

Sex differences in directional brain responses to infant hunger cries

Nicola De Pisapia^a, Marc H. Bornstein^b, Paola Rigo^a, Gianluca Esposito^c, Simona De Falco^a and Paola Venuti^a

Infant cries are a critical survival mechanism that draw the attention of adult caregivers, who can then satisfy the basic needs of otherwise helpless infants. Here, we used functional neuroimaging to determine the effects of infant hunger cries on the brain activity of adults who were in a cognitively nondemanding mental state of awake rest. We found that the brains of men and women, independent of parental status (parent or nonparent), reacted differently to infant cries. Specifically, the dorsal medial prefrontal and posterior cingulate areas, known to be involved in mind wandering (the stream of thought typical of awake rest), remained active in men during exposure to infant cries, whereas in women, activity in these regions decreased. These results show sex-dependent modulation of brain responses to infant requests to be fed, and specifically, they indicate that women interrupt mind wandering when

exposed to the sounds of infant hunger cries, whereas men carry on without interruption. *NeuroReport* 24:142–146 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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^aDepartment of Cognitive Science and Education, University of Trento, Trento, Italy, ^bChild and Family Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Public Health Service, Rockville, Maryland, USA and ^cKuroda Research Unit for Affiliative Social Behavior, RIKEN Brain Science Institute, Saitama, Japan

Correspondence to Nicola De Pisapia, DiSCoF – Department of Cognitive Sciences, University of Trento, Rovereto 38068, Italy
Tel: +39 0461 88 3087; fax: +39 0461 28 3066;
e-mail: nicola.depisapia@unitn.it

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Introduction

Lacking agency, new-born babies and young infants communicate their needs and physiological states mainly through vocalizing and facial expression. Infant cries communicate hunger, distress or the desire for physical closeness [1], and they effectively induce a broad range of caregiver responses, such as proximity [2] or endocrine reactions [3].

In the present study, we analysed sex differences in brain activations in response to infant hunger cries. Women and men, mothers and fathers have different relationships with their children. By many accounts, several cross-cultural in nature, human mothers provide more direct care to children than do fathers [4,5]. Maternal responses to infant cries are critical for infant survival and the development of wholesome mother–infant emotional bonding [6]. Women rate infant cries as more likely to evoke sympathy and caregiving than men, and men rate cries as more aversive, as eliciting more irritation and anger, and evaluate infants who cry as more spoiled [7,8].

Several neuroimaging studies have examined adult brain activity to infant cries, but so far, have produced conflicting findings [9]. Few neurobiological studies have included men. In one exception, Seifritz *et al.* [10] assessed female and male (parents and nonparents) responses to crying and laughter of unfamiliar infants; women showed greater prefrontal activation than men to infant vocalizations irrespective of parental status.

The main goal of our study was to investigate neural responses associated with listening to infant cries during rest and mind wandering. We asked participants to lie in the functional MRI (fMRI) scanner, and to think of nothing in particular, and so let their minds wander freely. They were told that they would hear various sounds intermixed with phases of rest and that they were required to do nothing with these sounds. In the key condition, participants heard cries of hungry babies.

We chose to study the brain's spontaneous reactions to infant cry, because immersion in 'internal' thoughts, without being focused on external stimuli, is acknowledged to be the most common mode of thinking, occupying almost half of our daily awake mental activity [11]. This situation has the additional advantage that it emulates ecological validity: when a baby begins to communicate a physiological or a psychological need through crying, this signal likely reaches a caregiver who is not already attending to the baby, but who is instead mind wandering or may be mentally focused elsewhere. The developing neuroimaging literature on mind wandering has shown that this mental state usually involves coherent and spontaneous low-frequency fluctuations in a specific brain network that includes medial prefrontal, posterior cingulate, hippocampus, superior temporal and inferior parietal regions, collectively called the default-mode network [12]. In particular, medial regions of the default-mode network (the medial prefrontal and the posterior cingulate cortex) are involved in self-reflection

and self-centred thinking [13]. By contrast, when an individual focuses on external stimuli, the default-mode network is deactivated [14]. Thus, the deactivation of the default-mode network is a reliable marker of the extent and efficiency of the observer's engagement with the external world [15]; for example, it is interpreted to indicate awareness in patients with disorders of consciousness (minimally conscious or vegetative state) during passive sentence listening [16]. The default-mode network encompasses brain regions that show task-induced deactivation, and although its activity is believed to represent on-going and organized cognitive processing that occurs when the brain is not actively involved in another task, its deactivation reflects an interruption of on-going mind wandering [17].

