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Cognitive Control: Exploring the causal role of the rTPJ in empathy for pain mediated by contextual information

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Abstract

Empathy determines our emotional and social lives. Extensive research has recognised the role of the right temporo-parietal junction (rTPJ) in social cognition, however there is less direct causal evidence for its involvement in empathic responses to pain. Given the rTPJ's role in the false beliefs and contextual information during social scenarios, we hypothesised that the empathic response to another's pain might depend on the rTPJ if participants were given information about people's intentions. Participants viewed videos of an actress freely showing or suppressing pain caused by an electric shock. During the task, participants either received 6Hz repetitive Transcranial Magnetic Stimulation (rTMS) over the rTPJ or sham vertex stimulation. Active rTMS had no significant effect on participants' ratings depending on the pain expression, although participants rated the actress' pain as lower during rTPJ perturbation. In contrast, rTMS accelerated the reaction times during pain suppression. In addition, we found that participants perceived the pain of the actress more intense when they knew that she would suppress vs. show it. These results suggest that the rTPJ may be involved in the process of attributing pain to others and provide new insights into people's behaviour in judging others' pain when it is concealed.

Keywords

Empathic accuracy, theory of mind, rTMS, rTPJ, contextual information

1. Introduction

Human empathy can be understood as our ability to understand and share the affective states of others, is crucial to our everyday social interaction and a fundamental component of social intelligence (Singer et al., 2004). As social beings, watching others suffer in reality, or even just observing them in the media, resonates strongly within us.

Typically, research distinguishes two complementary parts of empathy: cognitive empathy, the ability to cognitively infer the affective state of another person (Van Overwalle & Baetens, 2009) and emotional empathy, an affective state resulting from a partial and experiential sharing of another person's affective state (Bernhardt & Singer, 2012). Cognitive empathy and top-down regulation processes of affective states are also strongly related to self-other distinction (SOD), the ability to differentiate self- and other-related affective states (Shamay-Tsoory, 2011).

Cognitive and emotional empathy appear to operate at least in part independently on the neural level: Whereas cognitive empathy often recruits the so-called mentalizing network (e.g., ventromedial prefrontal cortex (vmPFC), temporoparietal junction (TPJ)), emotional empathy recruits networks related to emotion recognition and contagion (e.g., inferior frontal gyrus (IFG), intraparietal lobule (IPL); Shamay-Tsoory, 2011). Although the overall empathic response may be based on the complex interaction of both processes (Keysers and Gazzola, 2007), depending on the social context, it is believed that emotional and cognitive empathy represent two pathways to understanding others (Zaki & Ochsner, 2012; Spunt and Lieberman, 2013; Zaki, 2014).

A key hub of the mentalizing network and cognitive empathy is the right temporal parietal junction (rTPJ), whose important role in social cognition is widely recognised through an abundance of research. Indeed, the rTPJ is recruited during SOD, imitation control, and agency processing (Brass et al., 2009; Farrer & Frith, 2002; Ruby & Decety, 2001; Saxe & Powell, 2006; Saxe & Wexler, 2005). Furthermore, the rTPJ activates during adoption of the perspectives and belief of others (Schurz et al., 2014; Van Overwalle, 2009) and recognising false beliefs or encoding that someone’s mental state may differ from visible evidence (Ozdem et al., 2019). While the close connection between rTPJ activity and social cognition is well established in correlational studies, its causal role in the recognition or interpretation of someone's emotions is still unclear.

The investigation of people's ability to evaluate the emotions of others has often used pain as a model, potentially due to the robustness of pain in inducing empathic responses in an observer. First-hand pain is, in fact, highly motivational and able to induce adaptive avoidance (Price, 2000) and warning behaviours among conspecifics (Craig, 2004); while third-person pain motivates helping behaviours (Hein et al., 2010; Gallo et al., 2018).

Moreover, research on empathy for pain has provided ample evidence of the neural circuits involved in this experience (e.g., somatosensory cortices 1 and 2 (S1/S2); anterior and midcingulate cortex (ACC/MCC) and anterior insula (AI); Bernhardt & Singer, 2012). When people are asked to assess others' pain from facial expressions, they rely on regions associated with emotional empathy and simulation (Soyman et al., 2022). There is only some causal evidence for the rTPJ's involvement in processes of attributing pain to others (Coll et al., 2017). Nevertheless, to the best of our knowledge, no prior study introduced contextual information as a variable, investigating whether the involvement of the TPJ in the process of attributing pain to others is dependent on such information.

It was recently proposed that, in some situations, simulation and mentalizing networks may work together, opening up the perspective that these processes may work synchronously rather than in isolation, and that attribution of others' pain may rely on both networks rather than on simulation processes alone (Keysers & Gazzola, 2007). In line with this integrative view and in line with the evidence of the causal involvement of the rTPJ in holding false beliefs, inferring someone's level of pain from their facial expression might rely on the rTPJ if the inferring person is aware that the other person is trying to hide their pain.

Other evidence partially supporting this notion is the role the TPJ plays in encoding contextual information in relation to social scenarios (Gu et al., 2019). In particular, research has proposed that the TPJ may be necessary in mediating the social framing effect, or when a change in the description of a social dilemma (or a specific social component of this dilemma) significantly modulates a decision-maker's preference towards different options (Liu et al., 2020). In line with this, it is possible that the TPJ may also be sensitive to contextual information given around an emotion evaluation as part of an empathic experience. The contextual updating hypothesis (Geng and Vossel, 2013) suggests that the TPJ is essential for updating internal models of the internal or external context by integrating new information from the stimulus. TPJ recruitment in this process would be increased when the new information does not match the expectations of one's internal model. The TPJ may thus be necessary to update the expectations of the internal model when contextual information is provided about the intentions of a person to suppress or show pain.

