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Perception of suffering and compassion experience: Brain gender disparities

Roberto E. Mercadillo^a, José Luis Díaz^b, Erick H. Pasaye^{a,c}, Fernando A. Barrios^{a,*}^aInstitute of Neurobiology, Universidad Nacional Autónoma de México, Querétaro, Mexico^bSchool of Medicine, Universidad Nacional Autónoma de México, México D.F., Mexico^cNational Institute of Neurology and Neurosurgery "Manuel Velasco Suárez", México D.F., Mexico

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ABSTRACT

Compassion is considered a moral emotion related to the perception of suffering in others, and resulting in a motivation to alleviate the afflicted party. We compared brain correlates of compassion-evoking images in women and men. BOLD functional images of 24 healthy volunteers (twelve women and twelve men; age = 27 ± 2.5 y.o.) were acquired in a 3T magnetic resonance scanner while subjects viewed pictures of human suffering previously verified to elicit compassion and indicated their compassionate experience by finger movements. Functional analysis revealed that while women manifested activation in areas involved in basic emotional, empathic, and moral processes, such as basal regions and cingulate and frontal cortices, activation in men was restricted mainly to the occipital cortex and parahippocampal gyrus. These findings suggest that compassion and its moral elements constitute gender-relative subjective phenomena emerging from differently evolved neural mechanisms and socially learned features possibly related to nurturing skills.

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1. Introduction

The interactions between moral and emotional cognition have been recently studied in terms of moral emotions, which refer to a kind of emotions elicited during the perception of social transgressions encoded in attitudes and beliefs, and frequently imply an empathic component to infer the mental states in others (Bennett & Matthews, 2000; Kagan, 2005; Moll, De Oliveira-Souza, & Zahn, 2008; Nichols, 2002). In contrast to basic emotions that are elicited by stimuli that motivate clearly adaptive behaviors, such as fleeing in response to fear or attack elicited by anger (Ekman, 1993; Izard, 1992), moral emotions are related to the welfare of society as a whole or of individuals different from the person who experiences the emotion (Haidt, 2003).

Neurobiological approaches to moral emotions and reasoning have applied neuroimaging techniques to identify regional brain activity while the subjects process visual scenes, auditory statements, or moral dilemmas. The findings indicate activation in subcortical regions related to the experience of basic emotions, such as the amygdala, thalamus, insular cortex, and upper midbrain, but also in cortical regions linked to complex cognition, such as the

prefrontal and orbitofrontal cortices and the superior temporal sulcus (Casebeer, 2003; Greene & Haidt, 2002; Moll, de Oliveira-Souza, Bramati, & Grafman, 2002; Moll & Schulkin, 2009; Young & Koenigs, 2007).

Because it is strongly related to social cooperation (Damasio, 2006), compassion can be considered a moral emotion usually elicited by witnessing the suffering of others and resulting in a motivation to alleviate their perceived affliction (Haidt, 2003; Lazarus, 1991). Neuroimaging studies focused in the experience of compassionate attitudes and decisions of prosocial actions report neural activity related with theory of mind, empathy, and decision making involving the medial and inferior prefrontal cortex, temporo-parietal junction, cingulate cortex, insula and midbrain (Kedia, Berthoz, Wessa, Hiltun, & Martinot, 2008; Kim et al., 2009; Lutz, Brefczynski-Lewis, Johnstone, & Davidson, 2008; Moll et al., 2007).

In a recent validation of compassion-evoking pictures, Mercadillo and coworkers found that compassion experience includes attributes of basic negative emotions, such as displeasure and high arousal. Both women and men reported similar appraisals related to valence, arousal, and dominance when viewing compassion-evoking pictures representing human suffering in different contexts. Nevertheless, women's appraisals indicated a more intense experience of compassion and arousal when the compassion-evoking pictures depicted scenes of illness in particular, and reported lower dominance and higher arousal than men when viewing socially neutral pictures used as control stimuli (Mercadillo, Barrios, & Diaz, 2007).

* Corresponding author. Address: Institute of Neurobiology, Universidad Nacional Autónoma de México, Campus UNAM Juriquilla, Blvd. Juriquilla 3001, Querétaro, QRO 76230, Mexico. Fax: +52 442 238 1046.

E-mail address: barrios@inb.unam.mx (F.A. Barrios).

Although gender approaches are not reported in the neurobiology of compassion, some neuropsychological studies have shown gender differences in moral brain processing, emotional experience, and cognitive functions in which women manifest a pattern of brain activity related with emotional experience and strategies in resting electroencephalographic recordings (Jausovec & Jausovec, 2005). Also, women exhibit stronger defensive reactivity than men when viewing aversive pictures (Bradley, Codispoti, Cuthbert, & Lang, 2001) and report less control over the experience related to viewing pictures representing moral transgressions, such as intention to harm and frustration of goals (Javela, Mercadillo, & Ramirez, 2008). Neurobiological approaches report that women manifest a more intense activation of emotional-control brain areas when processing memories or sounds, while men manifest activation of cortical cognitive-control related areas (Canli, Desmond, Zhao, & Gabrieli, 2002; Flores-Gutierrez et al., 2009; Koch et al., 2007). Men exhibit more activation in frontal and temporal regions related to social learning and emotional concepts when viewing facial expressions depicting contempt, while women manifest activation in the insula when faces represent disgust (Aleman & Swart, 2008). Also, it has been suggested that women exhibit a more intense empathic sensitivity when viewing chimerical faces (Rueckert & Naybar, 2008) and moral-emotional understanding when perceiving unpleasant pictures, as inferred from their activity in insular and cingulate cortices (Harenski, Antonenko, Shane, & Kiehl, 2008). In reference to moral reasoning, women profusely elaborate moral judgments oriented to the care of others, whereas men tend to adjust their assessment based on a sense of duty (Bjorklund, 2003; Self & Olivarez, 1993). It has also been reported that women are more empathic in conflict-resolution situations, and that men manifest a lower activation of brain areas related to empathy when they observe a painful stimulus received by a person known to be unfair (de Wied, Branje, & Meeus, 2007; Singer et al., 2006).