Materials and methods

Participants

Eighteen healthy adults (nine women, mean age = 31.50 years, $SD = 4.27$; and nine men, mean age = 35.38 years, $SD = 4.63$) were recruited through the University of Trento webpage and local advertisements. Nine were parents of children older than 4 years (four females/five males) and nine were nonparents (five females/four males). All participants were right-handed, and none reported neurological or psychiatric disorders. Participants were ethnically homogeneous of European heritage. All participants provided written informed consent for participation. The procedures were approved by the ethical committee for experiments involving humans at the University of Trento.

Acoustic stimuli

In our main condition, we analysed brain responses to infant hunger cries vis-à-vis the adult at rest. We used 14 s for the rest period between acoustic stimuli. We also compared responses during hunger cries to two types of auditory control stimuli: white noise and atypical cries. All acoustic files were edited using the computer software Praat (<http://www.praat.com>) to normalize volume, equate for duration (10 s) and remove all background noise. A total of 10 acoustic excerpts of natural infant hunger cries from 10 1-year-old infants (five girls/five boys) were selected from a pool of home videos of typically developing infants who did not present any significant medical or developmental concerns (confirmed by their normal scores on the Child Behavior Checklist; [18]). Atypical cries were extracted from home videos of 10 (five girls/five boys) ~1-year-old infants who later, as children of ~3 years, were diagnosed with autism spectrum disorder (the clinical diagnosis was made by a child psychiatrist according to DSM-IV-R criteria and confirmed by ADI-R, ADOS-G). Atypical cries differ from hunger cries in morphological characteristics, especially their fundamental frequency (atypical cries > hunger cries). The fundamental frequency (f_0) is generated by vibration of the vocal folds and is heard as the pitch of the

cry. f_0 influences adult responses and caregiver perceptions: for example, higher-frequency cries are regularly perceived as more aversive and distressed than low-frequency cries [19]. To ensure that hunger cries and atypical cries were representative of the typical expected range of cry sounds for typical and atypical children, respectively, we analysed their f_0 . A long-term average spectrum (LTAS) was used to provide spectral information for each cry. For all cry stimuli, the first spectral peak (FSP) of the LTAS was obtained. FSP is the frequency value (in Hz) of the first amplitude peak across the LTAS. It is an estimate of the average f_0 of the cry episodes. The FSPs of hunger cries were $M = 526.87$ ($SD = 60.33$) and those of atypical cries were $M = 637.87$ ($SD = 66.56$), $F(1,16) = 18.80$, P less than 0.001.

Functional magnetic resonance imaging protocol

During functional scanning, participants were asked to listen passively to the acoustic stimuli presented binaurally at ~75 dB SPL using Serene Sound (Resonance Technologies, Northridge, California, USA) headphones, with stereo quality sound (40 Hz to 40 KHz frequency response) and passive scanner noise attenuation (30 dB). Participants underwent a single fMRI run in which stimuli were presented in a blocked design. Acoustic stimuli of each category (hunger cries, atypical cries, white noise) lasted 10 s, with an interstimulus interval of 14 s during which no stimuli were presented (rest). These stimulus categories were presented in a fixed order a total of 10 times. The 10 cry stimuli in each category were different, and they were pseudorandomized between participants. Each cry was presented once to minimize habituation effects.