To answer this question, we developed a task in which an actress is displayed receiving painful stimuli under two conditions: freely expressing or suppressing her pain. Before observing the videos and rating the actress' pain levels, participants were informed that the actress had been instructed to either express or suppress her pain (video stimuli labelled as pain being shown or suppressed). Along with the rating, reaction times (RT) were also assessed to investigate possible variations in inferential demand under the two conditions, especially considering that numerous studies have shown increased activation in the rTPJ as inferential demands increase (Vistoli et al., 2016; Henry et al., 2021). To investigate the causal role of the rTPJ, participants received 6Hz rTMS over the rTPJ or to sham stimulation over the vertex during the task.

Based on previous findings, we hypothesised that (i) participants would perceive more pain when the actress expresses vs. when she suppresses the pain (main effect of Video on ratings); (ii) participants would perceive more pain when they believe that the actress is suppressing her pain rather than expressing it (main effect of the Label on the rating); (iii) rTMS on the rTPJ disrupts the effect of the Label on ratings or RTs (TMS x Label interaction). Given the contextual updating hypothesis, rTMS might also disrupt the correct decoding of facial expressions of pain and the relationship to contextual information, especially if the information provided does not correspond to the actual emotions observed (TMS x Video x Label interaction).

2. Materials and Methods

2.1. Participants

Fourteen participants (9 female, 4 male, 1 not disclosed) participated in the present study. Participants were screened for exclusion criteria and only invited to the study, if they passed the safety screening for TMS collected twice, during recruitment and at the experimental session. All participants provided written consent and the study was accepted by the Medisch Ethische Toetsingscommissie of the Amsterdam Medical Center (application number 2019_025) prior to the start. The whole experiment lasted three hours for each participant and participants received 10 Euros per hour for their participation.

2.2. Procedure

First, we measured participants' resting motor threshold (rMT) over the right hemisphere. To do so, we measured the distance from inion to nasion to identify the centre of the head by connecting the two at the halfway mark. This line was crossed with the ear-to-ear line and the center of the brain was set as the location where the two lines met. We marked the approximate region of the right motor cortex as the right front quadrant. Then we applied single stimulations of gradually increasing intensity (starting with 45% of the stimulator's output intensity and increasing in steps of 5%, single pulses at least six seconds apart). Using three electromyography (EMG) electrodes on the left hand (one for the muscle, one for the index finger knuckle and one for the ground on the inner wrist), visualised with the Acquisition software (EMGworks), and participants' reports of muscle twitching (participants indicating once they felt a sensation in their left hand or index finger), we determined the motor hotspot and gradually decreased the intensity again to find the lowest stimulation intensity needed to produce motor-evoked potentials (MEPs) around 0.1 mV. We then tested this location using 10 pulses at the specified intensity by checking whether at least 5 out of the 10 pulses resulted in MEPs around 0.1 mV (mean rMT / SD = 51.71% / 3.29), and then set the stimulation intensity for the subsequent task at 90% of this value (mean stimulation intensity / SD = 46.00% / 3.56). Next, we marked the vertex [MNI coordinates (x, y, z) = 10, 0, 10] on the scalp. If participants had a stimulation intensity higher than 60% of the stimulator's output intensity, they were not further tested due to the unpleasantness of the stimulation. Neuronavigation (BrainSight) was used to physically mark the rTPJ [51, -54, 21].

Prior to the study, video stimuli were generated displaying a woman receiving real but tolerable shocks of varying intensity on her right hand and eliciting facial expressions of pain in line with the stimulation, ranging from mildly to annoyingly painful stimulation. During the pre-recorded videos, the woman was instructed to either freely show or suppress her facial expressions of pain in response to the shocks. Each video started with a neutral expression, which, following the delivery of the shock, led to a gradual change in facial expression until 1 sec after the video started. For the last second, the facial expression gradually changed back to neutral.

