invite neglect or maltreatment (53–55). Fundamental species-general responses to infant cries would suggest biological bases for generating appropriate caregiving behaviors as expressed by the nervous system. Understanding how mothers' brains respond to their infants' cries is therefore vital to optimizing care, as it is to diagnosing and obviating risk, to the next generation.

Results

Cross-Cultural Behavioral Observation of Infants and Mothers. Mothers in all countries showed within-country variation in all five response types but also demonstrated regular differences across response types ([Fig. 1A](#) and [Table S2](#)). Overall, combining countries, mothers were significantly unlikely to respond to infant distress by displaying affection, by distracting, and by nurturing, but mothers were significantly likely to respond to infant distress by picking up and holding and by talking to their infant. Some countries with smaller sample sizes ($n < 30$) of usable data (at least five infant distress vocalizations) did not reach significance for every behavior ([Supporting Information](#)). However, in every country, average odds ratios (ORs) for mothers' affection, distraction, and nurturance in response to their infants' vocal distress were below the transformed equivalent of 1, indicating that these responsive behaviors were unlikely. By contrast, average ORs for mothers to pick up and hold their infants and to talk to their infants in response to their infants' vocal distress were at or above 1 or its transformed equivalent, indicating that these responsive behaviors were likely. Looking across countries at maternal responses to infant vocal distress revealed culturally common parenting practices (i.e., virtually no country differences in ORs) ([Supporting Information](#)).

Mothers in 11 different countries around the world behaved with noteworthy consistency in promptly responding to their own infants' vocal distress by picking up and holding their infants and by talking to their infants as two likely contingent responses, and displaying affection, distraction, and nurturance as three unlikely contingent responses. In humans, infant cry is the earliest preverbal form of communication. Given their high biological relevance, infant-related stimuli capture adult attention and trigger physiological responses that prepare for action and speech (56). Evolutionary theories posit that parent responsiveness to infants plays a crucial role in child survival and so enhances reproductive success (24, 57). As evolutionary theorizing also appeals to the species-common genome, the shared biological heritage of some psychological processes presupposes their generality (58). We therefore reasoned that, because of their cross-cultural prevalence and significance for species survival, behaviorally common responses to infant cry may be subserved by neurobiological mechanisms embedded in mothers' nervous systems.

fMRI Experiments of Mothers' Brain Responses to Infant Cry. To uncover potential neurobiological underpinnings of specific maternal responses involving action and speech, we pursued a direct approach through fMRI in two main experiments, one of new primipara mothers' brain responses to their own infants' cry during the early postpartum period, and a second of more experienced mothers' brain responses to infant cries in contrast to other infant and adult emotional and control sounds. (In a third subsidiary fMRI experiment presented in [Supporting Information](#), we examined experienced mothers' and nonmothers' responses to generic infant cries.) fMRI allowed us to visualize locations of changes in brain metabolic activity that were correlated to the occurrence of stimuli linked to a young infant's vocal distress. Given our behavioral data, we hypothesized that infant cry (vs. other emotional and control sounds) would activate (*i*) the medial superior frontal gyrus, which includes the supplementary motor area (SMA) (59, 60) [known to be associated with two sets of functions especially relevant here: (*a*) preparing for movement and the conscious intention to move (61, 62), imagining to grasp (63), and experiencing an "urge" to move (64) and (*b*) as the "starting mechanism of speech" involved in preparing a verbal utterance and initiating vocal tract movement (65–69)]; (*ii*) the bilateral inferior prefrontal cortices (Broca's areas) associated with social speech processing (70); and (*iii*) the superior temporal gyri (STG) associated with processing complex sounds (71). (*iv*) We also hypothesized involvement of midbrain and striatum, known to play critical roles in maternal caregiving (72–74). To test these hypotheses about brain areas that would substantiate and presumably underlie universal observations from the cross-cultural behavioral observations, and to evaluate their generality, we studied mothers (and nonmothers) in three distinct cultures: the United States, China, and Italy. (For details about the participants, methods, and results of all fMRI experiments, see [Supporting Information](#).) Results with respect to the three main hypotheses are reported here (supplementary results for hypothesis *iv* are reported in [Supporting Information](#)).

fMRI experiment 1: New mothers in the United States. As hypothesized, we found one significant cluster of activation in the right pre-SMA, bilateral clusters of activation in the dorsolateral prefrontal cortex (includes Broca's areas) and in superior and middle temporal cortices, and one large bilateral cluster that included putamen, thalamus, and midbrain ([Fig. 1B](#)). For peaks of activity and cluster sizes, see [Table 1](#).

fMRI experiment 2: Experienced mothers in China. The main purposes of fMRI experiment 2 were to replicate, extend, and refine the results of fMRI experiment 1 in a second culture, to mothers who were more experienced with infants, and vis-à-vis emotional sounds other than infant cry. Results of fMRI experiment 2 replicated, extended, and refined results of fMRI experiment 1. The infant cry (IC) vs. noise control sound (NCS) contrast paralleled fMRI

