Familiarity From Facial Appearance Leads to Hypoalgesia

Arianna Bagnis,* Alexander Todorov,[†] Ilenia Altizio,* Valentina Colonnello,* Stefano Fanti,* Paolo Maria Russo,* and Katia Mattarozzi*

Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy, [†]Booth School of Business, The University of Chicago, Chicago, Illinois

Abstract: Social context has been shown to influence pain perception. This study aimed to broaden this literature by investigating whether relevant social stimuli, such as faces with different levels of intrinsic (based on physical resemblance to known individuals) and episodic (acquired through a previous experience) familiarity, may lead to hypoalgesia. We hypothesized that familiarity, whether intrinsic or acquired through experience, would increase pain threshold and decrease pain intensity. Sixty-seven participants underwent pain induction (the cold pressor test) viewing previously seen faces (Episodic Group) or new faces (Non-episodic Group) that differed in the level of intrinsic familiarity (high vs low). Pain threshold was measured in seconds, while pain intensity was measured on a rating scale of 0 to 10. The results did not show an effect of episodic familiarity. However, compared to low, high intrinsic familiar faces had an attenuating effect on pain intensity, even after controlling for pain expectation. These results suggest that physical features conveying a higher feeling of familiarity induce a top-down hypoalgesic modulation, in line with the idea that familiarity may signal safety and that the presence of familiar others reduce perceived threat-related distress. This study provides further evidence on the social modulation of pain and contributes to the literature on first impressions' influence on social behavior.

Perspective: *Consistent with the idea that familiar others signal safety and reduce the sense of threat, facial features conveying familiarity induce a top-down hypoalgesic modulation. This knowledge may contribute to understanding differences in pain perception in experimental and clinical contexts.*

Key Words: *Familiarity, Hypoalgesia, Pain perception, Top-down modulation, Facial appearance*

The presence and support of others are essential to human health and have relevant psychological and physiological consequences.[1,2] The Social Baseline Theory (SBT)[3] points out that proximity to social resources reduces the perceived distress associated with the threat. The SBT assumes that the human brain has evolved by learning that survival depends on others and that physiological needs are met more effectively when others are present.[4,5] Consistent with research showing that the presence of cospecifics reduces behavioral and autonomic responses to threat, clinical and experimental studies have shown that the social context intervenes in descending (ie, top-down) pain modulatory mechanisms.[6–10] Social context may lead to implicit or explicit pain expectations through conditioned or observational learning inducing placebo hypoalgesia or nocebo hyperalgesia.[1,9–15] A specific line of research shows that affectively familiar individuals (ie, significant others such

as parents and romantic partners) have a pain-attenuating effect.[16-19] Providing a feeling of protection and serving as a safety signal,[20] both active (ie, hand-holding) and passive (ie, mere physical proximity, photographs) presence of romantic partners reduces pain intensity and sensitivity in various clinical situations, such as recovery from surgery[21] and labor.[22] Pain reduction induced by the presence of affectively significant individuals has also been demonstrated in experimental paradigms using various measures such as thermal[23-25] and electric[26,27] stimulation and pressure pain.[28]

It is, therefore, reasonable to assume that familiarity—even when not conveyed by affectively familiar others—can signal the presence of resources to cope with threatening situations and, thus, lead to a similar pain-attenuating effect. Recent research shows that health care providers' facial features that convey feelings of familiarity led to reduced patients' pain perception during an invasive procedure in a clinical setting.[29] Patients' positive feelings of similarity and trust toward physicians predicted lower pain ratings,[30] and doctors' faces manipulated to look untrustworthy led to higher pain intensity with increased activity in brain regions associated with nociceptive pain, such as the insula and supplementary motor area.[31] Here, we aimed to investigate whether viewing strangers with different levels of nonaffective familiarity can modulate pain perception. We focused on 2 types of nonaffective familiarity, namely intrinsic (ie, based on physical resemblance to known individuals[32,33]) and episodic (ie, acquired through a previous experience[34]) familiarity. To assess the effect of intrinsic familiarity, participants were asked to report their pain during cold pressor test (CPT) while exposed to high familiar-looking versus low familiar-looking faces. Participants were split into 2 experimental groups to assess the effect of episodic familiarity. Half of them (ie, the Episodic Group [EG]) were exposed to high/low familiar-looking faces that they had already seen once, while the other half (ie, the Non-episodic Group [NG]) were exposed to completely new high/low familiar-looking faces. All participants were also exposed to a baseline control (no face) condition as well.

After the CPT, participants were also asked to report their experience in terms of anxiety, fear, pleasantness, and stress and to rate the faces in terms of how familiar/trustworthy/caring they looked.

We hypothesized that high familiar-looking faces and previously seen faces would increase the pain threshold and decrease pain intensity. Moreover, it is plausible that participants would benefit from an additive effect of intrinsic and episodic familiarity (ie, previously seen high familiar-looking faces). Given that individual differences such as pain expectations and personality traits (ie, catastrophizing, anxiety, and fear of pain) have been found to exert an influence on pain experience,[14,18,35] we controlled for these traits.

Methods

Design

A 3 within (high familiar, low familiar, no face) × 2 between (Episodic, Non-episodic) mixed-subjects design was used in this study (Fig 1A). Participants were randomly divided into 2 experimental groups: the EG was exposed to faces already seen the day before the procedure, and the NG was exposed to new faces. The total experiment lasted 5 days. Participants performed the CPT 3 times (on 3 consecutive days), and the order of the conditions (high familiar, low familiar, no face) was randomized across days.

Participants

A power analysis using G*Power software (Kiel Universität, Germany)[36] showed that a sample of 66 participants was required to achieve sufficient power (1-β > .95) for α = .05, assuming a medium effect (f = .20) and a correlation of .50 between repeated measures for 3 within (high familiar, low familiar, no face) × 2 between (Episodic, Non-episodic) mixed-model analyses of variance (ANOVAs). Eighty-six individuals were recruited to participate in the study. They were all Caucasian University students enrolled in the second year of Medicine and Surgery at the University of Bologna, Italy. Exclusion criteria included any current self-reported medical (eg, syncope, cardiovascular disease, pulmonary disease, vascular disease, chronic pain, or use of pain medication) or psychological (eg, psychiatric disorders, alcohol, or other drug abuse) conditions that might be influenced by the induced pain. Thirteen participants were excluded due to technical problems or because they did not complete the experimental sessions. In addition, data were checked for outliers (ie, z-scores > ±3 standard deviation [SD]). Six participants fell under this condition in pain threshold or pain ratings and thus were excluded. The final sample consisted of 67 participants. Of these, 34 (19 females, 15 males; M = 20.91 ± 1.90 years) were assigned to the EG, and 33 (19 females, 14 males; M = 20.32 ± 1.07 years) were assigned to the NG. The experimental procedures were approved by the Institutional Review Board of the University of Bologna. All participants signed an informed consent form. The real purpose of the study was not disclosed to the participants, but they were fully debriefed at the end of the study.

