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Pain influence on cognitive processing: an implicit emotional Go/NoGo task on an event-related potential study.

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ABSTRACT

The facial expression of pain is unique and distinct from the expression of basic emotions and its recognition has clear survival and communicative value. Distinct facial expressions of pain can warn others of imminent danger and elicit helping and emphatic behavior towards the individual experiencing pain. Contrary to the extensive research on facial expressions of basic emotions, little is known about brain processing of pain expressions. The present study aimed to unravel the modulating role of pain facial expressions on cognitive processing by using an emotional Go/NoGo task. For this purpose, eighteen healthy female volunteers (40-60 years, *mean* = 50.89 years, *SD* = 6.17) participated in a study, in which pain, happy and neutral faces were presented. Subjects were asked to press a button when they viewed a male face (Go trials), and to inhibit their response when a female face was presented (NoGo trials). Results indicated that pain faces elicited more commission errors and faster reaction times (RTs) than happy and neutral faces. Furthermore, it was shown that pain faces elicited larger N200 and reduced NoGo-P300 amplitudes than happy faces. Moreover, pain and neutral faces elicited larger NoGo-N200 amplitudes than happy faces. These findings suggest that pain faces were able to elicit empathic and arousal brain responses; and modulate both, response execution and inhibition.

Key words: pain; facial expression; cognitive processing; emotion; Go/NoGo; ERP; N200; P300.

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1. Introduction

The facial expression of pain is a prominent non-verbal behavior, unique and distinct from the expression of basic emotions (sadness, happiness, anger, contempt, disgust, fear and surprise) [8,23,29,39]. Although pain is often considered a private experience, recognition of pain in others has clear survival and communicative values. Thus, distinct facial expressions of pain can warn others of imminent danger and elicit helping and emphatic behavior towards the individual experiencing pain [44,50].

Behavioral observations and neuroimaging studies in healthy subjects have found that emotional facial stimuli may capture attention more readily than neutral stimuli, even in a reflexive or involuntary manner [5,7,18,24,45,46]. Most emotional studies were based on the assumption that such processing takes place only on a global valence-based level, allowing individuals to disentangle positive from negative emotions regardless of specific emotions. Nevertheless, in order to efficiently adjust own individual reactions to affective stimuli in social contexts, it is highly relevant to promptly and adequately recognize emotions in others [4]. In this sense, emotional faces can be processed very fast and even under limited awareness conditions. Thus, for instance, significant differences between anger, fear and sadness have been found at early stages of information processing [36]. Contrary to the extensive research on facial expressions of basic emotions, there is scarce information about the brain processing of implicit pain stimuli and its modulating role on attentional processes [23].

The emotional Go/NoGo task has been used extensively to investigate emotional processing in both, healthy adults and patients with affective disorders [27,38]. The fact that affective stimuli in this type of tasks are able to interfere with cognitive processing suggests that individuals are not only highly sensitive to such information, but also that they are unable to fully ignore those affective contents [12,17,33,45]. Furthermore, ERP and fMRI studies have revealed that negative stimuli, such as fearful or

angry facial expressions, require more attention and processing resources than positive stimuli, even when stimuli were presented after removing information from the face (like hair and neck)[49] or even if they were task irrelevant [15,17,45]. Moreover, negative stimuli also elicit time-consuming and disrupting cognitive performance, because their obvious adaptive value [1,7,12,19,26,41,45].

Studies using ERPs during Go/NoGo tasks, usually revealed augmented amplitudes mainly on N200 and P300 components in response to NoGo trials, because their appearance is much less probable than Go trials (≤25%) [13,14]. These components may reflect different sub-processes of response inhibition. Thus, for instance, **N200** (a negative-going component that peaks around 200-400ms after the stimulus) is particularly sensitive to conflict monitoring, showing that in a context of frequent Go responses, a NoGo response would require a behavioral inhibition, resulting in larger N200 amplitudes [2,10,14,16,54]. **P300** (a positive-going component that peaks around 300-700ms after the stimulus) is associated with motor inhibition itself (conflict resolution through response inhibition[14]) and its amplitude is modulated by the stimuli expectation degree [31]. Thus, P300 amplitudes seem to be linked to individual orientation reactions rather than to physical attributes of stimuli [35]. In consequence, those trials requiring a behavioral inhibition to highly significant stimuli may elicit larger P300 amplitudes [11-14]. Furthermore, it has been previously found that these ERPs are modulated by facial expressions, suggesting that facial expressions interact with response inhibition even at early stages of information processing [52,53]. Nevertheless, as far as we know, there is no clear evidence about how this interaction may occur. For example, *Zhang et al. (2012)* [53] found that positive (happy) and negative (angry and fearful) faces elicited lower Go-N200 amplitudes than neutral faces. On the other hand, positive and negative faces elicited larger P300 amplitudes than neutral faces. Contrarily, *Lewis et al. (2007)* [25] found that the presentation of negative (angry) faces produced larger N200 amplitudes than positive (happy) faces, with neutral faces falling in between. Thereby, it seems that this modulation may differ according to the stimulus characteristics and task methodology.

The aim of the present study was to investigate how implicit pain information may influence cognitive control processes, as well as its underlying neural brain mechanisms. For this purpose, and taking into account the previous research that highlighted the difference between positive and negative stimuli in control processes, ERPs generated during an emotional Go/NoGo paradigm with three different types of emotional facial stimuli (happy, neutral and pain faces) were recorded in healthy females. Based on previous studies [14,25,53], it was hypothesized that emotional information (happy and pain facial expressions) would modulate both response execution (Go trials) and response inhibition (NoGo trials). In addition, consistent with the notion that negative stimuli impair cognitive control, we expected to find longer reaction times and less accuracy to pain faces in comparison to happy and neutral faces. Moreover, due to its adaptive importance, we expected larger N200 and P300 amplitudes, in response to pain faces than in response to happy and neutral faces, showing greater conflict and significance for this emotion, respectively.