Biological research on cognitive and emotional processes requires consistency between subjective reports and their related physiological changes (Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005). Because women report more intense compassion and emotional appraisals related to emotions when viewing gestures and scenes of suffering, neurophysiological differences can be expected. The aim of the present study was to analyze gender differences in subjective compassion responses and their neurobiological foundations. We expected that, in response to experimentally evoked compassion experiences, women would show greater and more diverse neural activation than men in brain regions related to emotional experience, empathy, and prosocial actions such as prefrontal and cingulate cortex, insula, and temporoparietal junction.

2. Materials and methods

2.1. Preceding behavioral data and pilot study

In preparation for the functional MRI investigation, a behavioral study was applied using first-rate visual compassion-eliciting stimuli (Mercadillo, Barrios, & Diaz, 2007). Eighty-four pictures were selected from the International Affective Picture System (IAPS) and rated, as proposed in this archive, in the dimensions of valence, arousal, and dominance, where 1 indicates the lowest and 9 the highest rating. A compassion dimension was added where a score of 1 represented null compassion and 9 the greatest compassionate experience. With this method, 28 pictures evoking high compassion were obtained, and 28 pictures representing non-compassion-evoking stimuli were selected as controls, 14 depicting objects and landscapes and 14 showing customary social

scenes, such as people drinking coffee (information about the ratings of valence, arousal, dominance and compassion dimensions in each visual stimulus are presented in Tables 1–12 of the Supplementary material).

Prior to the MRI scanning presented in this research, six volunteers participated in a pilot study conducted to determine the appropriate mode to obtain the emotional appraisals during the fMRI session. Since the participants reported difficulty in remembering the 1–9 appraisal range and expressing the experience of more than one emotional dimension when viewing each picture, we decided to record only the absence or presence of compassionate feelings when viewing each picture. The subjects were instructed to press a key with one finger when they experienced a compassionate feeling or with the contralateral finger if they did not. The reaction time results obtained from the E-Prime response record (E-Prime responses achievement, Psychology Software Tools, Inc. Pittsburgh PA.) indicated that viewing the picture for two seconds was enough to produce the requested appraisal signal. Since repeated viewing of an image likely reduces the reported emotional experience, we decided to obtain the response only once during the MRI scanning to avoid habituation to the stimuli.

2.2. Participants

A different set of 24 healthy subjects in the same age and educational range as the behavioral study volunteers (twelve women and twelve men, mean age (M) = 27, standard deviation (s.d.) = 2.5 and mean of 15 years of education) participated in the fMRI sessions. In agreement with the procedures authorized by the Institutional Review Board (IRB), the ethical principles recommended by the American Psychological Association (O'Donohue & Ferguson, 2003), and the World Medical Association Declaration of Helsinki, all subjects gave written informed consent after the nature of the experiment was explained to them. Participants were strongly right-handed as measured by the Edinburgh Handedness Inventory and in good general health as confirmed by a clinical interview. The Mexican electronic version of the Symptom Check List 90 (González-Santos, Mercadillo, Graff, & Barrios, 2007) and a clinical interview verified the absence of current neurological and mental disorders. No subject was taking any medication or was paid for participating. As was already pointed out, no participant had previously seen the pictures they viewed during the study. All the imaging studies were conducted at the Neuroimaging Unit of the National Institute of Neurology and Neurosurgery, Mexico City.

2.3. Task parameters

The functional MRI session consisted of series conformed by 100 pictures alternating compassion- and non-compassion-evoking stimuli selected from a validated set of the International Affective Picture System (Lang, Bradley, & Curberth, 2005; Mercadillo, Barrios, & Diaz, 2007). Since compassion was reported by viewing expressions or situations manifested in social contexts, it is necessary to distinguish the neurocognitive functions related with the visual analysis of social context that may not involve compassionate processes *per se*. Thus, we decided to present two functional runs of visual stimuli contrasting compassion with both non-social and social conditions in an event-related design. The *Compassion-Objects* series contrasted the compassion-correlated brain activity (14 compassion-eliciting pictures depicting suffering in different contexts such as war scenes, sad facial expressions, and famine) from the activity related with viewing non-human scenes (14 emotionally neutral pictures representing objects or landscapes that were repeated to form a neutral background of 86 stimuli). The *Compassion-Social* series contrasted the compassion-correlated

brain activity (14 compassion-eliciting pictures depicting suffering in different contexts) from the activity related with viewing non-compassion-evoking social scenes (14 emotionally neutral social pictures such as people walking or waiting for the bus repeated to form a socially neutral background of 86 stimuli). Compassion- and non-compassion-evoking stimuli used in one series were totally different than the stimuli used in the other series and were pseudo-randomly distributed so that compassion-evoking pictures were separated by 12–25 s. Pictures were projected centrally every 2500 ms followed by a fixation cross for 500 ms. The sequence is illustrated in Fig. 1.

Participants saw the stimuli through the IFIS Presentation Response System (In Vivo Inc., Orlando, FL) screen situated in front of their eyes over the head coil. The presentation-response paradigm was executed and synchronized using E-Prime (Psychology Software Tools, Inc., Pittsburgh, PA). The presentation was synchronized in the same manner for all the subjects.

The IFIS response system was utilized to record the subjects' responses, verifying a compassionate/non-compassionate experience elicited during the observation of each of the pictures. In order to neutralize the average brain activation areas related to finger motor responses, 12 of the participants (six women, six men) were instructed to press a button with their right index finger if they experienced a compassionate feeling and a button with their left index finger in the absence of a compassionate feeling. The other 12 participants were instructed to respond in an inverse manner. In order to verify the proper understanding of the task, participants practiced in a mock procedure inside the scanner before the MRI session viewing 10 pictures different from those used in the study and by indicating their experience using the IFIS response system.

