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Double dissociation of neural responses supporting perceptual and cognitive components of social cognition: Evidence from processing of others' pain

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Models on how perceptual and cognitive information on others' mental states are treated by the cognitive architecture are often framed as duplex models considering two independent systems. In the context of the neuroscience of empathy analogous systems have been described. Using event-related potentials (i.e., ERPs) technique, we tested the hypothesis of temporal dissociation of two functional systems. We implemented a design in which perceptual (i.e., painful or neutral facial expressions) and contextual (i.e., painful or neutral related sentences) cues on others' mental states were orthogonally manipulated. Painful expressions selectively modulated the early activity at 110–360 ms over fronto-central and centro-parietal regions, whereas painful contexts selectively modulated the late activity at 400–840 ms over these same regions. Notably, the reactions to pain triggered by these cues added up when both were available, that is the joint reaction was characterized by additive effects. These findings favor a model assuming distinct neural paths of perceptual and cognitive processing, at least when the cognitive component is triggered by language.

The social environment is a source of copious multimodal information regarding others' sensations, feelings, beliefs and desires. Others' physical actions and facial/body expressions can be directly perceived, whereas a different source of information is contextually established and not directly observable, for instance when it is conveyed by language. Under appropriate circumstances, both perceptual and verbal information may trigger an empathic reaction in an observer, like when witnessing other's physical injury or hearing/reading about a sad event. The present investigation provides the first evidence of a double dissociation at both temporal and functional levels in the processing of perceptual and verbal information on others' pain by showing that each is separately processed in the brain even when both types of information are concurrently available.

Most of the theoretical views on how perceptual and verbal information on others' mental states is treated by the cognitive architecture are indeed framed as *duplex models* considering two levels, or systems, that operate according to different rules and modes of processing. The philosopher Goldman[1,2] distinguishes, for instance, low-level mindreading − which is characterized as a simple, primitive, automatic, and largely below the level of consciousness mechanism dedicated to the processing of social perceptual information − from high-level mind-reading − as committed to understand someone else's mental states by pretending his/her beliefs and desires. This distinction fits well with that of Tager-Flusberg and Sullivan[3], which refer to analogous levels termed social-perceptual and social-cognitive components of theory of mind (i.e., ToM). Both of these models belong to a rich tradition of theoretical frameworks that view the human mind as *dual*[4–7] and intend to explain thinking, reasoning, decision making and also social cognition as based on the operation of, at least, two systems − often named System 1 and System 2− characterized in a very similar way across the different models. Specifically, System 1 operates quickly, unconsciously and in an automatic fashion, whereas System 2 is slow, rule-based, deliberative, conscious and flexible[6]. To note, duplex models have been recently criticized[8–10], mostly because of the lack of empirical testing and rigorous conceptual clarity; in general, these critics agree that "evidence used to support dual theories is consistent with single-system accounts"[8] as well.

In the context of empathy for pain two systems similar to those theorized by Goldman[1,2] and Tager-Flusberg and Sullivan[3] have been proposed, with experience sharing on one side (vicariously sharing others' internal states)
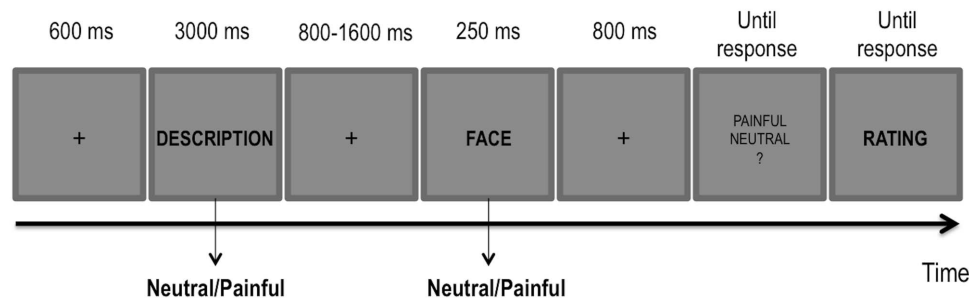
Figure 1 | Timeline and conditions in the present experiment.

and mentalizing on the other side (explicitly considering others' states)[11]. Notably, this functional distinction in the context of empathy for pain, is also shaped at the neuroanatomical level (i.e., neuropsychological dissociation) with experience sharing engaging the mirror neuron and the limbic systems (in particular the inferior frontal gyrus and the anterior insula)[13–17,20–21] and mentalizing engaging a subset of regions within medial prefrontal and temporal cortices and precuneus[12,14,16,18–21]. According to Schacter and Tulving[22], this convergence of dissociations corroborates the view that the two alleged systems are in fact separable. However, apparently in contrast to this evidence, there is also indication based on functional magnetic resonance imaging (fMRI) studies that pain related pictures and pain related words activate the same core empathic neural network, i.e., the secondary somatosensory cortex (i.e., SII), the insula, the right middle frontal gyrus, the left superior temporal sulcus and the left middle occipital gyrus[23]; furthermore, previous functional magnetic resonance imaging (fMRI) work reported the co-activation of the two systems during social interaction, actions and emotion understanding[24–28].

At the present, the evidence mentioned above does not clearly support temporal and functional dissociations between the two alleged systems, such that modulatory effects of one system on the other remain possible, and perhaps plausible. The issue of possible interactions between the two systems is at the present more than ever crucial in the field[11,27–32] and a critical aspect related to this debate is very well portrayed by Gonzalez-Liencres, Shamay-Tsoory and Brüne's question in their recent review (2013; p. 1543): "[…] do we first perceive the pain in others (unconsciously) and then process the context (consciously), or is contextual information relevant for the unconscious evaluation of another's pain?". Intuitively, one would expect that, when provided with proper and coherent contextually defined semantic information, reactions to physical signs of others' pain would get enhanced. Importantly, answering this question is relevant not only to studies on empathy, but encompasses social cognition conceptualizations as well.