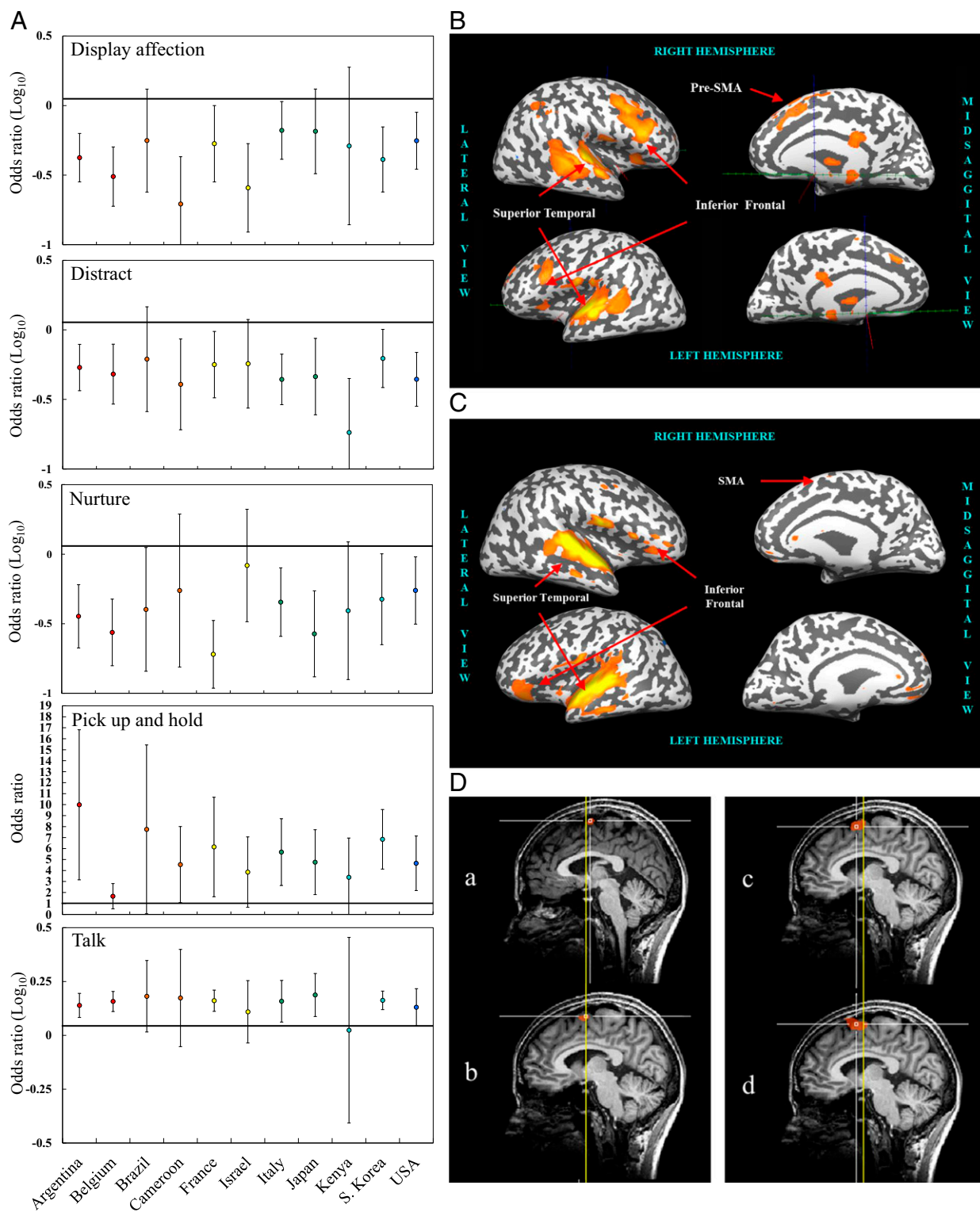


Fig. 1. Behavioral and fMRI responses to human infant cries. (A) Five types of maternal contingent responses to infant vocal distress in 11 countries. Display affection: Physical behaviors (kissing) or verbal statements (“I love you”). Distract: Encouraging the infant’s attention to a property, object, or event in the environment physically or verbally. Nurture: Feeding, burping, wiping the infant’s face or hands, or diapering the infant. Pick up and hold: Lifting and supporting some or all of the infant’s weight with the body. Talk: Vocalizing directed toward the infant. Reference lines for statistical significance are drawn. Except for talk, which has an absolute minimum of -1 , abscissae mark the absolute minima for transformed ORs. Means and 97.5% CIs. (B) US mothers. Graphical representation of brain regions resulting from the contrast own-infant cry vs. control noise in the whole group of new mothers at 3.5 mo postpartum. The top of the figure refers to the right hemisphere, the bottom to left hemisphere, the left to lateral views, and the right to midsagittal views. (C) Chinese mothers. Graphical representation of brain regions resulting from the contrast infant cry vs. control noise in the whole group of mothers at 7 mo postpartum. The top of the figure refers to the right hemisphere, the bottom to the left hemisphere, the left to lateral views, and the right to midsagittal views. (D) Chinese mothers. Sagittal brain views of pre-SMA and SMA-proper activation peaks (white squares) in the following contrasts (and coordinates): (a) IC vs. NCS ($x = 3, y = -4, z = 64$), (b) IB vs. NCS ($x = 6, y = -1, z = 61$), (c) AC vs. NCS ($x = 6, y = 5, z = 58$), and (d) IL vs. NCS ($x = 6, y = 5, z = 61$). The vertical anterior commissure (VAC) line ($y = 0$) is indicated in yellow.

Table 1. US mothers, own-infant cry vs. control noise

Region	Brodman area	Peak x	Peak y	Peak z	t	Voxels at q(FDR) < 0.01
Left <u>superior</u> and middle temporal gyri	41/42/22/21	-52	-20	9	9.75	20,705
Right <u>superior</u> and middle temporal gyri/insula	41/42/21/22/13	53	-20	6	8.57	21,803
Right <u>middle</u> frontal gyrus, precentral gyrus/insula	6/9/46/44/45/13	32	1	39	6.98	18,618
Left <u>putamen</u> /right putamen/thalamus (bilateral medial dorsal and ventral anterior nuclei)/bilateral midbrain (subthalamic nuclei)		-22	1	9	5.87	17,194
Right <u>pre-supplementary motor area</u> /bilateral medial frontal gyrus	6/8	2	4	63	5.83	6,558
Left <u>middle</u> and inferior frontal gyrus	9/44/46	-40	13	33	5.43	4,132
Left anterior insula	13	-31	22	9	5.25	744
<u>Left</u> and right ventral posterior cingulate cortex	23	-1	-32	27	5.11	1,122
Cerebellum (pyramis)		-16	-65	-30	5.09	2,067
Right supramarginal gyrus	40	47	-50	42	5.05	713
Right intraparietal sulcus	40	32	-53	36	4.75	870
Cerebellum (uvula)		8	-65	-30	4.61	547
Left <u>superior</u> and middle frontal gyri	9/10	-28	43	30	4.44	741

Brain regions (cluster peaks of activity are underlined), Brodmann area specifications, Talairach coordinates, *t* values, and cluster sizes resulting from the contrast own-infant cry vs. control noise in the whole group of participants (see Fig. 1B for graphical representation). Brodmann areas are missing for regions that fall outside the cerebral cortex (e.g., subcortical and cerebellar regions). qFDR, *P* value adjusted for the false discovery rate.

experiment 1 most closely and revealed increased activation in the right SMA and in two large bilateral clusters centered in the STG that extended to the inferior frontal gyrus [including Brodmann area (BA) 44 and 45], the insula, and the globus pallidus. Activation was also observed in one right cluster centered in the putamen (Fig. 1C). For peaks of brain activity and cluster size, see Table 2.

The infant laugh (IL) vs. NCS contrast revealed increased activation in the bilateral pre-SMA and in two large bilateral clusters centered in the STG. The left cluster extended to the middle temporal gyrus, the inferior frontal gyrus, and the insula. The anterior part of the right cluster included the temporal pole, the inferior (including BA 44 and 45) and middle frontal gyrus, the precentral gyrus, and the insula, whereas the posterior part of the same cluster extended to the supramarginal gyrus. Another peak of cerebral activation was observed in the clusters centered in the right inferior gyrus. Cerebral activation was also found in the left lateral globus pallidus, the right caudate body, and the right thalamus (the cluster extended to the lentiform nucleus) (Fig. S1). For peaks of brain activity and cluster size, see Table S3.

The infant babble (IB) vs. NCS contrast revealed peaks of cerebral activations at the right edge between pre-SMA and SMA-proper, in the right inferior frontal gyrus, and in two large clusters centered in the left STG—which extended to the middle and transverse temporal gyri, the inferior frontal gyrus (including BA 44), the postcentral gyrus and the insula—and the right STG that included the middle temporal gyrus, the inferior frontal gyrus (including BA 44 and 45), and the insula. We also observed subcortical activity in the bilateral thalamus and the left medial globus pallidus (Fig. S2). For peaks of brain activity and cluster sizes, see Table S4.

The adult female cry (AC) vs. NCS contrast revealed cerebral activations in the right pre-SMA and in one large cluster centered in the right STG that extended to the inferior and the middle frontal gyri, the insula, the thalamus, the putamen, and the midbrain in both hemispheres and to the globus pallidus and the amygdala in the right hemisphere (Fig. S3). For peaks of brain activity and cluster sizes, see Table S5.

Summary, fMRI experiment 3, and activation peaks analysis. The fMRI results from one Western and one Eastern culture confirm that new mothers hearing their own infants' vocal distress as well as

Table 2. Chinese mothers, infant cry vs. control noise

Region	Brodman area	Peak x	Peak y	Peak z	t	Voxels at q(FDR) < 0.05
Left superior <u>temporal</u> gyrus, inferior frontal gyrus, insula, globus pallidus	22/21/42/44/46/13	-48	-13	7	9.95	40,269
Right superior <u>temporal</u> gyrus, inferior frontal gyrus, insula, globus pallidus	22/21/44/45/13	57	-13	7	10.29	33,898
Left cerebellar declive		-15	-64	-20	6.03	9,002
Left anterior <u>cingulate</u> , medial frontal gyrus	32/10	-3	41	-5	4.78	1,711
Left superior frontal gyrus	9	-12	53	28	4.39	712
Right precentral gyrus	6	45	-1	46	4.18	867
Right putamen		21	2	13	4.15	847
Right cerebellar uvula		15	-85	-26	3.99	862
Right supplementary motor area	6	3	-4	64	3.88	302
Right inferior frontal gyrus	45	51	17	19	3.73	143
Left inferior semi-lunar lobule		-12	-64	-42	3.62	529
Left precuneus	7	-24	-64	31	-3.55	319
Left precentral gyrus	6	-63	-4	31	-3.56	201

Brain regions (cluster peaks of activity are underlined), Brodmann area specifications, Talairach coordinates, *t* values, and cluster sizes resulting from the contrast infant cry vs. control noise in the whole group of participants (see Fig. 1C for graphical representation). Brodmann areas are missing for regions that fall outside the cerebral cortex (e.g., subcortical and cerebellar regions). qFDR, *P* value adjusted for the false discovery rate.

experienced mothers hearing infant vocal distress generally activate brain areas linked to the intention (*i*) to move and to grasp (SMA), (*ii*) to speak (inferior frontal regions, SMA), and (*iii*) to process auditory stimulation (superior temporal regions). (*iv*) In addition, we found strong activity in other brain areas known to be associated with caregiving (midbrain, basal ganglia, cingulate, and insula) (75). Furthermore, we found similar results in a third fMRI experiment with experienced Italian mothers (Fig. S4 and Table S6). See [Supporting Information](#) for full details of fMRI experiment 3.

In fMRI experiment 2, SMA activated to all emotional sounds (IC, IL, IB, and AC) when contrasted with a control sound (NCS). However, each sound has a distinctive emotional valence, recruited different resources of the SMA, and activated different parts of the SMA (Fig. 1D). SMA is subdivided into pre-SMA and SMA-proper. The *y* coordinates of peak activations of the sounds used in fMRI experiment 2 lay along the anterior–posterior axis and ranged from $y = -4$ to $+5$. Pre-SMA is the portion of the SMA anterior to the vertical line intersecting the vertical anterior commissure (VAC or $y = 0$), and SMA-proper is posterior to the VAC (60). SMA-proper and pre-SMA, located in the medial superior frontal gyrus, are involved in motor and cognitive control and play active roles from motor planning to motor output and action (62, 76–78). Passive listening to nonverbal emotional vocalizations, such as crying, laughter, and speech, evokes responses in pre-SMA and SMA-proper, which in turn promotes action responses. Each is also involved in affective processing in emotion regulation (79).

