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Research Report

Subliminal presentation of other faces (but not own face) primes behavioral and evoked cortical processing of empathy for pain

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ABSTRACT

Current research on empathy for pain emphasizes the overlap in the neural response between the first-hand experience of pain and its perception in others. However, recent studies suggest that the perception of the pain of others may reflect the processing of a threat or negative arousal rather than an automatic pro-social response. It can thus be suggested that pain processing of other-related, but not self-related, information could imply danger rather than empathy, due to the possible threat represented in the expressions of others (especially if associated with pain stimuli). To test this hypothesis, two experiments considering subliminal stimuli were designed. In Experiment 1, neutral and semantic pain expressions previously primed with own or other faces were presented to participants. When other-face priming was used, only the detection of semantic pain expressions was facilitated. In Experiment 2, pictures with pain and neutral scenarios previously used in ERP and fMRI research were used in a categorization task. Those pictures were primed with own or other faces following the same procedure as in Experiment 1 while ERPs were recorded. Early (N1) and late (P3) cortical responses between pain and no-pain were modulated only in the other-face priming condition. These results support the threat value of pain hypothesis and suggest the necessity for the inclusion of own- versus other-related information in future empathy for pain research.

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1. Introduction

A large number of studies using functional MRI and, more recently, electrophysiology have used the presentation of stimuli depicting people in pain (i.e., people suffering from physical injuries or expressing facial expressions of pain) to characterize the neural underpinnings of empathic processing (Botvinick et al., 2005; Jackson et al., 2006a; Cheng et al., 2008a; Fan and Han, 2008; Han et al., 2008; Akitsuki and Decety, 2009; Decety, Yang, and Cheng, 2010). Results from these studies suggest that empathy for pain involves a somatosensory resonance mechanism between other and self which draws on the affective and sensory dimensions of pain processing (Jackson et al., 2006a). This mechanism provides crucial and rapid information to help us understand the affective states of others and respond to them (Decety and Lamm, 2006). Pain serves evolved protective functions not only by warning the suffering person, but also by impelling expressive behaviors that attract the attention of others (Craig, 2004).

Pain, however, includes a dimension that does not necessarily imply the onset of a pro-social response in the observer. This aspect can be directly related to the perception of threat and danger (Eccleston and Crombez, 1999; Williams, 2002; Yamada and Decety, 2009; Decety, 2011, 2010). This primitive aspect of pain processing, which is usually associated with an avoidance of the source of threat, seems in theory to conflict with the emergence of empathic concern, i.e., the motivation to approach the other. Therefore, it remains unclear how the perception of pain in others loses its threat value and instead triggers empathic behavior.

A behavioral study recently examined the hypothesis that the perception of others in pain is a potential threat to the self rather than eliciting empathic resonance and concern for the other. In this experiment, likable and dislikable affective words (i.e., honest versus rude) were subliminally tagged to faces using a priming technique. In this study, detection of pain was only facilitated by unconscious negative affective processing rather than by positive affective processing (Yamada and Decety, 2009). The results from this study suggest that both early and late visual processing of painful stimuli can be associated with potential threat and that the mere perception of pain does not automatically activate an empathic process, as is commonly believed to occur. Rather, what seemed to be first activated were a threat-detection system and possibly a general aversive response in the observer, instead of an empathic response. We call this hypothesis “threat value of pain hypothesis” (TVPH, hereafter).

1.1. Own versus other-related information

One critical issue which was not considered in the aforementioned study is the possible effect of the perception of self and other-related information on painful stimuli. Such perceptions should differ according to whether the painful stimuli are associated with either own or other face priming. In brief, pain stimuli associated to “other” priming should enhance the threat-detection system compared with information associated to “own” priming, since the other represents a stronger threat than the self. In contrast, pain-related information

primed by own-faces should not activate a strong automatic response because the instinct for self-preservation should prevent threat activation. Since the TVPH does not assume a shared representation of self and other, only warning stimuli (pain pictures primed by other-related information) should produce facilitation painful stimuli. On the contrary, the sensorimotor resonance hypothesis of empathy would predict that responses to pain stimuli should not be subject to a significant differentiation between self or other-related information.

Pain, in part, implies a somatically focused negative emotional state associated with discomfort and a perceived threat. Suffering refers to a perceived threat to the integrity of the organism. Other individuals can induce pain as well as the pleasure of being close. When other and the self are related to a pain stimuli task, a stronger threat reaction should be expected if the other is associated with pain-related information. In brief, pain/other association can induce a potential risk of insult to the self, and this should activate a faster negative arousal response.

With the purpose of test the TVPH, two experiments were conducted. In order to test the automatic bias of own versus other faces, we used a subliminal presentation of priming stimulus for both experiments. In the first experiment, a classification task with semantic stimuli of pain and neutral content was primed with own and other faces. In the second experiment, early and late evoked cortical processing to pain perception was recorded during a picture classification task (pain versus neutral) with own and other faces priming. Both the TVPH and the resonance empathy hypothesis of pain predict, regardless of priming categories, a general facilitation of pain stimuli processing (compared to neutral), because painful information is considered equally salient by the two interpretations. It is the processing of own versus other information of the priming stimuli that should help distinguish between the two theories. The empathy hypothesis predicts that the presence of own versus other information should produce similar results, due to the activation of shared neural representation between self and other. On the contrary, for the TVPH, processing of pain stimuli with other-related information should be subject to facilitation in comparison with other categories. Since this latter hypothesis posits that other-related information associated to pain stimuli should act as an alarm, only in the case pain stimuli should a shorter response be produced. Pain stimuli associated to self-related information should not produce differences compared to neutral stimuli because its processing would not be facilitated by the threat system.

1.2. Experiment 1

In empathy research, the use of sentences as stimuli (linguistic expressions) associated with pain versus neutral content is less common than the use of visual stimuli. Only the domain of chronic pain has used pain-related words, specifically with the Stroop and dot-probe paradigms (Crombez et al., 2000; Pearce and Morley, 1989; Pincus et al., 1998; Pincus and Morley, 2001; Roelofs et al., 2003, 2005). Semantic pain expressions could be disadvantageous because they imply a less direct pain induction compared with visual stimuli. For

example, Roelofs et al. (2005) argued that verbal stimuli may not evoke sufficiently powerful priming to test sensory pain-related words in selective attention processing measured with a modified Stroop task. They could, however, represent a type of stimulus that becomes relevant only as a function of relevant previous cues or contextual information (i.e., faces with expressions of pain). With regard to the hypothesis that the perception of others in pain activates the threat-detection system, one would expect that semantic pain expressions have a greater saliency and should also be processed faster than neutral stimuli, especially when they are primed by other face stimuli. Following the same logic, neutral stimuli should not be modulated based on own or other priming. Similarly, the same should be true for pain stimuli primed by own face, since those stimuli combinations do not themselves represent a direct threat to the self.

We created an experimental procedure to investigate how the processing of visual stimuli is affected depending on whether pain is expressed or not and, simultaneously, whether it is related to self or another individual. Participants were instructed to judge the emotional content of semantic pain expression (pain or neutral). To relate the semantic content of the expression directly to the own/other information, we used sentences constructed with the first or third person for both conditions (neutral and pain). Therefore, four explicit stimulus categories were present. Additionally, each trial was subliminally primed with a picture that could either be the face of the participant herself/himself or that of another individual of the same gender. The facial expression could express pain or neutrality.