Although the excellent spatial resolution of fMRI allowed localization of plausible neural underpinnings of experience sharing and mentalizing, its poor temporal resolution did not assist in deploying processing within the two streams in the temporal domain so that it is still unclear *if* and *when* a functional interplay between them occurs. For instance, it is unclear whether this functional interplay may occur for verbal information (e.g., description of an accident) coherent with an observed scene (e.g., painful face). By recording event-related potentials (ERPs), we tested the hypothesis of temporal and functional dissociations between perceptual and contextual routes of social cognition during empathy for others' pain. We implemented a design in which perceptual (i.e., pictures of faces with either painful or neutral expressions) and contextual information (i.e., sentences describing either a painful or neutral contexts) were orthogonally manipulated (see Figure 1). The domain of language is strictly related to the cognitive component of social cognition and ToM[3,33–37] and strong evidence supporting this claim comes from studies on deaf children who usually present delays in reasoning about intentions

and desires[38–43]. In this vein, the contextual information provided by sentences in the present study would require high level cognitive processing. Participants had to decide whether the face had a neutral or a painful expression by pressing one of two response keys and they were required to rate their subjective impression of empathy capability for each presented context/face. Three possible neural reactions to others' pain were monitored: *perception-based reaction* (a modulation of ERPs as a function of facial expressions), *context-based reaction* (a modulation of ERPs as a function of verbal information), and *joint reaction* (a modulation of ERPs as a function of both facial expressions and verbal information). At least, two alternative empirical scenarios were expected, supporting two distinct models. According to a model assuming distinct neural paths of perceptual and cognitive processing, modulations associated with the two cue categories, either perceptual and contextual, would have been selectively confined to different time windows of the ERP waveforms, i.e., perception-based and context-based reactions would have been dissociated in time; within this empirical scenario, the complete dissociation of the two systems would manifest as additive effects of perception-based and context-based reactions when both cues are available (i.e., when both facial expression and context show painful information). On the contrary, the other empirical scenario favoring the functional interplay of the two cues and systems would have revealed as interactive effects of them, demonstrating that contextual information designating others' pain may boost processing of painful facial expressions and/or that painful facial expressions may enhance processing of contextual information. The former of the two hypothesized empirical scenarios would also provide more substantial evidence in favor of a two-system model, since it would strongly suggest that the two systems operate independently of each other, and that neither system interacts with the other system[9].

Results

Behavioral results. Reaction times (i.e., RTs) exceeding each individual mean RT in a given condition $+/- 2.5$ SD and associated with incorrect responses were excluded from all analyses.

Individual mean proportions of correct responses and RTs were submitted to separate ANOVAs, both considering facial expression (painful vs. neutral) and context (painful vs. neutral) as within-subjects factors. The main effect of neither facial expression or of the context approached significance level, nor did the interaction (for mean proportions of correct responses: max $F = 3.670$; min $p = .071$, max $\eta_p^2 = .057$; for RTs max $F = 1.296$; min $p = .269$, max $\eta_p^2 = .014$; see Figure 2a).

Individual scores of the participants in the rating task were also submitted to repeated measure ANOVA considering the same factors. ANOVA showed significant effect of the interaction between facial expression and context factors ($F(1,19) = 18.910$, $p = .000346$, $MS_e = 1.095$, $\eta_p^2 = .143$). Post-hoc t-tests revealed that, when both facial expressions and context were painful, participants reported higher rates of subjective impression of empathy toward others' pain relative to the conditions in which only the facial expression ($t =$
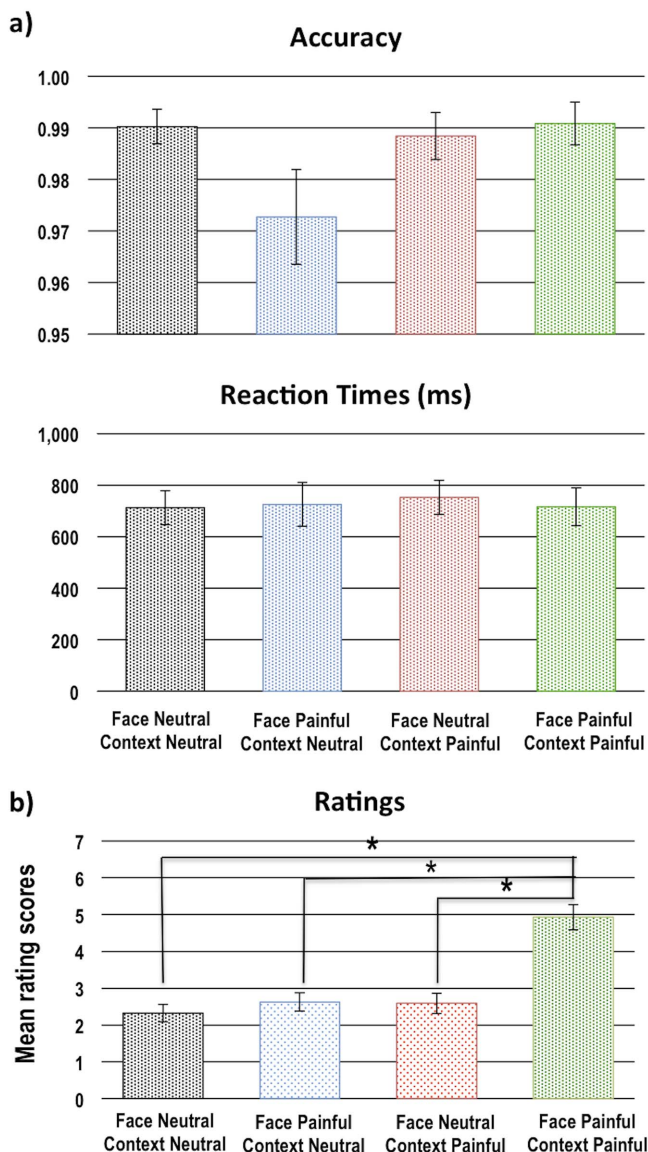
a)

Accuracy

Reaction Times (ms)

b)

Ratings

Figure 2 | (a) Bar charts displaying mean accuracy and mean RT for each experimental conditions and (b) bar charts of mean rating scores for each condition. Error bars represent standard errors. Colors of the bars relate to colors of the ERP waveforms for corresponding conditions.

6.769, $p = .000002$; $M_{diff} = 2.302$ [1.33, 3.27]), or context ($t = 6.015$, $p = .000009$; $M_{diff} = 2.341$ [1.23, 3.45]), or both of them were neutral ($t = 7.653$, $p = .000001$; $M_{diff} = 2.608$ [1.63, 3.58]). Figure 2b shows a bar chart of mean rating scores for each condition with standard errors. Main effects of both facial expression ($F(1,19) = 42.652$, $p = .000003$, $MS_e = .822$, $\eta_p^2 = .241$), and of context ($F(1,19) = 31.092$, $p = .000022$, $MS_e = 1.061$, $\eta_p^2 = .227$) were also significant.

