Social Cognitive and Affective Neuroscience, 2023, **18**(1), 1–10
DOI: https://doi.org/10.1093/scan/nsad033
Advance Access Publication Date: 30 May 2023
**Original Manuscript**

# You are fired! Exclusion words induce corticospinal modulations associated with vicarious pain

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## Abstract

Self- and vicarious experience of physical pain induces inhibition of the motor cortex (M1). Experience of social rejections recruits the same neural network as physical pain; however, whether social pain modulates M1 corticospinal excitability remains unclear. This study examines for the first time whether social exclusion words, rather than simulated social exclusion tasks, modulate embodied sensorimotor networks during the vicarious experience of others' pain. Participants observed visual sequences of painful and functional events ending with a superimposed word with social exclusion, social inclusion or non-social meaning. Motor-evoked potentials (MEPs) to single-pulse transcranial magnetic stimulation of the left M1 were recorded at 400 or 550 ms from word onset. MEPs tended to inhibit during the observation of pain, relative to functional events. Moreover, MEPs recorded at 400 ms from word onset, during pain movies, decreased following the presentation of exclusion, relative to inclusion/neutral words. The magnitude of these two modulations marginally correlated with participants' interindividual differences in personal distress and self-esteem. These findings provide evidence of vicarious responses to others' pain in the M1 corticospinal system and enhancement of such vicarious response in the earlier phases of semantic processing of exclusion words—supporting activation of social pain–embodied representations.

**Keywords:** transcranial magnetic stimulation; language; social exclusion; self-esteem; empathy for pain

## Introduction

Social exclusion or rejection induces an experience of social pain involving brain areas that overlap with those activated by physical pain (Kross *et al.*, 2011; Eisenberger, 2012, 2015), including affective and sensorimotor brain areas such as the anterior cingulate cortex (ACC), the insula and the somatosensory cortices (Eisenberger *et al.*, 2003, 2006; Onoda *et al.*, 2010; Somerville *et al.*, 2010; Kross *et al.*, 2011). However, most of the studies on social exclusion involve simulated exclusion situations, typically the Cyberball game (e.g. Eisenberger *et al.*, 2003), in which language processes are absent or play a secondary role. Yet, words themselves can convey a meaning of exclusion (Borelli *et al.*, 2018), which is likely to activate social pain representations.

In the present study, we aimed to investigate for the first time the semantics of social pain, examining whether words with the content of social exclusion and inclusion differentially modulate empathic brain activity tracked via motor-evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) of the primary motor cortex (M1). We focused on corticospinal excitability (CSE) assessed via MEP recording, as CSE is consistently reduced during self-pain (Farina *et al.*, 2001; Rohel *et al.*, 2021) and during the observation of pain in others (Avenanti *et al.*, 2005, 2006, Fecteau *et al.*, 2008; Avenanti *et al.*, 2009; Mahayana *et al.*, 2014), suggesting that it may reflect an empathic brain response to vicarious experience of others' pain.

A few studies have examined whether words with psychosocial or emotional connotations modulate CSE (Obhi *et al.*, 2011; Gough *et al.*, 2013), showing facilitatory MEP modulations when words associated with self-construal were primed before observing an action (Obhi *et al.*, 2011) or opposite effects of positive and negative action–related adjectives from flexor and extensor hand muscles, suggesting activations of approach and avoidance responses depending on word meanings (Gough *et al.*, 2013). However, none of the previous studies investigated the influence of words conveying social pain meanings on CSE.

Building on these prior studies, here we presented social exclusion/inclusion words associated with the observation of painful

**Received:** 20 December 2022; **Revised:** 12 April 2023; **Accepted:** 29 May 2023

and non-painful events to examine interactive priming effects, that is, whether exclusion words differentially modulate CSE, especially during the observation of pain in others. To this aim, we applied TMS over the left M1, while participants were presented with image sequences depicting painful or functional events, together with a superimposed word with social exclusion, social inclusion or neutral content. We hypothesized that the concurrent exposure to pain-related images and exclusion words would induce maximal CSE reduction, since the social exclusion meaning modulates the brain activity of the same pain network as watching pain events. To test this hypothesis, we decided to select a group of female participants, since there is considerable literature showing larger empathic responses in women [see Christov-Moore *et al.* (2014) for an extensive review]. Particularly relevant for our study, the observation of pain in others induces the larger CSE inhibition in women than in men (Sadeghiyeh *et al.*, 2017). Moreover, the presentation of hand movements (Cheng *et al.*, 2006) and body parts in painful situations (Cheng *et al.*, 2009) is associated with a stronger mu rhythm suppression in female than in male participants. Both CSE and mu oscillations are considered reliable indicators of sensorimotor resonance when participants perceive other people in painful situations (Avenanti *et al.*, 2005; Cheng *et al.*, 2008; Minio-Paluello *et al.*, 2009; Riečanský *et al.*, 2015, 2020).

Another main purpose of the present study was to track the timecourse of the effect of the social words during stimuli presentation by testing two different stimulation times, that is, 400 and 550 ms from the onset of the words. A recent meta-analysis has reported that comprehension of action-related words, in a simple semantic decision task, induces inhibitory effects on action execution early in time (i.e. within the first 400 ms after word presentation), while, at later intervals (i.e. after 450 ms), facilitation or null effects are commonly observed (García and Ibáñez, 2016). Similarly, previous electroencephalography (Dalla Volta *et al.*, 2014) and magnetoencephalography (Pulvermüller *et al.*, 2005; Klepp *et al.*, 2014) studies have found an early motor brain response (<400 ms from stimulus onset) for action-related words and verb processing. Despite the differences between this and previous investigations, it is likely that the comprehension of social words will occur in an early time window and consequently will influence brain motor activity during the perception of visual pain stimuli at 400 ms and, presumably, will not be present at a later period.