Functional magnetic resonance imaging data acquisition

Participants underwent MRI scanning at 4 T in a MedSpec Biospin MR scanner (Bruker Ettlingen, Germany) using an eight-channel birdcage head coil. Mild external head restraint was used to minimize head movement. Before collecting functional images, a high-resolution T1-weighted image of the entire brain (MPRAGE: 176 slices, GRAPPA acquisition with an acceleration factor of 2, field of view = $256 \times 256 \text{ mm}^2$, voxel size = $1 \times 1 \times 1 \text{ mm}^3$, $TI = 1020 \text{ ms}$, $TE = 4.18 \text{ ms}$, $TR = 2700 \text{ ms}$) was acquired for the purpose of spatial coregistration. Whole-brain functional data were acquired using echoplanar imaging, sensitive to blood oxygenation level dependent (BOLD) contrast (34 slices, tilted 18° from intracommisural plane, field of view = $192 \times 192 \text{ mm}^2$, voxel size = $3 \times 3 \times 3 \text{ mm}^3$, slice gap = 15%, flip angle = 73° , $TE = 33 \text{ ms}$, $TR = 2 \text{ s}$ per volume). We performed an additional scan 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. The experiment lasted 16 min and 10 s.

Functional magnetic resonance imaging data analysis

Imaging data analyses were carried out using BrainVoyager QX 2.1 (BrainInnovation B.V., Maastricht, The Netherlands). For preprocessing, we corrected for distortions in geometry and intensity in the Echo-Planar Imaging (EPI) images, and we applied distortion correction on the basis of the point-spread function data acquired before the EPI scans. Then, we performed 3D motion correction with trilinear interpolation and slice timing correction with ascending interleaved order using the first slice as a reference. Functional data were temporally high-pass filtered at three cycles/run length. A Gaussian kernel of 8 mm was applied to smooth the images spatially. Next, we aligned the first volume of each functional run to the high-resolution anatomy. Both functional and anatomical data were transformed into Talairach space [20] using trilinear interpolation. Predictor time courses were convolved with a canonical haemodynamic impulse response function starting at the beginning of each trial and included 3D-motion correction parameters.

Using general linear models, we explored the sensitivity of brain regions to cries of hungry, healthy infants. We identified brain regions that were more or less active during white noise compared with rest for all participants. This contrast allowed us to localize brain regions that – independent of sex or parent status – were responsive to sudden neutral sounds while individuals were resting and free to let their minds wander. Subsequently, we carried out orthogonal region of interest analyses within the individual regions identified in the previous contrast. For all reported contrasts, we used random effects and false discovery rate to correct for multiple comparisons.

Results

Consistent with the extant literature [21], the first analysis showed that, during white noise auditory stimulation, left and right superior temporal lobe regions were more active (in particular, centred on the Heschl's gyri, otherwise known as transverse temporal gyri; Brodmann area 41), whereas the dorsal medial prefrontal and posterior cingulate cortex (BA 23) regions – two key medial components of the

default-mode network – were less active (Table 1). A follow-up comparison of group differences (men versus women; parent versus nonparent) in activity during white noise compared with rest showed no differences (minimum $P = 0.12$), indicating that neither sex nor parenthood status affects these regions differently when listening to white noise compared with rest (Fig. 1b, for the male versus female comparison).

Our main analysis sought group differences during passive listening to hunger cries versus rest (men versus women, and parent versus nonparent) within each of the localized regions identified as more sensitive to sounds. The parenthood group contrast showed no difference (minimum $P = 0.16$). However, the sex group contrast showed significant differences in the two medial regions, namely the dorsal medial prefrontal cortex ($d.f. = 16$; M female group BOLD = -0.341 ; M male group BOLD = -0.004 ; SE = 0.15; $t = 2.22$; $P = 0.041$) and the posterior cingulate cortex ($d.f. = 16$; M female group BOLD = -0.342 ; M male group BOLD = -0.022 ; SE = 0.097; $t = 3.76$; $P = 0.001$). No sex group difference emerged in the left superior ($P = 0.10$) or the right superior temporal regions ($P = 0.57$). Thus, the sex difference consisted in men not deactivating in the dorsal medial prefrontal cortex and the posterior cingulate cortex during hunger cries relative to rest (Fig. 1a). Sex differences again emerged as significant when we directly compared hunger cries with white noise in both the dorsal medial prefrontal cortex ($d.f. = 16$; M female group BOLD = -0.268 ; M male group BOLD = 0.531; SE = 0.354; $t = 2.26$; $P = 0.03$) and the posterior cingulate cortex ($d.f. = 16$; M female group BOLD = -0.327 ; M male group BOLD = 0.544; SE = 0.193; $t = 4.50$; $P = 0.0003$), but not significant in either the left ($P = 0.75$) or the right ($P = 0.69$) superior temporal regions.