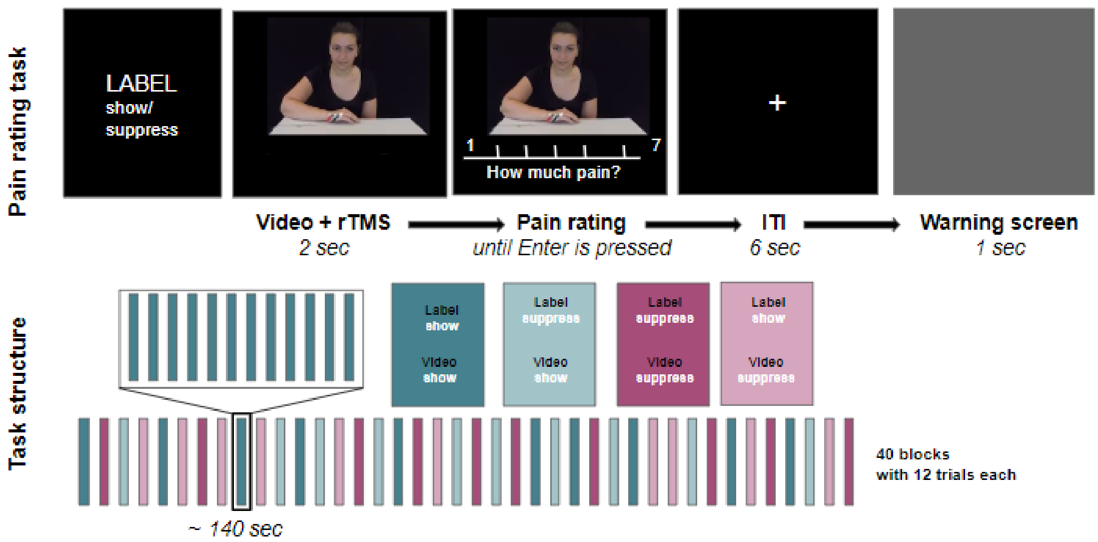

Figure 1. Overview of the task. Participants saw videos of a female receiving electrical stimulation in varying intensities on her hand, and then rated the pain they thought the woman felt.

These videos were shown to the participants in the task, who were asked to rate the pain of the woman in each video on a 6-point Likert scale from 1 ("no pain at all") to 7 ("very painful") (see Figure 1). Participants saw a total of 480 videos, distributed over 40 blocks with 12 trials each. Before each block, participants received two different types of information: that the person was freely showing (*label* = SHOW) or suppressing (*label* = SUPPRESS) the pain she felt. Unbeknownst to the participants, we included a *congruency* factor, whereby half of these information were labelled correctly, or congruently (e.g., participants were told it was a SHOW block and the woman was actually showing her pain), while the other half was incorrectly labelled, or incongruent (e.g., participants were told it was a SHOW block, but the woman was actually suppressing her pain). This division led to 10 blocks for each of the four conditions (label-video could either be congruent: SHOW-SHOW or SUPPRESS-SUPPRESS; or incongruent: SHOW-SUPPRESS or SUPPRESS-SHOW). The videos varied regarding the pain intensity delivered to the actress and accompanying facial reaction to the stimulation. The task was implemented in Presentation (Neurobehavioral Systems) and participants provided their answers via the keyboard.

Half of all blocks were accompanied by rTMS over the rTPJ using a MagStim Rapid^2 stimulator and a Figure-of-8 coil (Magstim Co Ltd). Participants were told a cover story that we were interested in two brain regions which would be stimulated during the task in separate blocks (one region on top of the head and another on the side of the head). In reality only the rTPJ received active stimulation, while sham stimulation was given over the vertex, with the coil and stimulation pointing away from the participants' heads. Block order was pseudorandomized into two different orders and counterbalanced across participants (6 vs. 8 participants for each order). Each trial of the task included two seconds of 6Hz stimulation (12 pulses) starting with the onset of the video, after which participants were asked to rate the pain of the woman. In sum, participants received 5760 pulses if they completed all blocks. Unfortunately, three participants missed the last three blocks and for three we had to lower the intensity of the stimulation during the task due to unpleasantness of the stimulation. However, due to the already small sample size, we included all participants into the analysis for who we were able to calculate means for all conditions.

2.3. Data analysis

Data analysis was conducted in RStudio (version 2021.09.0+351) and JASP (version 0.16.3.0). The two dependent variables were pain rating (i.e., the score that participants gave to the painful stimulations seen in the videos) and RT (i.e., the time it took participants to give the score). The 12 ratings for each of the 40 blocks (total number of ratings per participant = 480) were averaged to one rating per block, resulting in 40 ratings and RTs per participant (with the exception of three participants who had 14, 37 and 37, respectively; the participant with 14 ratings was excluded from further analyses as they did not have ratings for 4/8 conditions). These 40 average ratings divided into the three factors with two levels each (*Label*: show vs. suppress, *Video*: show vs. suppress, *TMS*: active vs. sham), resulting in 8 block types, each shown 5 times. According to the descriptive analyses, the pain ratings were normally distributed ($W = 0.98$, $p = .25$), while the RTs were not ($W = 0.51$, $p < .001$). We therefore log-transformed the RT data, which is a common approach in research to lessen the impact of outliers or skew (Whelan, 2008). The log-transformation did not fully normalise the distribution (W = 0.94, p < .001); but as it did slightly improve the data, all RT analyses were done using the log-transformed data. It is noteworthy that our data met the sphericity assumption, since we only have two levels of the repeated measure factor (Hinton et al., 2004), and research shows evidence of the robustness of the repeated-measure ANOVAs to non-normality when the sphericity assumption is met (Blanca et al., 2023).

In RStudio, both dependent variables were aggregated separately, thus creating an average pain rating and an average RT for each participant for each of the six factor combinations. In JASP, we calculated one three-way repeated-measures 2x2x2 ANOVA and one Bayesian ANOVA for each of the two dependent variables (with the factors *label*, *video*, and *TMS*). The interactions that emerged from the repeated-measures ANOVAs were further investigated through post-hoc tests.

Due to the small sample size, we calculated a post-hoc power analysis using WebPower (Zhang et al., 2018), implemented in RStudio (RStudio version 2022.07.0, build 548; R version 4.2.1) - to assess the effect size we could reliably detect. This analysis (hypothesised TMS x Label interaction effect, n = 13, *alpha* = .05, *beta* = .80) indicated a Cohen's f = 1.09.