2.5. Behavioral analysis

The frequency of compassionate experiences indicated by the subjects during the two series of stimuli through the finger movement in the IFIS response system was obtained for each participant. These responses given by both genders were compared applying a Mann–Whitney U test to estimate different experiences reported by genders.

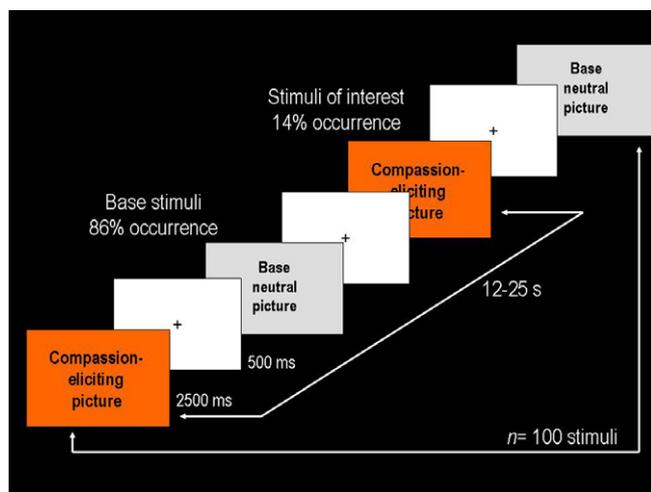


Fig. 1. Event-related design used in the presentation of visual stimuli. The series consisted of 100 pictures: 14 compassion-eliciting pictures depicting suffering in different contexts (stimuli of interest) and 86 neutral pictures representing objects or common social scenes (base stimuli). Each stimulus was presented for 2500 ms followed by a fixation cross for 500 ms. Stimuli of interest were randomly presented at 12–25 s intervals.

2.6. Functional image acquisition and analysis

Anatomical and functional pulse sequences covering the whole brain were performed on a 3.0 Tesla GE scanner (General Electric Medical Systems, Milwaukee, WI). Anatomical images were acquired using a high resolution 3D SPGR (spoiled gradient sequence): 140 slices, TR = 24 ms, TE = 5 ms, flip angle = 30°, with $1 \times 1 \times 1 \text{ mm}^3$ resolution voxels. For the functional image acquisition a BOLD EPI-GRE (blood-oxygen level dependent echo planar imaging gradient-echo) sequence was acquired over 30, 5-mm thick slices with no gap and $4 \times 4 \text{ mm}^2$ in plane resolution; TR = 3000 ms, TE = 30 ms, flip angle = 90°, FOV = 24 cm. All fMRI data were transferred to offline workstations using DICOM format and all the image analysis was executed using SPM5 (Wellcome Department of Imaging Neuroscience, <http://www.fil.ion.ucl.ac.uk/spm/>).

Pre-statistics image analysis included time slice correction to synchronize for inter-slice time difference; realignment for head movement; normalization for framing all the brain volume images into the MNI standard (Montreal Neurological Institute anatomical brain template); and spatial smoothing to limit size effect (Friston, 2007).

The stimuli of interest in our event-related design were the 14 compassion-evoking pictures distributed along each functional run. Since we performed a pseudo-randomized presentation, we extracted from the E-Prime record the onset vector for each subject indicating the event or stimulus of interest distributed along 100 time frames. The General Linear Model description matrix for each subject was defined using the 14 recorded onset vectors with zero duration and including the motion correction parameters calculated during the realignment process as multiple regressors. Contrast between conditions (Compassion vs. Objects pictures and Compassion vs. Non-compassion-Social pictures) was estimated as a first level statistical analysis for each subject. To estimate the average activation for all subjects in each functional series, a second level statistical analysis was estimated with a one-sample *t*-test using the first level contrast images of each subject. The same procedure was executed to estimate the average activation for women and for men. To contrast Gender vs. Gender we performed a second level two-sample *t*-test using the first level contrasts of females and males. Clustering was estimated by thresholding with False Discovery Rate (FDR) correction at $p = 0.05$ (illustrations of the matrix analyses executed in SPM 5 are presented in the Fig. 1 of the Supplementary material).

Cluster centroid coordinates of brain activation were estimated in SPM, and brain structure and function related data was acquired using the Talairach Daemon Client system (Lancaster et al., 2000) obtaining the approximate Brodmann area.

3. Results and discussion

No gender differences were observed in the frequency of reported compassionate experiences in the two series of stimuli as indicated by the Mann–Whitney U test. Neural correlates of finger movement indicating compassionate experience showed that both the 12 right- and the 12 left-finger responders manifested activation in the specific contralateral motor cortex regions (see Fig. 2 and Tables 13 and 14 of the Supplementary material).

While viewing compassion-eliciting stimuli alternated with pictures representing objects (Compassion-Objects series), the average of BOLD activation in all subjects was observed in the prefrontal cortex (BA 47, 46), Broca's area (BA 44), the bilateral superior parietal region (BA 7), occipito-temporal region (BA 37 and 19), anterior cingulate cortex (BA 24), and insula (B 13). Women exhibited a more diverse frontal and temporal activation as well as activation

in the anterior cingulate cortex (BA 24). Men manifested activation in the posterior cingulate region (BA 29) and cerebellum (see Table 1 and Figs. 2 and 3). The statistical comparisons *Women vs. Men* indicated activation in the anterior cingulate cortex in BA 24, while *Men vs. Women* showed null activation, indicating that all activations in men are canceled by the activations in women (see Table 1 and Fig. 2 of the Supplementary material).