Finally, as a secondary objective, in this study we tested whether participants' individual differences in self-esteem and empathy-related dispositions are related to reactivity to vicarious pain and social exclusion words. Personal distress in particular has been found to correlate with CSE response to pain-related and other emotional visual stimuli in several studies (Avenanti *et al.*, 2009; Borgomaneri *et al.*, 2014; De Coster *et al.*, 2014; Borgomaneri *et al.*, 2015a; Hortensius *et al.*, 2016; Borgomaneri *et al.*, 2021). Self-esteem has been reported to be closely associated with self-relevant emotions (Brown and Marshall, 2001) and neural responses to social pain situations (Onoda *et al.*, 2010; Eisenberger *et al.*, 2011). We tried to increase the self-relevance of the inclusion and exclusion words by taking advantage of the Spanish female gender mark (e.g. 'rechazad**a**' → rejected[fem]) to better engage our participants, all of whom were women. Based on this, we expected to find the CSE inhibition during vicarious pain to be related with individual differences in empathy-related traits, in particular personal distress. Moreover, we expected significant correlations between CSE responsivity to social exclusion words and self-esteem measures.

# Method

## Participants

Twenty-five female right-handed Spanish speaking students took part in the main study (mean age ± s.d.: 19.0 ± 0.7 years). None of them reported any visual or medical problems, or contraindication to TMS (Rossi *et al.*, 2009, 2011; Rossini *et al.*, 2015). Statistical power estimation was conducted by using the simulate function from the lmer4 package (Bates *et al.*, 2015) in R (R Core Team, 2018). A simulation of 1000 new data sets, each containing $n$ participants, were iterated by including the same structure used in the main analysis (stimulation time, visual sequence and social word as fixed factors and participants as a random effect). Trials from these data were randomly labeled as missing ones and excluded from the dataset. Separate estimations were run by steadily increasing differences for the three-way interaction, while observing the power for each difference. The percentage of models in which the effect of the three-way interaction from which the data were generated was detected (i.e. for which $P < 0.05$) was taken as the estimate of statistical power. For $n = 25$ simulated participants, we estimated a statistical power of 1 (i.e. in 1000 out of 1000 simulation runs, the model detected a significant three-way interaction).

All students gave informed consent and received course credit for volunteering. The Research Ethics Committee of the University of La Laguna approved this study, and the experiment was conducted according to the principles expressed in the Declaration of Helsinki.

## Visual stimuli

Visual stimuli consisted of 12 picture sequences, presented centrally on a 23 inch screen (resolution: 1920 × 1080 pixels; refresh rate: 60 Hz) located 80 cm away from the participants and selected from an initial sample of 26 stimuli. Each stimulus consisted of four frames presented sequentially. Frame 1 always depicted a female right hand from the first-person perspective, placed in the lower part of the screen, below an object (e.g. piece of cloth) that was situated at the top of the screen and aligned with participants' hand to maximize embodiment of the observed hand (Cardini *et al.*, 2013; Bucchioni *et al.*, 2016). The second frame was identical to frame 1 but included a tool (e.g. scissors) appearing on the left side of the screen. The third frame depicted the tool making contact with the hand or with the object. Finally, the last frame showed the accomplishment of the tool-hand or tool-object interaction, that is, pain actions and functional actions, respectively (Figure 1). It should be noted that several prior studies have reported motor inhibition following the observation of dangerous objects (Anelli *et al.*, 2012, 2013a,b; Mustile *et al.*, 2021). However, because we presented the same object (e.g. scissors) in both pain and functional action stimuli, any MEP difference between the two visual conditions cannot be merely due to the observation of a potentially dangerous object. The pictures were edited using Adobe Photoshop software to correct lighting, contrast and color.

To choose stimuli that better express a pain situation, we conducted a pilot study with 25 participants (10 females, 30.7 ± 11.6 years), who were asked to evaluate the degree of 'pain aroused' through a 5-point Likert scale ranging from 1 'no pain' to 5 'unbearable pain'. We selected the six different tool-hand pain sequences with the highest scores ($M \geq 3.40$) and the