3. Results

3.1. Pain ratings

We observed a main effect of TMS ($F_{(1,12)}$ = 15.30, p = .002, η^2 = 0.04; see Figure 2A and Table 1). The corresponding Bayesian ANOVA provided moderate evidence for H1 (BF_{incl} = 4.44). Participants rated the pain of the actress higher in the sham TMS (M = 3.51, SE = 0.12) than in the active TMS condition (M = 3.34, SE = 0.12).

Moreover, we observed expected main effects of Video ($F_{(1,12)}$ = 39.01, p < .001, η^2 = 0.27; see Figure 2B) and Label ($F_{(1,12)}$ = 28.95, p < .001, η^2 = 0.21; see Figure 2C), which were strongly confirmed by the Bayesian analysis (Video: BF_{incl} = 468.42; Label: BF_{incl} = 134.10). The main effect of Video showed that the participants gave higher ratings for videos in which the actress was told to express her emotions freely ("show" condition; M = 3.62, SE = 0.12) than for videos in which she was told to suppress her emotions ("suppress" condition; M = 3.22, SE = 0.11). In contrast, the main effect of Label showed that the participants gave higher ratings if they had been previously told that the actress had been instructed to suppress her emotions ("suppress" condition; M = 3.60, SE = 0.12) than when they had been previously told that the actress had been instructed to express her emotions freely ("show" condition; M = 3.24, SE = 0.12).

No interaction effects were found between Label x Video ($F_{(1,12)}$ = 2.35, p = .151, η^2 < .01), TMS x Video ($F_{(1,12)}$ = 0.05, p = .818, η^2 < .01), TMS x Label ($F_{(1,12)}$ = 0.02, p = .886, η^2

< .01) and TMS x Label x Video ($F_{(1,12)}$ = 0.36, p = .55, η^2 < .01). The lack of any interaction effects was partially confirmed by the Bayesian ANOVA (Label x Video: BF_{incl} = 1.37; TMS x Video: BF_{incl} = 0.87; TMS x Label: BF_{incl} = 0.74; TMS x Label x Video: BF_{incl} = 0.24), although many effects had inconclusive Bayes Factors between 3 and 0.33 with little evidence for either H1 or H0 (see Table 2).

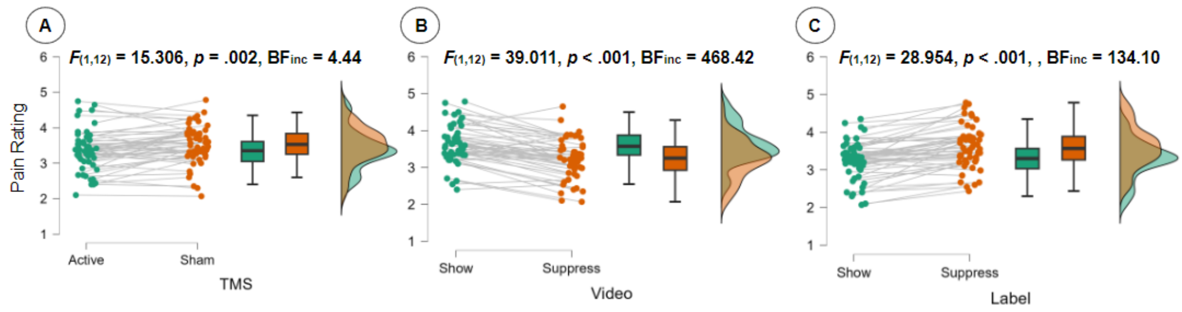

Figure 2. Significant pain rating results. A. Main effect of TMS: "Active" condition in green; "Sham" condition in orange. B. Main effect of Video: "Show" condition in green; "Suppress" condition in orange. C. Main effect of Label: "Show" condition in green; "Suppress" condition in orange. Please note, that the labelling was randomly assigned videos, so that videos in which the actress had suppressed her expressions were sometimes labelled as "Show", and sometimes as "Suppress".
The scattered dots in the graph on the left represent the averaged ratings given by the participants (8 per participant, one for each of the 8 combinations between factors levels). Lines between dots represent ratings of the same participants.The boxplots describe the distribution of ratings, dark line in the middle of the box being the median, the top/bottom of the box being the 75th/25th percentile, respectively, the top/bottom of the whisker being the maximum/minimum. The density plots show the distribution of the ratings with the peaks being the points where most of the values are concentrated.

Table 1. Repeated Measure ANOVA of the pain ratings.

Effects	*F(1,12)*	*p*	*eta²*	BFinc
TMS	**15.306**	**.002**	**0.047**	**4.446**
Label	**28.954**	**< .001**	**0.213**	**134.104**
Video	**39.011**	**< .001**	**0.272**	**468.422**
TMS x Label	0.021	.886	< 0.001	0.742
TMS x Video	0.055	.818	< 0.001	0.874
Label x Video	2.355	.151	0.007	1.377
TMS x Label x Video	0.366	.557	0.002	**0.247**

Note. Type III Sum of Squares. Significant effects are marked in bold. The last column indicates the result of a Bayesian ANOVA on the same data; red indicates evidence for an effect (Bayes Factor (BF) > 3); blue indicates evidence of absence of an effect (BF < 0.33).