While viewing pictures in the *Compassion-Social* series, both genders manifested activation in the prefrontal (BA 46, 47), the occipital (BA 19) and anterior cingulate cortices (BA 24), insula (BA13), and cerebellum. Women exhibited BOLD signals in thalamus and basal ganglia and a more diverse prefrontal (BA 47, 46 and 10), anterior cingulate (BA 24 and 32), and cerebellar activation. Activation in parahippocampal cortex (BA 36) was observed in men but not in women (see Table 2 and Fig. 4). The contrast

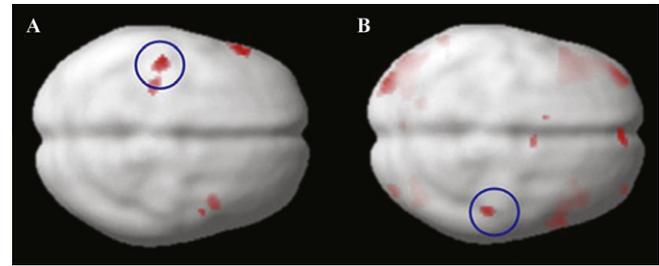


Fig. 2. Brain activity correlated with the index finger movement indicating compassionate experience (blue circle). A. Right finger responders: left postcentral gyrus ($Z = 5.17$; $-46, -19, 53$; Brodmann 2). B. Left responders: right postcentral gyrus ($Z = 4.90$; $50-24, 55$; Brodmann 2). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Activated brain regions identified by BOLD signal correlated with the experience of compassion while viewing pictures representing suffering alternated with pictures representing objects and landscapes.

Anatomical region	L/R	BA	Cluster size	Z value	MNI coordinates		
					x	y	z
<i>All subjects</i>							
Inferior frontal gyrus	R	9	83	3.96	52	22	18
Inferior frontal gyrus	L	47	125	4.19	-40	20	-12
Inferior frontal gyrus	L	44	473	5.49	-58	12	16
Middle frontal gyrus	R	6	56	3.99	36	-6	48
Middle frontal gyrus	L	6	23	3.96	-36	-2	44
Middle frontal gyrus	L	46	199	4.5	-48	26	18
Postcentral gyrus	L	2	103	4.21	-46	-24	40
Superior parietal lobule	R	7	316	4.68	30	-58	60
Precuneus	L	7	274	4.16	-22	-66	58
Middle temporal gyrus	R	37	2879	4.98	52	-70	10
Middle occipital gyrus	L	19	2080	4.75	-48	-80	14
Cingulate gyrus	L	24	296	4.49	-4	6	46
Insula	R	13	102	4.26	62	-34	22
Insula	L	13	126	4.24	-32	28	-4
<i>Women</i>							
Inferior frontal gyrus	R	44	158	3.57	56	22	6
Inferior frontal gyrus	L	44	81	4.38	-60	10	18
Inferior frontal gyrus	L	45	310	3.8	-50	28	14
Inferior frontal gyrus	R	47	21	3.41	42	30	-16
Middle frontal gyrus	L	9	36	3.41	-34	26	24
Middle frontal gyrus	R	46	104	3.66	48	28	18
Superior frontal gyrus	L	6	52	4.05	-4	32	54
Superior parietal lobule	R	7	124	3.59	32	-56	58
Superior temporal gyrus	R	22	45	3.46	52	-36	2
Middle temporal gyrus	R	37	1894	4.66	50	-72	10
Lingual gyrus	L	18	66	3.95	-10	-104	-4
Middle occipital gyrus	L	19	1228	4.1	-50	-74	-4
Anterior cingulate	L	24	259	4.04	2	26	8
<i>Men</i>							
Middle frontal gyrus	L	9	44	3.48	-30	32	28
Middle frontal gyrus	R	6	558	3.75	36	-6	50
Inferior frontal gyrus	L	44	3122	4.81	-58	12	16
Inferior frontal gyrus	L	47	132	3.65	-48	20	-12
Postcentral gyrus	L	2	323	3.75	-42	-26	40
Superior parietal lobule	L	7	263	3.37	-24	-64	64
Inferior parietal lobule	R	40	284	3.93	46	-26	42
Precuneus	R	7	670	3.97	6	-56	64
Middle temporal gyrus	L	37	1725	4.22	-50	-64	14
Precuneus	R	31	300	3.37	28	-78	32
Inferior occipital gyrus	R	19	2496	4.14	44	-80	0
Posterior cingulate	L	29	192	3.58	0	-48	10
Clastrum	L	*	67	3.32	-30	28	-4
Declive	L	*	114	3.32	-42	-74	-16
<i>Women vs. Men</i>							
Anterior cingulate		24	43	3.40	0	26	6
<i>Men vs. Women</i>							
Null							

Notes: Results for *All subjects*, *Women* and *Men* indicate significant activation at $p < 0.05$. when False Discovery Rate correction was applied. Results for *Women vs. Men* indicate significant activation at $p < 0.001$ with no correction. BA = approximate Brodmann area location obtained by using the Talairach Daemon Client system.