2. Material and methods

2.1. Participants.

Eighteen healthy right-handed females between the age of 40 and 60 (*mean age* = 50.89 years, *SD* = 6.17) participated in this study. Sociodemographic characteristics are shown in *Table 1*. Participants were selected from a list of volunteers recruited at the Open Balearic University for Seniors (UIB) and by posting weblogs on social network sites. Initial screening measures were conducted by telephone. All volunteers were asked to perform a telephone survey to determine medical history (current or past

presence of pain, medication, diseases, and depression). Inclusion criteria were the absence of chronic pain and depression, as well as the absence of pain sensation or use of medication during one week before the experimental session. Screening measures were conducted in the laboratory to twenty-one selected volunteers, before the experimental session, through a series of questionnaires (specified in the following section). Participants with a sum score in the BDI-II questionnaire higher or equal to ten were not included in the study [3], leading to three of the twenty-one selected volunteers being excluded. All subjects had normal or corrected vision, and none had a current or prior history of chronic pain, neurological disorders, or psychiatric disorders. All participants were verbally informed about the study at the time of recruitment and they signed an informed consent before testing. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of the Balearic Islands.

Table 1. Sociodemographic and Clinical data. Participant characteristics; mean, standard deviation (SD) and range are displayed for each questionnaire.

	Mean control group (n=18)	SD	Range
Age (years)	50.88	6.17	40 - 60
BDI score (0-63)	3.00	3.96	0 - 10
PANAS score (1-5)			
Positive affect	3.85	0.57	3 - 4.6
Negative affect	1.20	0.53	1 - 2.8
PVAQ score (0-80)	43.50	10.82	18 - 58
ERQ score (1-7)			
Reappraissal	5.08	1.58	1 - 6.83
Supression	2.87	0.98	1 - 4.75

Abbreviations: SD, *Standard deviation* ; BDI, *Beck Depression Inventory* ; PANAS, *Positive And Negative Affect Schedule* ; PVAQ, *Pain Vigilance and Awareness Questionnaire* ; ERQ, *Emotion Regulation Questionnaire* .

2.2. Questionnaires.

All participants underwent a semi-standardized interview to assess sociodemographic and clinical data. Thus, the Spanish versions of the Beck Depression Inventory (BDI-II) [3], the Positive and Negative Affect Schedule (PANAS) [48], the Edinburgh Handedness Inventory (EHI) [32], the Pain Vigilance and Awareness Questionnaire (PVAQ) [28], and the Emotion Regulation Questionnaire (ERQ) [21] , were completed. In addition, a pharmacological questionnaire was completed, asking about current medication and diseases. Participants rated the valence and arousal of the presented affective stimuli by using the Self-Assessment Manikin Scale (SAM) [5].

2.3. Emotional Go/NoGo task and procedure.

After participants completed the self-report questionnaires, they performed an implicit emotional Go/NoGo task. Emotional stimuli included happy, neutral and pain facial expressions from 8 individuals (4 females and 4 males) selected from a pool of 1-second video clips validated by *Simon et al. (2008)* [8,40] and used in previous studies from our lab [19] . Single frames from original video clips were captured at the peak of the facial expression (around 1000s from the original video onset) [19]. Then pictures were

transformed to black and white, adjusted for luminosity and the face was cropped in an oval (removing hair, neck, and surrounding parts) in order to assure a better focus on emotional expressions[6]. The task consisted of six blocks *(see Fig. 1)*. Each block contained 72 trials, of which 55 (77%) were Go trials (male faces) and 17 (23%) were NoGo trials (female faces), resulting in a total of 110 Go cues and 34 NoGo cues for each of the three emotion conditions (happy, neutral and pain). In each trial, a facial stimulus was presented for 500ms in the center of the black screen. The interstimulus interval (ISI) was pseudorandomized from 1300 to 1500ms to discourage anticipatory responses. A white fixation cross was displayed in the center of the screen at the beginning and during the ISI. The trial order was pseudorandomized to avoid the consecutive presentation of two NoGo cues within each block.

Before each block, subjects were given instructions to respond to male faces (Go trials) by pressing a button-pushing device, and inhibit their responses to female faces (NoGo trials). These task instructions were displayed on the computer screen and subjects pressed any button when ready to begin. They were required to respond as fast as possible without making mistakes. As facial expressions were task-irrelevant, the emotional component was implicit. Participants were first given the opportunity to practice in a block of 16 trials, where instead of faces, geometrical figures (triangles, squares and circles) with different colors (yellow and red) were shown. Red figures acted as Go cues and yellow ones as NoGo cues. Once it was determined that they were able to perform the task, the experimental trials started. The task was compiled and run using the software Presentation (Version 14.9, Neurobehavioral Systems, Inc., San Francisco, CA).

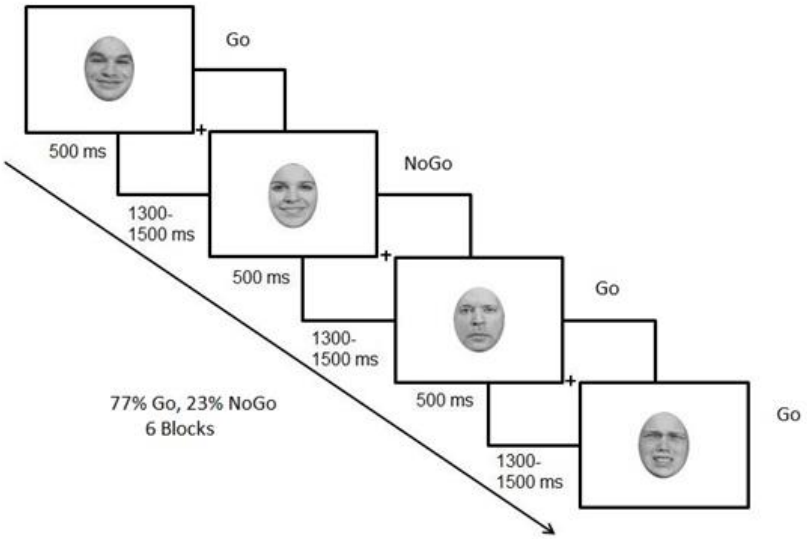

Fig 1. Stimuli presentation in the emotional Go/NoGo task.