However, pre-SMA and SMA-proper control motor behaviors (reach and speech) at different levels. Functional connectivity (80) reveals that the more rostral pre-SMA is involved in higher level cognitive processing of motor behaviors whereas the more caudal SMA-proper is involved in motor output of different kinds. Pre-SMA and SMA-proper also connect to different brain regions, which helps to explain functional differences between them. The pre-SMA is associated with brain regions that underlie cognitive and affective processing, such as the prefrontal cortex (81), the anterior premotor area, the cingulate cortex, and the medial prefrontal cortex (59). Pre-SMA is recruited in top-down integration subserving actions, plans, and motivation in volitional processes (62), as well as self-initiated actions, and is not triggered by external cues (82, 83). By contrast, the SMA-proper is connected with the primary motor cortex, the posterior premotor areas, the cingulate cortex, and parietal areas. SMA-proper is itself somatotopically organized (60) with cortical representation from the face (anterior) to the foot (posterior) (84, 85). The anterior portion of the SMA-proper (close to the border with pre-SMA) is involved in producing orofacial movements, vocalizations, and speech (65) and in bimanual coordination of finger movements (86). SMA-proper is therefore activated in conjunction with overt articulation and movement of the lips and hands (78). In accord, clinical data reveal that lesions of the SMA-proper produce language and motor impairments (87, 88), and transcranial magnetic stimulation confirms enhanced hand motor-evoked potentials to infant cry in women (89). Moreover, in contrast to the pre-SMA, the SMA-proper is activated by external triggers (83) and is involved with sequential processes (60). Our analysis revealed that only infant cry activated the (anterior) SMA-proper; other emotional sounds (IL, IB, and AC) activated the pre-SMA or the border between pre-SMA and SMA-proper (Fig. 1D).

Discussion

Some characteristics of children likely affect parents everywhere, perhaps in similar ways. By the end of the first trimester, fetuses are felt to move in utero (“quickening”) (90), a significant marker in the life of the child and in the lives and psyches of parents. Soon after birth, physiognomic features of the infant (a large head

dominated by a disproportionately large forehead, widely spaced sizable eyes, a small snub nose, an exaggeratedly round face, and a small chin) (91–93) prompt adults to express nurturance and solicitude (94–96). Moreover, many adult responses to infants are culturally common, such as the special vocal register of child-directed speech (97). Infant cries and maternal responses to them appear to function in the same way.

Distress vocalizations emitted when infants are separated from their mothers, hungry, or physically ill at ease (3, 15, 17, 98–100) are similar in many mammals, including humans. Infant cries interrupt cognition (101). Hearing infant cries, mothers (or other caregivers) promptly move to retrieve or establish contact and communication with offspring (2, 3, 5, 15, 17) and to nourish or defend them against predators (102–104). Indeed, caregivers in different species even display strong emotional and physiological responses to cries of nonoffspring (3, 28). For example, deer (*Odocoileus hemionus* and *Odocoileus virginianus*) mothers will approach a speaker playing distress vocalizations of infant marmots (*Marmota flaviventris*), seals (*Neophoca cinerea* and *Arctocephalus tropicalis*), domestic cats (*Felis catus*), bats (*Lasiorycteris noctovagans*), humans (*Homo sapiens*), and other mammals as though they were going to assist a fawn in distress. Does also emit contact calls when near that speaker, as they do when responding to their own fawns (16). Chimpanzees are the primate species closest to humans. Chimpanzee infants emit distress vocalizations rarely and only following physical separation from their mothers. In response to their infants’ distress vocalizations, chimpanzee mothers move to restore physical proximity and retrieve their infants (105). Thus, mothers in many species respond to their infants’ calls by orienting, approaching, retrieving, and vocalizing (106, 107).

In *The Expression of the Emotions*, Darwin highlighted the significance of infant distress signals (57), and, in detailing attachment theory, Bowlby underscored that “crying... plays an important part in the earliest phases of social interaction” between parent and child (24). Parental caregiving blends tuition and intuition. Some aspects of parenting are learned, as through culture, but parents also rely on their instincts in caregiving. The long evolutionary history of altricial human infant dependency on requisite adult caregiving suggests that some mechanisms associated with adult attentiveness and responsiveness to infants ought to be automatic and deeply ingrained in caregivers’ nervous systems. For example, parents have specific implicit cognitive (108), autonomic (109, 110), and CNS (111) reactions to human infant faces that differ from their responses to faces of human adults and faces of in-frahuman mammal infants and adults.

We expected that some types of maternal responsiveness to infant cry would be common across cultures. In accord with this expectation, we explored contingencies between their own infants’ vocal distress and maternal affection, distraction, nurturance, movement/contact, and speech, along with the neurobiological bases of those responses, in a wide variety of societies. Nearly 700 mother–infant dyads in nearly a dozen countries were observed in situ and closely analyzed. Across these social groups, new mothers preferentially and systematically responded to their infants’ vocal distress by picking up and holding and by speaking to their infants. Corresponding fMRI results confirmed that new mothers, hearing their own infant’s distress, and more experienced mothers, hearing infant cries, generally activate the SMA associated with the intention to move and speak, inferior frontal regions involved in the production of speech, and superior temporal regions linked to processing auditory stimuli (61–63, 78, 111). These automatic responses in brain and behavior appear to occur in advance of conscious awareness, as the brain evolved adaptive circuits in the service of reproductive success (19). SMA is associated with the programming, generation, and control of relevant motor action and speech sequences.

Notably, the neurobiological findings obtained for mothers but not for nonmothers ([Supporting Information](#)). These results accord

with others in the extant literature: Mothers exhibit more pronounced neural responses in brain areas involved in emotional processing in response to infant cry than do nonmothers (75, 112, 113), suggesting that mothers may experience the cry as an emotionally important signal which requires their attention. This result points to rapid plasticity in the maternal brain (29, 74, 114, 115). With as little as 3 mo postpartum experience, mothers' brains become responsive to particular infant facial and vocal stimuli.

The behavioral observations study recruited mothers from different parts of the world, but the three imaging experiments recruited mothers only from the United States, China, and Italy. Is there evidence that, following the cry of their child, similar brain structures that promote similar responsive behaviors are activated in mothers in still other countries? Imaging experiments from Israel, Japan, and the United Kingdom reveal involvement of the motor cortex in mothers listening to their own infants' crying, as well as looking at pictures of their own infants' faces or watching video registrations of their own children (112, 116–120).

We do not contend that mothers' behavioral responses to infant cry differ from their responses to other infant stimuli, but rather that mothers in different cultures preferentially respond to infant cry in certain ways (picking up and talking to their infants) and not other ways (distracting, showing affection, or nurturing) and that their prominent motor and vocal responses are supported by specific matching brain responses.

In the spirit of systems neuroscience, the convergence of behavioral and neurobiological modalities increases the validity of results and the added value of applying both methodologies, here in investigating parent sensitivity to infant cries. That conjunction is reinforced by related independent findings from the emerging neuroscience of parenting. Other methodologies [for example, event-related potentials (ERPs)] that address the timing and stages of neural responsiveness to infant cues complement fMRI data focused on neural architecture (121).

Caregiver responsiveness is vital to infant survival and hence continuation of the species, parent–infant bonding, and the wholesome development of the child. It has been argued that, whether experience-expectant or experience-dependent, hard-wired responses to newborn distress vocalizations exemplify an adaptive speed–accuracy trade-off (121, 122), in which responding to the infant in distress is preferred to delaying action because hesitation increases the risk of the infant suffering harm (123). Another evolved function of the human infant cry is to communicate phenotypic quality (fitness) to caregivers (6) because cries signal infant health status (4, 46, 123). Finally, responsiveness to infant distress, and not nondistress, is critical for infants' attachment security with parents, and prosocial behavior has long-lasting impact on children's well-being (3, 124, 125).