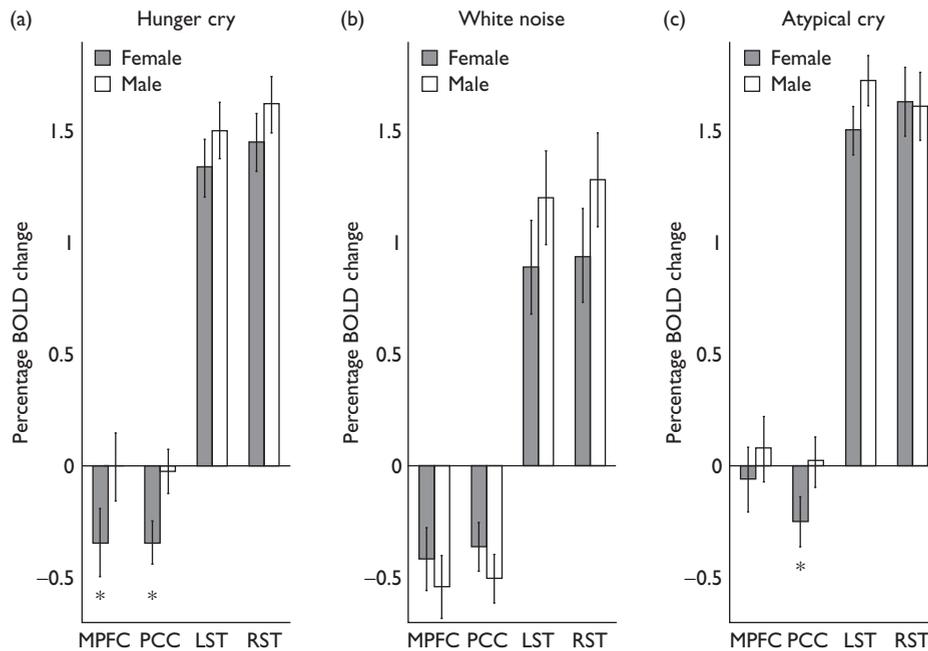
When examining sex group differences within the same regions for atypical cries (another emotionally charged stimulus produced by infants, but with a difference in frequency; see Materials and methods section) versus rest (Fig. 1c), we observed a significant difference only in the posterior cingulate cortex ($d.f. = 16$; M female group BOLD = -0.247 ; M male group BOLD = 0.019; SE = 0.109; $t = 2.44$; $P = 0.02$). There was no difference in the dorsal medial prefrontal cortex ($P = 0.35$) in the right superior temporal lobe ($P = 0.89$) or the left superior

Table 1 Passive-listening brain regions

Auditory brain regions (white noise > rest)	BA	Peak X	Peak Y	Peak Z	Number of voxels at $q(\text{FDR}) < 0.01$
Decreased activation (white noise < rest)					
Dorsal medial prefrontal cortex	9/10	3	47	28	3926
Posterior cingulate cortex	23	0	-46	25	1827
Increased activation (white noise > rest)					
Left Heschl's (transverse temporal) gyrus	41	-45	-19	7	6368
Right Heschl's (transverse temporal) gyrus	41	48	-13	4	7379

Brain regions resulting from the contrast white noise against rest in the entire group of participants. These regions serve as a mask for auditory-sensitive regions (both increase and decrease of activation) during passive exposure to sudden sounds. FDR, false discovery rate.