For the current study, hits and mistakes were analyzed. The relative number of false alarms or commission errors (CEs) (errors on NoGo trials (i.e., pressing the button when a female face appears) divided by the total number of NoGo trials and multiplied by 100), and the relative number of omission errors (OEs) (errors on Go trials (not pressing the button when a male face appears) divided by the total number of Go trials and multiplied by 100) for each of the three emotional facial conditions (happy, neutral and pain) served as primary measures to test the effects of affective modulation on behavioral inhibition and execution. The mean reaction time (RT) (in milliseconds) on correct Go trials for the three emotional facial conditions was used as a measure of emotional bias[14].

2.4. Electrophysiological recording and analysis.

To analyze electroencephalographic (EEG) activity, 46 scalp electrodes were mounted in an elastic cap and placed according to the International 10/20 system. An electrooculogram (EOG) channel was also obtained by placing one electrode above and another below the left eye. Activity was continuously recorded by using a QuickAmp amplifier, which was managed through the program BrainVision Recorder (BrainProducts, Munich, Germany). Electrodes were recorded against an average reference calculated by the amplifier. Electrode impedance was kept below 10kΩ. EEG and EOG signals were recorded with a sampling rate of 1000Hz, a frequency bandpass filter of .05 to 70 Hz and a 50Hz notch filter. EEG recordings were further processed off-line using BrainVision Analyzer (BrainProducts, Munich, Germany). A frequency bandpass filter of .05 to 35 Hz was applied. Eye movement artifacts were corrected by using Gratton & Coles algorithm [20]. For analyses of ERPs elicited by stimuli, EEG waveforms were segmented in epochs of 700ms duration (-100ms to 600ms relative to stimulus onset) and baseline corrected (from -100ms to 0ms). Before baseline correction, an artifact rejection protocol with the following criteria was applied: maximal allowed voltage step/sampling point = 100mV, minimal allowed amplitude = -100mV, maximal allowed amplitude = 100mV and maximal allowed absolute difference in the epoch = 100mV. Finally, EEG waveforms were averaged separately for each condition (happy, neutral, pain). Trials with incorrect behavioral responses were not included in the analyses. Relevant ERP components to target faces were identified by using a global maxima detection method, and analyzed in the time segments 200-350 and 350-550ms. The 200-350ms time segment was chosen to capture the well-known N200 component, which represents the conflict caused by a competition between the frequently (Go) and infrequently (NoGo) required responses [10,16]. The 350-550ms interval was chosen to detect the later P300 component, which is mainly associated with motor inhibition itself [14]. Nonetheless, as this last component is conformed by a set of peaks, the whole area was analyzed. Because of its topographical relevance [14,53,54], electrodes were grouped into following brain regions: frontal (F1, Fz and F2), fronto-central (FC1, FCz and FC2) and central electrodes (C1, Cz and C2).

In addition, amplitudes in the time windows 90-120ms and 140-190ms were also analyzed to capture N1 and P2 peaks, respectively. These results will be presented in the attached supplementary material.

2.5. Statistical analyses.

EEG data were statistically analyzed using multivariate analyses of variance (MANOVA) for repeated measures with the following repeated factors: EMOTION (happy, neutral and pain), TRIAL TYPE (Go vs. NoGo) and BRAIN REGION (frontal, fronto-central and central). **Task accuracy and RTs** were statistically analyzed using MANOVA for repeated measures with the factor EMOTION (happy, neutral and pain). For task accuracy, the factor TRIAL TYPE (Go vs. NoGo) was also included. Degrees of freedom were corrected using the Greenhouse-Geisser epsilon and post-hoc analyses were always corrected by Bonferroni.

In addition, subjective ratings elicited by the facial stimuli were analyzed using MANOVA with the factors GENDER (male vs. female) and EMOTION (happy, neutral and pain), in order to evaluate possible gender differences in **valence and arousal**. These results will be shown in the attached supplementary material.

3. Results

3.1. Behavioral data.

Accuracy

Regarding behavioral inhibition and execution (*see Fig.2a*), significant main effects were found on EMOTION [F (2,34) = 17.221, p<0.001]. Post-hoc analysis showed that participants made more errors for pain faces than for happy and neutral (all p<0.005). We also found a significant interaction effect between EMOTION and TRIAL TYPE [F (2,34) = 12.209, p≤0.001]. Post-hoc comparison indicated that participants made more CEs for pain stimuli than for happy and neutral (all p_s<0.05), while non-significant differences between emotions were found in OEs. Finally, analysis also revealed significant differences regarding the TRIAL TYPE, showing that participants made more OEs than CEs only in the happy faces condition (p<0.05, Bonferroni corrected).

Reaction time

Analyses of RT for correct Go trials (*see Fig.2b*) showed a significant main effect of EMOTION [F (2,34) = 14.143, p<0.001]. Post-hoc analysis indicated that when a pain stimuli was presented, participants had faster reactions times in comparison with happy and neutral stimuli (all p<0.005, Bonferroni corrected) and not significant differences were found between happy and neutral.