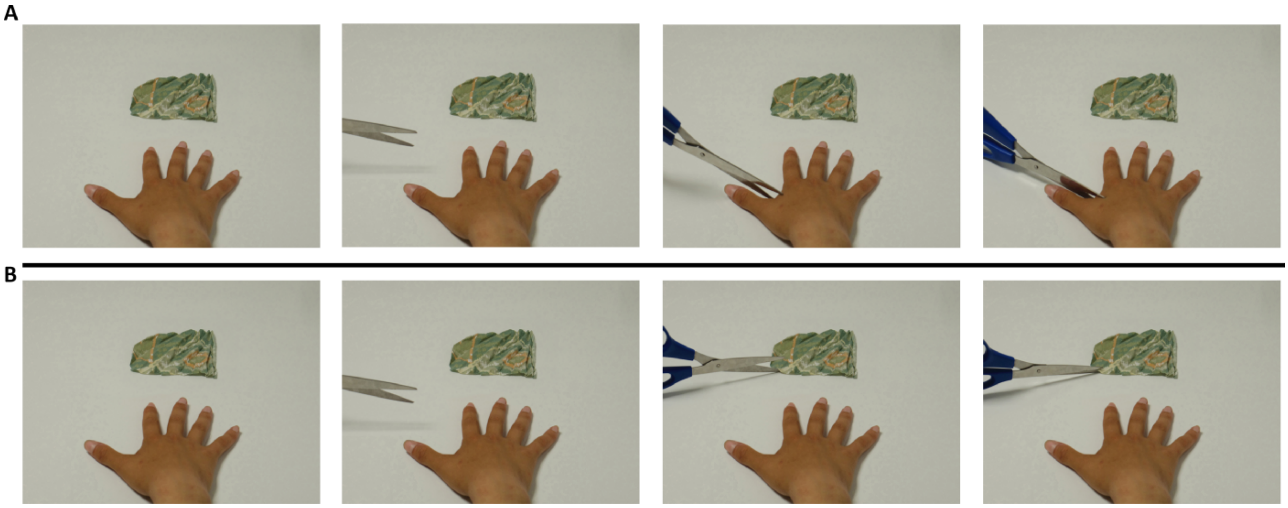


**Fig. 1.** The example of visual sequences representing (A) pain action and (B) functional action used in the experiment.

**Table 1.** The values of linguistic variables (obtained from the EsPal database) and social valence rating for inclusion, exclusion and neutral words

| Inclusion | | | | Neutral | | | | Exclusion | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Rating | Frequency | Length | | Rating | Frequency | Length | | Rating | Frequency | Length |
| Acogida [welcomed] | 4.25 | 3.73 | 7 | Acurrucada [curled up] | 2.00 | 2.43 | 10 | Abandonada [abandoned] | −4.75 | 3.49 | 10 |
| Apreciada [appreciated] | 4.50 | 2.95 | 9 | Despierta [awake] | 0.50 | 3.57 | 9 | Despedida [fired] | −3.75 | 3.51 | 9 |
| Incluida [included] | 4.75 | 3.91 | 8 | Distraída [distracted] | −1.50 | 2.50 | 9 | Excluida [excluded] | −4.75 | 2.83 | 8 |
| Invitada [Invited] | 4.65 | 3.17 | 8 | Levantada [standing] | 0.25 | 3.13 | 9 | Rechazada [rejected] | −4.75 | 3.42 | 9 |

*Note:* All of the words were presented in female grammatical gender to promote self-reference in our female participants.

corresponding functional sequences, where the same tools interacted with objects. The statistical comparison confirmed that the pain context (mean ± s.d.: 3.77 ± .87) produced a higher score than the functional context (1.23 ± .58; $t_{24} = -12.18$, $P < 0.001$).

## Linguistic material

We used Spanish adjectives expressing social inclusion, social exclusion and neutral states matched in frequency ($F_{2,9} = 1.51$, $P = 0.27$) and length ($F_{2,9} = 3.32$, $P = 0.08$). Additionally, through a normative study, 10 participants were asked to judge the social valence of the words using a bipolar scale (from −5 very excluded to 5 very included). The analysis of variance conducted on social ratings for the three categories of social words revealed a significative main effect ($F_{2,9} = 104.21$; $P < 0.001$; $\eta_p^2 = 0.96$). *Post hoc* comparisons confirmed that the inclusion words were perceived as more positive (4.54 ± .22) compared to the neutral (0.31 ± 1.43, $P < 0.001$) and exclusion words (−4.50 ± .50, $P < 0.001$). Also, the exclusion words were more negative compared to the neutral ones ($P < 0.001$).

Table 1 shows the words employed in the experiment and their scores in the variable.

## TMS and electromyography recordings

To explore CSE, MEPs from the right first dorsal interosseous (FDI) were recorded using a Biopac MP-35. Electromyography (EMG) signals were band-pass filtered (30–500 Hz), sampled at 5 kHz, digitized and stored on a computer for offline analysis. Pairs of silver-chloride surface electrodes were placed in a belly-tendon montage with ground electrodes on the right wrist. TMS was delivered over the left M1 through a Magstim 200 stimulator (Magstim, Whiteland, Dyfed, UK) connected to a figure-of-eight magnetic coil (70 mm outer diameter; peak magnetic field 2.2 Tesla). The intersection of the coil was held tangentially to the scalp with the handle pointing backward and laterally at 45° from the midline, resulting in a posterior–anterior current flow direction in the brain. The left M1 optimal scalp position was defined as the point where TMS consistently evoked the largest MEPs in the right FDI. During the experimental session, the intensity of the stimulator output was adjusted so as to obtain MEPs with a peak-to-peak amplitude of ∼1 mV in the relaxed FDI. The mean stimulation intensity (±s.d.) was 46.7 ± 9.8% of the maximum stimulation output.