1.3. Experiment 2

Recent studies have investigated the temporal dynamics of neural mechanisms underlying empathy for pain by recording event related brain potentials (ERPs). All previous reports (Han et al., 2008; Fan and Han, 2008; Decety et al., 2010c) have shown two basic correlates of empathy: an early and automatic response of stimulus type effects (pain versus non-pain, indexed by a N1 frontal component) and a second and controlled processing of empathy for pain (as indexed by a central-parietal P3 component). The neural processing of empathy seems to be modulated by the contextual reality of stimuli, by top-down attention to the pain cues (Han et al., 2008), as well as by the inhibition of bottom-up processing of the perception of pain in others by expertise (Decety et al., 2010c). Because of this contextual malleability of empathy neural dynamics, we expected an early and late modulation of pain-neutral differences dependent on own-other priming. Specifically, if the threat value of pain hypothesis is supported, an attenuation of differences between pain and neutral stimuli should be observed in the own face priming condition. In addition, following this hypothesis, the other-face priming should enhance the early and late response to painful stimuli.

We employed a similar methodology as the one used in experiment 1, but this time added the recording of cortical activity with ERPs. Moreover, instead of considering semantic stimuli we used as target pictures of painful and neutral situations, primed by own or other faces.

1.4. Predictions

The empathy hypothesis predicts that the results produced in response to own-information should be similar to those produced in response to other-information, due to the shared representation between self and other. In consequence, the pattern observed of RTs (experiment 1) and ERPs (experiment 2) elicited by pain and neutral stimuli should be no different following priming by self-information than following priming by other-information. On the contrary, according to the TVPH, processing RTs (experiment 1) and ERPs (experiment 2) of pain stimuli with other-related information should be facilitative in comparison with information from other categories. In consequence, there should only be discrimination between pain and neutral stimuli in the other-face priming condition. In the own-face priming condition, because no automatic reaction to threat would be activated, no difference between pain and neutral pictures would be observed in either behavioral performance or ERPs.

2. Results

2.1. Experiment 1

A main effect was observed for the word valence factor ($F(1,22)=14.63, p<0.001$). In general, reaction times were faster for pain-related words (mean=861, SD=372) than for neutral words (mean=896, SD=385). An interaction effect was found between face person and word valence factors [$F(1,24)=4.39, p=0.03$]. When participants were primed with their own faces, reaction times for pain-related words were not statistically different (mean=876, SD=384) from neutral words (mean=888, SD=373). When faces of others were used as primes, pain-related words showed shorter reaction times (mean=846, SD=359) than neutral words (mean=905, SD=396). Tukey HSD post-hoc comparisons yielded significant differences for pain versus neutral word valence when primed by other-faces ($p=0.02$). In

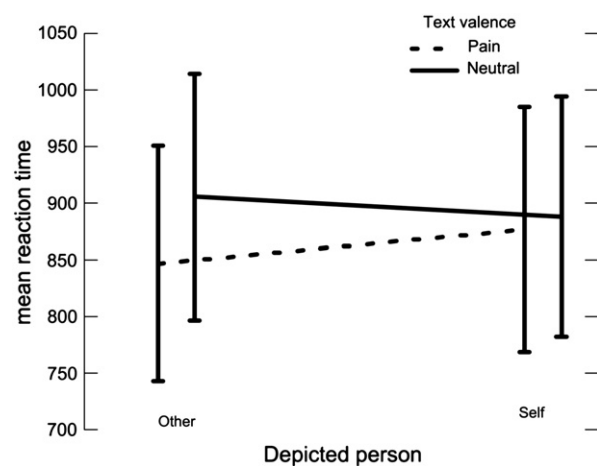


Fig. 1 – RT results from other- versus own-face priming (Face Person factor) and neutral versus semantic pain expression (Word Valence factor). Bars show a 95% t distribution confidence interval for each mean.

addition, semantic pain expressions elicited shorter reaction times when they were primed by other-face compared to own-face ($p=0.001$) (see Fig. 1).

No effects of person congruence ($F(1,33)=0.12, p=0.72$), valence congruence ($F(1,66)=0.03, p=0.85$) or interaction ($F(1,66)=1.43, p=0.23$) over reaction times were found.

Accuracy rates were computed, and a logit transformation [$y=\log(x/(1-x))$] was applied for normalization. An ANOVA procedure yielded no statistically significant effects. This can be explained by a ceiling effect in accuracy rates; as Table 1 details, most categories were answered with more than 90% mean accuracy.

To explore a potential gender difference, the same four-factor ANOVA model was performed after adding gender as a between-subject factor. No statistically significant effects of the gender factor were found, nor any interaction and thus no conclusion changed with respect to the results from the previous ANOVA.

2.2. Experiment 2

2.2.1. Behavioral data

2.2.1.1. Accuracy. Important differences regarding accuracy were found. A main effect of stimulus type (pain versus neutral; $F(1, 12)=5.90, p=0.03$) evidenced a better performance of the classification for pain stimuli (75.41%, $SD=3.1$) compared to neutral ones (68.91%, $SD=3.2$). No effects of priming were observed. An interaction of stimulus type \times priming ($F(1, 12)=9.73, p<0.01$) suggests a better classification of pain stimuli when they were primed by other faces. Post hoc comparisons show that only pain stimuli primed with other faces were better classified than

neutral stimuli primed by own faces ($p<0.01$) and pain primed with own faces ($p=0.29$, see Table 2). No other differences were significant.

2.2.1.2. RTs. Similar results to accuracy were found when analyzing the RTs. Stimulus type differences ($F(1, 12)=6.51; p=0.025$) showed shorter responses to pain stimuli (478 ms, $SD=44$) compared to neutral ones (537 ms, $SD=39$). Only a trend for priming effects was observed ($F(1, 12)=4.22; p=0.06$) suggesting shorter responses of stimuli primed with other faces. An interaction of stimulus type \times priming ($F(1, 12)=10.53, p<0.01$) and their corresponding post hoc comparisons evidenced that pain stimuli primed by other faces elicited significantly shorter responses (see Table 2) than neutral stimuli primed by own faces ($p<0.01$), pain stimuli primed by own-faces ($p<0.01$) and neutral stimuli primed by other faces ($p<0.05$).

2.2.2. ERPs

N1. A main effect of stimulus type was found ($F(1, 12)=28.29, p<0.005$), indicating that pain stimuli elicited less negative amplitude modulation than neutral stimuli. A electrode effect was significant too ($F(2, 24)=50.22, p<0.001$). More importantly, an interaction between electrode, stimulus type and priming ($F(2, 24)=7.46, p<0.05$) was observed. Post hoc comparison performed over this interaction (HSD test, $MS=11.27, df=24.00$) evidenced that only in Fz, pain versus neutral stimuli primed by other faces elicited significant differences ($p=0.001$, see Fig. 2). No differences of stimulus type primed by own faces were found in any other electrode and no other differences were found. Table 3 shows descriptive statistics.