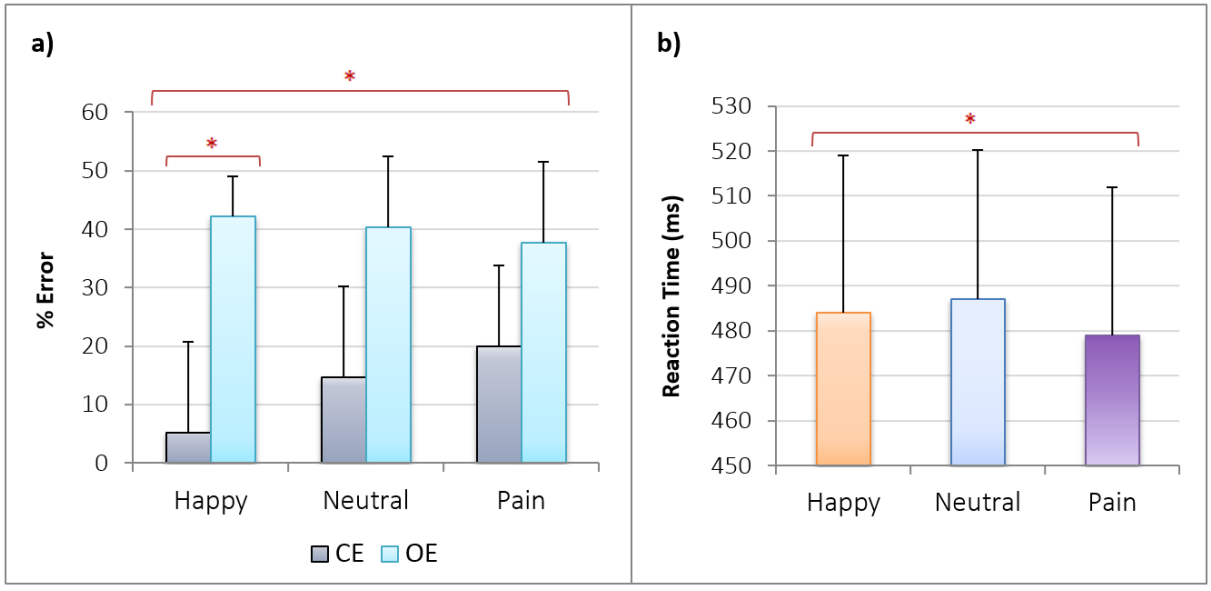

Fig 2. a) Mean values of Commission Errors (CE) and Omission Errors (OE) for the three different emotional facial expresions; Post-hoc analysis showed that participants made more CEs for pain faces than for happy and neutral; and they also made more OEs than CEs for happy faces. **b)** Mean values of Reaction times for hits (Go trials) and for the three different emotional facial expresions; Post-hoc analysis indicated that participants had faster RTs for pain faces than for happy and neutral. In both graphics, error bars represent standard deviation (SD) and * indicate significant differences (all ps<0.05).

A complementary table showing CEs and OEs rates, as well as reaction times (RTs) on Go trials during the emotional Go/NoGo task has been attached in the supplementary material (*Table 2*).

3.2. Electrophysiological data.

N200 amplitudes.

We found a significant main effect of TRIAL TYPE [F (1,17) = 5.497, p<0.05], indicating larger N200 amplitudes for NoGo trials than for Go trials (p<0.05) (*See Fig.3*). Besides, a main effect of EMOTION was found [F (2,34) = 11.363, p<0.001], in which pain and neutral faces evoked larger N200 amplitudes than happy faces (all p_s<0.05, Bonferroni corrected). There was also a non-significant trend in the EMOTION x TRIAL TYPE interaction [F (2,34) = 2.909, p = 0.08]. As shown in *Figure 4*, post-hoc analyses indicated that pain and neutral faces evoked larger N200 amplitudes in response to NoGo than to Go trials (all p_s<0.05). There were also lower NoGo-N200 amplitudes for happy faces than for neutral faces (p=0.001) (*See Fig.3*).