Cold Pressor Test

The CPT is considered a safe and standardized method for pain induction.[37] In this procedure, the participant's hand is immersed in an ice water bath for about 3 minutes. Afterward, the participant's hand is immediately dried and warmed. In our study, participants placed their nondominant hand in the cold tank, which was kept at a temperature of 2.5 °C (±.5 °C). Before immersion, they
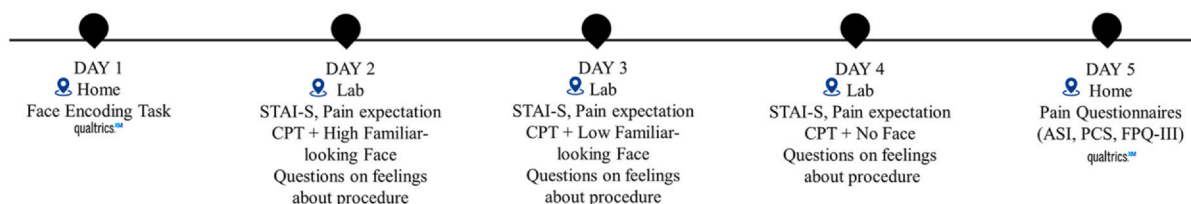
A)
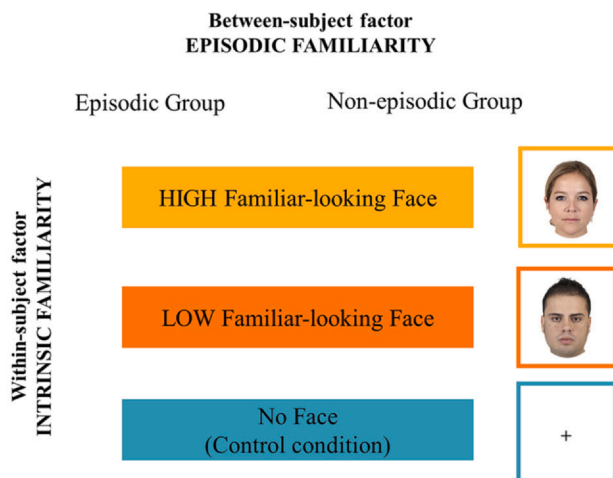
B)

Figure 1. Experimental design (**A**) and procedure (**B**). Panel A shows the experimental mixed design, while panel B shows the experimental procedure. Note that the order of conditions (high, low, no face) was randomized across days in the actual experiment.

were instructed to keep their hand open (rather than in a closed fist position) under water until the pain became unbearable. However, the cutoff time was set at 3 minutes, after which the participants were asked to remove their hands from the water. The participants were not informed about this maximum limit.

Familiarity Manipulation
Stimuli

The stimuli consisted of 24 emotionally neutral Caucasian faces (12 female faces) selected from the Chicago Face Database[38] according to their standardized appearance-based ratings of familiarity. Specifically, the faces were selected based on a standardized average (z score) of their familiarity ratings from an independent Italian sample of 342 (47 men; age M = 22.73, SD = 6.94 years) individuals. The final set included 12 low familiar-looking faces (6 men; M = 2.52, SD = .18) and 12 high familiar-looking faces (6 men; M = 4.76, SD = .38). Four additional faces (2 low familiar-looking faces and 2 high familiar-looking faces, gender-balanced) were used for practice trials.

Face Encoding Task

In order to manipulate experimentally the episodic familiarity, all participants performed a Face Encoding Task the day before (ie, day 1) the pain experimental induction. On the following days, participants assigned to the EG were exposed to the same faces that they rated during the Face Encoding Task, while participants

assigned to the NG were exposed to completely new faces (different from the faces they were presented with during the Face Encoding Task).

Sixteen images (800 × 600-pixel bitmap) depicting a frontal face image (8 high familiar-looking and 8 low familiar-looking, gender-balanced) were presented in a randomized order. To ensure continuous attention during the acquisition phase, participants were asked to rate each face on a scale of 1 (not at all) to 9 (extremely) on how familiar/trustworthy/dominant/attractive/typical/caring the face looks (see Supplementary Materials, Supplementary Table 1 for ratings' means and SDs of the stimuli used during the CPT). Participants rated each face on all traits at once. Each participant was assured that there were no right or wrong answers and that they should rely on their first impression. The task began with 2 practice trials to familiarize the participant with the task. Each trial was preceded by a fixation cross for 1 second

Measures
Demographics

At the beginning of the CPT session (ie, day 2), participants signed the consent form and were asked to provide their demographic information (ie, age and sex).

State of Anxiety

The level of state of anxiety before the CPT was measured with State-Trait Anxiety Inventory-State version (STAI-S[39]). STAI-S has 20 items for assessing state anxiety. All items are rated on a 4-point scale (from

"Almost Never" to "Almost Always"). Higher scores indicate greater anxiety. Reliability analysis yielded good internal consistency (Cronbach's alpha = .94).

Pain Expectation

Participants' expectation about the pain was measured on a 10-point Likert scale ("How much pain do you think you are going to feel?") to control for individual differences.

Pain Threshold and Pain Tolerance

Latency to pain threshold (ie, the time in seconds from hand immersion to the first pain rating, when the participant indicates that they feel pain by pressing the space bar) and pain tolerance (ie, the time in seconds from hand immersion to the time the participant voluntarily removes their hand) were measured in seconds using a stopwatch.

Pain Intensity

Pain intensity was measured on a verbal numerical rating scale of 0 to 10 (where 0 = no pain and 10 = the worst possible pain) every 20 seconds after the pain threshold and at the time the hand was removed from the water. It is important to note that the aim of collecting pain intensity ratings every 20 seconds after the threshold was 2-fold, namely to calculate average pain intensity and to control for the effect of time (ie, differences in time during the pain procedure, as acute cold exposure has been demonstrated to be dependent on habituation[40]).

Feelings About Procedure

After the CPT, participants were asked to answer questions to determine how emotional and stressful the experience was. The questions were as follows: 1) "How much anxiety did you feel during the procedure?" 2) "How much fear did you feel during the procedure?" 3) "How much unpleasantness did you feel during the procedure?" 4) "How much stress did you feel during the procedure?" Participants had to rate their answers on an 11-point scale (0 = "not at all" to 10 = "maximum extent").

Pain-Related Questionnaires

Level of anxiety, fear of pain, and pain catastrophizing were measured with the Anxiety Sensitivity Index-3 (ASI-3[41]), the Fear of Pain Questionnaire- III (FPQ- III[42,43]), and the Pain Catastrophizing Scale (PCS[44]), respectively.

ASI-3 is a 16-item self-report scale measuring concerns about possible negative consequences of anxiety symptoms; FPQ- III is a 30-item questionnaire that assesses fear of pain; and the PCS is a 13-item scale that quantifies the degree of pain-related catastrophizing, that is, the degree of exaggerated negative orientation toward actual or anticipated pain experiences. We administered these scales to make sure that the groups did not differ in personality traits related to pain perception. The pain-related questionnaires were analyzed using sum scores. Reliability analysis yielded a good internal consistency (Cronbach's alpha: ASI-3 = .87, FPQ-III = .89, PCS = .87).

Procedure

The total duration of the study was 5 days, as shown in Fig 1B. On day 1, participants performed a Face Encoding Task at home via Qualtrics. Over the next 3 days, participants performed the CPT at the laboratory and were exposed to faces they had seen during the Face Encoding Task (EG) or completely new faces (NG), depending on the experimental condition. Participants were also exposed to a no face condition (control). In total, the participants performed the CPT 3 times, that is, once per day to avoid a possible habituation effect among conditions within a day. The CPT was always conducted in the afternoon (from 2.00 to 5.00PM) to exclude any possible influence of variations in the time of day. On day 5, participants were administered pain-related questionnaires at home via Qualtrics.