P3. A main effect of electrode ($F(2, 24)=87.48, p<0.001$) revealed that a P3 response over the central and parietal areas was present (see Fig. 2). An effect of stimulus type ($F(1, 12)=5.99, p=0.03$) evidenced that pain stimuli increased the P3 positive voltage when compared to neutral stimuli.

Further, stimuli primed by other faces increased the response amplitude when compared to own face primed stimuli ($F(1, 12)=4.98, p=0.04$). Moreover, a stimulus type \times priming interaction ($F(2, 24)=10.10, p<0.01$) confirmed that pain stimuli, only when primed by other faces, elicited more positive amplitudes compared to all other conditions (Tukey HSD test, post hoc comparison to neutral primed by other face, as well as pain primed by own face, and neutral primed by own face, all $p<0.05$).

In order to clarify the specific localization of this pain \times other face priming effect, a stimulus type \times priming \times electrode confirmed the visual inspection which suggested a

Table 1 – Experiment 1: Mean and standard deviations for accuracy rates from all participants in the different stimuli categories.

Text person	Text valence	Face person	Face valence	Mean accuracy	Accuracy SD
Other	Neutral	Other	Neutral	0.96	0.12
Self	Neutral	Other	Neutral	0.91	0.24
Other	Pain	Other	Neutral	0.89	0.18
Self	Pain	Other	Neutral	0.93	0.15
Other	Neutral	Self	Neutral	0.92	0.13
Self	Neutral	Self	Neutral	0.92	0.19
Other	Pain	Self	Neutral	0.90	0.19
Self	Pain	Self	Neutral	0.90	0.16
Other	Neutral	Other	Pain	0.94	0.13
Self	Neutral	Other	Pain	0.92	0.18
Other	Pain	Other	Pain	0.88	0.20
Self	Pain	Other	Pain	0.93	0.17
Other	Neutral	Self	Pain	0.95	0.14
Self	Neutral	Self	Pain	0.92	0.19
Other	Pain	Self	Pain	0.91	0.18
Self	Pain	Self	Pain	0.92	0.15

The first two columns show which kind of textual stimulus was displayed for classification, the next two columns state which kind of facial priming preceded text, and the last two columns detail means and standard deviations for the corresponding category.

Table 2 – Experiment 2: Descriptive statistics of behavioral data.

Condition	Accuracy % (SD)	RTs ms (ES)
Pain stimuli primed by own face	69.23 (4.92)	564 (44)
Neutral stimuli primed by own face	71.07 (3.19)	552 (57)
Pain stimuli primed by other face	81.58 (2.08)	392 (55)
Neutral stimuli primed by other face	66.74 (3.96)	523 (42)

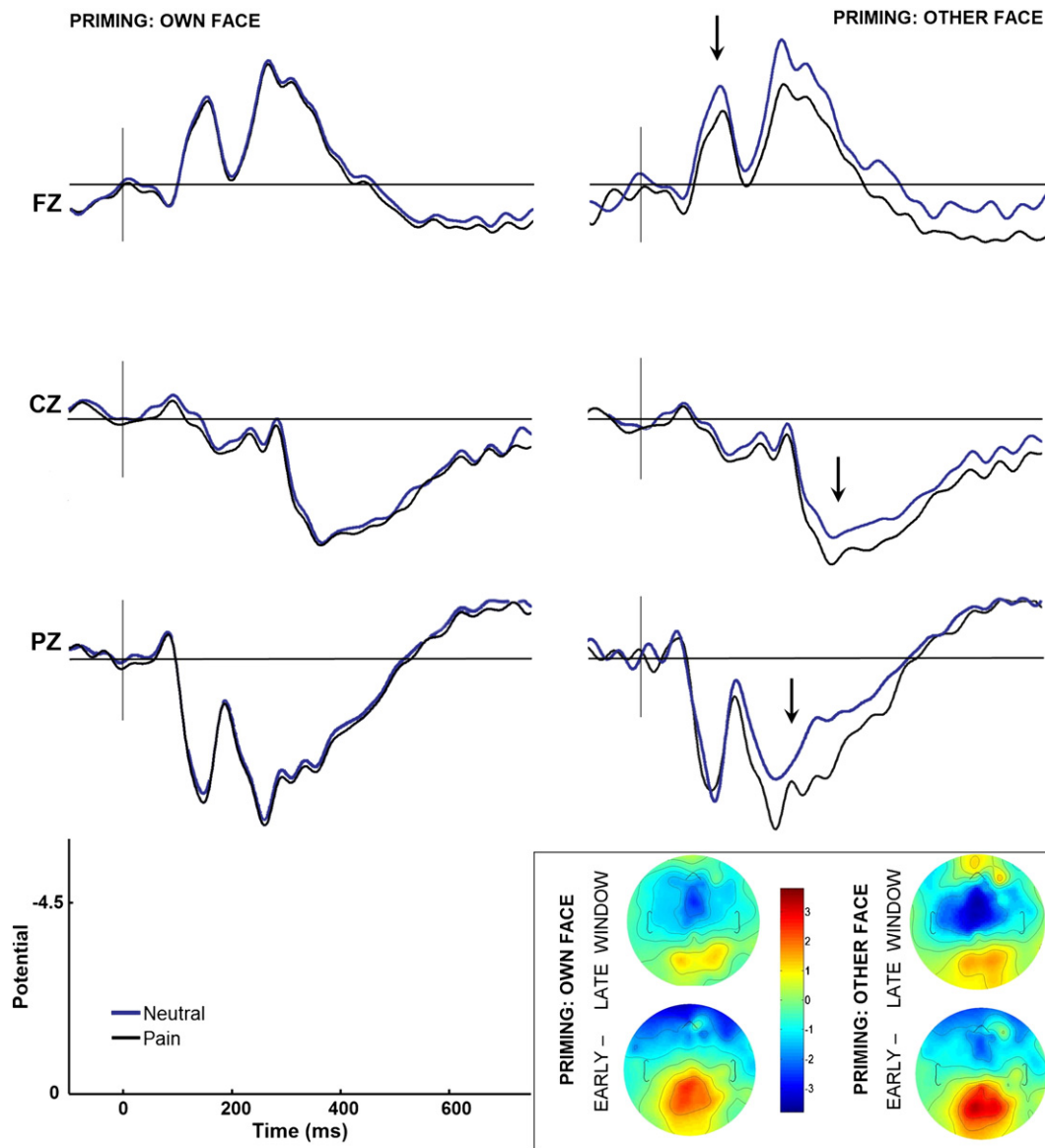


Fig. 2 – Cortical responses to painful and non-painful stimuli primed by own or other faces. ERPs to painful situations (black traces) and to neutral situations (blue traces) are shown in the own face priming cognition (left) and in the other face priming condition (right). Arrows are indicative of the statistical differences reported at N1 and P3 time windows. At the bottom, voltage scalp maps of early and late windows for the own and other-face priming are shown.