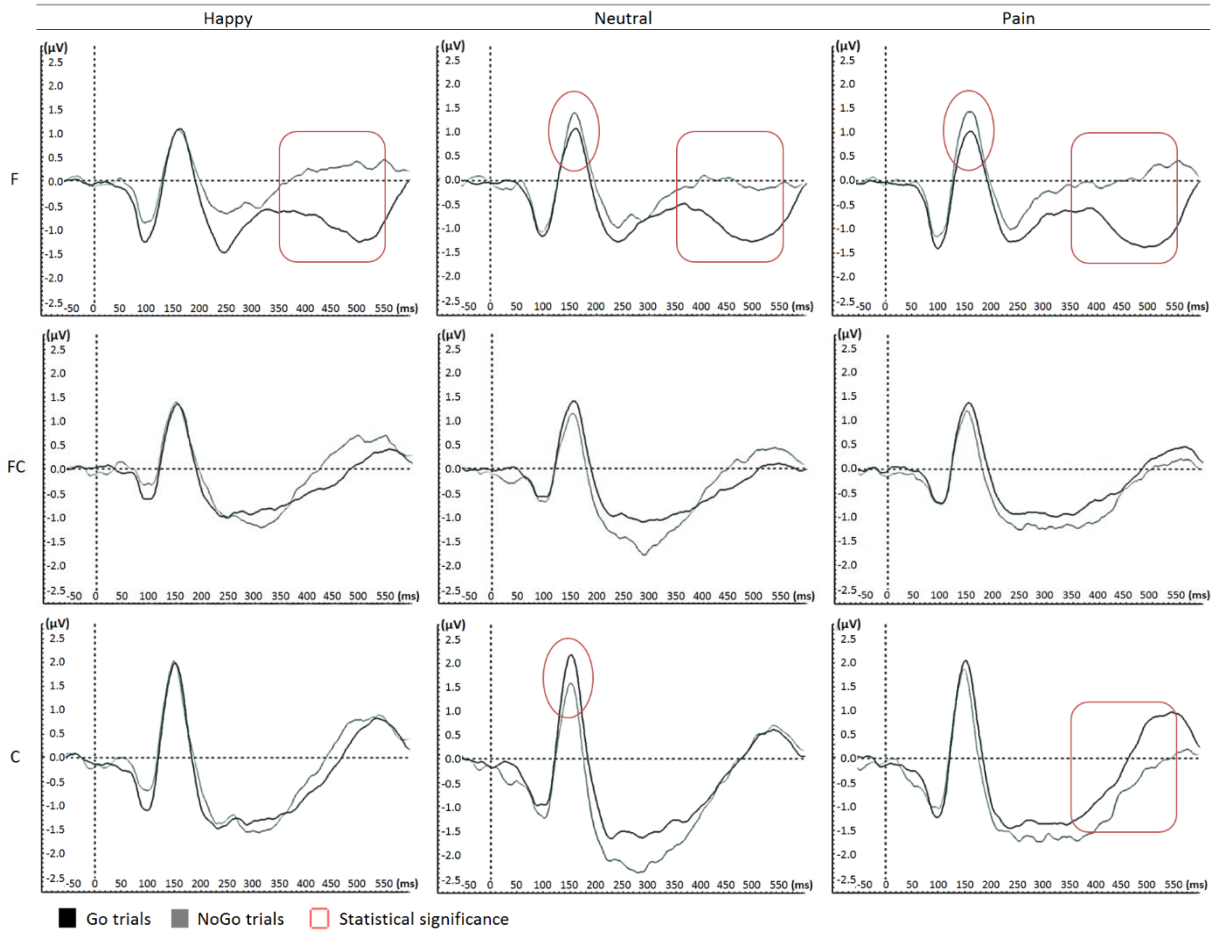

Fig 3. Stimulus-locked grand average waveforms from frontal, F (upper panel); frontocentral, FC (middle) and central, C (bottom panel) brain regions evoked by happy, neutral and pain stimuli in the emotional Go/NoGo task as a function of trial type (Go, black; NoGo, gray). In red circles statistical significances are standed out.

P300 amplitudes

The repeated measures ANOVAs revealed significant main effects of TRIAL TYPE [F (1,17) = 4.869, p<0.05] and EMOTION [F (2,34) = 5.079, p<0.03]. We also found significant BRAIN REGION x TRIAL TYPE [F (2,34) = 6.190, p<0.03], TRIAL TYPE x EMOTION [F (2,34) = 5.579, p<0.03] and BRAIN REGION x TRIAL TYPE x EMOTION interactions [F (4,68) = 3.694, p< 0.05]. As shown in *Figure 3*, data analyses revealed larger P300 amplitudes for NoGo than for Go trials in all emotions in frontal electrodes, while in central electrodes pain faces showed lower amplitudes for NoGo than for Go trials (all p_s<0.05, Bonferroni corrected). Moreover, in fronto-central and central sites, NoGo trials revealed larger P300 amplitudes for happy than for pain faces (all p_s<0.05, Bonferroni corrected).

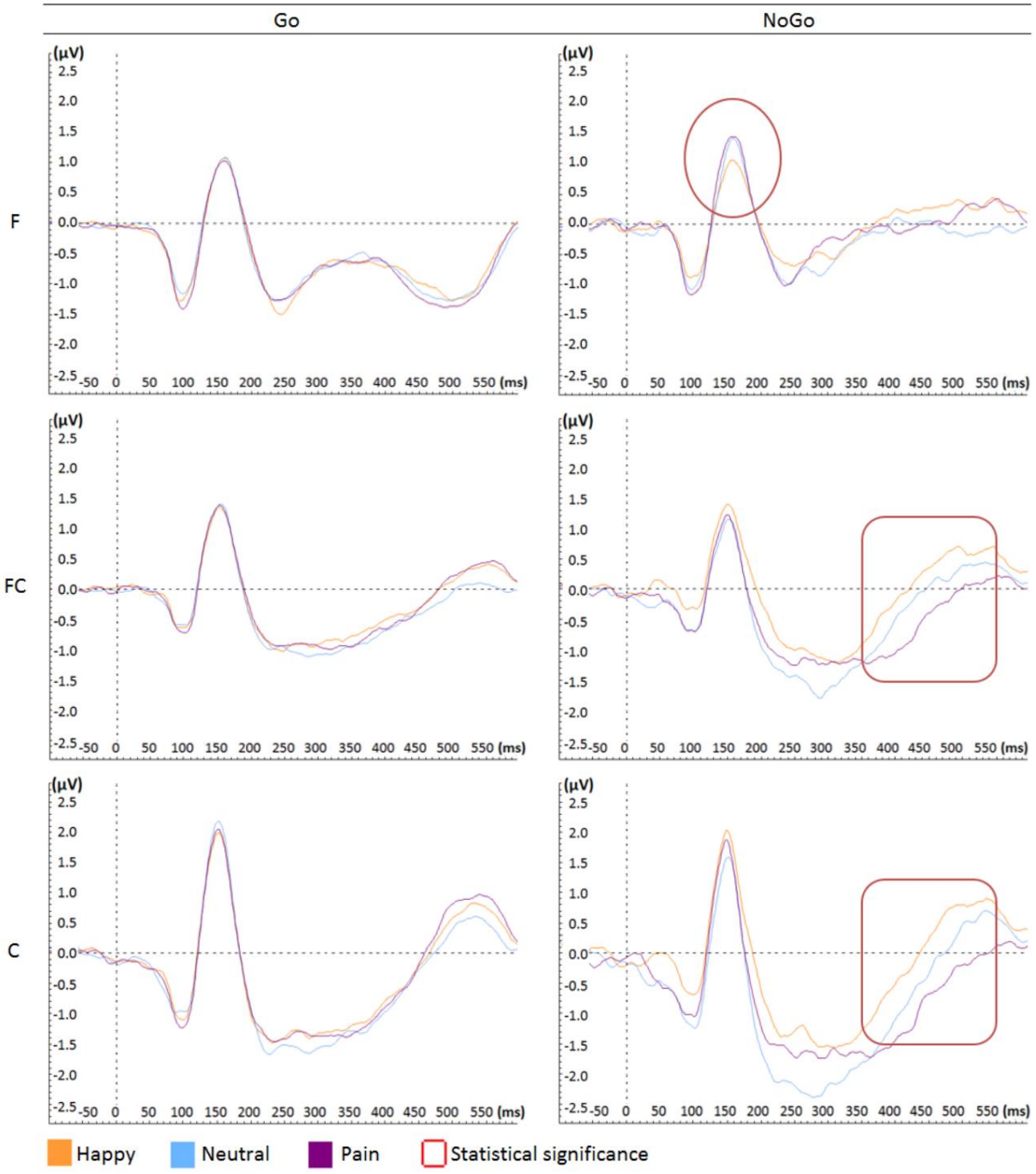

Fig 4. Stimulus-locked grand average waveforms from frontal, F (upper panel); frontocentral, FC (middle) and central, C (bottom panel) brain regions evoked by the total number of Go and NoGo trials in the emotional Go/NoGo task as a function of Emotions (happy in orange, neutral in blue and pain in purple). In red circles statistical significances are standed out.