ERPs. A repeated measure analyses of variance (ANOVA) of ERP amplitudes including facial expression (painful vs. neutral) and context (painful vs. neutral) as within-subjects factors was carried out for each ERP time-window and electrode pool. The significant threshold for all statistical analyses was set to .01. Because of the complex experimental design, exact p values, mean square errors (i.e., MS_e) and effect sizes (i.e., partial eta-squared, η_p^2) are reported. Confidence intervals (i.e., CIs, set at 99%) are defined only for paired t-tests and referred to difference of means (i.e., M_{diff}; as suggested by Cumming[44]). Planned comparisons relevant to test the hypotheses of the present experiment are reported.

Figure 3a shows grand averages of ERPs locked on face onset recorded at pooled fronto-central electrodes for each experimental condition (i.e., neutral context/painful facial expression, painful context/neutral facial expression, and painful context/painful facial expression) superimposed with ERPs elicited in the neutral condition (i.e., neutral context/neutral facial expression). Analogous patterns of ERP modulations were observed at centro-parietal pooled electrodes (fig. 3b). Mean amplitude values of each component were submitted to ANOVAs considering facial expression (painful vs. neutral) and context (painful vs. neutral) as within-subjects factors, separately for each region, i.e. fronto-central and centro-parietal pooled electrode sites.

N1. The ANOVA of the N1 mean amplitude values revealed main effects over none of the pooled electrode sites nor interactions between facial expression and context (all $Fs < 1$).

P2. The ANOVA carried out on P2 mean amplitude values revealed a significant main effect of facial expression at pooled fronto-central electrodes, $F(1,19) = 8.269$, $p = .01$, $MS_e = 1.785$, $\eta_p^2 = .118$, indicating that painful expressions elicited larger P2 (3.419 μV, $SD = 3.179$) than neutral expressions (2.559 μV, $SD = 3.217$) irrespective of the context. Neither the main effect of context nor its interaction with factors reached significance (all $Fs < .1$). At centro-parietal pooled electrodes, neither the main effects of facial expression and context nor their interaction reached significance (max $F = 3.609$; min $p = .073$; max $\eta_p^2 = .08$). Planned comparisons revealed that, at fronto-central electrode pooled sites, painful expressions elicited larger P2 amplitude than neutral expressions ($t = 2.876$, $p = .01$; $M_{diff} = .859$ [.004, 1.71]) irrespective of the context and that the condition in which both facial expression and context were painful did not elicit enhanced P2 amplitude compared to the condition in which only the face was painful ($t < 1$).

The results of sLORETA analysis revealed that the neural activity in the P2 time window that differentiated between painful and non-painful facial expressions (i.e., the perception-based reaction) was mainly localized in the left anterior insula extending into the IFG (Brodmann Area, BA, 47; peak Montreal Neurological Institute, MNI, coordinates: −30, 30, −5, Fig. 3a), core regions of the limbic and putative mirror neuron systems. This finding provides further support to the view that this early ERP reaction to pain was a reflection of the experience sharing component of empathy[13–17,20–21].