P3 central-posterior effect ($F(2, 24) = 14.24, p < 0.001$; see Fig. 2). Post hoc comparison performed over this interaction confirmed that only at Cz and Pz sites were pain stimuli primed by other faces statistically different from neutral stimuli primed

by other faces ($p < 0.01$ for Cz and $p < 0.001$ Pz). Importantly, no differences were found between pain and neutral stimuli when they were primed by own faces ($p = 0.86$ for Cz and $p = 0.73$ for Pz; see Table 3).

Table 3 – Experiment 2: Descriptive statistics of ERP data (N110 and P3).

Condition	N1 window: μV (SD)			P3 window: μV (SD)		
	Frontal	Central	Parietal	Frontal	Central	Parietal
Pain stimuli primed by own face	-2.71 (0.06)	-0.16 (-0.06)	2.30 (0.07)	-2.68 (0.19)	2.09 (0.22)	2.9 (0.17)
Neutral stimuli primed by own face	-2.89 (0.07)	-0.34 (0.08)	2.25 (0.06)	-2.74 (0.20)	1.98 (0.18)	2.8 (0.15)
Pain stimuli primed by other face	-1.98 (0.08)	-0.22 (0.07)	2.17 (0.09)	-2.23 (0.24)	3.4 (0.31)	4.02 (0.19)
Neutral stimuli primed by other face	-2.99 (0.07)	-0.46 (0.09)	2.04 (0.0)	-3.30 (0.20)	2.52 (0.11)	2.59 (0.20)

As in Experiment 1, we explored potential gender differences by performing the same four-factor ANOVA model after adding gender as a between-subject factor. No statistically significant effects of the gender factor we found, either main effects or interactions. In addition we performed an additional analysis with the factor stimuli repetition (since all stimuli was repeated twice). No main effects or interaction were observed.

3. Discussion

3.1. Experiment 1

This experiment was designed to test the TVPH when stimuli are associated with other-related information by measuring the extent to which reaction times to painful and neutral text classification are affected by priming with own or other facial expressions. Reaction time data indicate that the face person has an effect on response delays in a discrimination task between pain-related and neutral words. When the subject's face was used as a prime stimulus at the beginning of each trial, both pain and neutral verbs produced similar reaction times. However, when the face of the other person was used as a prime, pain words elicited a faster reaction.

When investigating reaction time data for simple relationships between text and priming face, no effect of person identity (self or other) or valence congruence was found. Therefore, an effect of face priming on reaction times does not support either of the two reasonable hypothesis to consider: (1) that valence/person congruence between text and face could produce shorter response times because of a response facilitation by preparation, or (2) that valence congruence accompanied by person incongruence (same valence expressed for own and other) could produce shorter response times because of an empathic effect (e.g., if first person pain facilitates the detection of pain in others, or if perception of pain in others speeds up the understanding of first person painful statements).

Instead of any congruence effects, our reaction time data show an effect of other-face priming on reaction times to text classification. This suggests that other-related information (other-face priming) affected the processing of painful semantic content. This latter result supports the hypothesis of pain as a proxy for activating the threat-detection system, since the non-threat stimuli combinations (neutral and painful semantic expression primed with the subject's own face and neutral expression primed with other-faces) did not facilitate responses.

It is well-known that emotion speeds up processing of sentences, compared with sentences of neutral content (Fischler and Bradley, 2006). Further, priming is stronger for emotional content compared to neutral (Abrams and Grinspan, 2007; Ruys and Stapel, 2008). The effect revealed by our study is thus consistent with previous studies that show that emotional processing modulates attention and perception of pain (Kirwilliam and Derbyshire, 2008; Lang 1995; Miron et al., 1989; Villemure and Bushnell, 2002).

Unexpectedly, we did not find an effect of the face's emotion (painful versus neutral) in the priming stimuli. A

possible explanation for this could be the use of an experimental design that involved strong subliminal priming (see general discussion), with a short presentation time and manipulation of the stimulus intensity. This may have made the priming stimuli less detectable (see supplementary data for more details on this procedure), which can reduce the processing of emotional information (Hsu et al., 2008), impeding any effect measured with RTs, especially if the distinction of the own-other stimuli was more salient. In addition, another potential factor is the use of only a few word stimuli and the effect of concomitant repetition. It has been reported that repetition of semantic stimuli lowers the salience of content and can even produce an attenuation of the cortical response (Bentin and Peled, 1990). A probable repetition effect could reduce the sensitivity of the experimental design to more slight semantic effects. Future studies with different priming time windows and a greater number of semantic stimuli may test whether the complementary effects of emotional face priming and the semantic content referred to as "own" or "other" modulate pain or neutral semantic expressions.

In order to record cortical measures of empathy for pain, a modified paradigm of pictures depicting neutral and pain situations primed by own and other faces was conducted with ERPs recordings.

3.2. Experiment 2

In Experiment 2, ERPs were recorded while participants performed a categorization task on painful and neutral stimuli, primed by their own face or other faces. Performance data showed a better classification of painful stimuli, especially when they were primed by other faces (pain stimuli primed with other faces were better classified than neutral stimuli primed by own faces). Regarding reaction times, a main effect of pain stimuli (collapsed for self and other priming) elicited shorter responses than neutral ones. Moreover, when pain stimuli were primed by other faces they elicited significantly shorter responses than all other conditions. In summary, the pain stimuli facilitated both performance and reaction times when primed by other faces.

In agreement with previous ERP reports, (Fan and Han, 2008; Han et al., 2008; Decety et al., 2010c) Experiment 2 evidenced a frontal early component (N1; over the anterior frontal area of the scalp) and a late centro-parietal waveform (P3) in response to pain and neutral pictures. Nevertheless, the pain-neutral differentiation at these early and late stages was only observed when pictures were primed by other faces. When pictures were primed by participants' own faces, no differences were observed in N1 and P3.

The use of pictures of others in a pain versus neutral images design to study empathy for pain is the most frequently used strategy in fMRI and ERP studies (e.g., Botvinick et al., 2005; Jackson et al., 2006a; Cheng et al., 2008a; Fan et al., 2008; Han et al., 2008; Akitsuki and Decety, 2009, Decety et al., 2010b). In a very consistent pattern, our results and previous ERP studies of empathy for pain showed an N1 differentiation (neutral pictures eliciting greater negative amplitudes) over the frontal area, as well as a late P3 over the centro-parietal region (pain pictures producing greater

positive amplitudes) (Fan et al., 2008; Han et al., 2008; Decety et al., 2010b). In addition to the amplitude modulation seen for pain versus neutral stimuli, the latency, morphology and scalp localization found in our study is very consistent with previous reports of empathy for pain (Fan et al., 2008; Han et al., 2008; Decety et al., 2010b). This convergence between our results and previous studies as well as the context of our study (processing painful stimuli) allows us to consider ERP measures as neural correlates of empathy processing.

The N1 response to empathy for pain can be considered a marker of the automatic activation of affective arousal/emotional sharing, which interestingly correlates with participants' unpleasantness ratings, and is related to the instantiation of an emotional state in the empathizer (Fan and Han, 2008; Han et al., 2008; Decety et al., 2010c). The prefrontal activity was elicited before the parietal component, which emerged after 380 ms. The P3 elicited in the empathy task is an index of cognitive evaluation, mainly related to stimulus access to memory and attention (Polich, 2007) and arousal (Dufey et al., 2011). In other words, P3 is an indicator of top-down attention to painful cues in the stimuli and the amplitudes correlated with subjective ratings of perceived pain and unpleasantness. Those components are considered as an early automatic component and a late top-down controlled component involved in the neural responses to perceived pain (Fan and Han, 2008; Han et al., 2008; Decety et al., 2010c).