## Design and procedure

The study involved a two stimulation time (400 ms and 550 ms) × a two visual sequence (pain and functional) × three social words (inclusion, exclusion and neutral) experimental design. The 12 visual sequences were combined with the 12 social words, generating a total of 144 trials: 24 pain-inclusion, 24 pain-neutral, 24 pain-exclusion, 24 functional-inclusion, 24 functional-neutral and 24 functional-exclusion. We used E-Prime software to control stimulus presentation and trigger TMS pulses. The task consisted of six blocks of 48 trials. Each trial involved a sequence of frames, as illustrated in Figure 2. The social word appeared for

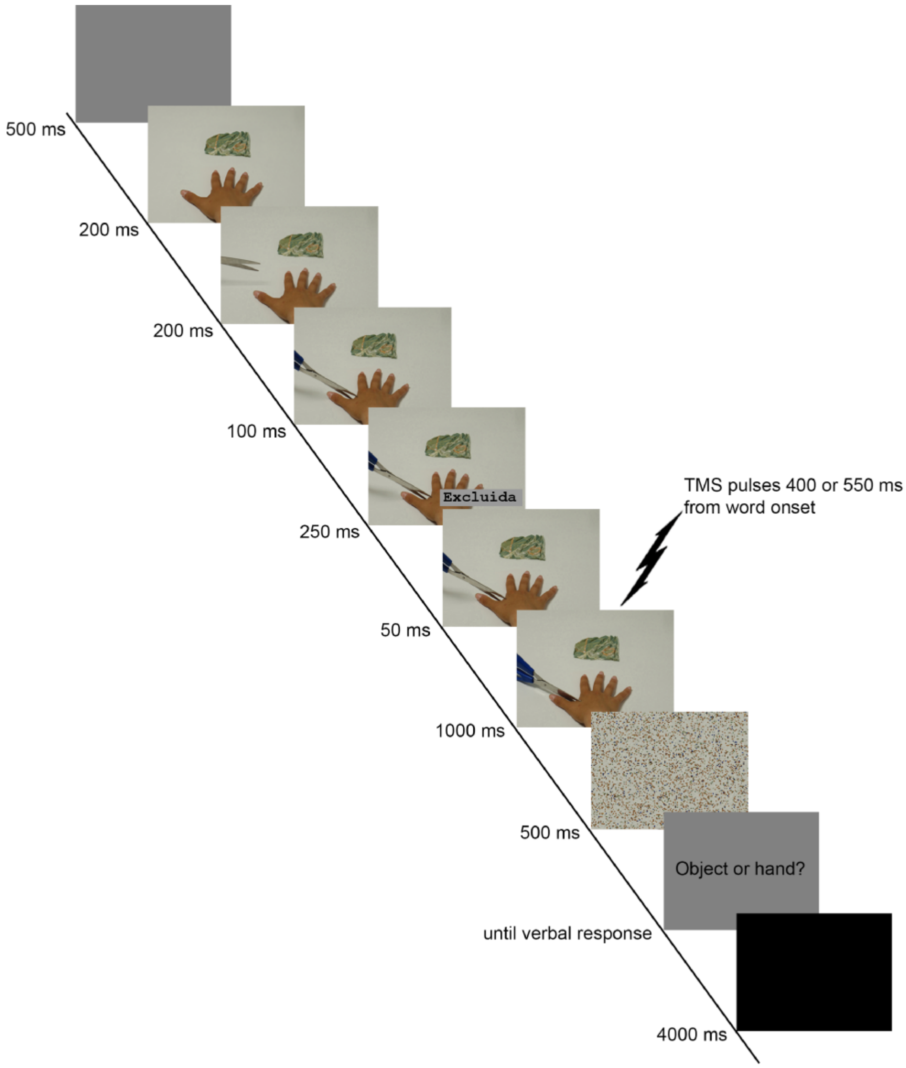


**Fig. 2.** The example of trial with a visual sequence of pain and a social exclusion word (translation: excluded) as background.

250 ms overlapping the hand or the object, in pain and functional events, respectively. Subsequently, the fourth frame representing the final course of the pain or the functional action was projected on the screen for 1000 ms followed by a 500 ms random-dot mask (obtained by scrambling the sample stimulus with image segmentation software). The TMS pulse was delivered at 400 or 550 ms from word onset, corresponding to 100 and 250 ms from frame 4 onset, respectively (Figure 2). Finally, the question 'Hand or object?' appeared on the screen. The participants had to verbally respond 'hand' in case of pain action context or 'object' in case of functional action sequence and an experimenter collected the answers. To avoid changes in CSE due to verbal response (Tokimura *et al.*, 1996; Meister *et al.*, 2003), participants were invited to answer 2–3 s after the question was presented (Tidoni *et al.*, 2013; Borgomaneri *et al.*, 2015b). After the response, a black screen appeared for 4 s, ensuring an inter-pulse interval of about 10 s to avoid changes in CSE due to TMS *per se* (Chen *et al.*, 1997). Each trial was presented twice.

To facilitate the participants' identification with the hand of the model depicted in the pain and no-pain sequences, we hid their right hand under a screen and kept it aligned with the hand in the clips.

Before and after the experimental session, two additional blocks of 20 MEPs, which served as baselines, were collected using TMS delivered with an inter-pulse interval of ~7 s. The comparison between the pre- (mean MEP amplitude ± s.d.: 0.91 ± .23) and post-baselines (0.91 ± .29) did not show any changes ($t_{24} = 0.08$, $P = 0.94$), confirming that the TMS itself did not affect CSE.

## Individual differences measures

At the end of the TMS session, participants filled in the Rosenberg Self-Esteem Scale (RSES) (Rosenberg, 1965) and the Interpersonal Reactivity Index (IRI) (Davis, 1996) questionnaires. The former is a widely used 10-item scale for evaluating global self-worth (Rosenberg, 1965), and the latter is a 28-item self-report survey consisting of four subscales: (i) fantasy scale (FS), (ii) perspective taking (PT), (iii) empathic concern (EC) and (iv) personal distress (PD), assessing different aspects of cognitive and affective empathy.