N2−N3. The ANOVAs of ERP amplitudes in the N2-N3 time window revealed a significant main effect of facial expression at both fronto-central pooled electrode sites, $F(1,19) = 12.875$, $p = .002$, $MS_e = 2.448$, $\eta_p^2 = .211$, and centro-parietal pooled electrode sites $F(1,19) = 19.656$, $p = .0003$, $MS_e = 3.212$, $\eta_p^2 = .319$. This effect was manifest as a positive shift of the ERP activity for painful facial expression (at fronto-central pooled sites .865 μV, $SD = 2.7$; at centro-parietal pooled sites 8.339 μV, $SD = 3.59$) relative to neutral expression (at fronto-central pooled sites -.390 μV, $SD = 2.43$; at centro-parietal pooled sites 6.563 μV, $SD = 3.56$). The main effect of context did not reach significance at both pooled sites (fronto-central pooled sites $F(1,19) = 1.252$, $p = .277$, $MS_e = 2.301$, $\eta_p^2 = .019$; centro-parietal pooled sites $F < 1$) nor did the interaction between factors (fronto-central pooled sites $F(1, 19) = 1.945$, $p = .179$, $MS_e = 1.164$, $\eta_p^2 = .015$; centro-parietal pooled sites $F(1, 19) = 1.261$, $p = .275$, $MS_e = 1.463$, $\eta_p^2 = .009$). Planned comparisons revealed that painful facial expressions elicited more positive N2−N3 amplitude than neutral facial expressions (at centro-central pooled sites: $t = 3.588$, $p = .002$; $M_{diff} = 1.255$ [.254, 2.26]; at centro-parietal pooled sites: $t = 4.433$, $p = .0003$; $M_{diff} = 1.777$ [.630, 2.92]). The condition in which both facial expression and context were painful elicited a joint reaction that was comparable to that elicited when only the face was painful (all $ts < 1$; i.e., the perception-based reaction). At centro-parietal pooled electrode sites, the reaction elicited by the condition in which both the face and the context were painful elicited a more positive shift than the condition in which only the context was pain-
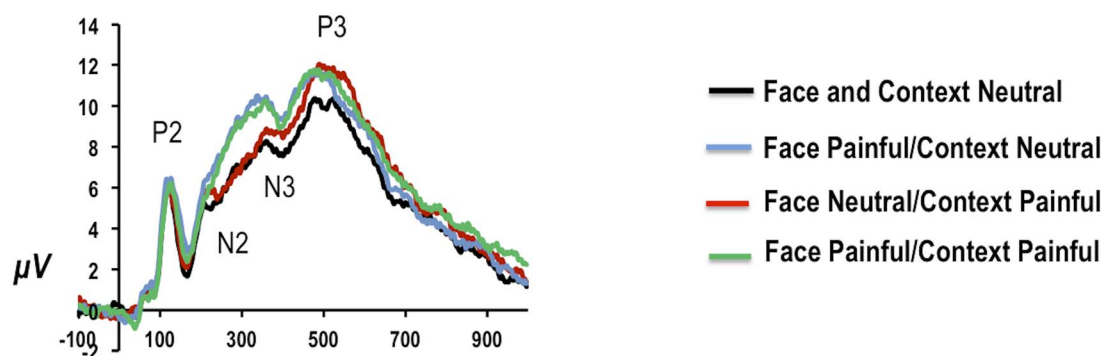
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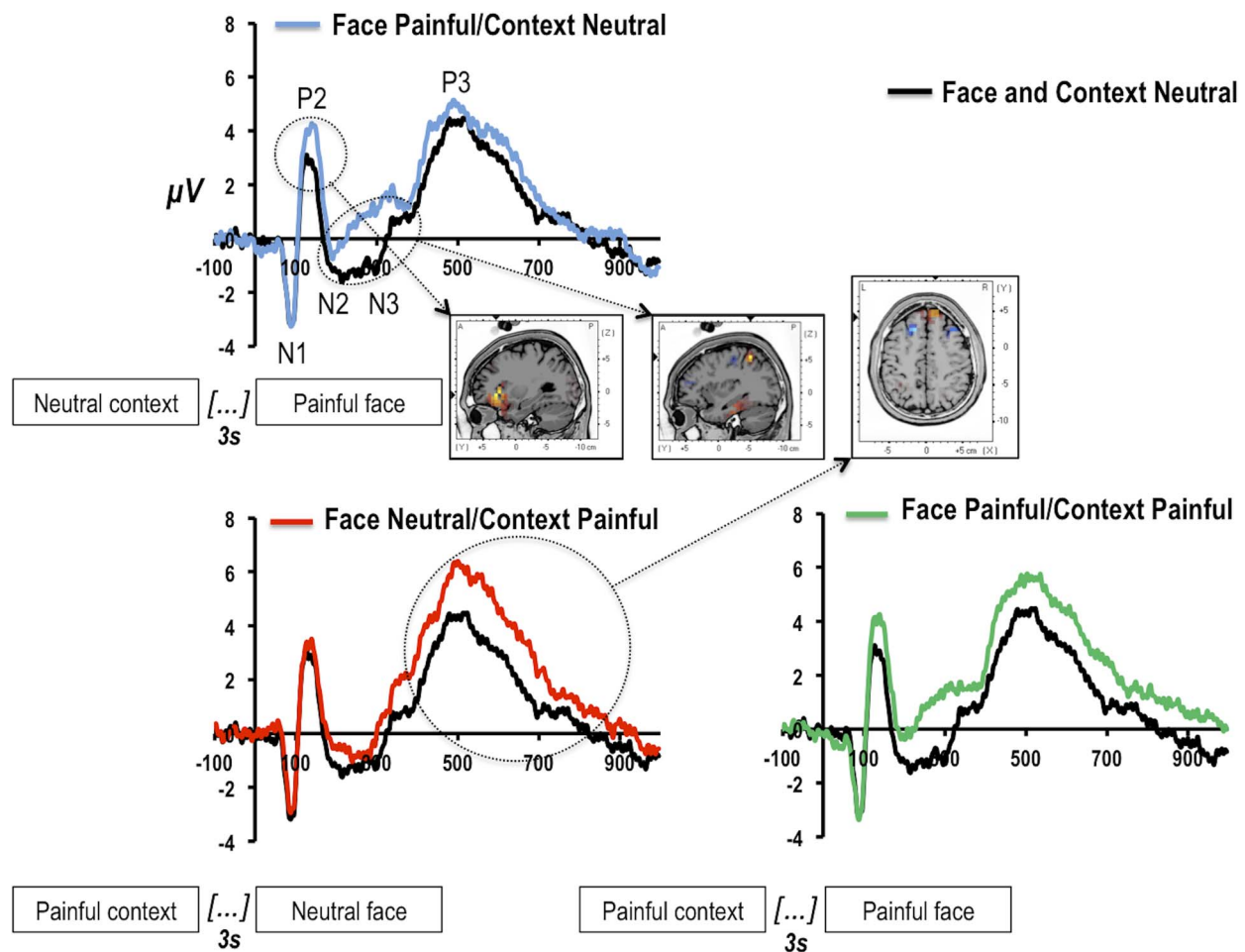
Figure 3 | (a) Grand averages of the face-locked ERP waveforms recorded at pooled fronto-central electrode sites for each experimental condition in comparison to the neutral condition (in black color). The perception-based reaction (i.e., reactions to painful facial expressions that were preceded by neutral contexts; in blue color) selectively involved the earlier portion of the ERP waveforms (i.e., P2 and N2−N3 components), which were significantly more positive in response to painful relative to neutral facial expressions. The context-based reaction (i.e., reactions to neutral faces preceded by painful contexts; in red color) selectively interested the P3, which was significantly more positive in response to painful relative to neutral contexts. The joint reaction (i.e., reactions to painful faces preceded by painful contexts; in green color) involved the P2, N2−N3 and the P3, which were significantly more positive when both the face and the context were painful relative to the neutral condition; the joint reaction was characterized by additive effects (i.e., no interaction) of reactions triggered by perceptual and contextual cues. The figure shows also source estimation of the P2 and N2–N3 activities in the painful vs. non-painful facial expression conditions (perception-based reaction; the left anterior insula/inferior frontal gyrus and the left inferior parietal lobule/intraparietal sulcus, respectively) and the source estimation of the P3 activity in painful vs. non-painful conditions as a function of contextual information (context-based reaction; the bilateral superior frontal gyri). (b) Grand averages the face-locked ERP waveforms of all conditions superimposed recorded at pooled centro-parietal electrode sites. The N2−N3 were selectively modulated by painful facial expressions, whereas the P3 was selectively modulated by painful contexts.

ful ($t = 3.423$, $p = .003$; $M_{diff} = 1.473$ [.242, 2.70]). At fronto-central pooled electrode sites this comparison did not show significant results ($t = 1.891$, $p = .074$; $M_{diff} = .919$ [-.471, 2.31]).

The results of sLORETA analysis revealed that the neural activity in the N2−N3 time window that differentiated between painful and non-painful facial expressions (i.e., the perception-based reaction) was mainly localized in the left inferior parietal lobule/intraparietal sulcus (BA 40; peak MNI coordinates: −35, −50, 55, Fig. 3a), core regions of the putative mirror neuron system and previously associated with the experience sharing component of empathy[13–17,20–21].

P3. The ANOVAs of the P3 amplitudes revealed a significant main effect of context at fronto-central pooled electrode sites, $F(1,19) = 8.504$, $p = .009$, $MS_e = 2.614$, $\eta_p^2 = .160$ (at centro-parietal pooled sites the main effect of context did not reach the significance level of .01, although an analogous trend was observed: $F(1,19) = 4.665$, $p = .044$, $MS_e = 2.705$, $\eta_p^2 = .078$). Painful contexts enhanced P3 amplitudes related to face stimuli (fronto-central pooled sites: 3.517 μV, $SD = 2.588$) relative to those following neutral contexts (front-central pooled sites: 2.462 μV, $SD = 2.69$). Similarly, at centro-parietal pooled sites painful vs. neutral context tended to elicit larger P3 amplitudes to face stimuli (8.144 μV, $SD = 2.38$) than neutral contexts (7.350 μV, $SD = 2.12$). The main effect of facial expression did not reach significance (all $Fs < 1$) nor did the interaction between factors (at fronto-central pooled sites: $F(1,19) = 3.429$, $p = .08$, $MS_e = .881$, $\eta_p^2 = .022$; at centro-parietal pooled sites $F(1,19) = 2.483$, $p = .132$, $MS_e = 1.233$, $\eta_p^2 = .019$). A planned comparison further confirmed that the condition in which both facial expression and context were painful was not significantly different from the condition in which only the description was painful (at both pooled sites all $ts < 1$).