3.2. Reaction Times

We observed a significant interaction effect between TMS and Video ($F_{(1,12)}$= 21.207; p < .001, η^2 = 0.32; see Figure 3A-D and Tables 2,3), showing that rTMS had a different effect on the RTs in the show vs. suppress videos. Bayesian analysis provided additional strong evidence for this interaction (BF_{incl} = 35.95) and Bonferroni-corrected post-hoc analysis revealed that under the sham TMS condition, participants were faster to give ratings to videos in which the actress was freely showing her emotions (*M* = 8.93, *SE* = 0.11) than when she was suppressing it (*M* = 9.24, *SE* = 0.11; see Figure 3A). This effect was altered during active 6Hz rTPJ stimulation, whereby participants were faster to give ratings in the "suppress" condition (*M* = 8.91, *SE* = 0.11) compared to the "show" condition (*M* = 9.20, *SE* = 0.11; see Figure 3B). Furthermore, participants were faster to rate freely expressed pain under sham (*M* = 8.93, *SE* = 0.11) compared to active perturbation of the rTPJ (*M* = 9.20, *SE* = 0.11; see Figure 3C). In contrast, they were faster to rate suppressed pain under active (*M* = 8.91, *SE* = 0.11) compared to sham stimulation (*M* = 9.24, *SE* = 0.1; see Figure 3D).

We also found an interaction between Label and Video ($F_{(1,12)}$= 14.413; p = .003, η^2 =0.09; see Figure 4A-C and Tables 2, 4), showing that the RTs during videos labelled as show vs. suppress was influenced differently by the label. In line with this, the effect was also strongly confirmed by the Bayesian analysis (BF_{incl} = 16.36). Post-hoc analysis showed that when participants were previously told that the actress would freely show her pain, they were faster to give ratings for the videos in which the actress actually suppressed the pain (*M* = 8.96, *SE* = 0.12) vs. when she actually showed it (*M* = 9.12, *SE* = 0.10; see Figure 4A). On the other hand, when participants were previously told that the actress would suppress the pain, they were faster to give ratings for the videos in which the actress actually showed her pain (*M* = 9.02, *SE* = 0.12) vs. when she actually suppressed it (*M* = 9.19, *SE* = 0.09; see Figure 4B). Post-hoc tests further showed that in the videos with suppressed pain, the Label "show" produced faster RTs (*M* = 8.96, *SE* = 0.12) compared to Label "suppress" (*M* = 9.19, *SE* = 0.09; see Figure 3D). Note that in the videos with freely showing pain, there was no significant difference in RTs between the two Labels ("show": *M* = 9.12, *SE* = 0.10; "suppress": *M* = 9.02, *SE* = 0.12).

We found no main effects of TMS ($F_{(1,12)}$ = 1.09, p = .316, $\eta^2 < .01$) or Video ($F_{(1,12)}$ = 0.15, p = .700, $\eta^2 < .01$), while a trend emerged for Label ($F_{(1,12)}$ = 4.12, p = .065, η^2 = 0.01). The Bayesian ANOVA provided moderate evidence for the Label effect (BF_{incl} = 5.19), which would suggest a faster rating when being told that the actress will freely show (*M* = 9.04, *SE* = 0.10) vs. suppress her pain (*M* = 9.10, *SE* = 0.10). Finally, no interaction effects were observed between TMS x Label ($F_{(1,12)}$ = 1.43, p = .254, $\eta^2 < .01$) and TMS x Video x Label ($F_{(1,12)}$ = 0.58, p = .458, $\eta^2 < .01$). However, in contrast to the frequentist ANOVA, the Bayesian ANOVA suggested strong to moderate evidence for both the inclusion of the main effects of TMS (BF_{incl} = 9.28) and Video (BF_{incl} = 19.36) and the interaction between TMS x Video x Label (BF_{incl} = 3.53). It is noteworthy that for both significant interaction effects (TMS x Video; Label x Video), pairwise Bayesian comparison showed evidence of effect only for Figure 3D and in Figure 4C.