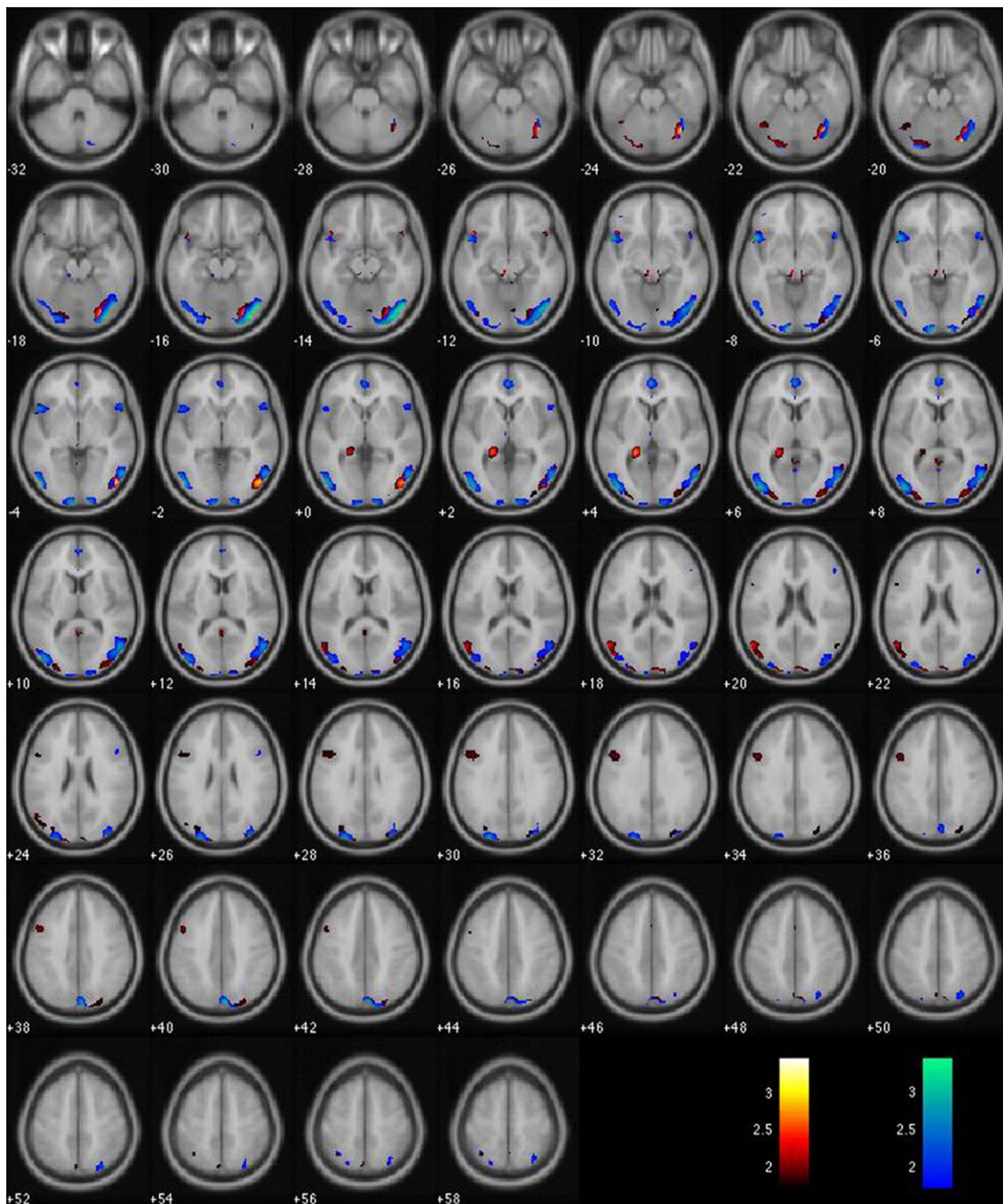


Fig. 3. Functional results in axial views while subjects were viewing pictures depicting human suffering alternated with pictures showing objects and landscapes in the run *Compassion-Objects*. Regions in red-yellow represent the activation manifested for men, and the regions in blue-green refer to the women's brain. Women manifested a higher activity in the frontal and the occipital cortices and the anterior cingulated cortex while men showed evidence for activity in the posterior cingulated cortex and cerebellum. The False Discovery Rate correction was used with $p = 0.05$ in all cases.

Women vs. Men showed that only women manifested activation in the left superior frontal gyrus and thalamus. The contrast *Men vs. Women* showed null activation (see Table 2 and Fig. 2 of the Supplementary material).

The activation of the insula and frontal regions in BA 6, 44, and 47 has been related to certain complex cognitive processes required for human social interactions and decisions based on the inference of the psychological states in others and the representation of one's own bodily state in social context (Craig, 2002; Kennedy, Semendeferi, & Courchesne, 2007; Knutson, McClellan,

& Grafman, 2008; Lang & Bradley, 2010; Pfeifer, Iacoboni, Mazziotta, & Dapretto, 2008; Rizzolatti & Fabbri-Destro, 2008; Singer et al., 2006; van der Gaag, Minderaa, & Keysers, 2007), motivation, emotional direction, and moral judgments (Greene, Nystrom, Engell, Darley, & Cohen, 2004; Moll, de Oliveira-Souza, Eslinger, et al., 2002; Moll et al., 2005), particularly in aversive situations (Schienle, Schafer, & Vaitl, 2008). These processes may be required for the decision to aid the suffering party, motivated not only by socially learned moral values, but also by the individual's own experience of situations categorized as aversive.

Table 2
Brain regions identified by BOLD signal correlated with the experience of compassion while viewing pictures representing suffering, alternated with pictures depicting habitual social scenes.