Both emotional and attentional processes seem to modulate empathy processing at early (N1) and late (P3) stages. That modulation can be understood within models of selective attention to threat (Bishop, 2008; Halgren and Marinkovic, 1995). N1 discrimination may index bottom-up sensory mechanisms sensitive to stimulus salience. In this regard, threatening stimuli facilitate early pre-attentional discrimination indexed by the visual complex N1/P1 (fronto-occipital; Dufey et al., 2011; but see Carretié et al., 2009 for the opposite valence modulation). The P3 may be considered a marker of top-down control mechanisms that support the processing of task-relevant stimuli. In this paradigm, the P3 would be understood as a marker of stimuli arousal triggered by the emotional content of pain stimuli (see Hajcak et al., 2010). Consistently, the P3 has been related to the integration of negative stimuli (fear) into the current context via controlled processing (Liddell et al., 2004). Thus, the N1/P3 discrimination of pain versus neutral stimuli can be understood as an early-automatic and late-controlled parallel process triggered by the potentially harm represented by other-face priming.

Our results show that other faces prime both the early automatic as well as the late-controlled process, suggesting a strong effect of contextual information on empathy for pain. More specifically, our data suggest that only when a more threatening stimulus (other) is used as prime does the cortical discrimination occur. In the same line, own face priming suppresses both the early and late discrimination between pain and neutral pictures. Both effects (own face priming suppression and other face priming discrimination) suggest that when empathy for pain process is triggered by a stimulus associated to heightened arousal and attention to threat related information, the early and late processes are discrim-

inated. This result supports the empathy' TVPH (Decety, 2010; Yamada and Decety, 2009).

The contextual dependence effects of N1 and P3 elicited in this study are consistent with the contextual malleability of empathy process. Neuroimaging studies have shown that the perception of pain in others is modulated by attentional demands (Fan and Han, 2008; Gun and Han, 2007), social relationship (Cheng et al., 2010; Singer et al., 2006), cognitive appraisal (Lamm et al., 2007), and implicit attitudes towards others (Decety et al., 2010a). In the same line, ERP studies of empathy for pain have shown early modulation by contextual reality of stimuli, and late modulation based on cognitive regulatory and task demands (Fan and Han, 2008; Han et al., 2008; Decety et al., 2010c; Li and Han, 2010). Our results are in agreement with recent reports on the influence of contextual cues in cognitive processing (Aravena et al., 2010; Barutta et al., 2011; Cornejo et al., 2009; Gleichgercht et al., 2010; Hurtado et al., 2009; Ibáñez et al., 2006, 2009, 2010a,b, 2010c, 2010d, 2011a, 2011b; Riveros et al., 2010; San Martín et al., 2010). Our study demonstrates an early and late modulation of cortical responses based on who is being contextually and implicitly associated to the pain stimuli. In another study of perception of pain recorded with ERPs (Li and Han, 2010), perspective taking was manipulated by asking the participants to classify neutral and pain pictures from a simulated self or other perspective. Late neural responses (P3) to perceived pain were reduced when participants performed the pain judgment task from the other perspective compared to the self perspective. This result suggests that a top-down controlled process is critical for empathy as one has to adopt others' psychological views in order to understand and simulate others' emotional states (Decety and Jackson, 2004, 2006). Although our result could be considered to some extent in contradiction with Li and Han's report, we think that own-other information should be not comparable to perspective taking. The contextual modulation of empathy under an alarm sign (i.e., other related information) implies a different process compared to a conscious and explicit simulation of self or other perspective, which in itself does not imply any alarm or danger. Combining perspective taking as well as external signal of threat would be a relevant topic for future research. Although further research is required to assess the exact effects of other-related information associated to pain stimuli, our results suggest that the threat value of pain can enhance an avoidance response within the empathy process. At a neurophysiological level, empathic processing would not only imply positive (e.g., empathic happiness) or negative (e.g., empathic concern) valence empathy (Light et al., 2009) but also more basic processes and reactions (such as avoidance versus sharing).

3.3. General discussion

3.3.1. The TVPH in empathy research

Following the TVPH, the interpretation of the results suggests that the faces of unfamiliar others are processed as more threatening than self. Since only the pain stimuli subliminally primed by other faces were behaviorally and neurally facilitated in both experiments, this supports the hypothesis of an alarm processing of threat information and its consequent automatic facilitation. Under the TVPH, only threat

information (pain stimuli primed by other-related information) will present a differentiation from non-threat stimuli. According to this hypothesis, pain stimuli primed by other faces should trigger the bottom-up saliency filters and automatically enhance the response to stimuli of learned biological relevance (e.g., danger).

Expressions of fear have an important value in survival, similar to those of pain. An individual expression of fear is beneficial if correctly followed by actions that promote recovery and survival, and protection from danger (Prkachin, 1997). Therefore, the signs of pain require rapid evaluation. Success in this regard will be transformed into adaptive behavior and emotional responses of the observer, including sympathy for the other (Goubert et al., 2005), but only when these are associated with a positive valence. Otherwise, the perception of pain may constitute a threat. In support of this theory, results from an fMRI study demonstrated that the expression of pain activates brain areas associated with the implicit processing of pain expression and triggers an emotional reaction characterized by a threat-related response (e.g., Simon et al., 2006).

The attention theory posits that the threat value of pain is evolutionarily and ontogenetically primitive and requires attention resources (Eccleston and Crombez, 1999). In relation to fear as an ontogenetic factor, it has previously been established that the threat of pain facilitates the processing of pain-related stimuli, which is why imminent pain is often the source of arousal and anxiety and is frequently a threatening experience (Eccleston et al., 1997). According to Ohman (1979) and Price (1988), pain is the warning archetype of body danger (actual or potential) because it interrupts, distracts, and demands attention. The threat of pain anticipates imminent pain as a preparatory effect to respond and increase awareness by assigning priority to the stimuli that show the presence of threat (Ohman, 1979). Pain serves to promote bodily health and integrity, as the congenital absence of fear for wounds or injuries significantly reduces the duration of human life (Williams, 2002).

Our results cannot be explained by own face processing or familiarity. Human adults show distinct behavioral responses to their own faces and those of others (Ma and Han, 2010; Tong and Nakayama, 1999). Own face distinctiveness and familiarity would predict shorter responses to self-related stimuli (Tacikowski and Nowicka, 2010). Nevertheless, our findings are not explained by familiarity since we found the opposite effect: Other faces selectively primed the pain stimuli. This is not a simple attentional or a facilitation effect of own face or familiarity, rather an automatic enhancement of the behavioral and cortical responses to pain stimuli and other-face association. This effect is possibly triggered by the negative valence of the alarm sign present in painful stimuli. Probably, this early response of threat-detection system interacts with the empathic resonance process at early and late stages, suggesting a more complex empathy process.