Figure 4 provides a schematic overview on how ERPs were modulated by the presentation of each combination of cues. Mean perception-based reaction, context-based reaction and joint reaction are represented here as the differential mean amplitude between the ERPs elicited in the critical condition for eliciting the reaction (i.e., painful facial expressions/neutral contexts for the perception-based reaction; neutral facial expressions/painful contexts for the context-based reaction; painful facial expressions/painful contexts for the joint reaction) and the ERPs elicited in the neutral condition (i.e., neutral facial expressions/neutral contexts). It is clear that the perception-based reaction mainly involved the early portion of the ERP waveforms (i.e., P2 and N2-N3 components), whereas the context-based reaction mainly interested the later portion of the ERP waveforms (i.e., P3). Notably, the effect of one cue was completely separate from the other cue, as evident when both cues, perceptual and contextual, were concurrently available. The reactions triggered by these cues (i.e., perception-based and context-based reactions) just added up in a simple way, that is the joint reaction was characterized by additive effects (i.e., no interaction) of the early perception-based reaction and the late context-based reaction.

The results of sLORETA analysis revealed that the neural activity in the P3 time window that differentiated between painful and non-painful conditions as a function of the context (i.e., the context-based reaction) was mainly localized in the bilateral superior frontal gyri (BA 8; peak MNI coordinates: 13, 42, 46, Fig. 3a), a core region of the mentalizing network[12,14,16,18–21].

In order to further corroborate the evidence of a double dissociation between perception-based and context-based reactions, we conducted an additional ANOVA including time window (P2 mean amplitude vs. P3 mean amplitude), facial expression (painful vs. neutral) and context (painful vs. neutral) as within-subjects factors. Notably, both the interaction time window x facial expression and time window x context were significant at pooled fronto-central electrodes, $F(1,19) = 13.019$, $p = .002$, $MS_e = .549$, $\eta_p^2 = .407$, and $F(1,19) = 10.281$, $p = .005$, $MS_e = .820$, $\eta_p^2 = .351$, respectively. At centro-parietal electrodes, the interaction between time window and context was also significant, $F(1,19) = 10.123$, $p = .005$, $MS_e = .830$, $\eta_p^2 = .348$ (the interaction between time window and expression was not significant, $p = .298$). These results further demonstrate the dissociated effects of pain expression and painful context on the early and late neural activities during perceiving information about others' pain.

Discussion

The present study showed that perceptual cues of others' emotional states (i.e., facial expressions; perception-based reaction) selectively modulated ERP responses in a time-window including the P2 and the N2−N3 components, and, in line with the previous work[45], such modulation was evident as a positive shift of the ERP waveforms when faces expressing painful expressions were displayed compared to when faces expressing neutral expressions were displayed. Moreover, the modulations of the P2 and N2−N3 amplitudes were independent of the context information shown before the presentation of face stimuli. This reaction appears to reflect the perceptual component of social cognition, and within the theoretical framework of studies on empathy, it was suggested that it is the ERP manifestation of experience sharing of others' pain[45–47]. This conclusion is further supported by the finding that the main potential sources of these responses were the left anterior insula/inferior frontal gyrus and the left inferior parietal lobule, regions that previous studies have linked to the experience sharing system[13–17,20–21].

The contextual cue, instead, selectively modulated a later ERP component, i.e., the P3, such that painful contexts elicited a larger P3 than neutral contexts (i.e., context-based reaction). The modulation of the P3 amplitudes by context was independent of the emotional states of the target, being similar for pain and neutral expressions. Notably, this later effect cannot be due to the time needed for the processing of the contextual information because of the variable interval interleaved between it and the presentation of the perceptual information (for further details, please see the Methods section). This reaction very likely reflects the cognitive component of social cognition, and the component termed 'mentalizing' in the context of the studies on empathy as also supported by source localization[11,45–47]. These results, although novel, are not necessarily surprising, as recent research in this field demonstrated the independence of brain regions involved in experience sharing and mentalizing, thus complementing the anatomical dissociation with evidence of functional dissociation[22]. Consistent with these findings, a meta-analysis of 200 neuroimaging studies on understanding of others' action goals showed that mirror neuron and mentalizing systems are rarely concurrently active, strongly suggesting that neither system subserves the other, but they are rather complementary[48]. However, it should be noted that the great majority of studies investigating how we understand others' mental states in general, and empathy in particular, triggered almost selectively either experience sharing or mentalizing by implementing experimental procedures that included one or the other type of cue (perceptual vs. cognitive/verbal[49–52]) dissociating *a priori* the possible contribution of the two and preventing the interaction between them from being disclosed.

In order to overcome such limitation, the present study orthogonally manipulated both types of cues. By virtue of this procedure, the novel, and surprising finding is that the concurrent presence of both painful cues did not elicit magnified neural reactions to others' pain, that is, when both cues of pain were available, the early perception-based reaction was not modulated by the presence of a painful context nor the later context-based reaction was modulated by the presence of a face expressing pain. In brief, the joint reaction was characterized by additive effects (i.e., no interaction) of perceptual and contextual cues. Apparently, a single-system account cannot explain this whole patter of findings.
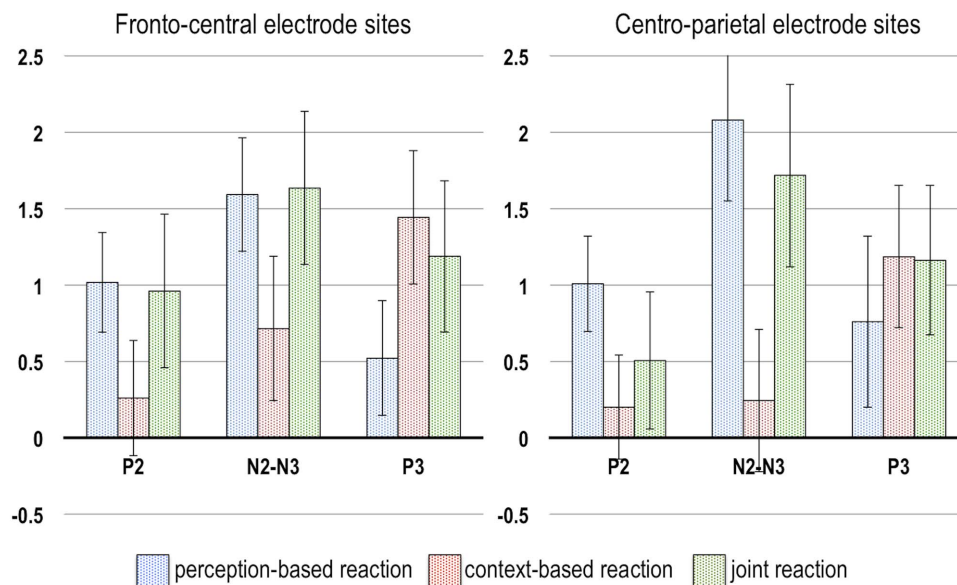
Figure 4 | Mean perception-based reaction, context-based reaction and joint reaction for each ERP temporal window at pooled fronto-central electrode sites (the left bar chart) and centro-parietal electrode sites (the right bar chart) computed as differential mean amplitudes between the critical condition for eliciting each reaction and the ERP elicited in the neutral condition. Error bars represent standard errors.