Studying offspring solicitation vocalizations and caregiver responsiveness contributes to understanding animal communication systems and caregiver investment and also speaks to the etiology, prediction, and prevention of child neglect and abuse. Caregiver reactions to infant crying are not always benevolent. Cries sometimes trigger caregiver maltreatment (126–128). Our results encourage further research on caregivers who may be at-risk for problematic responsiveness to infants. The data reported here reveal a propensity to act and to speak in response to infant vocal distress. However, whether the action and speech are positive and growth-promoting or negative and harmful may depend on idiosyncratic characteristics of the caregiver. Using brain imaging, it may be possible to identify caregivers who are unaware or reluctant to disclose such risks (38). For example, depressed mothers compared with nondepressed mothers (129–131), and mothers who abuse drugs compared with mothers with no such dependencies (132), show altered brain involvement (subcortical limbic regions, prefrontal cortex including SMA, and superior temporal cortex) and altered behavior in response to negative emotions expressed

by their own infants. Altered cerebral activations in specific brain circuits might compromise parental motivation or the implementation of behaviors attuned to the needs of the child. Screening and diagnosis could be combined with early intervention to sensitize parents and to enhance their understanding of the importance and meaning attached to infant cries. Such a multimodal therapeutic approach could lead to the introduction of an array of tools for parents to respond appropriately to optimize child care and manage negative feelings tantamount to child maltreatment.

Healthy human mothers are likely to pick up and hold and to speak to their infants in response to their infants' cry, and this specific complex of behavioral responsiveness is known to calm infants (133). A survey of more than 180 societies showed that infants cried less when they were responded to in this way (4), and a randomized controlled trial (RCT) demonstrated the effectiveness of this same response (26). Perhaps because of their evolutionary advantage, these reactions toward infants are specific and automatic, widespread culturally, and embedded neurobiologically in mothers.

Materials and Methods

Cross-Cultural Behavioral Observation of Infants and Mothers. All study procedures and consent documents were approved by the Institutional Review Board of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and mothers provided written informed consent. We first recruited, observed, and recorded 1 h of home-based naturalistic mother–infant interactions in 684 dyads in 11 countries, including Argentina, Belgium, Brazil, Cameroon, France, Kenya, Israel, Italy, Japan, South Korea, and the United States. Only primipara mothers and firstborn singleton healthy awake full-term 5.5-mo-olds participated, with approximately equal numbers of girls and boys in each country sample. (Detailed sociodemographic information for all participants appears in [Table S1](#).) Next, we carefully operationalized infant cries (distress vocalizations that indicated protest, complaint, anger, or upset and encompassed whining, fretting, fussing, whimpering, and full-blown distress) and five maternal response types (affection, distraction, nurturance, action, and speech) and coded video records of infants and mothers using mutually exclusive and exhaustive schemes to mark all behavior onsets and offsets to the nearest 0.10 s (for details of behavior durations, coding, and reliability see [Supporting Information](#)). Finally, we analyzed behavioral contingencies between maternal responses and infant cries in terms of odds ratios (ORs) ([Supporting Information](#)). Separately for each dyad, time units were tallied in two-by-two tables for each behavioral sequence, and ORs were computed for each table (134, 135). Odds ratios indicate the likelihood of mothers' responding to infant distress within a 5-s time window of the onset of a cry, with each response type compared with the likelihood of their initiating the same five behaviors outside of those time windows. This microanalytic strategy allowed us to examine in quantitative detail lead–lag sequences of infant cry–mother response, taking into consideration the timing of their interactions at the level of in-the-moment lived experiences.

fMRI Experiment 1: New Mothers in the United States. All study procedures and consent documents were approved by the Yale University School of Medicine Human Investigations Committee, and deidentified data were used in this study. Participants provided informed consent. We recruited 43 new primipara healthy European American middle-class mothers and their 3.5-mo-olds (56% male). Acoustic stimuli consisted of each mother's own-infant cry and own-infant noise (matched in pattern, intensity, and frequency range to their own infant's cry). Because each own-infant cry varied according to each infant's individual characteristics, the own-infant cry and matched control sounds were necessarily unique to each mother. Mothers underwent two fMRI scanning sessions at 3 tesla in a Siemens Trio full-body scanner. They heard 10 blocks of stimuli. Each block of 30 s was composed of own-infant cry or own-infant control sound. Imaging data analyses were performed with BrainVoyager QX version 2.0 (Brain Innovation; www.BrainVoyager.com) (see [Supporting Information](#) for preprocessing details). Using general linear models (GLMs), we analyzed whole-brain blood oxygenation level-dependent (BOLD) activity and contrasted activity during exposure to own-infant cry to activity during exposure to the own-infant control sound.

fMRI Experiment 2: Experienced Mothers in China. All study procedures and consent documents were approved by the East China Normal University Committee on Human Research. Participants provided written informed consent. We recruited 44 healthy Shanghai Chinese middle-class mothers of 7.6-mo-olds (57% male). Acoustic stimuli consisted of infant cries (ICs), infant

laughs (ILs), infant babbles (IBs), adult female cries (ACs), and noise control sounds (NCSs) (derived from and matched to ICs). ICs and ILs were retrieved from Oxford Vocal (OxVoc) Sounds (136) and public online databases. IBs, which can have characteristic sounds of the native language (137–139), were collected from native Chinese infants. ICs, ILs, and IBs came from children in the first year of life. Mothers underwent two fMRI scanning sessions at 3 tesla in a Siemens Trio Tim system. They heard 48 blocks of stimuli. Each block of 15 s consisted of one of the five sounds: IC or IL or IB or AC or NCS. Imaging data analyses were performed with BrainVoyager QX version 2.8 (Brain Innovation; www.BrainVoyager.com) (see [Supporting Information](#) for preprocessing details).

Using GLM, we analyzed whole-brain BOLD activity and created one statistical whole-brain map for each of the following contrasts: IC vs. NCS, IL vs. NCS, IB vs. NCS, and AC vs. NCS.

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Supporting Information

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Cross-Cultural Behavioral Observation

Mothers and Infants. Altogether, 684 families were recruited using methods common to developmental research with infants, including mass mailings, hospital birth notifications, patient lists of medical groups, newspaper birth announcements, and advertisements in newspapers. Infants weighed 2,500 to 5,000 g at birth. See Table S1 for demographic information by country. Argentine mother–infant dyads ($n = 99$) were recruited from metropolitan Buenos Aires (67% of the sample) and Córdoba Province (33%), an interior rural community. Belgian dyads ($n = 100$) were recruited from the Ghent (45%) and Antwerp (55%) metropolitan regions. Brazilian dyads ($n = 58$) were recruited from metropolitan Rio de Janeiro. Cameroonian dyads ($n = 29$) were Nso, an indigenous group that lives in northwest Cameroon. French dyads ($n = 49$) were recruited from Paris and its immediate banlieux. Israeli dyads ($n = 30$) were recruited from metropolitan Haifa. Italian dyads ($n = 92$) were recruited from Padua (55%), a northern city, and from the environs of Ruoti (45%), a southern town. Japanese dyads ($n = 49$) were recruited from the greater metropolitan Tokyo area. Kenyan dyads ($n = 26$) were Kamba, a Bantu group that lives in eastern Kenya. South Korean dyads ($n = 52$) were recruited from the Seoul metropolitan area. Dyads from the United States ($n = 100$) were all European American, recruited from the Washington, DC, metropolitan area, Maryland, and Virginia (77%), and from rural West Virginia (23%). Sample sizes per cultural group were designed so that the ratio of the smallest to largest would not exceed 1:4 (140).

Materials and Methods. Mothers and infants were video-recorded at home when the infant was awake and alert and the two were alone together, except for one female researcher who was a native of the same culture as the dyad. Infants were awake for virtually the entire observation (mean = 99.84%, SD = 0.01, range = 92 to 100%). We attempted to remain faithful to a principle of ecological validity by focusing on naturalistic interactions between mothers and infants in their most familiar setting (141, 142). Mothers were instructed that observations were intended to represent the dyad's typical routine and behavior and to disregard the researcher's presence insofar as possible; the researcher resisted talking to, making eye contact with, or otherwise reacting to the mother or infant while video-recording. Filming commenced after a conventional period of acclimation to the camera and the presence of the researcher (143, 144). At the conclusion of the home visit, mothers completed a demographic questionnaire originally written in English and translated into the native language of the mother using standard forward- and back-translation procedures by bilingual and bicultural developmental scientists who were natives of the countries studied (145–147).

As human infants reach the third month postpartum, motor cortex associations necessary for voluntary control of crying develop, and pitch and duration of cry stabilize, indicating that cry quality conveys information about intrinsic aspects of infant phenotypes (4, 123, 148).

