“Does my pain affect your disgust? Cross-modal influence of first-hand aversive experiences in the appraisal of others’ facial expressions”

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Supporting Information

Methods S1. Olfactory and thermal stimuli preselection

In line with previous studies from our group (Antico et al., 2018; Corradi-Dell’Acqua et al., 2016; Sharvit et al., 2015, 2018), in the olfactory preselection task, 9 odours (plus 10th odourless control) were delivered twice and in random order to each participant. The stimulus delivery was organized using the same cued-sniffing structure adopted in the main experiment, followed by a visual analog scale used for unpleasantness, identical to that in the main experiment for the rating of Reference trials. The olfactory-stimuli selection session lasted approximately 15 minutes.

As for the selection of thermal stimuli, we used a modified double random staircase (DRS) algorithm aimed at identifying stimuli of comparable unpleasantness (measured with the same VAS as for the odorants selection session) of the highly unpleasant odour selected for the main experiment (HD). Our DRS procedure is described in detail in our previous researches (Antico et al., 2018; Sharvit et al., 2015, 2018), and can be resumed as follows. Participants rated a sequence of thermal stimuli in which the temperature selected in each trial was selected based in the rating provided in prior trials. At each trial participants first saw a 1 sec long fixation-cross, followed by the text string “Temperature is changing” and concomitant delivery of the heat stimulation. Each thermal event was composed of 3 sec of rise time, 2 sec of plateau at the target-temperature, and 3 sec of return to baseline (37°C). The speed of the temperature rise and the temperature return was automatically adjusted according to the plateau in order to maintain both a rise time and a return time of approximately 3 sec each. The pleasantness scale was presented just after the 2 sec of plateau stimulation, when the temperature started to return to baseline, and lasted until participant provided a response.

In particular, trials rated as more unpleasant than the given cut-off (corresponding to the rating of HD) led to a subsequent lowered temperature, whereas trials less unpleasant than the given cut-off led to a subsequent higher temperature. To prevent participants from learning the relationship between their rating and the subsequent temperature, two independent staircases were presented randomly (initial thermal stimulations for the two staircases: 41°C and 43°C; temperature change in each step: 3°C; temperature change in trials in which the rating crossed the threshold: 1°C; maximum temperature possible: 52°C). The session ceased when each staircase was associated with 4 direction changes in the sequence, with the associated temperatures being averaged together to lead to subject-specific HP target stimulus, which varied on a participant-by-participant basis, but converged around the average value of 47.06°C (SD 1.96). Based on this temperature, we selected one additional temperature associated with more neutral ratings (LP), corresponding to an average value of 43.14°C (SD 2.30). This session lasted approximately 10 minutes.

Methods S2. Validation of face stimuli

We took 32 video-clips from the Montreal Pain and Affective Face Clips database (Simon et al., 2006, 2008), depicting the 8 models (4 males) engaged in painful, disgusted, surprised and neutral expressions. Each of these 32 video-clips was fed to the Computer Expression Recognition Toolbox (CERT) (Littlewort et al., 2011) to obtain automated frame-by-frame analysis of 20 facial AUs responses. For each of the 20 AUs, and for each clip, we calculated the average value of CERT output across all frames in the 1 second-video. These values were subsequently averaged across the 8 models, to get a unique facial response scalar for each AU and each state. Keep in mind that the CERT output reflects the likelihood for a specific AU response, as described by the distance of the extracted data vector from a support vector machine (SVM) hyperplane classifying whether or not a facial response occurred (Littlewort et al., 2011). As such measure is difficult to evaluate in absolute term, we used as baseline the output associated with neutral expressions, in which no facial response contraction is employed (Simon et al., 2006, 2008). Hence, for each unit *u*, and for each of the three affective states *s*, we calculated a facial engagement index i_{su} as follows:

$$i_{su} = \frac{Resp_{su} - Resp_{nu}}{\max(Resp - Resp_n)}$$

where $Resp_{su}$ is the CERT output in one specific state and unit, $Resp_{nu}$ is the CERT output in the neutral state for the same unit. The higher the difference, the stronger the response likelihood in one specific state, as opposed to the neutral. This differential response was scaled with the largest differential response obtained across all three states and all 20 AUs $max\ (Resp - Resp_n)$. The resulting index i_{su} is expected to be 0 for neutral-like facial response, and 1 for the most pronounced facial response in this dataset. The obtained indexes were used to create templates for facial expression pain, disgust and surprise as opposed to neutral on FACSGen software (cases in which $i_{su} < 0$, reflecting stronger response in Neutral expressions, were replaced with 0). Importantly, as CERT does not estimate AU 27 (mouth stretching) (Littlewort et al., 2011), we assumed that large modulations of this specific AUs in the videos would be classified as an AU 26 response (jaw drop). Thus, by adopting an exploratory approach, we created initially five templates, with two variations of pain and surprise, one fully reflective of the CERT output, and another in which i_{su} for AU 26 data were instead recoded as AU 27. The disgust template was characterized by $i_{su} \leq 0$ for AU 26, and therefore was associated only with one template. Furthermore, although FACSGen allows customizing each AU separately, it should be acknowledged that combining modulations of AU 1, 2 and 4 might lead to minor visual artefacts in the facial expressions. For these reasons, we carried out a validation pilot of the created templates, in order to insure that they truly convey the desired state.