To the best of our knowledge, this is the first report of a double dissociation in healthy participants of neural reactions to others' pain based on perceptual and contextual information, favoring a model of social cognition in which perceptual and cognitive components are dissociated at both temporal and functional levels, at least when the cognitive component is triggered by language. Importantly, when both types of cues of others' pain were available, the subjective impression of empathy was doubled, exactly as expected by an additive model in which the outputs of two different systems are summed up, suggesting that both systems may equally contribute in generating a subjective experience of empathy. Furthermore, when only one type of cue of others' pain was available, the subjective impression of empathy did not significantly differ from the condition in which both cues were neutral, suggesting not only that the two systems may equally contribute, but that they are both necessary for a subjective experience of empathy. In this vein, our findings do not invalidate previous fMRI evidence for co-activation of the two systems during social interaction, actions and emotion understanding[24–28], but they suggest that the observed pattern of co-activation is to be reconsidered in light of the highly finer temporal resolution offered by the ERP approach. By using this technique, our findings strongly suggest that the two systems are triggered in different time windows, and that 'cooperation' between the two is not to be intended as 'interaction' between them, but rather as the 'contribution' that they may offer to the good functioning of the complex machine devoted to social cognition.

Methods

Participants. Before running the present experiment, we established to enter into ERP analyses data from 20 participants because of existing literature in this field that suggests it is an appropriate sample[45–46,53]. Data were then collected from 23 volunteer healthy students (7 males) from the University of Padova (mean age: 25 years, SD = 3.3; two left-handed) because data from 3 participants (2 males) were discarded from analyses due to excessive electrophysiological artifacts. All reported normal or corrected-to-normal vision and no history of neurological disorders. Twenty participants (5 males; mean age: 25 years, SD = 3.5; one left-handed) were then included in the final sample. All participants gave their informed consent according to the ethical principles approved by the University of Padova.

Stimuli. The stimuli were 32 Caucasian face stimuli, 8 females and 8 males with either a neutral or painful expression[45], and 32 sentences describing either a painful or neutral situation. The sentences were comparable with regard to their syntactic complexity, i.e., all declarations, with the same phrase structure grammars, i.e., noun

phrase (adjective and noun; i.e., "This person") + verbal phrase (verb and noun phrase, e.g. "has got a severe toothache", or verb and propositional phrase, e.g., "does yoga three times per week "). The face stimuli were scaled using an image-processing software so that each face fit in $2.9° \times 3.6°$ (width $\times$ height) rectangle and the sentences were presented on three lines at the center of the screen in a $1.73° \times 3.9°$ (width $\times$ height) virtual rectangle from a viewing distance of approximately 70 cm. Stimuli were presented on a 17-in cathode ray tube monitor controlled by a computer running E-prime software.

Experimental design. Each trial began with the presentation of a fixation cross at the center of the screen (600 ms), followed by a sentence (i.e., contextual cue; 3000 ms) describing either a neutral or a painful condition. After a blank interval (800–1600 ms, jittered in steps of 100 ms), a face (i.e., perceptual cue) was displayed for 250 ms with either a neutral or a painful expression. The sequence of events of each trial is depicted in Figure 1. The jittering of the blank interval between the contextual and the perceptual cue was crucial as it avoided any possible bias due to the time needed to process the sentence by smearing electrical activity related to the contextual cue before presenting the face.

Participants had to decide whether the face had a neutral or a painful expression by pressing one of two response keys. Participants were told that on each trial they would have been presented with a sentence describing either 1) a neutral situation involving an individual (i.e., neutral context; e.g., "This person loves playing classical guitar") or 2) a painful situation (i.e., painful context: "This person is undergoing a hurting injection"). Each sentence was followed by the picture of the individual taken in the 1) painful condition (i.e., expressing a painful facial expression) or in 2) a different moment (i.e., expressing a neutral facial expression).

In brief, this manipulation resulted in four combinations in which participants knew that a painful condition would have been characterized either by a context, by a facial expression or by both of these cues. At the end of each trial, participants were required to rate their subjective impression of empathy capability on a 7-points Likert scale for each presented context/face. Following a brief session of practice in order to familiarize with the task, participants performed 320 trials (i.e., 5 blocks, 80 trials for each combination of perceptual and contextual cues).

Electrophysiological recording and analyses. The EEG was recorded from 64 active electrodes distributed over the scalp in accordance with the international 10/20 system placed on an elastic Acti-Cap, referenced to the left earlobe. The EEG was re-referenced offline to the average of the left and right earlobes. Horizontal EOG (i.e., HEOG) was recorded bipolarly from two external electrodes positioned laterally to the left and right external canthi. Vertical EOG (i.e., VEOG) was recorded from Fp1 and one external electrode placed below the left eye. The electrode impedance was kept less than 10 KΩ because of the highly viscous electro-gel and the properties of active electrodes.