A complementary table showing mean N200 and P300 amplitudes, averaged across nine recorded fronto-central scalp sites (F1, F2, Fz, FC1, FC2, FCz, C1, C2 and Cz) for each trial type (Go and NoGo) and emotional facial expression (happy, neutral and pain) has been attached in the supplementary material (*Table 3*).

4. Discussion

The aim of the present study was to investigate the influence of implicit pain information in cognitive control processes and its underlying neural brain mechanisms in healthy subjects, by using an emotional Go/NoGo task on an event-related potential study.

The hypotheses were that emotional information (happy and pain facial expressions) would modulate both response execution (Go trials) and response inhibition (NoGo trials). It was also hypothesized that pain faces would elicit longer reaction times and less accurate responses, as well as larger N200 and P300 amplitudes, than happy and neutral faces.

According to behavioral data, participants had significantly **more CEs** (errors during NoGo trials) **to pain faces** than to happy and neutral faces, and not significant differences were found within OEs (errors on Go trials), suggesting that pain faces created more difficulties for response inhibition. These results are in line with the well-known theory that negative stimuli impair cognitive control due to its adaptive importance [7,9,12,19,41,45]. Contrary to what we hypothesized, **RTs for pain faces were faster** than for happy and neutral. However, even though our results did not match with our hypothesis, *Rohr et al. (2012)* [36] highlighted the differences that can be found between emotions, not only due to its valence but its relevance in social interactions. Accordingly, whereas pain is an emotion that is unconditionally negative, as fear or anger, it has relevant cue for delivering effective care and social support [43,44,50]. *González-Roldan et al. (2011)* [19], also stated that viewing another person expressing acute pain without knowing the source of pain could be linked to a more empathetic behavior from the observer. Besides, other studies have stand out the influential role of arousal on RTs. *Pessoa et al. (2013)* [34] reported that fearful expressions decreased reaction time relative to neutral faces during stop-signal task in healthy subjects, because the emotional stimuli were rated as more arousing than neutral ones. *Nakic et al. (2006)* [30] observed this RT decrease for highly and arousing negative words but not for moderately negative words. Therefore, for future studies we recommend to further analyze arousal ratings, to check if subjects find pain faces more arousing than happy and neutral ones.

Regarding electrophysiological data, similar to the general Go/NoGo tasks with non-emotional stimuli [2,53], we observed larger N200 and P300 amplitudes for NoGo than for Go responses. These results show the conflict: frequent Go cues create a prepotent tendency to respond that must be inhibited in NoGo cues [38], suggesting that our task was valid to characterize brain responses of inhibition process. Furthermore, we found that **pain faces elicited larger N200 and reduced NoGo-P300 amplitudes** than happy faces. We also found that **pain and neutral faces elicited larger NoGo-N200** amplitudes than happy faces. N200 component represents the conflict caused by the competition between the frequently (Go) and infrequently (NoGo) required responses [10,16]. As hypothesized, our results indicate that pain faces enhance this conflict. These results are in line with *Williams (2002)* [50] and *Saarela et al. (2006)* [44] studies, which show that pain faces need to be processed with a higher priority than happy faces because are more relevant and arousing, due to its clear survival and empathetic value [44,50]. Similarly, *Lewis et al. (2007)* [25] found that the presentation of angry faces produced larger N200 amplitudes than happy faces, with neutral faces falling in between. They explained these results suggesting that it could reflect more urgent recruitment of attentional processes needed to regulate anxiety during stimulus appraisal (effortful emotion regulation). Nevertheless, we did not expect that neutral faces would also elicit larger NoGo-N200 amplitudes than happy faces. However, previous studies have shown similar results [25,51] suggesting that neutral faces

could elicit larger amplitudes because its ambiguous nature. Several studies have demonstrated that neutral stimuli are subject to interpretive bias. *Yoon et al. (2008)* [51] focused their study on the interpretation of neutral facial expressions, with and without an anticipatory speech threat on the task, by anxious and non-anxious individuals. They found out that socially anxious individuals are characterized by an interpretive bias regardless of the threat manipulation. In contrast, non-anxious individuals interpreted neutral faces in a negative manner only when they were in the threat condition. In a similar way, as in our experiment neutral faces were mixed with pain faces, that could have caused a negative influence on the interpretation. On the other hand, regarding P300 component, we found that just NoGo-P300 amplitudes vary as a function of affective valence. Contrary to our expectations, our results show that **pain faces elicited significant lower NoGo-P300 amplitudes** than happy faces in frontocentral and central brain regions. This component is associated with motor inhibition itself [14], and it is well established that the lower the probability of an stimulus and greater its significance, the larger the amplitude of P300 [11]. Then, due to its significant adaptive value, we hypothesized to find larger P300 amplitudes for pain than for happy faces. Nonetheless, we have to take into consideration the fact that P300 amplitude is affected by expectancies generated by the sequence of stimuli preceding the eliciting stimulus [11]. For example, *Squires et al. (1976)* [42] observed that successive repetitions of one kind of stimuli were associated with decreases in P300 amplitudes. Then, taking into account that our results suggest that neutral faces could have been interpreted as pain faces, happy faces would have been more unexpected than pain faces, eliciting larger NoGo-P300 amplitudes.