Infant cry and each maternal behavior were coded in separate passes through the records. All responsive behaviors of mothers could cooccur (e.g., mothers could talk to the infant while picking up and holding the infant). Infant base rates of vocal distress were coded in real time from records using a purpose-designed computer program. A cry was counted if it lasted at least 3 s and was separated from another cry by at least 2 s. Cry episodes that were separated by less than 2 s were counted as one. A maternal behavior was considered a response when it followed the onset of infant vocal distress

within 5 s; derivation of this window was based on a review of extensive published work and features of the current dataset, such as durations, gaps between onsets, and visual plots of mother and infant behaviors (149–151). (For rationales for the parameters used as well as reliability data for coding, see ref. 152.) Coders were first trained to reliability [κ (κ) ≥ 0.60] on a standard set of records (153, 154); coder reliability was checked every 10 records to guard against coding drift; and intercoder agreement was calculated using at least 10% of each sample. With three exceptions, reliability for the six codes separately for the 11 countries ranged from 0.60 to 0.98 (86 to 99% agreement), indicating acceptable levels of intercoder reliability (154, 155). Mothers' displays of affection in Belgium ($\kappa = 0.57$), France ($\kappa = 0.47$), and Kenya ($\kappa = 0.46$) had at least 98% agreement between coders. If fewer than five occurrences of infant distress were observed, the value of the OR was regarded as missing for that dyad because there was not a sufficient sample of the behavior from that dyad to draw conclusions about behavioral contingency (134, 135, 156).

Coding produced timed event-sequential data, which were then formatted for sequential analysis using the Sequential Data Interchange Standard (134, 156). Sequential analysis is applied to elucidate temporal patterns in sequentially recorded events, describes dynamic patterns of interaction in real time, and explains the behavior of each interactant by evaluating contingency between the two. Five sequential variables occurring within a 5-s time window dependent on the onset of infant vocal distress for mother display affection, distract, nurture, pick up and hold, and talk were computed. We used the Generalized Sequential Querier program (GSEQ) version 5.1.09 (www2.gsu.edu/~psyrab/gseq/) to conduct simple and sequential statistical analyses. Single-sample t tests determined whether pairs of behaviors were significantly contingent within countries, and analyses of covariance (ANCOVAs) determined cultural differences in the odds of responding to infant cries.

Power Analysis. Post hoc power analyses were computed to determine whether the sample size of infants who cried at least five times was adequate to detect medium effects ($f = 0.25$) with $\alpha = 0.05$ in single-sample t tests within countries and ANCOVAs across countries (157). The single-sample t tests were adequately powered (power > 0.80) for all countries except Brazil (power = 0.70), Cameroon (power = 0.67), Israel (power = 0.78), and Kenya (power = 0.55). The ANCOVAs with three covariates across 11 countries had adequate power to detect medium (power = 0.95) and large (power = 0.99) effects. Hence, when judging country moderation of contingency, we gave more weight to the ANCOVAs across countries than the individual country t tests, especially for Brazil, Cameroon, Israel, and Kenya.

Preliminary Analyses. Before data analysis, univariate and multivariate distributions of the dependent variables and potential covariates (i.e., child age and mother age and education) were examined for normality, homogeneity of variance, outliers, and influential cases. The ORs for mother response to infant vocal distress with affection, distraction, nurturance, and speech were log-transformed (158). Because there were some odds of 0 and the log of 0 is undefined, a constant of 0.10 was added before the transformation so that the minimum transformed value was -1 and the value corresponding to an untransformed OR of 1 was $\log_{10}(1.10) = 0.041393$. Although the natural log is often used to transform ORs, we used the common \log_{10} because it has the same distribution as the natural log and is easier to interpret. The

OR for mother picks up and holds, given infant vocal distress, was not transformed because no transformation would improve its distribution. Instead, we followed parametric analyses with non-parametric analyses for this variable. Analyses were conducted on transformed variables, excluding outliers. Outliers were identified by exploring residuals, box plots, and Cook's distance of transformed variables in least squares models by country; one outlier was identified and excluded for display affection, pick up and hold, and talk in response to infant distress. Preliminary analyses indicated few systematic infant gender differences; therefore, gender was excluded from the analyses.

Results. ANCOVAs, controlling for infant age and maternal age and education (if significantly associated with the ORs), were performed to investigate cultural group differences in mothers' responses to infant distress. The main effect of cultural group was nonsignificant in all tests: (i) display affection toward the infant given infant vocal distress, $F(10, 374) = 1.48, P = 0.14, \eta^2_p = 0.04$; (ii) distraction, $F(10, 383) = 0.79, P = 0.64, \eta^2_p = 0.02$; (iii) nurturance, $F(10, 366) = 1.23, P = 0.27, \eta^2_p = 0.03$; (iv) pick up and hold, $F(10, 383) = 1.26, P = 0.25, \eta^2_p = 0.03$ [however, the Kruskal–Wallis test was significant, $\chi^2(10) = 19.92, P = 0.030$, and pairwise tests indicated that the contingency between infant distress vocalization and pick up and hold the infant was stronger in South Korea than in Belgium, but ORs were above 1.00 in all samples, suggesting that this difference was only one of degree]; and (v) speech, $F(10, 380) = 0.37, P = 0.96, \eta^2_p = 0.01$. The lack of cultural differences in maternal responses to infant distress indicates that these behavioral responses are culturally common.

fMRI Experiments

Some methods and procedures were common to all three fMRI experiments. Only women participated because, in the behavioral observation, only mothers were observed and because research indicates a sex dimorphism in brain responses to infant cries (112, 159). Participants reported no neurological or psychiatric disorders or birth complications, and all were right-handed. All participants gave written informed consent for voluntary participation following procedures approved for fMRI experiment 1 by the Yale University School of Medicine Human Investigations Committee, for fMRI experiment 2 by the East China Normal University Committee on Human Research, and for fMRI experiment 3 by the Ethical Committee at the University of Trento for Experiments Involving Humans.

All auditory stimuli were prepared by removing all nontarget cry sounds, such as background conversations, noises, and baby vegetative sounds. For fMRI experiments 1 and 2, control sounds were derived from white noise matched to own-infant or generic infant cry on sound intensity and frequency range and duration and projected onto the sound envelope of the cry; for fMRI experiment 3 the control sound was white noise. The resulting comparison sounds controlled for stimulus volume, intensity pattern, and frequency range without sounding anything like an actual infant cry.

To focus on activations in large cortical regions, we used a conservative whole-brain threshold for multiple comparisons [for fMRI experiment 1, $q(\text{FDR}) P < 0.01$ and, for fMRI experiment 2 and experiment 3, $q(\text{FDR}) P < 0.05$] (160). We set the threshold for fMRI experiment 1 activation map at 0.01 to reduce the size of activated clusters and thereby improve the interpretation of results.

fMRI Experiment 1: New Mothers in the United States. Mothers' mean age = 33.19 y (SD = 7.14), and infants' SD = 0.57 mo.

Acoustic stimuli. Acoustic stimuli consisted of the cry of their own infants (own-infant cry) and matched own-infant noise. Mothers made audio records of their own baby within 2 wk after delivery. Acoustic files were edited using the computer software Cool Edit Pro Version 2.0 (Syntrillium Software).

fMRI protocol. During functional scanning, mothers listened to acoustic stimuli presented binaurally using headphones (foam earplugs were used for scanner noise attenuation). Acoustic stimuli lasted 30 s, with an interstimulus interval of 10 s, during which no stimuli were presented (rest). Beeps (lasting 4 s) were inserted at 10, 20, and 30 s of each block. Mothers were instructed to press a button after each beep to ensure full attention to all sounds. All mothers were familiarized with all sounds before being scanned to habituate surprise effects. Each sound block was presented in a pseudorandom order.

fMRI data acquisition. Whole-brain functional images were acquired using an echo-planar imaging (EPI) sequence with the following parameters: echo planar T2*-weighted gradient-echo, 30 axial slices, 3.125-mm in-plane resolution; 5-mm thick, skip 0, matrix size 64×64 , flip angle = 80° , echo time (TE) = 30 ms, repetition time (TR) = 2,000 ms. Each of the two BOLD-fMRI runs consisted of 200 whole-brain images per mother; each run lasted 6 min and 50 s. Before collecting functional images, high-resolution T1-weighted anatomical images were obtained [3D magnetization-prepared rapid acquisition with gradient echo (MPRAGE), 176 slices, matrix size 256×256 , TE = 3.66, TR = 2,530 ms], and anatomical T1-weighted echo-planar images (spin-echo, 30 axial slices, 3.125-mm in-plane resolution 5-mm-thick, skip 0, matrix size 64×64 , TE = 4 ms, TR = 300 ms) were acquired to be coplanar with the functional scans for spatial registration.

fMRI data analysis. For preprocessing, 3D motion correction with trilinear interpolation and slice timing correction with ascending interleaved order, using the first slice as reference, were performed. Functional data were temporally high pass-filtered at three cycles per run length. A Gaussian kernel of 6.25 mm was applied to spatially smooth the images. The first volume of each functional run was then aligned to the high-resolution anatomy. Both functional and anatomical data were transformed into Talairach space using trilinear interpolation. Predictor time courses were convolved with a canonical hemodynamic impulse response function, starting at the beginning of each block, and included 3D-motion correction parameters.