Prior to the CPT

After giving consent to participate, all participants were contacted by email at home on day 1 and given a Qualtrics link to the Face Encoding Task. The link was sent on a well-defined schedule to ensure that participants completed the task within 24 hours before the CPT.

The CPT

On the next 3 days (day 2, day 3, day 4), participants performed the CPT individually in the Bologna University Psy-Lab at the Morgagni-Pierantoni Forlì Hospital.

On arrival at the laboratory, participants were greeted by the experimenter. To ensure that they could immerse themselves in the situation, they were told: "[.] imagine you are in a hospital for a clinical test. The test will be conducted by a healthcare professional who can be seen on the computer monitor on the desk where you are sitting." Before the test began, participants were told that they could stop the task at any time. After the participants sat down, the experimenter went behind a screen so as not to be visible during the procedure. At the beginning of the session, participants signed the consent form and were asked to provide their demographic information. They also indicated their current anxiety levels using the STAI-S,[39] and their expectation about the pain. Then, CPT instructions were provided entirely through the computer, written on the right side of the screen, next to the face that ostensibly represented the health care professional conducting the procedure. Participants had to press the space bar after reading the instructions to advance. Once participants had immersed their hands in the water, the face was presented (18 cm high × 21 cm wide) at 80 cm viewing distance from the center of a 19-inch computer monitor, subtending a visual angle of approximately 12.83 to 14.95°. The face (or fixation cross in the No Face condition) remained in the center of the screen for the entire

duration of the CPT, and the participant was asked to look at it during the whole procedure. In total, each participant was exposed to 2 faces (high- and low-familiar conditions) and to a fixation cross (no face condition). During each CPT, each participant, whether belonging to the EG or NG, was exposed to a single face, which could have been low or high familiar-looking, depending on the condition, randomly selected from the stimulus set. Faces were gender-balanced across conditions (eg, if the participant saw a female low-familiar face, then he/she saw a male high-familiar face. See Supplementary Materials, Supplementary Table 2 for analyses controlling for gender face stimuli. No significant effect of gender was found on pain threshold and pain intensity). The order of the conditions (No Face, Low, High) was randomized across days (see also Supplementary Materials, Supplementary Table 3 for analyses controlling for day order on pain intensity. No significant effect of day order was found on pain intensity). During the CPT, participants were instructed to immerse their hand in the water and to rate their pain.

We used the E-Prime software (Psychology Software Tools, Inc., Pittsburgh, PA, USA, http://www.pstnet.com/) for stimulus presentation and response data collection throughout the procedure in the laboratory.

Following the CPT

After the CPT, participants were asked to answer questions about how they felt during the procedure in terms of anxiety, fear, unpleasantness, and stress.

Participants were blind to the aims of the study and the experimental within- and between-subjects manipulations. However, to check whether the manipulation of within-subjects (High vs Low intrinsic familiarity) and between-subjects (EG vs NG) familiarity was successful, participants were asked at the end of the procedure whether they had ever seen the face shown during the experiment before and how much the face looked familiar to them. Participants were also asked to rate faces in terms of trustworthiness and caringness to control their impression of the health care professional who ostensibly conducted the procedure.

Finally, on day 5, participants received a second Qualtrics link containing the 3 pain-related questionnaires (ie, ASI-3, FPQ-III, PCS).

Data Analysis

Supplementary Fig 1 shows the data analysis overview. First, we tested whether the experimental manipulations (ie, intrinsic familiarity and episodic familiarity) worked as intended. After the CPT, participants were asked how much the face shown in the experiment looked familiar to them and whether they had ever seen the face shown in the experiment. To check for intrinsic familiarity, an F-test was calculated to evaluate differences between high and low intrinsic familiar conditions on familiarity ratings across experimental groups. To check for episodic familiarity, recognition was considered accurate if participants

from the EG recognized faces seen during the encoding task and if participants from the NG did not falsely recognize faces.

Preliminary analyses were then conducted to examine participants' characteristics. EG versus NG differences in demographic variables, anxiety state (STAI-S), pain expectation, and pain-related questionnaires were calculated using t-tests, χ^2-tests, and F-tests as appropriate. As anxiety state and pain expectation are state measures that can vary from day to day, differences within conditions were also explored. For the following analyses, total scores (ie, regardless of within conditions) were used for variables that did not differ between conditions and groups. Bivariate correlations were performed to determine the relationship between the dependent variables (ie, pain outcomes and feelings about the procedure) and the STAI-S, pain expectation, and pain-related questionnaires. Finally, a t-test was calculated to evaluate differences between high and low intrinsic familiar conditions on trustworthiness and caring judgments across experimental groups.

Consistent with CPT studies[34,45-47] and as described above ("Measures"), we calculated the following dependent pain measures: 1) mean scores for pain threshold (ie, time in seconds from hand immersion to first pain rating) and 2) mean pain ratings (ie, average pain intensity) during CPT for all participants. Pain tolerance (ie, the time in seconds from the time the hand is immersed to the time the participant voluntarily removes the hand from the water) was not analyzed as all participants kept their hand in the water until the end of the procedure (ie, the 3-minute interval).

To examine familiarity effects, pain threshold and pain intensity outcomes were analyzed using mixed ANOVAs, with Intrinsic Familiarity (High Familiar-looking Face, Low Familiar-looking Face, No Face) as a within-subjects factor and Episodic Familiarity (EG, NG) as a between-subjects factor. To control for the effect of time (ie, differences in time during the pain procedure), individual ratings of pain intensity (collected every 20 seconds after threshold) were also analyzed using a mixed ANOVA (within-subject factors: Intrinsic Familiarity, Time; between-subjects factor: Episodic Familiarity). Analyses of covariance (ANCOVAs) were also run using the variables that were significantly different among groups or significantly correlated with dependent variables as covariates. Following recommendations when conducting ANCOVAs for mixed design,[48] all covariates were centered (ie, subtracting the mean covariate score from each covariate score) before entering them into the models. Finally, we were also interested in examining the modulation of familiarity on questions after the CPT, namely participants' feelings about the procedure (ie, anxiety, fear, unpleasantness, stress). Accordingly, a mixed multivariate analysis of variance (MANOVA, within-subject factor: Intrinsic Familiarity; between-subjects factor: Episodic Familiarity) was computed. For F-tests, partial eta-squared (η_p^2) were calculated as effect sizes. Significant main effects or interactions were followed up by posthoc Bonferroni adjusted analyses.