EEG, HEOG and VEOG signals were amplified (pass band 0.01–80 Hz) and digitized at a sampling rate of 250 Hz. The EEG was segmented into 1200-ms epochs starting 100 ms prior to the onset of the faces. The epochs were baseline-corrected based on the mean activity during the 100-ms pre-stimulus period, for each electrode site. Trials associated with incorrect responses or contaminated by large horizontal eye movements, eye blinks or other artifacts (exceeding ± 30 μV, ± 60 μV and ± 80 μV, respectively) were discarded from analysis, which accounted for the exclusion

of an average of 6% of trials. Separate average waveforms for each condition were then generated time-locked to the presentation of the face stimuli. Statistical analyses of ERPs mean amplitudes focused on N1 (90–100 ms), P2 (110–180 ms), N2−N3 (200–360 ms) and P3 (400–840 ms). The time window between 200 and 360 ms was labeled N2−N3 relating to a previous study[47]. Mean ERPs amplitude values were measured at pooled electrode sites selected from fronto-central (Fz, F1, F2, F3, F4, F5, F6, FCz, FC1, FC2, FC3, FC4, FC5, FC6) and centro-parietal (CPz, CP1, CP2, CP3, CP4, CP5, CP6, Pz, P1, P2, P3, P4, P5, P6) electrodes according to visual inspection and previous work[46–47]. ERP reactions to others' pain are known to manifest as positive shifts of the ERP waveforms in trials related to pain (e.g., painful facial expressions, painful stimulations applied to body parts of other people) compared to trials in which neutral conditions with regard to pain are displayed (i.e., neutral facial expressions, neutral stimulations applied to body parts of other people)[46–47,53–55].

As expounded in the Introduction, we monitored the *perception-based reaction* (a positive shift elicited by painful facial expressions compared to the condition in which both facial expressions and contexts were neutral), the *context-based reaction* (a positive shift elicited by contexts describing painful situations compared to the condition in which both facial expressions and contexts were neutral), and the *joint reaction* (a positive shift elicited by the condition in which both the facial expression and the context were painful compared to the condition in which both of them were neutral).

The standardized Low Resolution Brain Electromagnetic Tomography (sLORETA)[56] was used for brain localization of the potential sources of ERP reactions. sLORETA extrapolates 3D statistical maps from EEG data of the possible sources of scalp-recorded ERP components. Using sLORETA, 3D maps and stereotaxic information about current density source of neural activity modulated by the painful vs. non-painful manipulation were derived from the present EEG dataset. The analysis was conducted following the creation of a boundary element method (BEM) model, including cortical and skin, with about 5000 nodes from magnetic resonance imaging (MRI) data, the selection of a temporal window in which ERP responses differentiated between painful and non-painful conditions, and a location-wise inverse weighting from the Minimum Norm Least Square (MNLS) analysis with estimated variances.