Anatomical region	L/R	BA	Cluster size	Z value	MNI coordinates		
					x	y	z
<i>All subjects</i>							
Inferior frontal gyrus	R	46	32	4.82	54	32	10
Inferior frontal gyrus	R	47	7	4.63	42	32	-14
Postcentral gyrus	L	2	5	4.9	-60	-18	34
Middle occipital gyrus	L	18	76	4.96	-34	-88	4
Fusiform gyrus	L	19	719	5.29	-42	-72	-10
Cingulate gyrus	L	24	6	4.63	0	-8	42
Insula	L	13	247	5.32	-40	24	-2
Cerebellum/culmen	R	*	1322	5.75	32	-42	-26
Cerebellum/declive	L	*	32	4.85	-32	-86	-18
<i>Women</i>							
Inferior frontal gyrus	R	47	165	4.2	36	20	-16
Inferior frontal gyrus	R	46	126	4.18	52	38	4
Superior frontal gyrus	L	10	590	5.3	-26	56	18
Inferior parietal lobule	L	40	53	4.18	-42	-28	34
Cingulate gyrus	R	24	131	4.07	8	22	26
Cingulate gyrus	L	24	289	5.46	0	-8	42
Cingulate gyrus	L	32	225	4.32	-4	28	36
Insula	L	13	151	4.54	-40	24	-2
Thalamus medial dorsal nucleus	L	*	270	4.63	0	-22	2
Lentiform nucleus/putamen	L	*	81	4.07	-14	4	6
Culmen	R	*	1501	5.23	28	-42	-26
Culmen	L	*	251	4.13	-40	-54	-20
Declive	R	*	200	4.32	10	-74	-20
Declive	L	*	326	4.04	-32	-86	-14
<i>Men</i>							
Superior frontal gyrus	R	6	29	3.39	10	16	68
Precentral gyrus	R	44	1670	4.3	48	18	0
Precentral gyrus	L	6	51	3.39	-48	4	26
Superior parietal lobule	R	7	157	3.51	34	-52	54
Superior parietal lobule	L	7	454	3.77	-22	-58	68
Precuneus	R	19	198	3.62	30	-76	38
Postcentral gyrus	R	2	305	3.78	46	-28	66
Inferior occipital gyrus	R	19	4991	4.55	46	-74	-8
Fusiform gyrus	L	19	4752	4.62	-42	-70	-8
Cingulate gyrus	R	24	266	3.31	10	20	30
Insula	L	13	2376	4.52	-36	22	-2
Parahippocampal gyrus	R	36	76	3.6	48	-24	-12
Parahippocampal gyrus	L	*	70	3.53	-26	-18	-14
Substantia nigra	R	*	232	3.47	20	-18	-12
<i>Women vs. Men</i>							
Superior frontal gyrus	L	9	88	3.38	-12	56	26
Superior frontal gyrus	L	10	33	4.00	-24	54	18
Thalamus	L	*	7	3.16	2	-24	4
<i>Men vs. Women</i>							
Null							

Notes: Results for *All subjects*, *Women* and *Men* indicate significant activation at $p < 0.05$, when False Discovery Rate correction was applied. BA = approximate Brodmann area location obtained by using the Talairach Daemon Client system.

Parietal activation in BA 7 manifested for all subjects in the *Compassion-Objects* series suggests that compassion experience involves visuo-motor coordination and semantic processes (De Carli et al., 2007; Greene et al., 2004; Moll, de Oliveira-Souza, Bramati et al., 2002; Prehn et al., 2008; Tettamanti et al., 2002, 2009) while the occipital-temporal activation in BA 19 and BA 37 implies detailed analysis of mutilation scenes and object recognition (Dong et al., 2000; Schupp et al., 2007). It is reported that the spatial frequencies presented in some pictures of the IAPS influences the emotional appraisal when viewing the picture, particularly in objects (Delplanque, N'Diaye, Scherer, & Grandjean, 2007). Therefore, it seems necessary to consider that some physical characteristics of the preceding picture may influence the perceptual analysis. Nevertheless, in this case, the absence of occipital and temporal activation for all subjects in the *Compassion-Social* series could imply that the semantic and visual processes are required to analyze social scenes whether they do or do not elicit compassion.

A more diverse activation of cingulate, parahippocampal and cerebellar regions related to decision making, motor control, and spatial representation was more readily observed in the *Compassion-Social* than in the *Compassion-Objects* series. As occurs with auditory stimuli (Zaehle, Clapp, Hamm, Meyer, & Kirk, 2007), these results suggest that neutral social scenes may prime the activation of brain areas related to social cognition regarding the unexpected appearance of an aversive picture of suffering. Differences between genders were more noticeable in the *Compassion-Social* than in the *Compassion-Objects* series (see Tables 1 and 2 and Fig. 5). Activation in female prefrontal cortex and thalamus suggests that this priming constitutes a more salient effect in women. In addition, behavioral data presenting women's higher arousal appraisals when observing non-compassion-evoking social scenes but not in objects (see Tables 6 and 10 in the Supplementary material) suggest that gender differences could be attributable not only to the experience of compassion but to a general emotional analysis of social scenes.