Table 1. Means and Standard Deviations on Intrinsic Familiarity for Both Experimental Groups

	TOT (N = 67)		EG (N = 34)		NG (N = 33)	
	M	SD	M	SD	M	SD
High-familiar	5.48	2.08	5.19	2.04	5.77	2.04
Low-familiar	3.69	1.97	3.26	1.81	4.12	2.05

Abbreviation: M, Mean; EG, Episodic Group; NG, Non-episodic Group: TOT, Total

Results

Manipulation Check

Both experimental manipulations (ie, intrinsic familiarity and episodic familiarity) were successful. The selected images were perceived as differing in intrinsic familiarity. ANOVA on intrinsic familiarity showed a significant effect of Intrinsic Familiarity ($F_{(1, 67)} = 65.24$, $P < .001$, $\eta_p^2 = .48$), while no significant effect was found for Episodic Familiarity (ie, the group, $F_{(1, 67)} = 3.33$, $P = .07$, $\eta_p^2 = .03$), or the interaction between Intrinsic Familiarity and Episodic Familiarity ($F_{(1, 67)} = .02$, $P = .89$, $\eta_p^2 = .00$). Table 1 reports means and SDs of intrinsic familiarity across groups. See also Supplementary Materials for individual participants' data on intrinsic familiarity (Supplementary Fig 2).

For episodic familiarity, participants' recognition accuracy was high for both high (EG = 88%; NG = 79%) and low (EG = 88%; NG = 76%) intrinsically familiar faces. That is, whereas participants in the EG correctly recognized the faces that they had seen before, participants in the NG correctly did not recognize these faces. In the Supplementary Materials, we report the main analyses and results on pain outcomes performed only on participants who were 100% accurate (N = 50). Results show no differences between these participants and the total sample (Table S4).

Concerning the inferences from face stimuli, MANOVA showed a significant effect of Intrinsic Familiarity, $F_{(2, 64)} = 65.14$, $P < .001$, Wilk's $\Lambda = .33$, $\eta_p^2 = .67$, on trustworthiness ($F_{(1, 65)} = 100.37$, $P < .001$, $\eta_p^2 = .61$) and caring ($F_{(1, 65)} = 116.73$, $P < .001$, $\eta_p^2 = .64$) judgments, showing that both judgments were significantly larger for high familiar-looking faces than for low familiar-looking faces. No significant effect was found for Episodic Familiarity (trustworthiness: $F_{(1, 65)} = 1.10$, $P = .30$, $\eta_p^2 = .02$; caring: $F_{(1, 65)} = .41$, $P = .52$, $\eta_p^2 = .01$), or the interaction between

Intrinsic Familiarity and Episodic Familiarity, $F_{(2, 64)} = 1.14$, $P = .32$, Wilk's $\Lambda = .96$, $\eta_p^2 = .03$. Table 2 shows the means and SDs of trustworthiness and caring ratings of high familiar-looking faces and low familiar-looking faces across groups.

Participants' Characteristics

The 2 groups of participants (EG vs NG) did not differ in terms of sex distribution (EG: F = 19, M = 15; NG: F = 19, M = 14, χ^2 (1, N = 67) = .20, $P = .54$) and age (EG: M = 20.91 ± 1.90, NG: M = 20.32 ± 1.08, t (66) = 1.52, $P = .13$). Similarly, no significant differences in anxiety state (STAI-S scores) within conditions ($F_{(2, 128)} = 1.75$, $P = .18$, $\eta_p^2 = .03$) and between groups ($F_{(2, 128)} = .41$, $P = .66$, $\eta_p^2 = .01$) were found before the procedure. This was also the case for pain expectation among conditions ($F_{(2, 128)} = .12$, $P = .88$, $\eta_p^2 = .01$) and between groups ($F_{(2, 128)} = 1.76$, $P = .17$, $\eta_p^2 = .03$).

Table 3 reports psychological characteristics in terms of anxiety (ASI-3), catastrophizing (PCS), and fear of pain (FPQ-III), which were measured after the procedure. Experimental groups were found to be significantly different in terms of fear of pain. Accordingly, FPQ-III scores were used as covariates in the main analyses.

Table S5 reports correlations between dependent variables (ie, pain threshold, average pain intensity, feelings about the procedure) and STAI-S, pain expectation, and pain-related questionnaires. STAI-S were found to be correlated with feelings about the procedure (ie, anxiety, fear, and stress), while pain expectation with all the dependent variables. PCS and FPQ-III were correlated with pain threshold. Accordingly, they were used as covariates in the main analyses.

Effect of Familiarity on Pain Outcomes

Table 4 reports means and SDs on pain threshold and pain intensity across conditions and by groups.

Pain Threshold

ANOVA on pain threshold showed no significant main effect for Intrinsic Familiarity ($F_{(2, 130)} = .82$, $P = .91$, $\eta_p^2 = .001$), Episodic Familiarity ($F_{(1, 65)} = .56$, $P = .46$, $\eta_p^2 = .009$), or the interaction ($F_{(2, 130)} = .65$, $P = .52$, $\eta_p^2 = .01$), between Intrinsic Familiarity and Episodic Familiarity (Supplementary Fig 3). Since pain expectation and PCS scores were found to be correlated with

Table 2. Means and Standard Deviations of Trustworthiness and Caring Ratings of High Familiar-Looking Faces and Low Familiar-Looking Faces Across Experimental Groups

	HIGH FAMILIAR-LOOKING FACES						LOW FAMILIAR-LOOKING FACES					
	TOT (N = 67)		EG (N = 34)		NG (N = 33)		TOT (N = 67)		EG (N = 34)		NG (N = 33)	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Trustworthiness	6.72	1.38	6.53	1.46	6.91	1.28	4.19	1.70	4.09	1.71	4.30	1.70
Caring	6.34	1.43	6.09	1.50	6.61	1.32	3.90	1.83	3.94	1.86	3.85	1.82

NOTE. N = 67.
Abbreviation: EG, Episodic Group; NG, Non-episodic Group: TOT, Total

Table 3. **Psychological Characteristics for Both Experimental Groups**

	TOT (N = 67)		EG (N = 34)		NG (N = 33)		T	P
	M	SD	M	SD	M	SD		
ASI-3	21.27	10.12	20.79	8.28	21.76	11.84	.39*	.35
PCS	24.48	8.16	23.74	8.14	25.24	8.24	.75*	.23
FPQ-III	77.33	14.64	73.44	10.94	81.33	16.92	2.27*	.01
STAI-S	33.48	6.46	34.48	6.61	32.46	6.24	−.14*	.89
Pain expectation	6.58	1.68	6.54	1.64	6.61	1.72	1.27*	.21

Abbreviations: M, Mean; EG, Episodic Group; NG, Non-episodic Group: t, independent samples t-test; TOT, Total
*df = 65.

Table 4. **Means and SDs on Pain Threshold and Pain Intensity Across Conditions and by Groups**

	HIGH FAMILIAR-LOOKING FACE MEAN (SD)			LOW FAMILIAR-LOOKING FACE MEAN (SD)			NO FACE MEAN (SD)		
	TOT	EG	NG	TOT	EG	NG	TOT	EG	NG
Pain threshold	19.26 (15.33)	20.45 (16.52)	18.03 (14.14)	14.69 (26.27)	20.83 (19.91)	16.44 (11.29)	19.25 (14.76)	19.45 (17.45)	14.93 (11.63)
Pain intensity	7.30 (1.43)	7.28 (1.29)	7.31 (1.58)	7.69 (1.43)	7.52 (1.47)	7.86 (1.40)	7.61 (1.59)	7.60 (1.43)	7.60 (1.76)

NOTE. N = 67.
Abbreviation: EG, Episodic Group; NG, Non-episodic Group: TOT, Total

pain threshold, and experimental groups were found to differ in FPQ-III scores, ANCOVAs with them as covariates were also run. ANCOVA with pain expectation as a covariate showed that pain expectation was significantly related to pain threshold ($F_{(1, 64)} = 8.54$, $P < .01$, $\eta_p^2 = .12$), but again no significant main effect was found for Intrinsic Familiarity ($F_{(2, 128)} = .08$, $P = .91$, $\eta_p^2 = .001$), Episodic Familiarity ($F_{(1, 64)} = .55$, $P = .46$, $\eta_p^2 = .008$), or the interaction ($F_{(2, 130)} = .65$, $P = .52$, $\eta_p^2 = .01$) between them, indicating that pain expectation did not change the effects of episodic and intrinsic familiarity on pain threshold. Pain threshold was also analyzed using ANCOVA with the stable personality traits (ie, PCS and FPQ-III scores) as covariates, but both were found to be not significant (PCS: $F_{(1, 63)} = 1.02$, $P = .32$, $\eta_p^2 = .02$; FPQ-III: $F_{(1, 64)} = 2.41$, $P < .13$, $\eta_p^2 = .04$).