## Data analysis

MEP amplitudes were measured peak-to-peak in mV. We removed MEPs associated with incorrect responses (<1%) or preceded by the EMG background deviating ≥2 s.d. from the mean (~5%) that may affect the MEP size (Devanne *et al.*, 1997). Then, we computed median MEPs for each condition and normalized their distribution through the Yeo–Johnson transformation (Yeo and Johnson, 2000). Lastly, MEP amplitudes were analyzed with a linear mixed model, using the lme4 package in R (Bates *et al.*, 2015). The stimulation time (400 and 550 ms), visual sequence (pain and functional) and social word (inclusion, neutral and exclusion) were defined as fixed factors, while participants were accounted for as a random effect in the model. All fixed effects were contrast-coded before analyses using sum coding so that each model's intercept represented the mean value of each predictor (Schad *et al.*, 2020). We used planned comparisons to test the specific effect of words within each visual sequence and each stimulation time. We applied the false discovery rate (FDR) correction (Benjamini and Hochberg, 1995) to adjust for multiple comparisons.

The analysis of normalized MEP evidenced a marginal reduction of CSE for the pain visual sequences relative to the functional ones. Also, during pain observation, we found an early MEP inhibition for social exclusion words, compared to inclusion and neutral words (see the Results section). To explore whether individual differences in self-esteem and empathy-related dispositions predicted the CSE suppression during the different conditions, a simple correlation analysis and a stepwise regression model were performed. To this end, we computed a 'vicarious pain' index, reflecting the MEP suppression for the pain condition as the difference between the normalized median MEPs during pain *vs* functional sequences. Also, to express changes in M1 excitability during the processing of exclusion words in a pain context, we calculated an 'exclusion' index by subtracting the normalized median MEPs during the pain-inclusion conditions from the normalized median of the MEPs during the pain-exclusion conditions. These two MEP indices were entered in a correlation analysis with the RSES and IRI scores, followed by a stepwise regression in which questionnaires scores showing significant correlations were entered as predictors of the MEP indices. All statistical analyses were performed using R Studio (version 1.1.419) software.

# Results

## Neurophysiological data

Our first directional hypothesis that pain observation induced M1 corticospinal inhibition was supported by a main effect of context ($F_{1,264} = 3.37$; one-tailed $P = 0.034$; $\eta_p^2 = 0.01$), with lower MEPs for pain (–.03 ± 1.00) than those for functional context (0.03 ± 1.00) (Figure 3A).

Importantly, the linear mixed model also showed a significant three-way interaction ($F_{2,264} = 3.15$; $P = 0.04$; $\eta_p^2 = 0.02$). To assess our hypotheses, we tested the effect of the social words in a pain context during the early stage of semantic processing (Figure 4A). As expected, exclusion words induced MEP reduction compared to neutral ($P = 0.03$) and inclusion words ($P = 0.03$), which did not significantly differ from one another ($P = 0.94$). By contrast, in a functional context, MEPs were not affected by word content (all $P \geq 0.33$). Moreover, in line with our predictions, when the pulse was delivered at 550 ms from word onset, no differences in MEPs were found, either in pain (all $P \geq 0.58$) or functional sequences (all $P \geq 0.75$), confirming that the CSE modulation by exclusion words occurred within a relatively early time window.

## Relation between changes in motor excitability and personality traits

The two MEP indices representing the two modulations reported in the previous paragraph were entered into a correlation analysis. The results of simple correlations are reported in Table 2.

We found that the 'vicarious pain' index negatively correlated with PD ($r = –0.41$, $P = 0.04$), indicating that participants with the higher PD scores showed larger MEP inhibition during vicarious pain. In addition, we found a negative correlation between the 'exclusion index', i.e. MEP suppression for exclusion words relative to inclusion words during vicarious pain and the RSES ($r = –0.43$, $P = 0.03$), indicating that participants with the higher RSES scores showed stronger MEP inhibition for social exclusion words during vicarious pain.