Our study shows that the processing of semantic content as well as pictures of pain is automatically enhanced by other face and attenuated by own face priming, suggesting an early activation of threat or alarm signals. In a study that reached a similar conclusion, Yamada and Decety (2009) proposed that threat processing could occur earlier or at least at the same

time as any empathic processing. These results suggest the processing of pain based on the dimension of threat value rather than on empathy, inviting us to reconsider the current research on empathy for pain. These results advocate a more complex and intertwined processing of pain as salient information. It is likely that the pain matrix that includes the anterior insula, somatosensory cortex, periaqueductal gray matter, and anterior cingulate cortex is activated in pain stimuli tasks, not only as an empathic resonance response, but also as a complex interaction between empathy and avoidance. Importantly, the same neural network, which includes the amygdala, responds to any unpleasant and salient stimuli (e.g., disgusting), and its involvement in empathy for pain may thus reflect the detection and reaction to aversive salient stimuli (Benussi et al., 2008; Ibañez et al., 2010c; Ogino et al., 2007).

Although the existence of unconscious priming processing is controversial due to the marked individual differences in stimuli processing time (Torres and Raz, 1994), our study used a very robust priming paradigm with a very high processing threshold. Importantly, no participant reported being aware of the presentation of a stimulus outside the semantic expressions in any experiment, nor reported having recognized face identities or emotional expressions. Regarding the presentation procedure, we employed a procedure to some extent different from the previous pain priming study of Yamada and Decety (2009), which used a monitor capable of a 120-Hz refresh rate. For the subliminal presentation of priming stimuli, they used masking before and after showing the text. Priming involved three frames on the screen (25 ms). Our procedure, on the other hand, did not require masking. Since this study was designed to test a priming procedure in both behavioral and ERPs design, we avoided masking since it could potentially contaminate such measures. Using a 120-Hz monitor was not justified because a faster frame rate is usually compensated for by input lag, a delay in display response associated with signal processing inside the image device that has a magnitude that is independent of the refreshing rate. As a result, ours is a subliminal face presentation procedure that can be applied with common LCD monitors having a 75-Hz refresh rate.

No gender differences were found in this experiment. Although greater pain sensitivity among female participants has sometimes been reported in relation with empathy (Cheng et al., 2008a,b; Han et al., 2008; Kring and Gordon, 1998; Singer et al., 2006), many other fMRI studies (Jackson et al., 2006a; Lamm et al., 2011 for meta-analyses) have not observed any gender differences. Future studies under other experimental conditions (different thresholds of subliminal priming, greater numbers of semantic stimuli) should establish whether these results are due to the experimental design or the stable insensitivity of gender in priming conditions.

Although any subliminal primes must be presented for a short time, different time thresholds (e.g., from 8 to 50 ms) and stimuli parameters (such as intensity) can increase or reduce visibility (Eimer and Schlaghecken, 2003; Wiens, 2006). Moreover, different thresholds of subliminal stimuli can enhance or reduce automatic processing in spite of any conscious perception (Eimer and Schlaghecken, 2003; Wiens,

2006). Consequently, we claim that very strong subliminal priming (short time interval of stimuli presentation, 12 ms, and a reduced output intensity of 20) would permit the more salient self-other distinction but may attenuate small effects of emotional expression.

3.3.2. Relevance for empathy for pain research

Our result favors the predictions of the TVPH over those of the empathy hypothesis. Given the shared representation assumption (of self and other) in the empathy hypothesis, the N1 and P3 should discriminate pain from neutral stimuli in both priming conditions (own- and other-information). However, our results reveal a differentiation between pain and neutral stimuli only in the ‘other’ priming condition. In terms of the TVPH, these results can be interpreted as follows: When no source of danger is present (own-face priming) the automatic response to threat is not activated and consequently no behavioral or N1/P3 differences between painful and neutral stimuli are observed. In contrast, when a source of potential threat is present (other-face priming) an automatic alarm response yields a cortical discrimination between pain and neutral stimuli. Our results fit well with this interpretation of the TVPH.

Most cognitive neuroscience studies of empathy that have used the perception of pain in others as a means to elicit empathy processing in the observer did not include stimuli associated with the self (i.e., own faces) (Jackson et al., 2005; Jackson et al., 2006b; Cheng et al., 2008b; Lamm et al., 2007, 2010). However, recent studies indicate that processing of the self is distinguished from other information processing (Platek et al., 2008; Zaki et al., 2007). Our study suggests the importance of including a double dimension (own versus other) in priming or as a context in empathy studies to directly observe the effect of the association of stimuli to own- or other-attributes. The investigation of the neurological mechanisms underpinning empathy for pain could become more specific if one can demonstrate differential activation when painful stimuli are associated implicitly or explicitly to own- or other-related information. Notably, the fMRI studies of own- versus other-face show significant differences in areas related to empathy, such as the insula and anterior cingulate cortex (Kircher et al., 2001; Simon et al., 2006). Future neuroimaging studies of empathy would benefit from the use of pain stimuli designs that differentially activate processing related to own and other.

Although our data give more support to TVPH than to the empathy hypothesis, some alternatives would explain the results. For instance, it is possible to conclude that shared self-other representations during empathic processing may interact with threat activations in a context-dependant manner. Unfortunately, this complementary explanation is beyond the present result and calls for future research. There are also other possible explanations that could be tested in the future. For example, the Cannon–Bard theory might predict different responses to images of self emotion versus other emotion. In a similar vein, evolutionary perspectives would help to explain why no effects of own faces were observed (own faces are a very unusual stimulus and we are not frequently exposed to this stimuli). In addition, automatic responses to threat have an evolutionary developed adaptive value whereas empathic

behavior has emerged on the basis of pro-social values. Probably, empathy is a complex combination of basic-automatic and socially emergent processes which must be disentangled into its different sub-aspects. These are important areas for further exploration but they are topics that are far beyond our current design and will be the targets of additional research.

3.3.3. Conclusion

In summary, experiment 1 showed a facilitation of semantic painful expression processing when participants were primed with other face, regardless of the emotional expression. No facilitation was observed for painful expressions primed with own face or neutral expressions primed with either own or other. Experiment 2 elicited similar results using pictures instead of semantic stimuli, but this time providing evidence of cortical attenuation for pain-neutral differentiation in the own-face priming condition, and preserved pain-neutral differentiation in the other-face priming condition. Those subliminal effects influenced both the early (N1) and late (P3) evoked cortical responses to empathy for pain. Both experiments support the hypothesis of pain threat value in empathy for pain.

4. Experimental procedures

4.1. Experiment 1

4.1.1. Participants

A total of 38 participants were recruited, 17 female (ages: $M=25.6$, $SD=4.38$) and 21 male (ages: $M=24.8$, $SD=2.5$) students, to participate in the study. All participants provided written consent in agreement with the Declaration of Helsinki. None had a neurological or psychiatric history. The study was approved by the University Ethics Committee.