Pain Intensity

ANOVA on average pain intensity showed a significant effect of Intrinsic Familiarity ($F_{(2, 130)} = 4.39$, $P < .01$, $\eta_p^2 = .06$), while no significant effect was found for Episodic Familiarity ($F_{(1, 65)} = .14$, $P < .71$, $\eta_p^2 = .002$), or the interaction between Intrinsic Familiarity and Episodic Familiarity ($F_{(2, 130)} = .88$, $P < .42$, $\eta_p^2 = .01$). Posthoc comparisons showed that participants reported less average pain intensity in the high (M = 7.30, SD = 1.43) than in the low (M = 7.69, SD = 1.43) intrinsic familiar condition (Fig 2), while no differences with the No Face condition were found. Pain expectation and FPQ-III scores were used as covariates in 2 separated ANCOVAs. Pain expectation was found to be a significant covariate ($F_{(1, 64)} = 76.36$, $P < .001$, $\eta_p^2 = .54$). However, adding pain expectation did not change the effects of intrinsic and episodic familiarity. There was a significant effect for Intrinsic Familiarity ($F_{(2, 128)} = 4.31$,

$P = .01$, $\eta_p^2 = .06$) and no significant effect for Episodic Familiarity ($F_{(1, 64)} = .16$, $P = .69$, $\eta_p^2 = .003$), or the interaction between Intrinsic Familiarity and Episodic Familiarity ($F_{(2, 128)} = .89$, $P = .41$, $\eta_p^2 = .01$). FPQ-III scores were not a significant covariate ($F_{(1, 64)} = .35$, $P = .85$, $\eta_p^2 = .01$).

To control for differences across time during the pain procedure, ANOVA on pain intensity ratings with Time as a within-subject factor was performed. Results indicated that there was a significant effect of Intrinsic Familiarity ($F_{(2, 84)} = 7.57$, $P < .001$, $\eta_p^2 = .15$) and Time ($F_{(6, 252)} = 24.21$, $P < .001$; $\eta_p^2 = .37$). A significant interaction between Intrinsic Familiarity and Time was also found ($F_{(12, 504)} = 2.69$, $P < .05$, $\eta_p^2 = .06$). Interestingly, posthoc comparisons revealed that pain intensity ratings were lower in the high compared to low intrinsic familiar and no face conditions between +20 seconds and +80 seconds from pain threshold, while at +100 seconds and +120 seconds (ie, the last ratings) there were no differences among conditions (Fig 3).

Effect of Familiarity on Feelings About Procedure

MANOVA on anxiety, fear, unpleasantness, and stress reported by participants after the CPT showed no significant main effects for Intrinsic Familiarity ($F_{(8, 58)} = .87$, $P = .55$, Wilk's $\Lambda = .89$, $\eta_p^2 = .11$), Episodic Familiarity ($F_{(4, 62)} = 1.24$, $P = .30$, Wilk's $\Lambda = .93$, $\eta_p^2 = .07$), or the interaction between Intrinsic Familiarity and Episodic Familiarity ($F_{(8, 58)} = .24$, $P = .98$, Wilk's $\Lambda = .97$, $\eta_p^2 = .03$).

Discussion

Based on studies showing a pain attenuating effect induced by the presence of affectively familiar
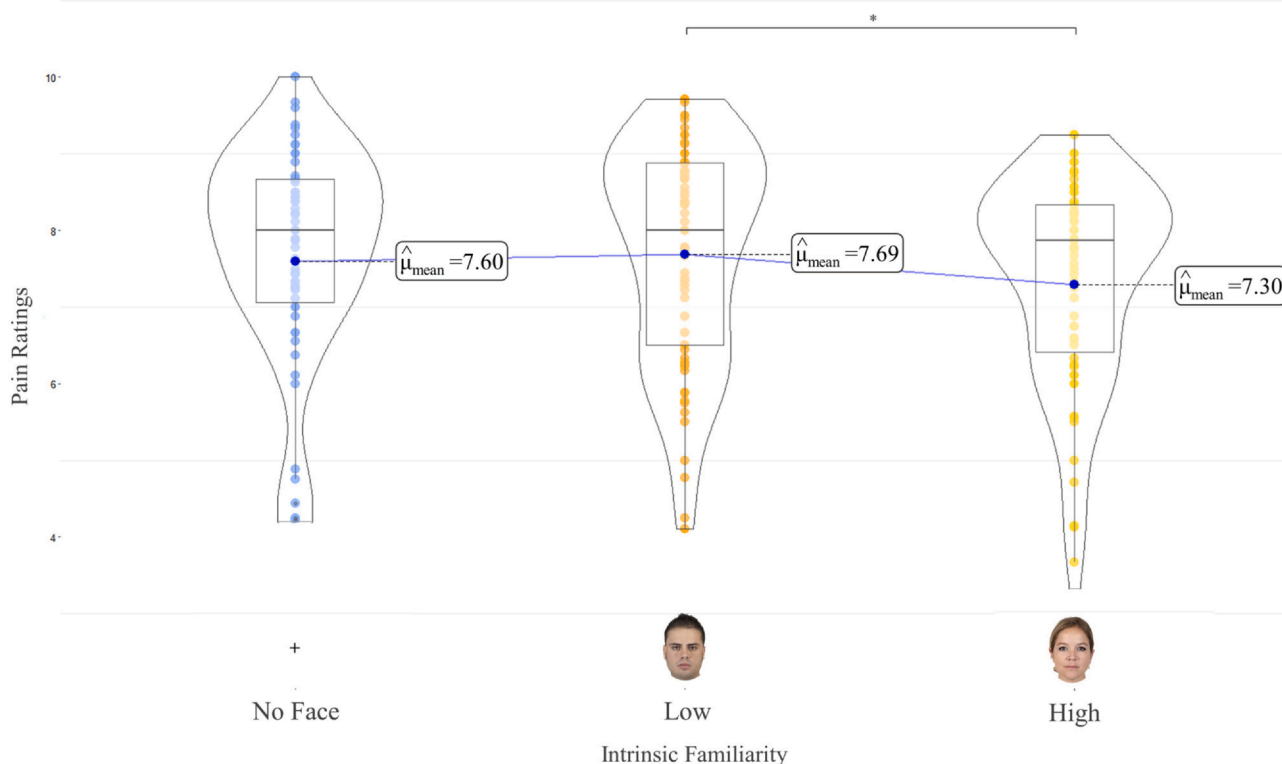
Figure 2. Violin plots of pain ratings for each condition (ie, No face, High familiar-looking face, Low familiar-looking face), reporting posthoc comparisons between conditions. Each violin represents data distribution and includes a standard box plot, which indicates the summary statistics (median, interquartile range). Means are depicted by the dark blue dot. Colored dots represent pain ratings for each participant. *P < .05.

others,[3,17,18,23,28,45] the aim of the present study was to test the effect of nonaffective familiarity on pain perception. Specifically, we aimed to investigate whether nonaffective familiar faces would have an impact both on pain threshold and perceived pain intensity. To assess intrinsic (ie, based on facial appearance and thus on physical features resemblance to known individuals) and episodic familiarity (ie, acquired through a previous experience), half of the participants (ie, the EG) were

exposed, during CPT, to high/low familiar-looking faces that they had seen before on 1 occasion, while the other half (ie, the NG) were exposed to new high/low familiar-looking faces.