Additional results. In line with the extant literature, we also observed activations in the dorsolateral prefrontal cortex and the insula, posterior cingulate cortices, and inferior parietal cortex (Table 1). These cerebral structures underlie social cognition involved in integration of feelings, cognitions, and actions (161, 162) and control behaviors in response to emotionally and socially relevant stimuli among women (43, 162) and empathy in mothers (43, 163–167).

fMRI Experiment 2: Experienced Mothers in China. Mothers' mean age = 30.5 y (SD = 2.2), and infants' SD = 2.3 mo.

Acoustic stimuli. IC and IL sounds were retrieved from the following public online databases: sounddogs (<https://www.sounddogs.com/>), soundbible (<https://www.soundbible.com/>), audio4fun (<https://www.audio4fun.com/>), and freesound (<https://freesound.org/>). Acoustic files were edited using the computer software Audacity 2.1.0 (<https://sourceforge.net/projects/audacity/>) and Adobe Audition CC 2015 (Adobe Systems Incorporated; www.adobe.com/it/products/audition.html).

fMRI protocol. During functional scanning, mothers listened to acoustic stimuli presented binaurally at ~ 80 dB using headphones with stereo quality sound (150 Hz to 10 KHz frequency response; foam earplugs were used for scanner noise attenuation). To ensure full attention to all sounds, participants were told that, after the scanning session, they would evaluate their feelings and emotions associated with each sound category. Sounds were presented in pseudorandomized sets of five (one sound from each acoustic category).

fMRI data acquisition. Whole-brain functional images were acquired using an EPI sequence with the following parameters: 33 slices, field of view (FOV) = 220×220 mm², voxel size = $3.4 \times 3.4 \times 3.5$ mm³, slice gap = 25%, flip angle (FA) = 90° , TE = 30 ms,

TR = 2,000 ms per volume. Additionally, high-resolution T1-weighted anatomical images (3D MPRAGE, 192 slices, matrix size 256×256 , TE = 2.34, TR = 2,530 ms) were acquired for spatial registration with the functional scans. The session consisted of 308 whole-brain images per mother, including two dummy scans at the start of each time series to allow for T1 equilibration. Two BOLD fMRI functional runs each lasted 10 min.

fMRI data analysis. For preprocessing, 3D motion correction was performed with trilinear interpolation and slice timing correction with ascending interleaved order, using the first slice as reference. Functional data were temporally high pass-filtered at three cycles per run length. A Gaussian kernel of 8 mm was applied to spatially smooth the images. The first volume of each functional run was then aligned to the high-resolution anatomy. Both functional and anatomical data were transformed into Talairach space using trilinear interpolation. Predictor time courses (one for each sound condition) were convolved with a canonical hemodynamic impulse response function, starting at the beginning of each sound, and included 3D-motion correction parameters.

Additional results. Across the four comparisons, prominent functional involvement included structures associated with emotional regulation and affect, self-relevant processes, memory (spatial and episodic), and attention.

In the IC vs. NCS contrast (Fig. 1C and Table 2), additional cerebral activations were observed in left clusters centered in the anterior cingulate cortex—which extended to the superior frontal gyrus, in the medial superior frontal gyrus and in the cerebellum—and in one bilateral cluster centered in the precentral gyri. We observed high deactivation in the left precuneus.

In the IL vs. NCS contrast (Fig. S1 and Table S3), cerebral activation also appeared in clusters centered in the right precentral gyrus (which extended to the middle frontal gyrus), in the left superior and middle frontal gyri, in the right occipital cortex, in the right cerebellar tonsil and in the bilateral uvula; activation in the left uvula included other cerebellar regions as the declive, the semilunar lobule, and the culmen. Finally, deactivated clusters were observed in the bilateral middle frontal cortex, the left precentral and the right postcentral gyri, the left parahippocampal gyrus, and the perirhinal cortex in the medial temporal lobe.

In the IB vs. NCS contrast (Fig. S2 and Table S4), cerebral activations also appeared in the right middle gyrus, in the left inferior semilunar lobule and right uvula of the cerebellum. Peaks of cerebral deactivation were observed in the bilateral retrosplenial area of the cingulum, in the left entorhinal cortex, the superior occipital gyrus, the right superior frontal sulcus, the postcentral and the angular gyri, the temporal pole, the parahippocampal gyrus, the posterior cingulate cortex, and the precuneus.

In the AC vs. NCS contrast (Fig. S3 and Table S5), cerebral activations also appeared in the left dorsolateral prefrontal cortex, anterior cingulate cortex, and bilateral uvula of the cerebellum. Peaks of cerebral deactivation were observed in clusters centered in the left middle frontal gyrus, the left precentral gyrus, the right medial and superior frontal gyri, the bilateral postcentral gyrus, and posterior cingulate cortices, the right middle cingulate cortex, the precuneus, and the left superior occipital gyrus.

Supplementary fMRI Experiment 3: Experienced Mothers and Inexperienced Nonmothers in Italy.

Mothers and nonmothers. Twelve healthy females (mean age = 32 y, SD = 3.98), six primiparas (mean age = 34 y, SD = 2.96) and six nulliparas (mean age = 30 y, SD = 4.04), participated.

Acoustic stimuli. Cries from 10 female and 10 male 1-y-olds were edited using Praat computer software (www.praat.com). A total of 20 acoustic excerpts of natural infant cries were selected from a pool of home videos and presented with comparable episodes of intensity- and duration-matched white noise. Stimuli were presented in a single fMRI run in a blocked design. Stimuli (cry and

white noise) lasted 10 s, with an interstimulus interval of 14 s of silence (rest). The two types of stimuli were presented in a fixed order a total of 10 times. The 20 cry stimuli were different, and they were pseudorandomized between participants. Each cry was presented once to minimize habituation effects. The experiment lasted ~16 min.

fMRI protocol. Women underwent fMRI scanning at 4 tesla in a MedSpec Biospin MR scanner. Imaging data analyses were performed as in fMRI experiment 1, and whole-brain BOLD activity contrasted exposure to infant crying with white noise. During functional scanning, participants listened passively to the acoustic stimuli presented binaurally at 75 dB sound pressure level (SPL) using Serene Sound headphones (Resonance Technologies), with stereo quality sound (40 Hz to 40 KHz frequency response) and passive scanner noise attenuation (30 dB).

fMRI data acquisition. Whole-brain functional data were acquired using echo-planar imaging, sensitive to BOLD contrast [34 slices, tilted 18° from intracommisural plane, FOV = 192×192 mm², voxel size = $3 \times 3 \times 3$ mm³, slice gap = 15%, flip angle (FA) = 73° , TE = 33 ms, TR = 2,000 ms per volume]. A high-resolution T1-weighted image of the whole brain [MPRAGE: 176 slices, generalized auto-calibrating partial parallel acquisition (GRAPPA) with an acceleration factor of 2, FOV = 256×256 mm², voxel size = $1 \times 1 \times 1$ mm, TI = 1,020 ms, TE = 4.18 ms, TR = 2,700 ms] was acquired for the purpose of spatial coregistration. An additional scan was performed to measure the point-spread function of the acquired sequence, which served for distortion correction as is expected with high-field imaging. The experimental session consisted of 489 whole-brain images per participant, including four dummy scans at the start of each time series to allow for T1 equilibration.

fMRI data analysis. For preprocessing, distortions in geometry and intensity in the EPI images were corrected, and distortion correction was applied on the basis of the point spread function (PSF) data acquired before the EPI scans (168). Then, the signal preprocessing was the same as fMRI experiment 2. Both functional and anatomical data were transformed into Talairach space using trilinear interpolation. Predictor time courses were convolved with a canonical hemodynamic impulse response function, starting at the beginning of each trial, and included 3D-motion correction parameters.

Results. Results of fMRI experiment 3 (Fig. S4 and Table S6) replicated results of fMRI experiment 1 and experiment 2 for mothers revealing increased activation in right pre-SMA, two bilateral clusters in the inferior frontal cortex, two large bilateral clusters in the superior temporal cortex, and bilateral midcingulum.

Additional Results. Differences between mothers and nonmothers were then analyzed within each area revealed by the main contrast. In most regions, there was no difference (minimum $P = 0.15$). However, nonmothers showed more activation compared with mothers in right inferior frontal ($df = 10$; mean mother group BOLD = 1.494; mean nonmothers group BOLD = 2.362; SE = 0.318; $t = -2.729$; $P = 0.02$) and right pre-SMA ($df = 10$; mean mother group BOLD = 0.535; mean nonmothers group BOLD = 1.372; SE = 0.338; $t = -2.484$; $P = 0.03$). Mothers are presumably more experienced than nonmothers and have been exposed to infant cries for years, and thus know when and how to respond to babies. Decreased activity in this brain area in experienced mothers compared with activation in novices has been observed previously (169).