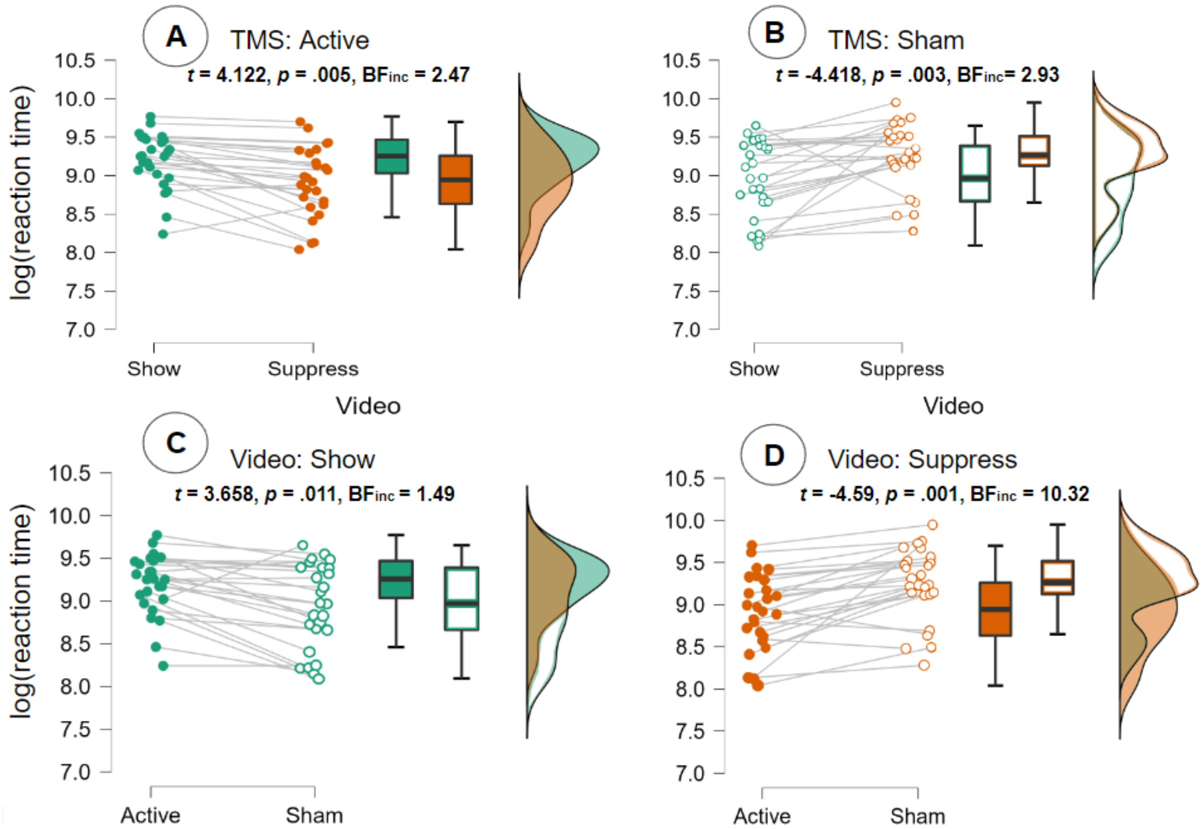

Figure 3. Reaction Time results. Interaction effect of TMS x Video: A. Comparison between TMS "Active" (full dots) with Video "show" (in green) and Video "suppress" (in orange). B. Comparison between TMS "Sham" (empty dots) with Video "show" (in green) and Video "suppress" (in orange). C. Comparison between Video "show" (in green) with TMS "active" (full dots) and TMS "sham" (empty dots). D. Comparison between Video "suppress" (in orange) with TMS "active" (full dots) and TMS "sham" (empty dots). The scattered dots in the graph on the left represent the averaged ratings given by the participants (8 per participant, one for each of the 8 combinations between factors levels). Lines between dots represent ratings of the same participants.The boxplots describe the distribution of ratings, dark line in the middle of the box being the median, the top/bottom of the box being the 75th/25th percentile, respectively, the top/bottom of the whisker being the maximum/minimum. The density plots show the distribution of the ratings with the peaks being the points where most of the values are concentrated.

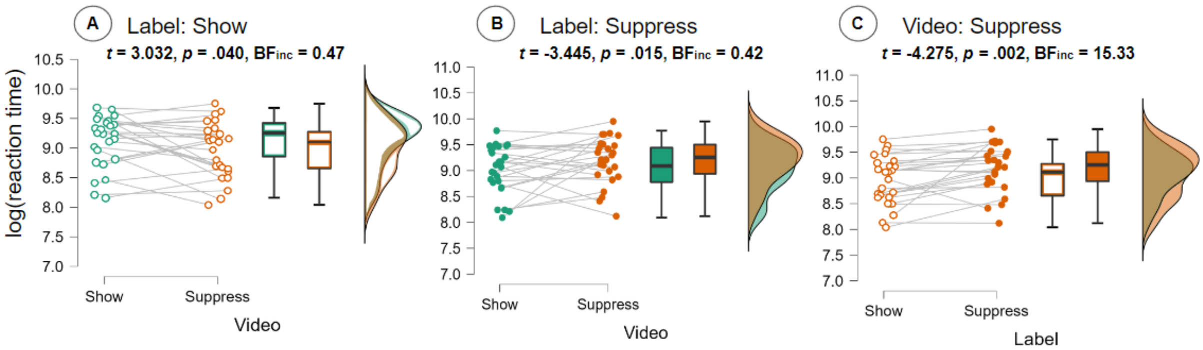

Figure 4. Reaction Time results. Interaction effect of Label x Video: A. Comparison between Label "show" (empty dots) with Video "show" (in green) and Video "suppress" (in orange). B. Comparison between Label "suppress" (full dots) with Video "show" (in green) and Video "suppress" (in orange).

C. Comparison between Video "suppress" (in orange) with Label "show" (empty dots) and Label "suppress" (full dots). The scattered dots in the graph on the left represent the averaged ratings given by the participants (8 per participant, one for each of the 8 combinations between factors levels). Lines between dots represent ratings of the same participants.The boxplots describe the distribution of ratings, dark line in the middle of the box being the median, the top/bottom of the box being the 75th/25th percentile, respectively, the top/bottom of the whisker being the maximum/minimum. The density plots show the distribution of the ratings with the peaks being the points where most of the values are concentrated.

Table 2. Repeated Measure ANOVA of the reaction times for the pain ratings.

Effects	*F (1,12)*	*p*	*eta²*	BF_{incl}
TMS	1.095	.316	0.004	**9.28**
Label	4.129	.065^{T}	0.013	**5.192**
TMS x Label	1.438	.254	< 0.001	1.548
Video	0.156	.700	0.007	**19.366**
TMS x Video	**21.207**	**< .001**	**0.321**	**35.953**
Label x Video	**14.413**	**.003**	**0.095**	**16.360**
TMS x Label x Video	0.588	.458	0.006	**3.531**

Note. Type III Sum of Squares. Significant effects are marked in bold. The last column indicates the result of a Bayesian ANOVA on the same data; red indicates evidence for an effect (Bayes Factor (BF) > 3); blue indicates evidence of absence of an effect (BF < 0.33).