We found that the presence of a relevant social stimulus, such as a face that looks familiar, modulates an unpleasant sensory and emotional experience by having a top-down analgesic effect on pain. Neuroimaging studies have shown that expectations and beliefs based
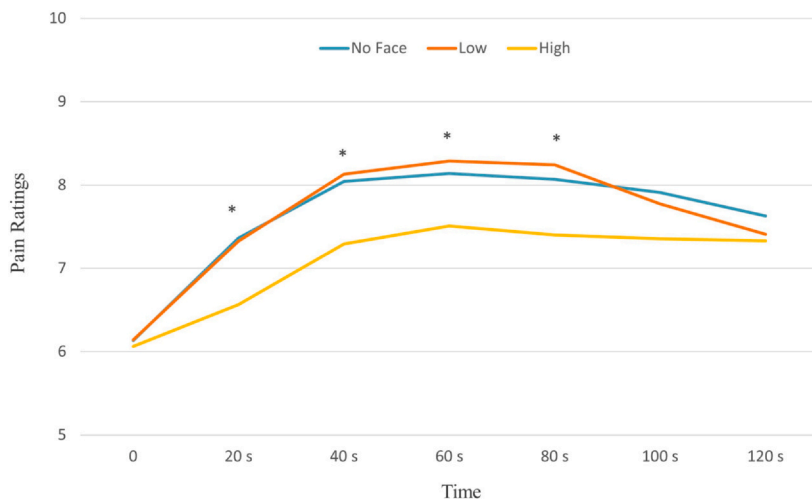
	No Face	Low	High
0	6.13 ± 1.82	6.14 ± 1.71	6.06 ± 1.81
20 s	7.37 ± 1.83	7.33 ± 1.58	6.56 ± 1.47
40 s	8.05 ± 1.79	8.13 ± 1.55	7.29 ± 1.58
60 s	8.14 ± 1.69	8.29 ± 1.72	7.51 ± 1.74
80 s	8.07 ± 1.81	8.24 ± 1.60	7.40 ± 1.86
100 s	7.91 ± 1.83	7.77 ± 1.71	7.36 ± 1.89
120 s	7.63 ± 1.91	7.41 ± 1.87	7.33 ± 2.16

Means ± SD by Conditions

Figure 3. Pain ratings by conditions across time. Line plot shows pain ratings by conditions across time. Asterisks indicate the time intervals when ratings during high intrinsic familiar conditions differ significantly from ratings during low intrinsic familiar conditions and no face conditions (*P < .05). Table reports means and SDs by conditions at each time interval.

on what typically occurs in the individual's environment influence perception by inducing changes not only in sensory brain regions (ie, bottom-up mechanisms) but also in regions involved in interpreting incoming information (ie, top-down mechanisms), such as cingulate and prefrontal cortices.[9,49-51] This evidence highlights the importance of top-down processes associated with contextual and social information influencing pain perception.[52] Consistently, we showed that the perceived pain intensity differed according to the level of intrinsic familiarity of the faces presented during the procedure. In line with our hypotheses and previous studies showing that the presence of affectively familiar individuals is associated with placebo hypoalgesia,[18] physical features that conveyed a higher feeling of familiarity had an attenuating effect on pain. The effect of the presence of an intrinsically familiar face emerged on the actual pain experience, while no effect was found on pain onset (ie, pain threshold). This is not surprising as self-reported pain is more likely to be influenced by emotional and social information than pain threshold.[53]

Conversely, the results did not show an effect of episodic familiarity and, hence, did not support its effect on the cold pain measures, at least with regard to the manipulation of episodic familiarity employed in this study. Even though participants accurately recognized the faces they had seen the day before, this nonsignificant result might be somewhat limited by the fact that face encoding from only 1 experience was not sufficient to affect pain perception. This is consistent with what has been found in studies of animal models on the regulatory effect of familiarity on anxiety-like behavior.[54] Specifically, anxiety has been shown to be sensitive to the frequency of prior experience (ie, multiple training sessions) with a stimulus, and thus we can assume that pain is affected by this frequency as well. Further studies with a stronger manipulation of episodic familiarity (eg, face encoding with more than one presentation) should be carried out to test this possibility. However, it is also possible that episodic and intrinsic familiarities are processed differently. As an important determinant of face evaluation, intrinsic familiarity has been shown to influence social behaviors.[32,33] As such, in line with studies on the positive evaluation of typical faces,[55,56] high familiar-looking faces may be evaluated as more positive and safer because of the common characteristics shared with affectively familiar individuals. In fact, we did find that high familiar-looking faces were perceived as more trustworthy and caring. This positive association[57] could explain the placebo hypoalgesia effect of high familiar-looking faces and the null effect on pain of previously seen faces just on 1 occasion.

Importantly, the present study, conducted in an experimental setting, replicates and extends recent evidence that inferences of familiarity from health care professionals' facial features explain a significant proportion of the variance in pain intensity during a real medical procedure.[29] Overall, both results converge in identifying intrinsic familiarity as contributing to the top-down process of pain perception; an effect that is found regardless of whether the pain is experimentally or clinically induced. One possible interpretation of this effect, which needs further investigation, could be that a high familiar-looking face represents a reassuring stimulus that triggers a feeling of safety and thus reduces pain intensity. In line with SBT,[3] individuals with facial features that convey a sense of familiarity and safety, similar to affectively familiar individuals, could be perceived as a social resource that can provide protection and care to cope with threatening situations. This is also consistent with neuroimaging studies that have shown that pain relief induced from the presence of familiar people is positively associated with the activation of brain areas related to safety signals and reward processing, such as the ventromedial prefrontal cortex and the nucleus accumbens, respectively.[23,58] However, additional research must be conducted to examine whether familiarity with facial appearance can serve as a safety stimulus and whether the underlying mechanism acting on pain perception is related to safety and reward mechanisms.[59]

Interestingly, the effect of high intrinsic familiarity (ie, lower average pain intensity compared to low intrinsic familiarity and the no face baseline) persisted over time. Only toward the end of the painful procedure average pain intensity decreased even when a low familiar-looking face was present and when the face was not present at all, possibly due to a pain habituation effect. Previous evidence suggests that pain increases over the course of the CPT and then reaches a plateau or decreases, likely because habituation to the cold benefits humans through increased skin temperature and decreased shivering.[40,60] Indeed, in contexts in which pain is unlikely to be associated with bodily damage (as in an experimental condition where participants are embedded in a painful but controlled procedure), it is adaptive to habituate to it. Moreover, habituation has been shown to be influenced also by social factors, as whether a situation is potentially threatening or not is often learned by observing other individuals, especially caregivers.[59] Here, high familiar-looking faces, probably acting as a safety signal and reward, may have helped to modulate the pain habituation and induce placebo hypoalgesia since the early moments of pain experience. The present findings may help to further understand why studies examining analgesic effects in the presence of strangers compared to alone conditions often yielded contradictory results.[18] For example, it is possible that unmeasured perceptual differences (ie, intrinsic familiarity) between strangers' faces may have influenced earlier results.