Finally, we want to mention other data results. According to behavioral data, contrary to the literature [13,14], we did not found significant more CEs than OEs. What is more, we found significant higher OEs than CEs for happy stimuli. During the experimental session, participants reported difficulties to differentiate female (NoGo trials) from male faces (Go trials). After the experiment, we presented the faces again and they pointed mainly emotional faces as the more difficult ones because the distinguishing characteristics were not clear. Hence, they could have interpreted happy male faces as NoGo cues, increasing the OEs. Considering ERP data, we found that in the central brain regions, pain faces evoked lower NoGo-P300 amplitudes than Go-P300. Even though this result does not agree with our earlier discussion, previous research demonstrates that the P300 component is associated with other processes such as attention, motivation and memory mechanisms [37]. Besides, other studies show that P300 amplitude can change according to the brain region, being different in frontal than central regions [22]. Then, we could contemplate that pain information had a different impact than happy and neutral stimuli for Go and NoGo trials, due to other involved mechanisms. On the other hand, although the EMOTION x TRIAL TYPE interaction did not reach significant values, a tendency was observed. That may suggest that pain and neutral stimuli were the principal cause of this larger NoGo-N200 than Go-N200 component, enhancing the conflict between frequent and infrequent responses[38].

There are, however, some **limitations of our study** that should be considered. First, we had a small group of participants (just 18 in front of a mean of approximately 30 in the studies we have analyzed). Second, the average age was 51 years, while most of the cited research studied children, adolescents and young adults. This is particularly important because it has been shown that age has an impact on the P300 amplitude for example [54]. Then, the effect of individual differences such as age should be investigated. Third, our study has a gender limitation because our sample consisted only of women and all Go trials were male faces. Significant gender effects in brain activations to emotional faces and

affective pictures have been previously reported [38,39,40]. Thus, it has an important methodological effect and further research should reproduce a similar investigation introducing male participants and an equal amount of male and female faces for Go and NoGo trials, to discard gender bias and fully demonstrate that pain caused less accuracy in attentional tasks independently of the gender. Nevertheless, we did not take into consideration this gender effect when planning the study because we focused it on how emotions affected response inhibition and execution, regardless of whether the target was female or male. Still, we were particularly interested in these gender effects, so we decided to independently analyze its impact in our study (results are shown in the supplementary material).

5. Conclusion

In summary, the results of our study add evidence to the notion that emotional information modulates N200 (conflict monitoring) and P300 components (response inhibition). Also, according to our interpretations, pain facial expressions seem to be processed differently than other negative valence facial expressions, as anger or fear. Pain facial expressions appear to elicit empathic and arousal brain responses as reflected by more CEs, faster reaction times and amplitude enhancements of the N200 component seconds after stimulus onset (in comparison with happy and neutral faces). Our findings, thus, provide further support for the idea that emotional information from faces is processed beyond valence under conditions of limited awareness. For this reason, more studies focused on pain stimuli should be conducted to clarify their specific neural brain implications.

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Supplementary material

In this section other graphics, tables and supplementary research have been attached, with the aim of solving possible curiosities of the reader.

Statistical analyses:

1. *Behavioral data.*

Table 2 presents CEs and OEs rates, as well as reaction times (RTs) on Go trials during the emotional Go/NoGo task. These data were used to create *Figure 2*.

Table 2. Behavioral results of cognitive control during the emotional Go/NoGo task.

Variables	Emotional Go/NoGo					
	Happy faces		Neutral faces		Pain faces	
	Mean	SD	Mean	SD	Mean	SD
NoGo errors (CE)	5.20%	6.79	14.65%	12.05	20.01%	13.87
Go errors (OE)	42.24%	15.44	40.38%	15.44	37.65%	13.79
Go RTs (ms)	484.05	35.05	487.09	33.15	478.96	32.89

CE, Commission Error rates ; OE, Omission Error rates; Go RTs (ms), Reaction Time on correct Go trials in milliseconds.

2. *Electrophysiological data.*

Table 3 represents mean N200 and P300 amplitudes, averaged across nine recorded fronto-central scalp sites (F1, F2, Fz, FC1, FC2, FCz, C1, C2 and Cz) for each trial type (Go and NoGo) and emotional facial expression (happy, neutral and pain).

Table 3. Mean N200 and P300 amplitudes on the emotional Go/NoGo task.

Trial type	Emotion	N200		P300	
		Mean	SD	Mean	SD
Go	Happy	-1.778	1.080	-0.335	0.897
	Neutral	-1.915	1.000	-0.486	0.910
	Pain	-1.892	1.058	-0.362	0.825
	Total Go	**-1.862**	**1.030**	**-0.394**	**0.841**
NoGo	Happy	-1.808	1.390	0.245	0.710
	Neutral	-2.407	1.173	-0.025	0.949
	Pain	-2.251	0.973	-0.311	0.838
	Total NoGo	**-2.155**	**1.122**	**-0.030**	**0.759**

N200 and P300 are mean amplitudes in microvolt averaged across nine recorded fronto-central scalp sites (F1, F2, Fz, FC1, FC2, FCz, C1, C2 and Cz).

Supplementary research:

1. N1 and P2 components.

With an exploratory character, 90-120ms and 140-190ms time intervals were analyzed to capture N1 and P2 peaks, respectively. In the following section results from the statistical analyses and a brief discussion are shown. We want to emphasize that it is an initial analysis, and therefore the interpretations made are just a first analysis that must be further contrasted.

Table 5. Mean N1 and P2 peaks amplitudes on the emotional Go/NoGo task.

Trial type	Emotion	N1		P2	
		Mean	SD	Mean	SD
Go	Happy	-1.154	0.743	2.044	0.962
	Neutral	-1.079	0.715	2.120	0.872
	Pain	-1.297	0.754	2.032	0.868
	Total Go	**-1.177**	**0.717**	**2.065**	**0.884**
NoGo	Happy	-0.925	0.854	1.886	0.754
	Neutral	-1.278	0.643	1.980	0.907
	Pain	-1.415	0.901	2.046	0.957
	Total NoGo	**-1.206**	**0.739**	**1.971**	**0.786**

N1 and P2 peaks are mean amplitudes in microvolt averaged across nine recorded fronto-central scalp sites (F1, F2, Fz, FC1, FC2, FCz, C1, C2 and Cz).