4.1.2. Materials

4.1.2.1. Facial stimuli. We used standard methodology for own and other faces (Keenan et al., 1999; Ma and Han, 2010; Miyakoshi et al., 2010; Sui et al., 2006; Tacikowski and Nowicka, 2010). “Other faces” were pictures taken of the faces of a male and a female participant (not the actual participant of the experiment, in order to obtain other-face stimuli), who were trained to adopt neutral facial expressions. Pained expressions were obtained by showing the participants a set of extremely painful pictures (that would elicit spontaneous mimicry of a similar pained expression in the participant). Before conducting the experiment, pictures of each actual participant (own faces) were obtained using the same procedure as for other face stimuli. In order to test the possible difference between own and other stimuli regarding valence, arousal and attractiveness, an independent study was conducted with 122 participants (just after all participants’ recordings were performed) who were asked to rate each stimuli. No differences were obtained in either neutral or pain facial expressions with respect to valence, arousal and attractiveness (see supplementary data, section rating study).

In summary, for each participant, four face pictures were considered: neutral and pained expressions of another face and neutral and pained pictures of the participant's own face (see supplementary data regarding participant picture selection). The selected photographs were then standardized based on their size, brightness, and intensity. To eliminate any possible distractions, only the eyes, nose, and mouth regions were selected. All faces were cut as an ellipse with a 10:14 aspect ratio. All images were resized to 300 (height) by 214 (width) pixels to be displayed at the center of a 1280×1024 screen. All pictures were taken in black and white, and the final results were normalized (using the total available dynamic range).

4.1.2.2. Semantic stimuli. Eight Spanish verbs were selected, four related to painful situations and four unrelated. They were written in the reflexive form, both in first and third person. Word lists were extracted from a previously validated set of stimuli (Ibáñez et al., 2006) controlled for frequency, class, emotional content, arousal and length. The resulting word stimuli are listed in Table 4.

4.1.3. Procedure

A software program running on Python was created to present one word stimulus at a time from the list and to measure reaction times in a task in which participants were asked to judge whether each stimulus was related or unrelated to pain. Four subliminal priming conditions (own face and other face with neutral and pain expressions) were utilized (see supplementary data for details about subliminal presentation). Each of the 16 word stimuli was presented twice in each of the four priming conditions, resulting in 128 trials (16×2×4). Each trial consisted of the following steps: (1) a face stimulus was presented for 13.3 ms, (2) a word stimulus appeared 200 ms later and remained until the subject's answer was given, and (3) the text disappeared immediately, followed by an inter-

trial interval of 1000 ms before the start of the next trial (see Fig. 3).

After shooting and selecting the pictures of a subject's neutral and painful facial expressions as described in the previous section, the participant entered the faraday cage (used for EEG recordings) to ensure the same conditions for all participants (particularly in terms of lighting).

Two practice trial blocks were presented to each subject. Participants were first instructed to answer with the "neutral" button (unrelated to pain) as fast as possible after reading each semantic stimulus. Only neutral textual stimuli were presented during this trial block. In a second practice trial block, participants were instructed to respond with the "pain" button (related to pain) after each semantic pain expression. They were asked to read each word and press the "painful" button as fast as possible. After these two trial blocks, subjects were instructed to answer with the "painful" button after reading text related to pain and with the "neutral" button otherwise. The button press for the pain versus neutral responses was counterbalanced between subjects. After the experiment, an off-line questionnaire was introduced in order to test if any of the participants perceived any faces. No reports of facial perception were obtained, confirming the lack of awareness of the priming procedure.

4.1.4. Data analysis

Histograms were inspected to remove outlier observations (an overall accuracy of less than 0.8) and the data for trials that had reaction times (RTs) lower than 200 ms or higher than 3000 ms. After this preprocessing, only the correct answers from 33 subjects were considered. This measure was subjected to a natural log transformation, to compensate for skewed distributions. An ANOVA model was fitted to the transformed reaction time data with the following within-subject factors: text person (1st or 3rd), word valence (neutral or painful), face person (own or other), and face expression (neutral or painful). A second ANOVA model was fitted to the same data, considering whether both text and picture had the same valence, and/or the same person (either 1st or 3rd). Only two within-subject factors were included: valence congruence and person congruence. Accuracy rates were normalized using a logit transformation [$y = \log(x/(1-x))$].

4.2. Experiment 2

4.2.1. Participants

A total of 13 students participated in the experiment (7 female, ages: $M=22.32$, $SD=2.52$; and 6 male, ages: $M=21.9$, $SD=2.31$). All participants were right handed according to the Edinburgh inventory (Oldfield, 1971), and signed a consent form in agreement with the Declaration of Helsinki. None had a neurological or psychiatric history. The study was approved by the University Ethics Committee.

4.2.2. Materials

4.2.2.1. Priming stimuli. The same methodology as the one used in experiment 1 was employed to obtain facial stimuli for priming presentation. However, since we did not obtain any effect of face-emotional expression in experiment 1, we

Table 4 – Experiment 1: Semantic expressions used in the paradigm, separated by two attributes: person (first or third) and valence (neutral or pain).

Person	Valence	Text in Spanish	English translation
Third	Neutral	Se enteró	He/she realized
		Se aburrió	He/she got bored
		Se distrajo	He/she got distracted
	Pain	Se quedó	He/she stayed
		Se golpeó	He/she hit him/herself
		Se cortó	He/she cut him/herself
First	Neutral	Se quebró	He/she broke (e.g., a bone)
		Se cayó	He/she fell down
		Me enteré	I realized
	Pain	Me aburrí	I got bored
		Me distraje	I got distracted
		Me quedé	I stayed
Pain	Me golpeé	I hit myself	
	Me corté	I cut myself	
	Me quebré	I broke (e.g., a bone)	
		Me caí	I fell down

The additional columns show examples in Spanish and their English translations.

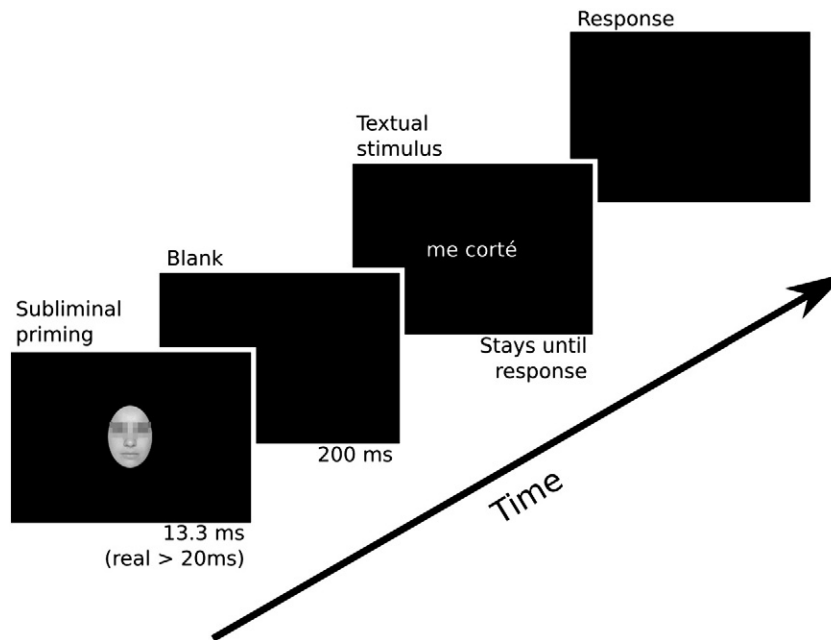


Fig. 3 – Timing of events in one trial. The meaning of the sentence in Spanish is “I cut myself.” Eyes are shown pixelized for anonymity, but were presented undistorted during the experiment.

included only the neutral expressions from participants and other face stimuli. Consequently, for each participant, two faces were considered: a neutral face of another participant and a neutral face of the participant herself/himself (see supplementary data regarding participant picture selection). All stimuli were selected, standardized, resized, normalized and the faces cut to an ellipse as detailed in experiment 1. As in Experiment 1, no differences were obtained in own versus other facial expressions with respect to valence, arousal and attractiveness (see supplementary data).