Previous studies[61] point to a crucial role of expectations shaping the top-down modulation of pain perception. Indeed, pain expectation enhances the possibility of a decrease in pain threshold and an increase in perceived pain intensity due to nocebo hyperalgesia.[8] Consistently, our results showed that pain expectation had a significant negative and positive relationship with pain threshold and perceived pain intensity, respectively, as individuals with a higher expectation of feeling pain during the procedure had a lower pain threshold and reported higher pain intensity. However, even when

controlling for pain expectation, our study still provides evidence for a hypoalgesic effect induced by the social context (ie, the presence of a high familiar-looking face), as the effect of intrinsic familiarity on pain intensity described above remained significant.

Some limitations of the present study should be acknowledged. First, several factors have been shown to impact day-to-day variations in pain.[62] Although the CPT was conducted always in the afternoon (from 2.00 to 5.00PM) to exclude possible influences due to diurnal fluctuations in the nociceptive system, other variables such as fatigue or menstrual cycle were not controlled. Second, we did not collect data on participants' specific attitudes toward the health care providers, which were experimentally represented by the face displayed. However, since our sample consisted of medical students, we may assume that they do not have negative attitudes toward health care providers and do not perceive them as threatening. More importantly, participants rated high familiar-looking faces as more trustworthy and caring than low familiar-looking faces. Finally, since CPT is characterized by cold habituation toward the end of the immersion period, future studies using other pain induction methods are needed to disentangle the temporal characteristics of the effect.

Conclusions

Our results show that placebo hypoalgesia, namely a reduction in reported pain perception, can be induced by individuals conveying a higher feeling of familiarity. This supports the idea that the presence of familiar others reduces threat-related responses, even if the familiarity is based only on facial appearance. It is not surprising that humans have learned to cope with painful situations by relying on perceptual cues of familiarity, highlighting the importance of a social stimulus with a higher safety signal without necessarily being affectively relevant.

Finally, the present results extend previous studies that have shown the influence of first impressions on social behavior,[63,64] suggesting that social inferences can influence not only decision-making but also an unpleasant sensory and emotional experience such as pain.

Acknowledgments

Appendix A. Supplementary Data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpain.2023.06.012.

References

1. Atlas LY: A social affective neuroscience lens on placebo analgesia. Trends Cogn Sci 25:992-1005, 2021

2. Brown JL, Sheffield D, Leary MR, Robinson ME: Social support and experimental pain. Psychosom Med 65:276-283, 2003

3. Coan JA, Sbarra DA: Social Baseline Theory: The social regulation of risk and effort. Curr Opin Psychol 1:87-91, 2015

4. Clark A: Whatever next? Predictive brains, situated agents, and the future of cognitive science. Behav Brain Sci 36:181-204, 2013

5. Hrdy SB: Evolutionary contextof human development: The cooperative breeding model. In: Salmon CA, Shackelford TK, editors. Family Relationships: An Evolutionary Perspective. 3. Oxford, Oxford University Press; 2007. pp 39-68,

6. Colagiuri B, Schenk LA, Kessler MD, Dorsey SG, Colloca L: The placebo effect: From concepts to genes. Neuroscience 307:171-190, 2015

7. Colloca L, Benedetti F: Placebo analgesia induced by social observational learning. Pain 144:28-34, 2009

8. Colloca L, Sigaudo M, Benedetti F: The role of learning in nocebo and placebo effects. Pain 136:211-218, 2008

9. Damien J, Colloca L, Bellei-Rodriguez C-É, Marchand S: Pain modulation: From conditioned pain modulation to placebo and nocebo effects in experimental and clinical pain. Int Rev Neurobiol 139:255-296, 2018

10. Okusogu C, Colloca L: Placebo hypoalgesia: Above and beyond expectancy and conditioning. Curr Opin Behav Sci 26:75-81, 2019

11. Farin E, Gramm L, Schmidt E: The patient-physician relationship in patients with chronic low back pain as a predictor of outcomes after rehabilitation. J Behav Med 36:246-258, 2013

12. Ferreira PH, Ferreira ML, Maher CG, Refshauge KM, Latimer J, Adams RD: The therapeutic alliance between clinicians and patients predicts outcome in chronic low back pain. Phys Ther 93:470-478, 2013

13. Hunter T, Siess F, Colloca L: Socially induced placebo analgesia: A comparison of a pre-recorded versus live face-to-face observation. Eur J Pain 18:914-922, 2014

14. Vlaeyen JWS, Hanssen M, Goubert L, Vervoort T, Peters M, van Breukelen G, Sullivan MJL, Morley S: Threat of pain influences social context effects on verbal pain report and facial expression. Behav Res Ther 47:774-782, 2009

15. Vögtle E, Barke A, Kröner-Herwig B: Nocebo hyperalgesia induced by social observational learning. Pain 154:1427-1433, 2013

16. Che X, Cash R, Chung S, Fitzgerald PB, Fitzgibbon BM: Investigating the influence of social support on experimental pain and related physiological arousal: A systematic review and meta-analysis. Neurosci Biobehav Rev 92:437-452, 2018

17. Hornstein EA, Fanselow MS, Eisenberger NI: A safe haven: Investigating social-support figures as prepared safety stimuli. Psychol Sci 27:1051-1060, 2016

18. Krahé C, Springer A, Weinman JA, Fotopoulou A: The social modulation of pain: Others as predictive signals of salience – A systematic review. Front Hum Neurosci 7:1-21, 2013

19. Mogil JS: Social modulation of and by pain in humans and rodents. Pain 156:S35-S41, 2015

20. Bowlby J: Developmental psychiatry comes of age. Am J Psychiatry 145:1-10, 1988

21. Kulik JA, Mahler HI: Social support and recovery from surgery. Health Psychol 8:221-238, 1989

22. Kennell J, Klaus M, Mcgrath S, Robertson S, Hinkley C: Continuous emotional support during labor in a US hospital: A randomized controlled trial. JAMA J Am Med Assoc 265:2197-2201, 1991

23. Eisenberger NI, Master SL, Inagaki TK, Taylor SE, Shirinyan D, Lieberman MD, Naliboff BD: Attachment figures activate a safety signal-related neural region and reduce pain experience. Proc Natl Acad Sci 108:11721-11726, 2011

24. Master SL, Eisenberger NI, Taylor SE, Naliboff BD, Shirinyan D, Lieberman MD: A picture's worth: Partner photographs reduce experimentally induced pain. Psychol Sci 20:1316-1318, 2009