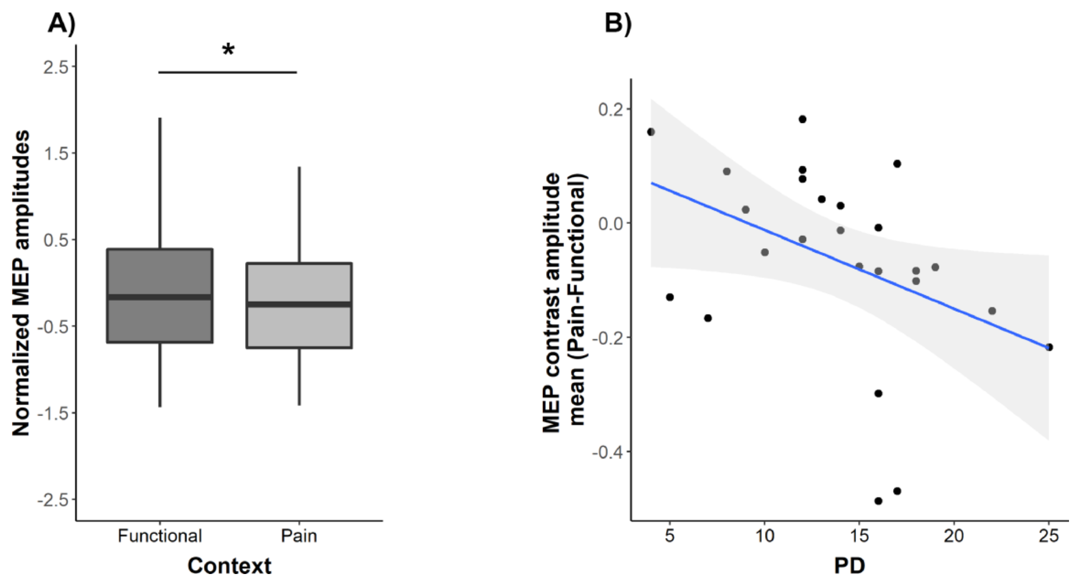


**Fig. 3.** (A) A boxplot representing the main effect of context and showing a reduction of normalized MEP amplitudes during the presentation of pain relative to functional visual sequences. Asterisks denote the significant comparison $P < 0.05$. (B) A scatterplot of the relationship between an index representing the main effect of context (normalized MEP contrast pain–functional events) and IRI's PD scores. The PD scale showed a trend for negative correlation with the MEP contrast, with larger motor inhibition observed in participants with higher PD scores.

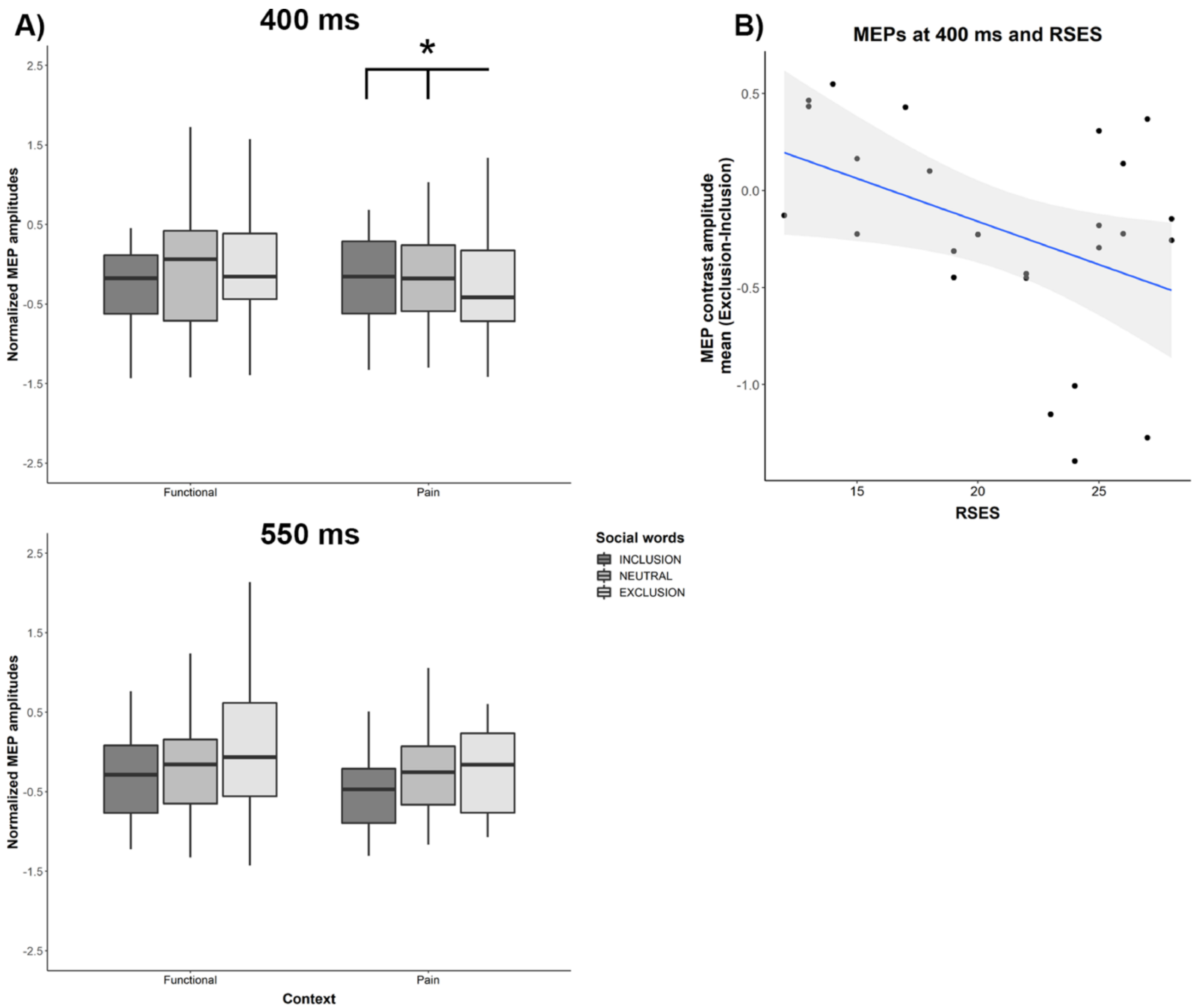


**Fig. 4.** (A) A boxplot showing normalized MEP amplitudes during the presentation of social inclusion, social neutral and social inclusion words in a pain visual sequence at 400 ms (top of the panel) and 550 ms (bottom of the panel) from the stimulus onset. Asterisks denote significant planned comparisons $P < 0.05$. (B) A scatterplot of the relationship between an index representing the effect of social word content on vicarious pain response (normalized MEP contrast exclusion–inclusion words at 400 ms) and the RSES. The RSES showed a trend for negative correlation with the MEP contrast, with larger motor inhibition observed in participants with the higher RSES scores.