Table 3. Post hoc comparison for TMS x Video.

Comparisons		Mean Difference	SE	*t*	p_{bonf}	*Cohen's d*	BF_{incl}
active show	**sham show**^{C}	**0.266**	**0.073**	**3.658**	**.011**	**0.612**	1.49
	active suppress^{A}	**0.289**	**0.070**	**4.122**	**.005**	**0.666**	2.47
	sham suppress	-0.044	0.042	-1.061	> .999	-0.102	**0.25**
sham show	active suppress	0.023	0.042	0.563	> .999	0.054	**0.22**
	sham suppress^{B}	**-0.310**	**0.070**	**-4.418**	**.003**	**-0.713**	2.93
active suppress	**sham suppress**^{D}	**-0.333**	**0.073**	**-4.59**	**.001**	**-0.767**	**10.32**

Note. Significant effects are marked in bold. Superscripts A-, B, C and D denote the effects given in Figure 3. The last column indicates the result of Bayesian *t*-tests on the same data; red indicates evidence for an effect (Bayes Factor (BF) > 3); blue indicates evidence of absence of an effect (BF < 0.33).

Table 4. Post hoc comparison for Label x Video.

Comparisons		Mean Difference	SE	*t*	p_{bonf}	*Cohen's d*	BF_{incl}
show show	suppress show	0.102	0.052	1.943	.391	0.235	0.76
	show suppress[A]	**0.153**	**0.050**	**3.032**	**.040**	**0.351**	0.47
	suppress suppress	-0.072	0.040	-1.790	.517	-0.165	**0.24**
suppress show	show suppress	0.051	0.040	1.271	> .999	0.117	**0.23**
	suppress suppress[B]	**-0.173**	**0.050**	**-3.445**	**.015**	**-0.399**	0.42
show suppress	**suppress suppress[C]**	**-0.224**	**0.052**	**-4.275**	**.002**	**-0.516**	**15.33**

Note. Significant effects are marked in bold. Superscripts A, B, C and D denote the effects given in Figure 3. The last column indicates the result of Bayesian *t*-tests on the same data; red indicates evidence for an effect (Bayes Factor (BF) > 3); blue indicates evidence of absence of an effect (BF < 0.33).

4. Discussion

This study investigated the rTPJ's causal contribution to pain empathy when people are given contextual information about others' intentions to freely display or suppress their pain. Our findings showed that TMS on the rTPJ influenced both participants' empathic perception and how quickly participants rated.

Active 6Hz rTPJ stimulation lowered participants' empathic pain ratings. This result confirms the previous work emphasizing the importance of rTPJ in the processing of social stimuli (Carter and Huettel, 2013; Decety and Lamm, 2007). In line with our results, rTPJ perturbation reduced the intensity of pain perceived in others (Coll et al. 2017), which confirms that rTPJ inhibition may reduce behavioural and brain measures related to the cognitive-evaluative component of empathy.

Behavioural results of the rating data also showed that participants gave higher pain intensity ratings to observed pain that was openly shown in the videos, compared to suppressed, independently of the contextual information given beforehand. This result is in line with studies where people rate freely expressed pain higher than suppressed pain (Poole and Craig, 1992).

Additionally, results revealed that people over-estimated the pain of the actress when they were told that she was suppressing it, independently of the actual video. This is consistent with studies showing that contextual information modulates the perception and recognition of facial emotions (Milanak and Berenbaum, 2014), especially when they are more difficult to decode (Bublatzky et al., 2020). It has been suggested that when the inferential weight is higher and multiple information sources are present, in our case the video and the label, the observer may privilege one of the two information sources, making one more salient than the other (Mendolia, 2021). Specifically, the fact that the “suppress” label significantly increased the perceived pain could depend on an overcompensation mechanism adopted by the participants when faced with emotions that are more difficult to decode. Not only does the suppressed pain expression in itself require more inferential effort, but the previous information indicating that pain will be suppressed creates the expectation of such inferential effort. Klein (2019) suggested that overestimating others' emotions may also be a mechanism for social approval motives, i.e., that people prefer to overestimate others' emotions because this indicates their effort and empathy.

Of note, we would have expected a modulation effect of TMS by such contextual information, but it should be mentioned that the contextual information used here did not completely overlap with the information used in previous studies investigating the role of the TPJ in modulating the social framing effect (Gu et al., 2020). The specific nature of the contextual information we used might explain the lack of any interactive effect with rTPJ stimulation. Specifically, the contextual information might have been perceived by participants as competing with the information presented in the video, especially under conditions of incongruence. Other studies showed that TPJ was specifically involved in mental state attribution but not in executive functions, such as response selection among competitors, suggesting that the TPJ might be less involved in processes of detection and resolution of incongruities (Vistoli et al., 2016).

Contrary to what we expected, no interaction effect between Label and Video emerged from the frequentist ANOVA, although the Bayesian ANOVA did not provide conclusive evidence.