25. Montoya P, Larbig W, Braun C, Preissl H, Birbaumer N: Influence of social support and emotional context on pain processing and magnetic brain responses in fibromyalgia. Arthritis Rheum 50:4035-4044, 2004

26. Coan JA, Schaefer HS, Davidson RJ: Lending a hand: Social regulation of the neural response to threat. Psychol Sci 17:1032-1039, 2006

27. Morriss J, Bell T, Johnstone T, van Reekum CM, Hill J: Social domain based modulation of neural responses to threat: The different roles of romantic partners versus friends. Soc Neurosci 14:398-408, 2019

28. Duschek S, Nassauer L, Montoro CI, Bair A, Montoya P: Dispositional empathy is associated with experimental pain reduction during provision of social support by romantic partners. Scand J Pain 20:205-209, 2019

29. Mattarozzi K, Caponera E, Russo PM, Colonnello V, Bassetti M, Farolfi E, Todorov A: Pain and satisfaction: Healthcare providers' facial appearance matters. Psychol Res 85:1706-1712, 2020

30. Losin EAR, Anderson SR, Wager TD: Feelings of clinician-patient similarity and trust influence pain: Evidence from simulated clinical interactions. J Pain 18:787-799, 2017

31. Anderson SR, Gianola M, Medina NA, Perry JM, Wager TD, Losin EAR: Doctor trustworthiness influences pain and its neural correlates in virtual medical interactions. Cereb Cortex 33:3421-3436, 2023

32. Verosky SC, Todorov A: Differential neural responses to faces physically similar to the self as a function of their valence. Neuroimage 49:1690-1698, 2010

33. Verosky SC, Todorov A: When physical similarity matters: Mechanisms underlying affective learning generalization to the evaluation of novel faces. J Exp Soc Psychol 49:661-669, 2013

34. Wang Y, Qi Z, Hofmann SG, Si M, Liu X, Xu W: Effect of acceptance versus attention on pain tolerance: Dissecting two components of mindfulness. Mindfulness 10:1352-1359, 2019

35. Tracy LM: Psychosocial factors and their influence on the experience of pain. Pain Reports 2:4, 2017

36. Faul F, Erdfelder E, Lang A-G, Buchner A: G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical. Behav Res Methods 39:175-191, 2007

37. Mitchell LA, MacDonald RA, Brodie EE: Temperature and the cold pressor test. J Pain 5:233-237, 2004

38. Ma DS, Correll J, Wittenbrink B: The Chicago face database: A free stimulus set of faces and norming data. Behav Res Methods 47:1122-1135, 2015

39. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA: Manual for the State-Trait Anxiety Inventory (Form Y). Palo Alto, CA, Consulting Psychologists Press; 1983

40. Yurkevicius BR, Alba BK, Seeley AD, Castellani JW: Human cold habituation: Physiology, timeline, and modifiers. Temperature 9:122-157, 2022

41. Schmidt NB, Joiner TE: Structure of the Anxiety Sensitivity Index psychometrics and factor structure in a community sample. J Anxiety Disord 16:33-49, 2002

42. Di Tella M, Ghiggia A, Testa S, Castelli L, Adenzato M: The fear of pain questionnaire: Factor structure, validity and reliability of the Italian translation. PLoS One 14:e0210757, 2019

43. McNeil DW, Rainwater AJ: Development of the fear of pain questionnaire - III. J Behav Med 21:389-410, 1998

44. Sullivan MJL, Bishop SR, Pivik J: The Pain Catastrophizing Scale: Development and validation. Psychol Assess 7:524-532, 1995

45. Edwards R, Eccleston C, Keogh E: Observer influences on pain: An experimental series examining same-sex and opposite-sex friends, strangers, and romantic partners. Pain 158:846-855, 2017

46. Kristiansen FL, Olesen AE, Brock C, Gazerani P, Petrini L, Mogil JS, Drewes AM: The role of pain catastrophizing in experimental pain perception. Pain Pract 14:E136-E145, 2014

47. Patanwala AE, Norwood C, Steiner H, Morrison D, Li M, Walsh K, Martinez M, Baker SE, Snyder EM, Karnes JH: Psychological and genetic predictors of pain tolerance. Clin Transl Sci 12:189-195, 2019

48. Schneider BA, Avivi-Reich M, Mozuraitis M: A cautionary note on the use of the Analysis of Covariance (ANCOVA) in classification designs with and without within-subject factors. Front Psychol Front Res Found 6:474, 2015

49. Bagnis A, Celeghin A, Mosso CO, Tamietto M: Toward an integrative science of social vision in intergroup bias. Neurosci Biobehav Rev 102:318-326, 2019

50. Eippert F, Finsterbusch J, Bingel U, Büchel C: Direct evidence for spinal cord involvement in placebo analgesia. Science 326:404, 2009

51. Summerfield C, De Lange FP: Expectation in perceptual decision making: Neural and computational mechanisms. Nat Rev Neurosci 15:745-756, 2014

52. Wiech K: Deconstructing the sensation of pain: The influence of cognitive processes on pain perception. Science 354:584-587, 2016

53. Stuginski-Barbosa J, Silva RS, Cunha CO, Bonjardim LR, Conti AC de CF, Conti PCR: Pressure pain threshold and pain perception in temporomandibular disorder patients: Is there any correlation? Rev Dor 16:22-26, 2015

54. Lungwitz EA, Stuber GD, Johnson PL, Dietrich AD, Schartz N, Hanrahan B, Shekhar A, Truitt WA: The role of the medial prefrontal cortex in regulating social famil-iarity-induced anxiolysis. Neuropsychopharmacology 39:1009-1019, 2014

55. Ryali CK, Goffin S, Winkielman P, Yu AJ: From likely to likable: The role of statistical typicality in human social as-sessment of faces. Proc Natl Acad Sci 117:29371-29380, 2020

56. Sofer C, Dotsch R, Wigboldus DHJ, Todorov A: What is typical is good: The influence of face typicality on perceived trustworthiness. Psychol Sci 26:39-47, 2015

57. Dotsch R, Hassin RR, Todorov A: Statistical learning shapes face evaluation. Nat Hum Behav 1:1, 2016

58. Younger J, Aron A, Parke S, Chatterjee N, Mackey S: Viewing pictures of a romantic partner reduces experimental pain: Involvement of neural reward systems. PLoS One 5:e13309, 2010

59. Griffin AS: Social learning about predators: a review and prospectus. Learn Behav 32:131-140, 2004

60. De Paepe AL, Williams AC de C, Crombez G: Habituation to pain: A motivational-ethological perspec-tive. Pain 160:1693-1697, 2019

61. Blasini M, Corsi N, Klinger R, Colloca L: Nocebo and pain: An overview of the psychoneurobiological mechan-isms. Pain Reports 2:1-9, 2017

62. Aviram J, Shochat T, Pud D: Pain perception in healthy young men is modified by time-of-day and is modality de-pendent. Pain Med 16:1137-1144, 2015

63. Todorov A, Oh D: The structure and perceptual basis of social judgments from faces. Adv Exp Soc Psychol 63:189-245, 2021

64. Todorov A, Olivola CY, Dotsch R, Mende-Siedlecki P: Social attributions from faces: Determinants, consequences, accuracy, and functional significance. Annu Rev Psychol 66:519-545, 2015