**Table 2.** Pearson's coefficient of simple correlations between MEP indexes and questionnaires scores

| | RSES | FS | PT | EC | PD |
|---|---|---|---|---|---|
| 'Vicarious pain' index | $r = 0.25$ | $r = -0.01$ | $r = 0.37$ | $r = 0.26$ | $r = -0.41^*$ |
| 'Exclusion' index | $r = -0.43^*$ | $r = 0.22$ | $r = -0.25$ | $r = -0.01$ | $r = 0.37$ |

*This denotes the significant results ($P < 0.05$).

Then, to assess the specificity of these findings, we conducted two stepwise regression analyses with PD and the RSES as factors and the physiological indexes as a dependent variable. The first regression model with the vicarious pain index as a dependent variable was found to be significant ($R^2 = 0.16$, $F_{1,23} = 4.56$, $P = 0.04$), showing that only PD tended to predict MEP inhibition during vicarious pain ($\beta = -0.01$, $P = 0.04$; Figure 3B). The second regression model with the exclusion index as a dependent variable was also found to be significant ($R^2 = 0.18$, $F_{1,23} = 5.13$, $P = 0.03$), confirming that the RSES was the only significant predictor of the index ($\beta = -0.4$, $P = 0.03$; Figure 4B). These results confirm that PD uniquely tended to predict the physiological changes associated with vicarious pain, whereas the RSES scores specifically tended to predict the CSE modulation reflecting social exclusion words (early) processing during vicarious pain observation. It should be noted that the regression models do not survive FDR correction and therefore should be interpreted with caution.

## Discussion

This is the first study to examine the neurophysiological underpinning of the semantics of social exclusion during vicarious experience of others' pain. Instead of inducing social exclusion via the Cyberball game as in prior work (Eisenberger et al., 2003, 2006; Onoda et al., 2010; Somerville et al., 2010; Kross et al., 2011), participants were presented with semantic cues of exclusion and inclusion while seeing painful or non-painful events. Participants' CSE was measured by means of MEPs collected during the final frame of the visual stimuli, at two time points after the onset of the social word.

Several aspects are remarkable in our findings. First, as expected, pain sequences tended to reduce MEP amplitudes relative to functional sequences, in line with prior evidence highlighting CSE reduction during not only first-person but also vicarious experience of pain (Farina et al., 2001; Avenanti et al., 2005, 2006, Fecteau et al., 2008; Avenanti et al., 2009; Mahayana et al., 2014; Rohel et al., 2021). Vicarious CSE reduction tended to be stronger in participants scoring higher at the PD scale, a subscale of the IRI assessing the tendency to feel distress in oneself when exposed to others' distress (Davis, 1996). Importantly, for pain sequences preceded by exclusion words, there was a consistent CSE reduction relative to inclusion or neutral words; this effect was specific to the earlier timing (400 ms), while no modulation effect of exclusion words was obtained at later timing (550 ms) or for functional sequences. This inhibitory CSE modulation suggests an activation of (social) pain representations associated with understanding exclusion meanings during pain observation. These results support our hypothesis that social exclusion words induce social pain, which shares neural representations with self- and vicarious pain experience. Individual differences in self-esteem tended to marginally predict the amount of MEP modulation for exclusion words during pain sequences, suggesting that exclusion words mobilize self-engagement.

## Words hurt: CSE reduction for exclusion words in pain sequences

Previous and current studies suggest that some adjectives work as powerful exclusion signals. Eisenberger et al. (2011) presented participants with accepting and rejecting feedback words (e.g. 'intelligent' and 'boring'), ostensibly chosen by another individual (a confederate) to describe a participant's previously recorded interview, and observed larger activity in pain-related brain areas for rejection-related words. By contrast, in the present experiment, we presented no evaluative context, and social words were unrelated to the participants' task. Consequently, the effects of exclusion words observed here are associated with spontaneous processing of word meaning, in an apparently automatic way. Inclusion words did not modulate CSE relative to neutral words, suggesting that social exclusion connotation is critical to induce motor modulations.

As predicted, the modulatory effect of exclusion words was obtained in the earlier time window (400 ms) and entirely faded in the later time window (550 ms), consistent with prior reports that words' semantic processing occurs within 400 ms from linguistic stimulus onset [Pulvermüller et al., 2005; Dalla Volta et al., 2014; Klepp et al., 2014; see García and Ibáñez (2016) for a review]. The results therefore confirm that the meaning of the semantics of social exclusion is processed in this early temporal window, in which the CSE modulation was observed.