4.2.2.2. Picture stimuli. Participants were shown 160 static visual stimuli, consisting of pictures of different body parts (40 for hand and 40 for foot, repeated twice) that were previously used and validated in behavioral, MEG and fMRI studies (Cheng et al., 2008a; Jackson et al., 2006a). Half of the pictures depicted body parts under non-painful situations (Neutral) and in the other half of the stimuli were painful situations with several types of pain (mechanical, thermal, and pressure). For each pain situation, a neutral picture involved the same settings without any painful component. All these situations depict familiar events from everyday life. The visual angle of stimuli was matched and they were presented in the center of a black background of a 18-in. color monitor. Each stimulus was 8 cm (width) × 6 cm (height).

4.2.3. Procedure

A software program running on Python was created to present one picture at a time from the list and to measure reaction times in a task in which participants were asked to judge whether each picture was related or unrelated to pain. Two subliminal priming conditions (own face and other face neutral expressions) were included (see supplementary data

for details about subliminal presentation). Each picture (neutral and pain) was presented once in each of the two priming conditions, resulting in 160 trials (40 × 2 × 2). Each trial consisted of the following steps: (1) a face stimulus (own or other) was presented for 13.3 ms (priming); (2) 400 ms later, a picture stimulus appeared for 500 ms and then the subject's answer was given, followed by; (3) an inter-trial interval of 1000 ms before the start of the next trial (see Fig. 4). Painful and non-painful stimuli were presented in a pseudo-random order (controlling for no more than 2 consecutive same valence picture presentations).

After picture selection (following the steps detailed in experiment 1), the participant entered the faraday cage for EEG recordings). After a practice trial block, participants were instructed to answer with the “neutral” button (unrelated to pain) or a “pain” button (related to pain) as fast as possible after seeing each picture. The button press for the pain versus neutral responses was counterbalanced between subjects. After this trial block, the EEG recording began. As in experiment 1, the offline questionnaire designed to evaluate the stimuli perception reported no facial perception during the task.

4.2.4. ERP data acquisition and processing

Electroencephalographic (EEG) data were acquired with a 128 channel Electrical Geodesics Inc. (EGI) system, GES300, consisting of Hydrocel Geodesic Sensor Net, Net Amps and Net Station software (Electrical Geodesics Inc.). EEG data were sampled at 500 Hz and 0.1–100 Hz analog filtered. Impedances were kept under 50 k Ω . EEG data were continuously recorded by default to vertex and offline re-referenced to linked mastoids. A band pass digital filter between 0.5 and 30 Hz was applied to remove unwanted frequency components. EEG

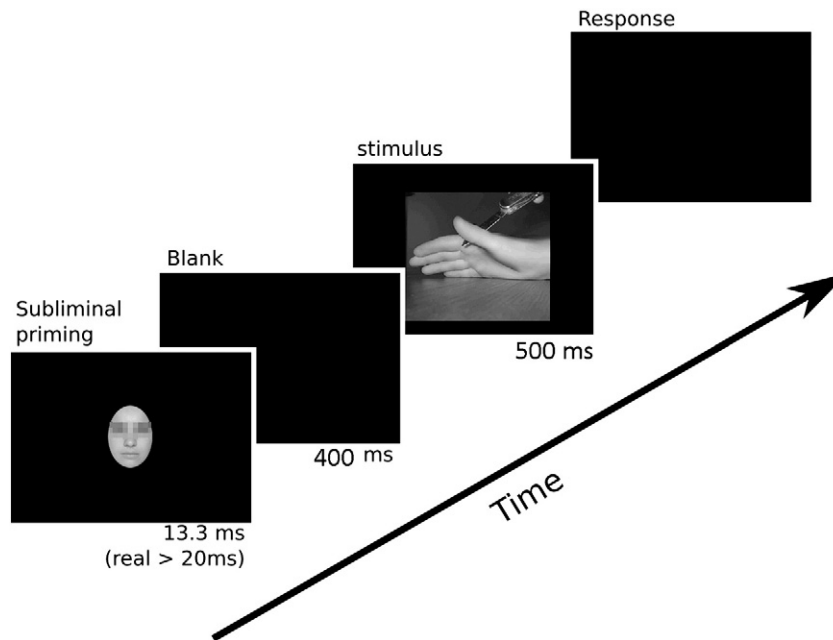


Fig. 4 – Schematic representation of trial sequence: a face stimulus (own or other) was presented for 13.3 ms (priming), then 400 ms later a picture stimulus appeared for 500 ms and then the subject's answer was given, and followed by an inter-trial interval of 1000 ms (not shown in the figure) before the start of the next trial. Eyes are shown pixelized for anonymity, but were presented undistorted during the experiment.

data were segmented offline into 1 s epochs spanning from 200 ms pre-stimulus to 800 ms post-stimulus for stimulus-locked segments. EEG channels with visually detectable artifacts (e.g., eye blink, channel drift and gross movement) were isolated using the Net Station Waveform Tools (NSWT) and discarded from the analysis. In addition, automatic ICA and adaptive autoregressive modeling was performed to discard further artifacts.

4.2.5. Data analysis

Behavioral data (accuracy and RTs) were calculated for each subject in each condition. Outliers with RTs outside ± 2.5 SD were deleted. An ANOVA model was fitted to transform behavioral and ERP data with the following within-subject factors: stimulus type (neutral or painful) and priming (own or other facial stimulus).

For ERPs, a strategy for channel selection based on the observed effects (and previously reported in ERPs studies of empathy: Decety et al., 2010c) was used: The time course analysis for three representative electrodes (Fz, Cz and Pz) was included as an additional within-subject ANOVA factor (electrode). Nevertheless, following a reviewer observation, we performed an additional analysis including midline, left and right lateral electrodes sites (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4). As expected, only midline electrodes (Fz, Cz and Pz) yield significant effects of stimulus type and priming. Consequently we did not include lateral sites but only midline electrodes (Fz, Cz and Pz). Accordingly, a $2 \times 2 \times 4$ (stimulus type \times priming \times electrode) analysis was carried out for ERPs, which were analyzed by considering mean amplitude values: (1) an early window consisted of a fronto-central negative component between 90 and 150 ms (N1) and a late P3 at central-posterior sites between 300 and 450 ms (Decety et al., 2010c). The

ANOVA's degrees of freedom for post hoc comparisons were corrected using the Tukey's HSD method.

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