Regarding participants’ RTs, evidence of an interactive effect between TMS and Video emerged. Under sham stimulation, participants were quicker to make judgements about the pain experienced by the person in the video when it was openly shown rather than suppressed, regardless of the information provided previously. Analogous to the pain rating results, this finding could intuitively be explained by the fact that inferring someone else's pain when it is suppressed may require more cognitive effort compared to situations in which pain is openly shown. This enhanced cognitive demand could plausibly translate into longer RTs.

Interestingly, under active stimulation, the previous result was reversed: When the rTPJ was disrupted, subjects were faster to give ratings when pain is suppressed rather than openly shown. This result supports the role of the rTPJ in the speed of social judgement (Costa et al., 2008). More specifically, post hoc tests revealed a slowing of RTs for the "show" condition and a speeding up in the "suppress" condition under active TMS. The former aligns well with the main effect of TMS on ratings: since the rTPJ is recruited in the process of pain attribution, its perturbation could slow down the speed of inference as well as the perceived intensity of pain (Coll et al. 2017). The speeded RTs in the “suppress” condition, which was confirmed with strong evidence by Bayesian post-hoc comparison, is an interesting finding worth discussing. Assuming that the level of inferential demand may differ between the "show" and "suppress" conditions, such that suppress stimuli may require more efforts to make inferences about the pain of others, it is possible to hypothesise that the reversal of RTs between the sham and active TMS depends on the involvement of the rTPJ in supporting such complex inferences. Specifically, if the TPJ supports difficult inferences about the others’ mental states, which could result in longer RTs due to increased pondering, its disruption might compromise this pondering process by making the subjects' judgement more reckless, resulting in shorter RTs. This hypothesis is supported by studies that have indeed shown stronger activation in the rTPJ as inferential demands increased (Vistoli et al., 2016; Henry et al., 2021). Moreover, the contextual updating hypothesis (Geng and Vossel, 2013) suggests that the TPJ is essential for the evaluation and integration of stimulus information with internal models of task performance and expectations. It would appear that mismatches between new sensory information and expectations produce the greatest responses from the TPJ because they represent the most significant updates to the internal model. It is possible that suppress videos represent a form of violation of the default assumption that a person in pain should show facial expressions of pain. Such a violation should engage the rTPJ more to update the internal model and this increased engagement could result in longer decision times during pain evaluation. Disruption of the rTPJ could break this updating mechanism and the associated commitment, shortening the subjects' RTs.

Contrary to what we expected, we found evidence of absence for a modulation effect of the TMS on RTs regarding contextual information. This result is in line with our rating data and suggests that the rTPJ region we targeted is less involved in using contextual information for social judgements.

Regarding the interactive effect between the label and the video, it appears that participants who thought the actress showed pain were quicker raters when a video were presented where the actress suppressed the pain; conversely, when they thought the actress suppressed pain, they were quicker with videos where the actress openly showed pain. These results suggest that in the presence of information about pain suppression, whether presented in the video or suggested in the label, participants relied on the simpler source to evaluate, either the label "show" (in the case of concurrent video "suppress") or the video "show" (in the case of concurrent label "suppress").This confirms the hypothesis that as the inferential weight increases, there is a tendency to focus on a single source of information (Mendolia, 2021). This would explain why participants' RTs were slower in the condition of concurrent video "suppress" and label "suppress": It is possible that the source that became salient in the decision-making process was the "show" label, i.e., the easiest to process. However, it should be noted that it remains counterintuitive that participants were not significantly faster in the condition of concurrent video "show" and label "show." Therefore, further studies investigating the relationship between videos and contextual information are necessary.

The present study had some strengths and limitations worth mentioning. First, a small sample size, resulting in lower power may have hidden smaller effects of Cohen's $f > 1.09$. The present study thus needs replication, especially for the effects with inconclusive BFs. Second, given the task length and the unpleasantness of rTMS, some subjects did not complete the entire task. Lastly, we did not measure self-experience ratings. Many empathy models propose that incorporating one's own affective experiences is crucial for comprehending the experiences of others. This should be considered in future studies. Despite these limitations, the present study partly confirms and expands the previous literature, while providing new evidence of the rTPJ's role in judging others' pain. Our results are underlined regarding their robustness through concurrent Frequentist and Bayesian analyses, as well as Bonferroni corrected post-hoc effects.

In conclusion, this study provides new insights into the involvement of the rTPJ in inferences about others' pain. If these findings are replicated, they may indicate that the rTPJ can be considered a valid target for stimulation when studying mechanisms of self-other control in socio-emotional processes like empathy. Shedding light on the role of the rTPJ in the process of attributing pain to others should be considered of importance in order to gain a deeper understanding of both the contribution of this brain region to social judgement and the phenomenon of empathy for pain. Furthermore, comprehension of the rTPJ's involvement in empathy for pain could provide useful clinical tools for dealing with conditions in which this ability is impaired.

5. Data availability

The data for this study can be found here.

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7. Author Contributions (Brand et al., 2015)

HH: Investigation, Data Curation, Formal analysis, Writing - Original Draft, Writing - Review & Editing, Supervision; **EO:** Investigation, Data Curation, Formal analysis, Writing - Original Draft, Writing - Review & Editing; **KB**: Conceptualization, Methodology, Software; Writing - Review & Editing; **VG**: Conceptualization, Resources, Writing - Review & Editing, Supervision, Funding acquisition; **CK**: Conceptualization, Resources, Writing - Review & Editing, Supervision, Funding acquisition.

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9. Declarations of Interest

All authors declare that they have no financial interests or potential conflicts of interest.

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