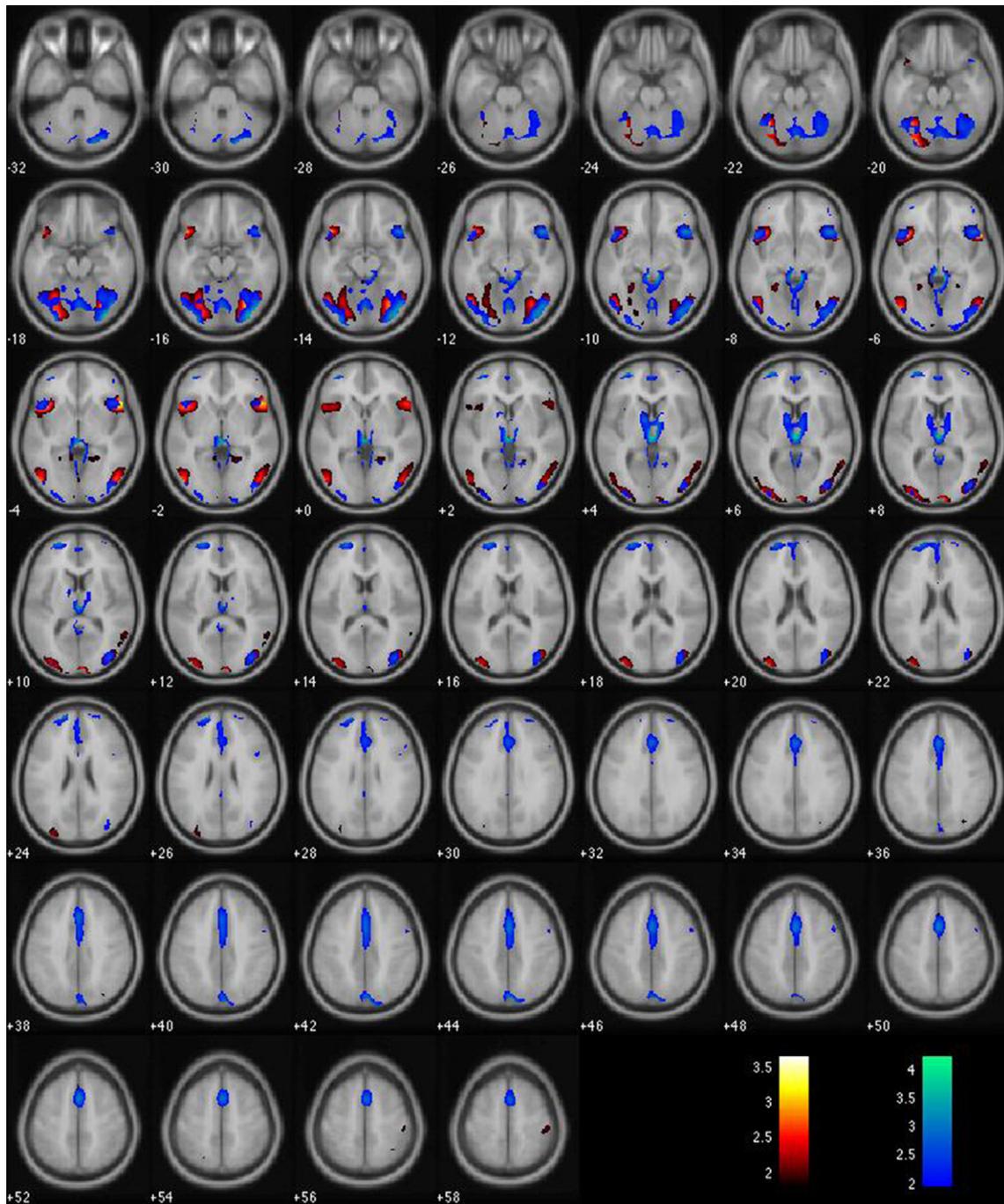


Fig. 4. Functional results in axial views while subjects were viewing pictures depicting human suffering alternated with pictures representing common social scenes in the run *Compassion-Social*. Regions in red-yellow represent the activation manifested for men, and the regions in blue-green refer to the women's brain. Women manifested a higher activity in the frontal cortex and the anterior cingulate cortex while men showed evidence for activity in the parietal and occipital cortices. The False Discovery Rate correction was used with $p = 0.05$ in all cases.

Brain activity for *all subjects* in prefrontal and cingulate cortices, precuneus, and insula in both functional series agreed with previous neuroimaging reports and indicates that the event-related design used in this study reflects the compassionate attitudes, experiences, and prosocial decision-making presented in other studies (Kedia et al., 2008; Kim et al., 2009; Lutz et al., 2008; Moll et al., 2007). Moreover, cognitive functions of the identified brain areas and interconnections between them are also related with basic processes of emotional recognition, somatic states, attention, and human memory formation (Adolphs, Tranel, & Damasio, 2003; Buckner, Kelley, & Petersen, 1999; Posner, Sheese, Odludas,

& Tang, 2006; Rolls, 2005). In particular, prefrontal activity in BA 9 and 46 and parietal activity in BA 7 have been related with working memory processing (Baddeley, 2003; Owen, McMillan, Laird, & Bullmore, 2005) and was observed more in the *Compassion-Objects* than in the *Compassion-Social* series, suggesting that although the non-compassion control stimuli in both series were repeated, the prefrontal and parietal activation observed was related to cognitive processes required to analyze the compassion experience in social context.

In agreement with our hypothesis, the present findings indicate that women accomplish the complex emotional-cognitive process