Caveat. These findings concerning higher brain activities induced by infant cries can only indicate certain mental states and attitudes in women (intention to move and speak, listening) because they are reverse inferences linked to the results (170). Activations of specific brain areas can occur for a variety of reasons, and, because the fMRI findings are not directly linked to the behavioral findings, the fMRI findings are supportive of the cross-cultural findings and guide future fMRI investigations.

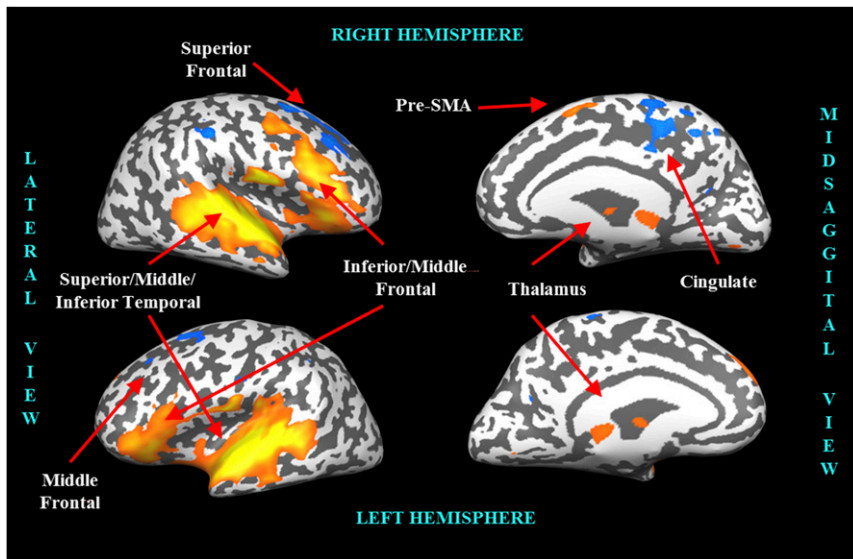


Fig. 53. Chinese mothers. Graphical representation of brain regions resulting from the contrast AC vs. NCS in the whole group of participants. The top figure refers to the right hemisphere, the bottom figure the left hemisphere, the left figure lateral views, and the right figure midsagittal views.

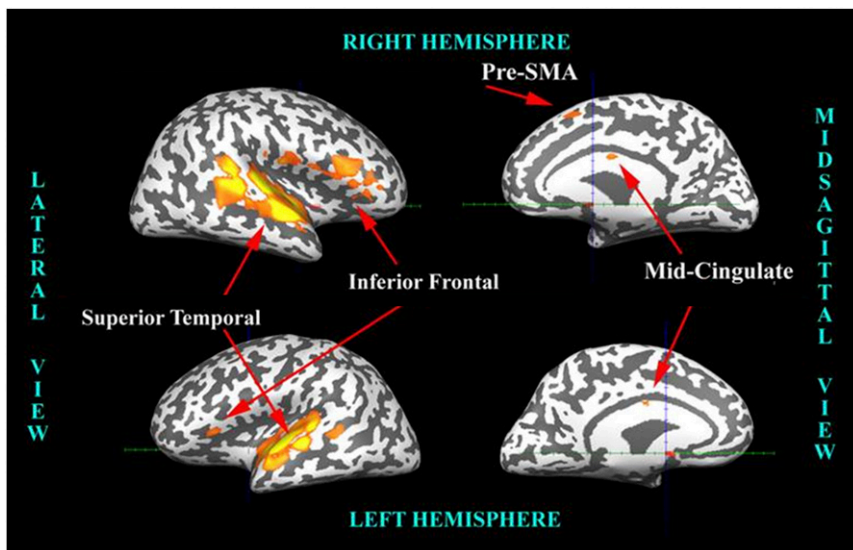


Fig. 54. Italian mothers and nonmothers. Graphical representation of brain regions resulting from the contrast IC vs. NCS in the whole group of participants. The top figure refers to the right hemisphere, the bottom figure the left hemisphere, the left figure lateral views, and the right figure midsagittal views.

Table S2. Descriptive statistics and tests of contingency for odds ratios given infant vocal distress in the behavioral observation

Response to infant distress	Argentina	Belgium	Brazil	Cameroon	France	Israel	Italy	Japan	Kenya	South Korea	United States	TOTAL
Mother displays affection	-0.37 (0.67) t(59) = -4.78, P < 0.001, d = -0.62	-0.51 (0.73) t(47) = -5.21, P < 0.001, d = -0.75	-0.25 (0.79) t(19) = -1.66, ns, d = -0.37	-0.71 (0.66) t(16) = -4.67, P < 0.001, d = -1.13	-0.27 (0.75) t(30) = -2.35, P < 0.05, d = -0.42	-0.59 (0.75) t(23) = -4.12, P < 0.05, d = -0.84	-0.18 (0.75) t(51) = -2.13, P < 0.05, d = -0.29	-0.19 (0.77) t(26) = -1.53, ns, d = -0.29	-0.29 (0.89) t(11) = -1.29, ns, d = -0.37	-0.39 (0.68) t(34) = -3.73, P < 0.001, d = -0.63	-0.25 (0.78) t(58) = -2.88, P < 0.01, d = -0.38	-0.35 (0.74) t(384) = -10.20, P < 0.001, d = -0.52
Mother distracts infant	-0.27 (0.65) t(60) = -3.74, P < 0.001, d = -0.48	-0.32 (0.76) t(49) = -3.35, P < 0.01, d = -0.47	-0.21 (0.80) t(19) = -1.40, ns, d = -0.31	-0.39 (0.66) t(17) = -2.80, P < 0.05, d = -0.66	-0.25 (0.66) t(31) = -2.49, P < 0.05, d = -0.44	-0.24 (0.77) t(24) = -1.85, ns, d = -0.37	-0.36 (0.65) t(51) = -4.40, P < 0.001, d = -0.61	-0.34 (0.69) t(26) = -2.83, P < 0.01, d = -0.54	-0.74 (0.67) t(13) = -4.33, P = 0.001, d = -1.16	-0.21 (0.59) t(34) = -2.48, P < 0.05, d = -0.42	-0.36 (0.75) t(59) = -4.11, P < 0.001, d = -0.53	-0.32 (0.70) t(393) = -10.19, P < 0.001, d = -0.51
Mother nurtures infant	-0.45 (0.85) t(55) = -4.30, P < 0.001, d = -0.57	-0.56 (0.83) t(48) = -5.07, P < 0.001, d = -0.72	-0.40 (0.92) t(18) = -2.07, ns, d = -0.48	-0.26 (1.11) t(17) = -1.16, ns, d = -0.27	-0.72 (0.66) t(30) = -6.40, P < 0.001, d = -1.15	-0.08 (0.91) t(21) = -0.63, ns, d = -0.13	-0.34 (0.87) t(49) = -3.15, P < 0.01, d = -0.45	-0.57 (0.75) t(24) = -4.10, P < 0.001, d = -0.82	-0.41 (0.86) t(13) = -1.96, ns, d = -0.52	-0.32 (0.95) t(34) = -2.27, P < 0.05, d = -0.38	-0.26 (0.92) t(57) = -2.50, P < 0.05, d = -0.33	-0.41 (0.88) t(376) = -9.91, P < 0.001, d = -0.51
Mother picks up and holds infant	9.98 (26.70) t(60) = 2.63, P < 0.05, d = 0.34	1.66 (4.06) t(49) = 1.15, ns, d = 0.16	7.75 (16.43) t(19) = 1.84, ns, d = 0.41	4.54 (7.19) t(18) = 2.15, P < 0.05, d = 0.49	6.14 (12.04) t(30) = 2.32, P < 0.05, d = 0.42	3.86 (7.58) t(23) = 1.85, ns, d = 0.38	5.68 (10.90) t(51) = 3.09, P < 0.01, d = 0.43	4.76 (7.62) t(27) = 2.61, P < 0.01, d = 0.49	3.39 (6.18) t(13) = 1.44, ns, d = 0.39	6.84 (7.90) t(34) = 4.38, P < 0.001, d = 0.74	4.66 (9.60) t(59) = 2.95, P < 0.01, d = 0.38	5.61 (13.68) t(393) = 6.69, P < 0.001, d = 0.34
Mother talks to infant	0.14 (0.21) t(58) = 3.50, P < 0.001, d = 0.46	0.16 (0.16) t(48) = 5.04, P < 0.001, d = 0.72	0.18 (0.35) t(19) = 1.77, ns, d = 0.39	0.17 (0.47) t(18) = 1.23, ns, d = 0.28	0.16 (0.14) t(31) = 4.92, P < 0.001, d = 0.87	0.11 (0.35) t(24) = 0.97, ns, d = 0.19	0.16 (0.35) t(55) = 2.43, P < 0.05, d = 0.34	0.19 (0.26) t(27) = 3.00, P < 0.01, d = 0.57	0.02 (0.75) t(13) = -0.09, ns, d = -0.02	0.16 (0.13) t(34) = 5.73, P = 0.001, d = 0.97	0.13 (0.33) t(59) = 2.06, P < 0.05, d = 0.27	0.15 (0.30) t(392) = 6.91, P < 0.001, d = 0.35

Except for "Mother picks up and holds infant," data are transformed odds ratios, mean (SD), excluding outliers; t tests tested whether the odds ratio was significantly different from 0.04139269 [$\log_{10}(1.10)$]. ns, $P > 0.05$.