1. Gallese, V. & Goldman, A. Mirror neurons and the simulation theory of mind-reading. *Trends Cogn. Sci. (Regul. Ed.)* **2**, 493–501 (1998).
2. Goldman, A. I. *Simulating Minds: The Philosophy, Psychology, and Neuroscience of Mindreading.* New York: Oxford University Press, (2006).
3. Tager-Flusberg, H. & Sullivan, K. A componential view of theory of mind: evidence from Williams syndrome. *Cognition* **76**, 59–89 (2000).
4. Epstein, S. Integration of the cognitive and the psychodynamic unconscious. *Am. Psychol.* **49**, 709–724 (1994).
5. Sloman, S. A. The empirical case for two systems of reasoning. *Psychol. Bull.* **119**, 3–22 (1996).
6. Evans, J. St. B. T. In two minds: Dual process accounts of reasoning. *Trends in Cogn. Sci.* **7**, 454–459 (2003).
7. Evans, J. St. B. T. & Stanovich, K. E. Dual-process theories of higher cognition: Advancing the debate. *Perspect. Psychol. Sci.* **8**, 223–241, 263–271 (2013).
8. Osman, M. An evaluation of dual-process theories of reasoning. *Psychon. Bull. Rev.* **11**, 988–1010 (2004).
9. Keren, G. & Schul, Y. Two is not always better than one: A critical evaluation of two-system theories. *Perspect. Psychol. Sci.* **4**, 533–550 (2009).
10. Kruglanski, A. W. & Gigerenzer, G. Intuitive and deliberative judgments are based on common principles. *Psychol. Rev.* **118**, 97–109 (2011).
11. Zaki, J. & Ochsner, K. The neuroscience of empathy: progress, pitfalls and promise. *Nat. Neurosci.* **16**, 1907–1907 (2013).
12. Amodio, D. M. & Frith, C. D. Meeting of minds: the medial frontal cortex and social cognition. *Nat. Rev. Neurosci.* **7**, 268–277 (2006).
13. Avenanti, A., Bueti, D., Galati, G. & Aglioti, S. M. Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. *Nat. Neurosci.* **8**, 955–960 (2005).
14. Decety, J. The neuroevolution of empathy. *Social Neuroscience: Gene, Environment, Brain, Body* **1231**, 35–45 (2011).
15. Keysers, C., Kaas, J. H. & Gazzola, V. Somatosensation in social perception. *Nat. Rev. Neurosci.* **11**, 417–428 (2010).
16. Lamm, C., Decety, J. & Singer, T. Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage* **54**, 2492–2502 (2011).
17. Lamm, C. & Singer, T. The role of anterior insular cortex in social emotions. *Brain. Struct. Funct.* **214**, 579–591 (2010).
18. Rizzolatti, G. & Sinigaglia, C. The functional role of the parieto-frontal mirror circuit: interpretations and misinterpretations. *Nat. Rev. Neurosci.* **11**, 264–274 (2010).
19. Saxe, R. & Kanwisher, N. People thinking about thinking people - The role of the temporo-parietal junction in "theory of mind". *Neuroimage* **19**, 1835–1842 (2003).
20. Shamay-Tsoory, S. G., Aharon-Peretz, J. & Perry, D. Two systems for empathy: a double dissociation between emotional and cognitive empathy in inferior frontal gyrus versus ventromedial prefrontal lesions. *Brain* **132**, 617–627 (2009).
21. Fan, Y., Duncan, N. W., de Greck, M. & Northoff, G. Is there a core neural network in empathy? An fMRI based quantitative meta-analysis. *Neurosci. Biobehav. Rev.* **35**, 903–911 (2011).
22. Schacter, D. L. & Tulving, E. What are the memory systems of 1994? In Schacter D.L. & Tulving E. (Eds.), *Memory Systems* (1–38). Cambridge, MA: MIT Press (1994).
23. Gu, X. & Han, S. Neural substrates underlying evaluation of pain in actions depicted in words. *Behav. Brain Res.* **181**, 218–223 (2007).
24. Brass, M., Schmitt, R. M., Spengler, S. & Gergely, G. Investigating action understanding: Inferential processes versus action simulation. *Curr. Biol.* **17**, 2117–2121 (2007).
25. Iacoboni, M. *et al.* Watching social interactions produces dorsomedial prefrontal and medial parietal BOLD fMRI signal increases compared to a resting baseline. *Neuroimage* **21**, 1167–1173 (2004).
26. Rizzolatti, G. & Craighero, L. The mirror-neuron system. *Annu. Rev. Neurosci.* **27**, 169–192 (2004).
27. Spunt, R. P., Falk, E. B. & Lieberman, M. D. Dissociable Neural Systems Support Retrieval of How and Why Action Knowledge. *Psychol. Sci.* **21**, 1593–1598 (2010).
28. Spunt, R. P., Satpute, A. B. & Lieberman, M. D. Identifying the What, Why, and How of an Observed Action: An fMRI Study of Mentalizing and Mechanizing during Action Observation. *J. Cogn. Neurosci.* **23**, 63–74 (2011).
29. Gonzalez-Liencres, C., Shamay-Tsoory, S. G. & Brüne, M. Towards a neuroscience of empathy: Ontogeny, phylogeny, brain mechanisms, context and psychopathology. *Neurosci. Biobehav. Rev.* **37**, 1537–1548 (2013).
30. Perry, A. & Shamay-Tsoory, S. G. Understanding emotional and cognitive empathy: A neuropsychological perspective. In Baron-Cohen, S., Tager-Flusberg, H., & Lombardo, M.V (Eds.), *Understanding Other Minds: Perspectives from Developmental Social Neuroscience* (178–194). Oxford: Oxford University Press (2013).
31. Waytz, A. & Mitchell, J. P. Two Mechanisms for Simulating Other Minds: Dissociations Between Mirroring and Self-Projection. *Curr. Dir. Psychol. Sci.* **20**, 197–200 (2011).
32. Zaki, J., Hennigan, K., Weber, J. & Ochsner, K. N. Social Cognitive Conflict Resolution: Contributions of Domain-General and Domain-Specific Neural Systems. *J. Neurosci.* **30**, 8481–8488 (2010).
33. Strickland, B., Fisher, M., Keil, F. & Knobe, J. Syntax and intentionality: An automatic link between language and theory of mind. *Cognition* **133**, 249–261 (2014).
34. Kidd, D. C. & Castano, E. Reading literary fiction improves theory of mind. *Science* **342**, 377–380 (2013).
35. de Villiers, J. The interface of language and theory of mind. *Lingua* **117**, 1858–1878 (2008).
36. Astington, J. W. E. & Baird, J. A. *Why Language Matters for Theory of Mind.* New York, NY, US: Oxford University Press (2005).
37. Hale, C. M. & Tager-Flusberg, H. The influence of language on theory of mind a training study. *Dev. Sci.* **6**, 346–359 (2003).
38. Scott, C., Russell, P. A., Gray, C. D., Hosie, J. A. & Hunter, N. The interpretation of line of regard by prelingually deaf children. *Soc. Dev.* **8**, 412–426 (1999).
39. Tomasuolo, E., Valeri, G., Di Renzo, A., Pasqualetti, P. & Volterra, V. Deaf children attending different school environments: Sign language abilities and theory of mind. *J. Deaf Stud. Deaf Educ.* **18**, 12–29 (2013).
40. Peterson, C. C., Wellman, H. M. & Slaughter, V. The mind behind the message: Advancing theory of mind scales for typically developing children and those with deafness, autism, or Asperger syndrome. *Child Dev.* **83**, 469–485 (2012).
41. Schick, B., de Villiers, P., de Villiers, J. & Hoffmeister, R. Language and theory of mind: A study of deaf children. *Child Dev.* **78**, 376–396 (2007).
42. Peterson, C. C., Wellman, H. M. & Liu, D. Steps in theory-of-mind development for children with deafness or autism. *Child Dev.* **76**, 502–517 (2005).
43. Peterson, C. C. Theory-of-mind development in oral deaf children with cochlear implants or conventional hearing aids. *J. Child Psychol. Psychiatry* **45**, 1096–1106 (2004).
44. Cumming, G. *Understanding the New Statistics: Effect Sizes, Confidence Intervals, and Meta-Analysis.* New York: Routledge (2012).
45. Sheng, F. & Han, S. Manipulations of cognitive strategies and intergroup relationships reduce the racial bias in empathic neural responses. *Neuroimage* **61**, 786–797 (2012).
46. Fan, Y. & Han, S. Temporal dynamic of neural mechanisms involved in empathy for pain: An event-related brain potential study. *Neuropsychologia* **46**, 160–173 (2008).
47. Sessa, P., Meconi, F., Castelli, L. & Dell'Acqua, R. Taking one's time in feeling other-race pain: an event-related potential investigation on the time-course of cross-racial empathy. *Soc. Cogn. Affect. Neurosci.* **9**, 454–63 (2014).
48. Van Overwalle, F. & Baetens, K. Understanding others' actions and goals by mirror and mentalizing systems: A meta-analysis. *Neuroimage* **48**, 564–584 (2009).
49. Gallese, V., Keysers, C. & Rizzolatti, G. A unifying view of the basis of social cognition. *Trends Cogn. Sci. (Regul. Ed.)* **8**, 396–403 (2004).
50. Hickok, G. Eight Problems for the Mirror Neuron Theory of Action Understanding in Monkeys and Humans. *J. Cogn. Neurosci.* **21**, 1229–1243 (2009).
51. Papeo, L., Corradi-Dell'Acqua, C. & Rumiati, R. I. "She" Is Not Like "I": The tie between language and action is in our imagination. *J. Cogn. Neurosci.* **23**, 3939–3948 (2011).
52. Saxe, R. Against simulation: the argument from error. *Trends Cogn. Sci. (Regul. Ed.)* **9**, 174–179 (2005).

53. Decety, J., Yang, C. & Cheng, Y. Physicians down-regulate their pain empathy response: An event-related brain potential study. *Neuroimage* **50**, 1676–1682 (2010).
54. Han, S., Fan, Y. & Mao, L. Gender difference in empathy for pain: An electrophysiological investigation. *Brain Res.* **1196**, 85–93 (2008).
55. Li, W. & Han, S. Perspective taking modulates event-related potentials to perceived pain. *Neurosci. Lett.* **469**, 328–332 (2010).
56. Pascual-Marqui, R. D., Esslen, M., Kochi, K. & Lehmann, D. Functional imaging with low resolution brain electromagnetic tomography (LORETA): a review. *Methods Find. Exp. Clin. Pharmacol.* **24**, 91–95 (2002).

Author contributions

P.S. developed the study concept. All authors contributed to the study design. F.M. performed testing and data collection. P.S. and F.M. performed the data analysis and interpreted the data. P.S. and F.M. drafted the manuscript, and S.H. provided critical revision. All authors approved the final version of the manuscript for submission.

Additional information

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