N1 component:

A significant main effect of EMOTION was found [F (2,34) = 13.563, p<0.001] (Greenhouse-Geisser corrected). The post-hoc analysis revealed that pain faces elicited larger N1 amplitudes than neutral and happy, and N1 amplitudes were also larger for neutral than for happy (all p_s<0.05, Bonferroni corrected).

N1 component is related to attention, which is especially relevant for the processing of emotional stimuli (larger N1 amplitudes imply greater attention)[47]. Previous studies suggest that emotional stimuli receive preferential attention and perceptual processing than non-emotional stimuli [7,45,46]. Although our results support the claim that negatively valenced stimuli are more effective in capturing attentional resources than neutral stimuli, do not support the widely accepted idea that positively valenced stimuli also attract more attention. As our results suggest that happy faces captures even less attention than neutral faces, one possible explanation could be the theorized facilitation implicit in the processing of positive faces. *Eastwood et al. (2003)*[12], suggested that negative faces capture attention more effectively than positive faces, and thus more effectively distract attention away from the primary task of processing the gender of the faces. Then, negative faces seem to be more effective at involuntarily attracting or capturing attention than positive faces.

P2 component:

A significant interaction effect between BRAIN REGION x EMOTION x TRIAL TYPE was found [F (4,68) = 4.080, p < 0.05] (Greenhouse-Geisser corrected). The post-hoc analyses showed that in frontal electrodes pain and neutral faces elicited larger NoGo-P2 amplitudes than happy faces (all p_s<0.05). In addition, pain and neutral faces elicited larger NoGo-P2 than Go-P2 amplitudes. Whereas in central electrodes neutral faces elicited lower NoGo-P2 than Go-P2 amplitudes (all p_s<0.05, Bonferroni corrected).

P2 component is related to some aspect of higher-order perceptual processing and visual search modulated by attention and emotional interaction. As demonstrated in *Furutsuka (1989)* study, were target stimuli elicited larger P2 amplitudes than non-target stimuli, we expected to find larger Go-P2 than NoGo-P2 amplitudes. Moreover, due to the emotional modulation, we expected to find for pain and happy faces larger P2 amplitudes than for neutral faces. Nevertheless, our results suggested that Go-P2 amplitude did not vary as a function of affective valence, but NoGo-P2 did: pain and neutral faces revealed larger NoGo-P2 amplitudes than happy faces in frontal sites. That means that when a response must be inhibited, pain and neutral faces receive more attention and increase perceptual processing than happy stimuli. Taking into account these findings, it is suggested the existence of a pain effect over response inhibition, which implies greater perception processing and attention than happy faces *[Ashley, V (2004); Carretié, L (2001); Eimer, M (2003); Kubota, JF (2007); Smith et al (2003)]*. Moreover, neutral faces results, could be explain due to its ambiguous nature [51].

2. Valence and arousal ratings.

As explained in the discussion, our study has a gender limitation because our sample consisted only of women and all Go trials were male faces. Significant gender effects in brain activations to emotional faces and affective pictures have been previously reported [38,39,40]. Thus, it has an important methodological effect and further research should reproduce a similar investigation introducing male participants and an equal amount of male and female faces for Go and NoGo trials, to discard gender bias and fully demonstrate that pain caused less accuracy in attentional tasks independently of the gender. Anyway, we analyzed the impact of this limitation in our study, and the results are shown in this section.

Subjective ratings elicited by the facial stimuli were analyzed using MANOVA with the factors GENDER (male vs. female) and EMOTION (happy, neutral and pain), in order to evaluate possible gender differences in valence and arousal.

Valence

Regarding valence, a significant main effect of EMOTION was found [F (2,34) = 161.568, p<0.001]. Post-hoc analysis showed that participants rated pain faces as the most unpleasant stimuli followed by neutral and finally happy faces (all p_s<0.01). Furthermore, a significant interaction effect between GENDER and EMOTION was found [F (2,34) = 10.413, p<0.001]. Post-hoc comparisons shown that pain and neutral female and male faces were considered as more unpleasant than happy ones (p<0.001). In addition, female pain faces were considered as more unpleasant than neutral female faces (p≤0.005). We also found that happy female faces were considered more pleasant than happy male faces (p<0.005) and pain female faces were considered less pleasant than pain male ones (p<0.005).

Arousal

Regarding arousal, significant interaction effects between TRIAL TYPE and EMOTION were found [$F(2,34) = 9.331$, $p \leq 0.001$]. Post-hoc analysis shown that female pain faces were rated as more arousing than female happy faces ($p < 0.005$, Bonferroni corrected), but not significance was found in male faces. Moreover, the analysis revealed that pain faces were assessed as more arousing in female than in male faces ($p \leq 0.01$, Bonferroni corrected).

Our data revealed that participants rated **happy female faces as more pleasant than happy male faces,** and **pain female faces as more unpleasant and arousing than pain male faces.** Also **pain female faces were rated more arousing than happy female faces, but this difference was not found in male faces**. These results suggest that women empathize more with women than with men. Conversely, *Schulz et al (2007)* [38] found that female participants had greater sensitivity overall to emotional expressions in male than female faces. In addition, *Simon et al* (2006) [39] found stronger amygdala activation to pain male expression compared to neutral and anger ones, but not to female pain faces. They interpreted this lack of amygdala response to female pain expressions as a spontaneous top-down inhibition of the defense response and the promotion of helping behavior. We also found significant gender effects in brain activations to emotional faces and affective pictures in other studies *[Killgore et al (2001); McClure et al (2004) and Hofer et al (2006), Kemp et al (2004), respectively].* After our analysis, to clarify gender effects on brain activity elicited by pain faces, we highly recommend that further research should reproduce a similar investigation introducing male participants and an equal amount of male and female faces for Go and NoGo trials.

We want to emphasize that it is an initial analysis, and therefore the interpretations made are just a first analysis that must be further contrasted.