Table S3. Chinese mothers: IL vs. NCS

Region	Brodmann area	Peak x	Peak y	Peak z	t	Voxels at q(FDR) < 0.05
Right <u>superior</u> temporal gyrus, temporal pole, inferior and middle frontal gyri, precentral gyrus, supramarginal gyrus, insula	6/9/13/22/38/40/45/47	54	-10	7	17.62	55,532
Left <u>superior</u> and middle <u>temporal</u> gyri, inferior frontal gyrus, insula	13/22/47	-51	-10	4	14.79	51,213
Left <u>posterior</u> (declive, semi-lunar lobule, <u>uvula</u>) and anterior (culmen) cerellum		-18	-67	-23	5.31	27,048
Right <u>precentral</u> gyrus, middle frontal gyrus (premotor cortex)	6	45	-1	46	4.99	2,791
Right medial frontal gyrus (pre-supplementary motor area)	6	6	5	61	4.36	1,818
Left superior frontal gyrus	9	-27	47	28	4.00	609
Left lentiform nucleus (lateral globus pallidus)		-18	-1	-5	3.99	1,267
Right <u>thalamus</u> , lentiform nucleus (putamen, lateral globus pallidus)		6	-10	4	3.99	6,944
Right caudate (body)		12	-16	25	3.64	315
Left medial frontal gyrus	10	-3	56	10	3.59	276
Left middle frontal gyrus	9	-54	20	25	3.59	445
Left medial frontal gyrus (supplementary motor area)	6	-6	-1	70	3.45	149
Right cerebellar tonsil		21	-58	-42	3.35	106
Right inferior frontal gyrus	47	33	29	-11	3.27	183
Right occipital lobe	17	8	-97	-2	3.27	142
Right posterior cerellum (uvula)		33	-82	-23	3.26	113
Left middle frontal gyrus (premotor cortex)	6	-27	8	52	-3.56	246
Left medial temporal lobe (perirhinal cortex)	36	-30	-28	-14	-3.57	124
Right postcentral gyrus	3	51	-19	37	-3.71	923
Right middle frontal gyrus (premotor cortex)	6	24	14	52	-4.24	1,086
Left precentral gyrus	4	-51	-13	28	-4.50	1,620
Left parahippocampal gyrus (entorhinal cortex)	34	-15	-10	-20	-4.60	305

Brain regions (peaks of activity in extensive clusters are underlined), Brodmann area specifications, Talairach coordinates, t values, and cluster sizes of brain regions resulting from the contrast IL vs. NCS in the whole group of participants. Brodmann areas are missing for regions that fall outside the cerebral cortex (e.g., subcortical and cerebellar regions).

Table S4. Chinese mothers: IB vs. NCS

Region	Brodman area	Peak x	Peak y	Peak z	t	Voxels at q(FDR) < 0.05
<u>Right superior</u> and middle temporal gyri, transverse gyrus, inferior frontal gyrus, postcentral gyrus, insula	13/22/40/41/44/47	60	-4	4	14.47	36,312
<u>Left superior</u> and middle temporal gyri, inferior frontal gyrus (pars orbitalis), insula	13/22/41/44/45/47	-54	-10	4	13.72	50,328
<u>Left posterior</u> (inferior semi-lunar lobule, declive) and anterior cerebellum		-12	-73	-41	6.39	9,509
Right middle frontal gyrus	9/46	42	14	25	5.56	3,186
Right <u>posterior</u> (uvula) and anterior (culmen, dentate) cerebellum		15	-76	-32	5.20	5,533
Right inferior frontal gyrus (pars orbitalis)	47	39	26	10	4.19	1,416
Right middle frontal gyrus (premotor cortex)	6	45	2	46	4.07	2,477
<u>Left and right thalamus</u>		-6	-7	4	3.69	1,561
Right medial frontal gyrus (supplementary motor area)	6	6	-1	61	3.56	320
Left lentiform nucleus (medial globus pallidus)		-21	-16	-2	3.32	132
Right posterior cingulate cortex	31	9	-43	43	-3.26	135
Right parahippocampal gyrus		27	-34	-8	-3.53	331
Right superior frontal sulcus		18	2	52	-3.66	217
Right precuneus	7	9	-64	43	-3.69	507
Left superior occipital gyrus	19	-36	-76	25	-3.84	513
Right temporal pole	38	48	17	-29	-4.04	922
Right angular gyrus	39	36	-73	31	-4.34	1,938
Left posterior cingulate cortex (retrosplenial area)	30	-18	-58	16	-4.37	1,353
Right posterior cingulate cortex (retrosplenial area)	30	15	-49	13	-4.41	1,460
Right <u>postcentral</u> gyrus, supramarginal gyrus	2/40	51	-28	37	-4.78	2,458
Left medial temporal lobe (entorhinal cortex)	28	-18	-4	-26	-4.93	649

Brain regions (peaks of activity in extensive clusters are underlined), Brodmann area specifications, Talairach coordinates, t values, and cluster sizes of brain regions resulting from the contrast IB vs. NCS in the whole group of participants. Brodmann areas are missing for regions that fall outside the cerebral cortex (e.g., subcortical and cerebellar regions). For two cortical clusters (right parahippocampal gyrus and superior frontal sulcus), the BA was not reported because the activation peaks fall in white matter.

Table S5. Chinese mothers: AC vs. NCS

Region	Brodman area	Peak x	Peak y	Peak z	t	Voxels at q(FDR) < 0.05
<u>Right and left superior</u> temporal gyrus, inferior and middle frontal gyri, insula, globus pallidus (only right), putamen, thalamus, right amygdala (only right), midbrain (substantia nigra)	9/13/22/44/45/47	54	-10	7	15.70	162,798
<u>Left and right posterior</u> cerebellum (uvula), anterior cerebellum		-15	-70	-32	5.74	27,779
Right medial frontal gyrus (pre-supplementary motor area)	6	6	5	58	4.19	1,261
Left dorsolateral prefrontal cortex	9	-12	50	34	4.09	3,429
Left anterior cingulate cortex	32	-3	41	-5	3.23	121
Right posterior cingulate cortex	31	15	-52	16	-3.16	229
Left posterior cingulate cortex	30	-12	-58	16	-3.16	109
Left superior occipital gyrus	19	-33	-76	25	-3.18	150
Left middle frontal gyrus	8	-21	23	37	-3.19	130
Left precentral gyrus	4	-12	-31	61	-3.24	502
Right precuneus	7	9	-46	55	-3.33	280
Right medial frontal gyrus	9	9	32	31	-3.34	161
Left postcentral gyrus	2	-51	-19	31	-3.38	209
Left middle frontal gyrus (premotor cortex)	6	-27	8	55	-3.87	1,318
Right middle and <u>posterior</u> cingulate cortex	24/31	9	-34	40	-3.89	3,895
Right postcentral gyrus	2	54	-25	37	-4.14	1,629
Right superior frontal gyrus	6/8	18	5	52	-5.30	7,657

Brain regions (peaks of activity in extensive clusters are underlined), Brodmann area specifications, Talairach coordinates, t values, and cluster sizes of brain regions resulting from the contrast AC vs. NCS in the whole group of participants. Brodmann areas are missing for regions that fall outside the cerebral cortex (e.g., subcortical and cerebellar regions).

Table S6. Italian mothers and nonmothers: Contrast cry vs. white noise

Region	Brodmann area	Peak x	Peak y	Peak z	t	Voxels at q(FDR) < 0.05
Right superior temporal gyrus	22/41/42	45	-13	-2	19.75	15,831
Left superior temporal gyrus	22/41/42	-57	-22	10	15.72	11,368
Right inferior frontal gyrus	44/45	42	17	13	7.22	1,464
Left inferior frontal gyrus	44/45	-39	20	13	6.16	254
Mid-cingulate gyrus	24	0	-10	31	6.06	66
Right presupplementary motor area (superior frontal gyrus)	6	6	14	55	3.99	214

Brain regions, Brodmann area specifications, Talairach coordinates, t values, and cluster sizes of brain regions resulting from the contrast cry vs. white noise in the whole group of participants in fMRI experiment 3.