Although we demonstrated that social exclusion words modulated CSE, it is not obvious how this happens. First, unlike in other studies on embodied meaning, our words were rather abstract, referring to social events rather than action words (Buccino et al., 2005; Tomasino et al., 2010; Vitale et al., 2021), or objects with motor affordances (Gough et al., 2013). Second, neuroimaging studies have shown that the feeling of social exclusion mainly activates the affective and sensorimotor components of pain (Eisenberger et al., 2011; Kross et al., 2011; Gyurak et al., 2012). However, we observed the CSE changes in M1 corresponding to the FDI representation. A possible explanation could be that the CSE modulation produced by exclusion words was caused indirectly, as a cascade effect, by the initial activation of the pain network, but it is also possible that the neural processes flow in the opposite direction; that is, words first modulate motor system excitability, which in turn activates the pain network. We cannot decide between these alternatives, since the stimulation method used here offers a partial view of the underlying brain processes. It provides a measure of CSE associated with a specific hand muscle but tells us nothing about the role of other important regions of the cortex involved in social pain or the functional connectivity between them. The neurosemantic study of social exclusion should be completed with other stimulation protocols such as repetitive TMS, which has demonstrated the important role of the prefrontal cortex in downregulation of social pain (Riva et al., 2012; He et al., 2020; Li et al., 2022).

## Empathy and reactivity to pain visual sequences

Participants with the higher PD scores tended to show stronger reduction in the MEP amplitude during the observation of pain sequences. The PD scale measures the tendency of an individual to feel distress in response to another's emotional distress, reflecting a form of primitive self-oriented empathy, consisting in experiencing the discomfort observed in others (Davis, 1996). PD has been frequently reported to be associated with CSE response to pain or emotional stimuli (Avenanti et al., 2009; Borgomaneri et al., 2014; De Coster et al., 2014; Borgomaneri et al., 2015a; Hortensius et al., 2016; Borgomaneri et al., 2021) and vicarious responding in other affective and sensorimotor brain regions (Saarela et al., 2007; Cheetham et al., 2009; Preis et al., 2015). In the present study, the model's hand was presented from an egocentric view and the adjectives were selected to fit with the participants' gender, all conditions that may have increased identification with the observed model, particularly in those with high PD, favoring their embodiment of the observed pain and, consequently, the strength of vicarious CSE responding.

## Self-esteem and reactivity to social exclusion words

CSE response to exclusion words during pain observation tended to be greater in participants with high self-esteem. Prior work has shown that people with high self-esteem exhibit more irrational reaction (McFarlin and Blascovich, 1981; Blaine and Crocker, 1993) and poorer self-regulation (Baumeister et al., 1993, 1996; Lambird and Mann, 2006) after exposure to ego threats or negative feedback; moreover, they show higher sensitivity to criticism compared to people with low self-esteem (Shrauger and Lund, 1975; Schlenker et al., 1976). Based on these prior results, and in view of the self-relevance of the exclusion words that we used in our study, it is likely that participants with high self-esteem tended to be more affected by social exclusion meanings compared to subject with low self-esteem, resulting in stronger activation of (social) pain representations, which, in turn, would be associated with CSE reduction.

On the other hand, a few studies on social exclusion reported that low self-esteem is associated with increased sensitivity to social pain, reflected by a stronger ACC activation (Onoda et al., 2010; Eisenberger et al., 2011). However, our study and the previous ones differ in many methodological aspects. We measured here fast and automatic physiological responses in the range of milliseconds, indexed by MEP modulation, which reflects the momentary change in motor brain activity; by contrast, the aforementioned studies employed low–temporal resolution neuroimaging techniques and found that self-esteem was negatively related to the activity of the ACC and the insula, whose activity was not tested here. Therefore, the two correlational patterns may correspond to the activity of different networks and probably to different times in the flow of neural signals.

## Conclusion

In sum, we found that seeing pain in others tended to suppress CSE, particularly in participants with a strong disposition to feel personal distress, supporting the notion of a vicarious response to others' pain in the observers' motor system. Remarkably, unlike other studies related to brain response to social exclusion events, this is the first one to use verbal labels in a non-social context rather than virtual social exclusion tasks. We have shown that some self-relevant words can work as powerful social exclusion signals, modulating CSE during vicarious pain. Moreover, the amount of this modulation shows a marginal correlation with participants' self-esteem.

It should be noted that, in the present study, we tested only female participants, considering just their biological sex. So, to generalize our results to the entire population, including men, and to assess whether gender differences modulate the processing of social pain, further research is necessary.

## Data availability

All stimuli, the experimental data and the scripts used for their collection and analysis can be viewed and downloaded from the Open Science Framework (OSF): https://osf.io/xs93f/?view_only=e84b1f164d2147b59118e81784d691d7.

## Author contributions

Francesca Vitale (Methodology, Software, Formal analysis, Investigation, Data curation, Writing—original draft and Funding acquisition), Mabel Urrutia (Methodology, Data curation), Alessio Avenanti (Conceptualization, Methodology, Supervision, Writing—review & editing, Funding acquisition) and Manuel de Vega (Conceptualization, Resources, Methodology, Writing—review and editing, Supervision, Project administration, Funding acquisition).

## Funding

This work was supported by grants from Ministerio de Ciencia, Innovación y Universidades and the European Regional Development Funds (grant RTI 2018-098730-B-I00 awarded to M.d.V. and the Research Training Predoctoral grant BES-2016-078438 awarded to F.V.) This work was also supported by the Ministry of University and Research, National Recovery and Resilience Plan, project MNESYS (grant PE0000006), and grants from the BIAL Foundation (grant 347/18), Fondazione del Monte di Bologna e Ravenna (grant 1402bis/2021) awarded to A.A.

## Conflict of interest

The authors declared that they had no conflict of interest with respect to their authorship or the publication of this article.

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