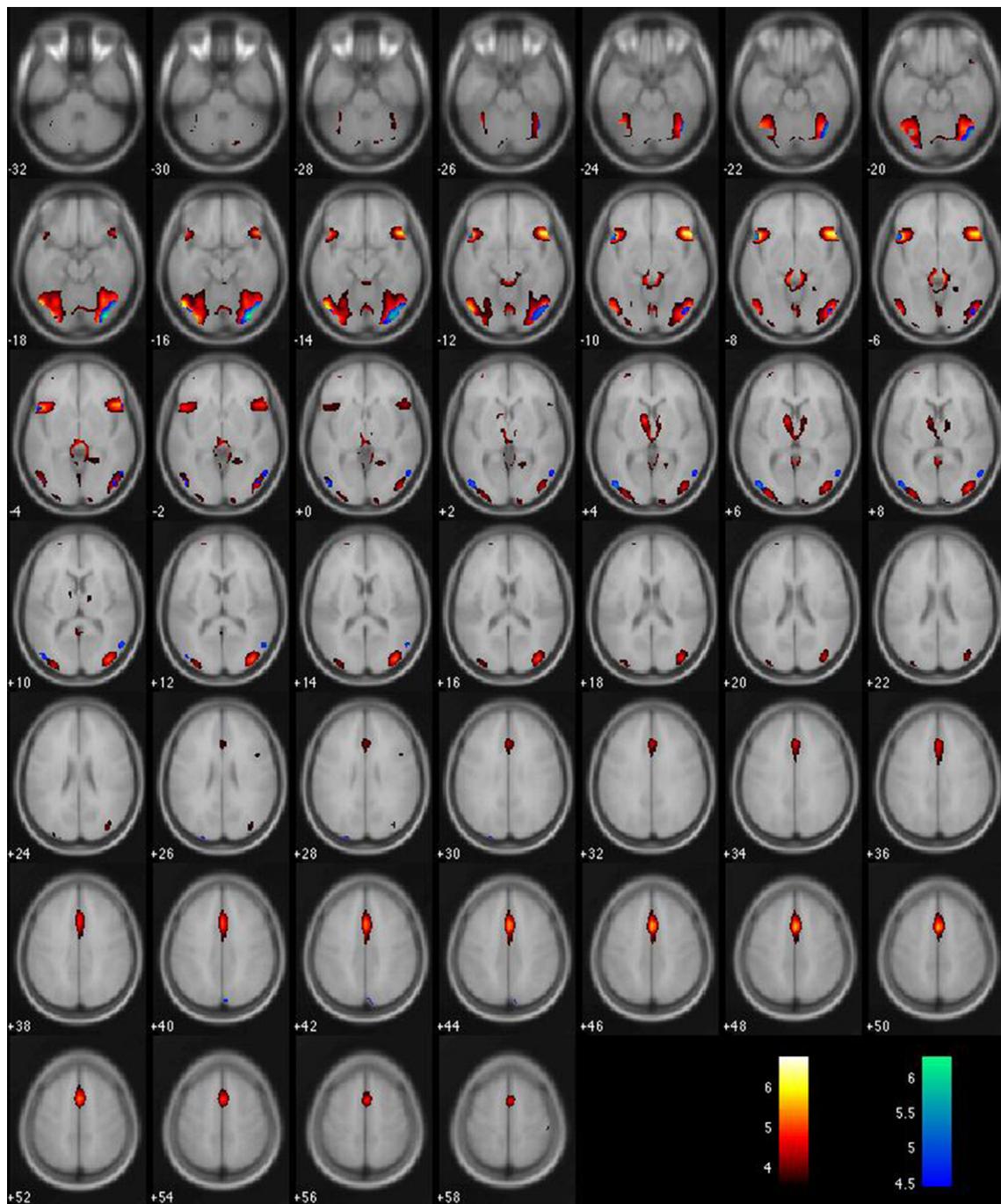


Fig. 5. Functional results in axial views representing both compassionate conditions applied. *Compassion-Objects*: blue; *Compassion-Social*: red. Image shows activation of prefrontal and cingulate cortex in both conditions. Cerebellar activity was identified only in the *Compassion-Social* run. The False Discovery Rate correction was used with $p = 0.05$ in all cases.

defined as compassion through a more elaborate brain processing than men by engaging prefrontal and cingulate cortices. The results agree with gender differences reporting a greater emotional sensitivity in women when viewing aversive and suffering situations (Bradley et al., 2003; Garcia-Garcia, Dominguez-Borras, SanMiguel, & Escera, 2008; Harenski et al., 2008; Javela, Mercadillo, & Ramirez, 2008) and women's moral reasoning directed to the care of others (Bjorklund, 2003). Only women manifested activity in the thalamus, necessary to maintain continuous afferent and efferent neural signals, and the putamen. With the caudate nucleus, the putamen forms the striatum complex of the basal ganglia, whose function has been associated with motor regulation and also with the experience of love, sexual selection, and reward systems through its reciprocal connections with the cerebral cortex (Aron et al., 2005; Bianchi-Demicheli, Grafton, & Ortigue, 2006). Also, women showed a greater activation in the cerebellum, a structure governing fine movement control that is also involved in judgment (Baillieux, De Smet, Paquier, De Deyn, & Marien, 2008), selective attention (Bugalho, Correa, & Viana-Baptista, 2006) and affective experiences (Rapoport, van Reekum, & Mayberg, 2000). The cerebellum may play a role in the decision to execute helping actions.

Our results suggest that compassion mechanisms evolved differentially in women, probably in connection with social skills including maternal preverbal communication and emotional

responses to helpless offspring (Campbell, 2008; Febo, Numan, & Ferris, 2005; Leibenluft, Gobbin, Harrison, & Haxby, 2004; Lenzi et al., 2009). They could also be explained by differential cultural expectations influencing moral judgments (Reeder, Kumar, Hesson-McInnis, & Trafimow, 2002; Tilley, 2004). This occurs in Mexican society, where differential sexual education reinforces in women the expressions of emotions related with inferring sadness or pain states and promotes the development of behaviors involving the care of people. Alternatively, the socially accepted masculine role emphasizes behaviors based in norms and rejects expressions believed to be feminine (Díaz-Guerrero, 1984, 1994; Saldívar-Hernández, Ramos-Lira, & Romero, 2008). The apparent incongruence between a similarly reported compassion experience and the BOLD activations of men and women may reflect different cognitive and emotional mechanisms eliciting a similar appraisal behavior.

Some experimental restrictions may influence the interpretation of the brain activity presented in this work. Arousal appraisals manifested higher scores in compassion stimuli than non-compassion evoked pictures used as control, so brain activity correlated with compassion could reflect the influence of arousal. In this sense, although compassion generally involves aversive situations qualified as high arousal, it could be essential, for future studies, to control the experimental conditions presenting similar arousal qualities to cancel the effect of this dimension. Similarly, as explained in the discussion of the occipital and temporal activity related with the visual analysis, it is necessary to consider the physical characteristics of the stimuli in order to differentiate the compassion process from the visual processes *per se*. Also, to improve this design it is possible to consider stimuli novelty in all cases to avoid possible effects related with mnemonic functions.

Further research of reported compassionate experience and related neurobiological mechanisms will require an integral neurocognitive approach capable of discriminating possible causal factors of the observed gender differences. It would be important to study compassion by considering qualitative differences in experimental designs that come closer to real life situations (Todorov, Harris, & Fiske, 2006) and by defining the features of the visual stimuli that elicit empathy and motivate compassionate intentions and behaviors.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bandc.2011.03.019.

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