Fig. 1



Percentage BOLD (blood oxygenation level dependent) signal change versus rest in men and women in three conditions: (a) hunger cry, (b) white noise and (c) atypical cry. Asterisks indicate significant differences between males and females' percentage BOLD change ($P < 0.05$). Deactivation in the dorsal MPFC and the PCC during hunger cry – distinctive of the mind-wandering interruption – took place only for the female group, but not for the male group. During atypical cry, this sex difference was significant only in the PCC, but not in the dorsal MPFC. For precise coordinates of regions, see Table 1. Error bars are SEs. LST, left superior temporal gyrus; MPFC, medial prefrontal cortex; PCC, posterior cingulate cortex; RST, right superior temporal gyrus.

temporal lobe ($P = 0.09$). Thus, the sex difference in the dorsal medial prefrontal cortex (i.e. only the female group deactivated) was specific to hunger cries; it was not found in closely matched atypical cries.

Discussion

In this experiment, adult participants passively listened to hunger cries of infants, cries of typically developing infants and white noise. Participants were simply resting in the scanner and not required to perform any task or even to pay attention to the auditory stimuli. During exposure to hunger cries compared with rest and white noise, the brain activity of women and men differed considerably in two key medial nodes of the default-mode network, namely, the dorsal medial prefrontal cortex and the posterior cingulate cortex (BA 23). Specifically, activity in these regions decreased in women, but not in men. During exposure to atypical cries (sounds closely matching hunger cries, but with higher fundamental frequency), the sex difference emerged only in the posterior cingulate cortex, but not in the dorsal medial prefrontal cortex.

Deactivation in the default-mode network is a common response to sounds that recruit attention during passive sensory tasks [21]. Researchers studying brain function generally assume that presentation of a stimulus or a task will increase neural activity in the brain relative to a resting

state. However, many tasks result in decreases in blood flow or blood-oxygenation indexes of neural activity relative to a 'resting' baseline, a phenomenon referred to as task-induced deactivation. This change may occur when resources shift from on-going, internally generated processing typical of 'resting' states to processing required by an exogenous task. Research shows that task-induced deactivation occurs consistently in default-mode network regions, and researchers speculate that 'rest' is actually a state of organized cognitive activity involving many processes, including monitoring the external environment, monitoring body image and state and processing emotions [15,17,22,23]. Included among these possible resting activities are on-going internal 'thought' processes that humans experience during resting consciousness, sometimes referred to as a 'stream of consciousness'. Because these 'thought' processes are generally self-initiated and self-referential, and not related to specific exogenous task demands, they have been reported as 'task-unrelated thoughts' [24]. As task-induced deactivation magnitude increases across task conditions, the frequency of task-unrelated thoughts decreases [17]. Internally generated cognitive activities (such as task-unrelated thoughts) are suspended because of reduced availability of resources when attention shifts from on-going, internal processes to performance of an exogenous task. As an auditory target detection task increases in difficulty (i.e. increased processing demands), multiple brain regions show

correlated decreases in the BOLD signal (i.e. more negative task-induced deactivations values) relative to the resting state [17].

In this experiment, we observed a medial default-mode network deactivation in both sex groups during passive exposure to white noise; by contrast, dorsal medial prefrontal and posterior cingulate cortical activity did not deactivate in men during exposure to hunger cries, but instead remained at the same level as during rest. These medial cortical regions are key nodes of the default-mode network associated with self-reflection activities [13], and thus these results suggest that women interrupt their mind wandering when they are exposed to infant hunger cries, whereas men carry on without interruption.

We found no difference in the response to hunger cries depending on parental status. The size of the sample did not allow us to make further sex comparisons within each parental group (parent and nonparents). Nonetheless, our results are indicative of an 'alloparental care' predisposition among women, a result common in several mammalian species where adult females act as cooperative breeders and share responsibility for infant care [25].

Conclusion

We found a sex difference in brain responses to hunger cries in medial default-mode network regions: specifically, women decrease activity in these regions when they suddenly and passively hear infant hunger cries, but men do not. In functional terms, this finding suggests that, whereas the female brain during hunger cries interrupts on-going mind wandering, the male brain continues in self-reflection typical of awake resting states.

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Conflicts of interest

There are no conflicts of interest.

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