The resulting 5 templates (2 versions of pain, 2 surprise, 1 disgust) were used to create a large database of static faces. In particular, we created hybrid expressions, obtained through weighted mean between each combination of two different templates (or between one template and a neutral expression). Overall, there were 11 pairs of interest, for each of which we created 9 hybrid stimuli, characterized by the following weightings: 0.00-1.00; 0.14-0.86; 0.29-0.71; 0.43-0.57; 0.50-0.50; 0.57-

0.43; 0.71-0.29; 0.86-0.14; 0.10-0.00. E.g., Pain-Disgust hybrids at 0.71-0.29 weighting were obtained by summing the Pain indexes multiplied by 0.71 with the Disgust indexes multiplied by 0.29. This led to 99 expressions which were implemented on 8 independent facial identities, thus leading to an overall of 792 stimuli. Please note that the facial identities used during the validation phase were different from those used in the main experiment.

Finally, we recruited an independent population of 20 subjects (10 men, age 23.30±4.07 years, range 18-32), and engaged them in a classification task in which they saw the 792 stimuli in random order. In each trial, a stimulus picture was presented only for 500 msec at the centre of the screen, and disappeared afterwards. At the bottom of the screen, the two response options remained visible and corresponded to the two states contributing to the hybrid stimulus used in this trial (e.g., “PAIN” and “NEUTRAL”). Participants were prompted to select, with no time constraint, which label was mostly descriptive of the stimulus presented by pressing one of two available keys on the keyboard. Following a response, the labels disappeared and were followed by an inter-trial interval of 1 sec. As the task was self-paced, there was no fixed duration, although the overall session never exceeded 40 minutes.

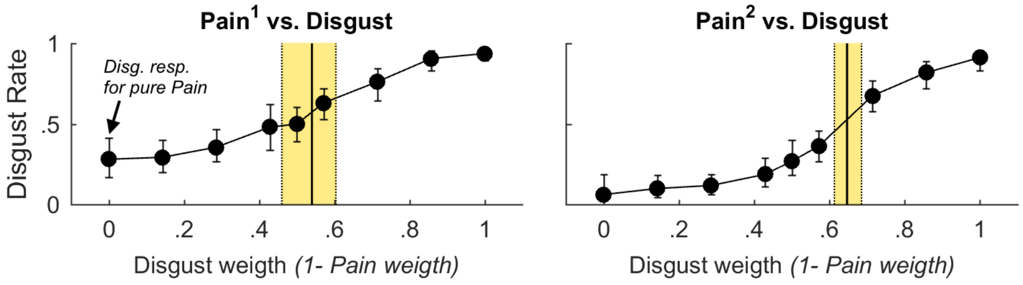

***Figure S1**. Data associated with the two variants of Pain-Disgust hybrid expressions related respectively to the presence of AU26 (variant 1) and AU 27 (variant 2). To identify, for each pair of stimuli, the weightings leading to the highest ambiguity, we fitted data to a sigmoid function. Black vertical lines refer to the point of the subjective equality (PSE) and dashed lines and yellow areas correspond to bootstrap-based 95% confidence intervals.*

In the analysis, we calculated for each hybrid stimulus the relative amount of instances in which one label was chosen with respect to the other. As visible in Figure S1, data follow a sigmoid function, consistently with previous studies implementing hybrid expressions (Mrug et al., 2015; Qiao-

Tasserit et al., 2017). To identify, for each pair of stimuli, the weightings leading to the highest ambiguity, we fitted individual data to a sigmoid function expressed as follows:

$$y = a + \frac{b}{(1 + e^{-s*(x-PSE)})}$$

where *y* represents participants' response, *x* the weighting, *a* the intercept (in Figure S1a, the amount of "pain" responses when the expression is entirely disgusted), *b* the maximum (the changes in responses from an entire painful, to an entire disgusting expression), *PSE* the point of subjective equality (reflecting the weighting value in which the two options were chosen with equal probability), and *s* the slope (the steepness of the curve at PSE). For each subject and for each continuum, we fitted the function to the data, with predefined starting values (*a* = 0, *b* = 1, *s* = 0.1, *PSE* = 0.5) and range constraints (between 0 and 1) for all parameters. The fitting was run using the the *lsqcurvefit* function as implemented in Matlab R2012a (Mathworks, Natick, MA). Parameter estimates for each subject and continuum were considered reliable only if associated with a goodness of fit of at least $R^2 \geq 0.75$ (this condition was not met only in 11 out of 220 [11 continua*20 subjects] cases).

***Table S1**. Average parameters of sigmoid function fitted on 11 independent continua (bracket values refer to 95% confidence intervals). Gray cells refer to hybrid configurations used in the main experiment together with weighting values corresponding to the estimated PSE (e.g., PSE = 0.61 in Pain*^{2} *vs. Neutral refers to Neutral weighted 0.61 and Pain*^{2} *weighed 0.39 [1-PSE]).*

	A	***b***	***PSE***	***S***	***R***^{2}
Pain^1 *vs. Neutral*	0.02 [0.01, 0.06]	0.94[0.90, 0.96]	0.50[0.46, 0.55]	0.30[0.20, 0.46]	0.97[0.96, 0.98]
Pain^2 *vs. Neutral*	0.03 [0.01, 0.05]	0.94[0.90, 0.96]	0.61[0.57, 0.65]	0.35[0.23, 0.53]	0.97[0.94, 0.98]
Disgust vs. Neutral	0.03 [0.02, 0.05]	0.95[0.92, 0.96]	0.53[0.50, 0.57]	0.23[0.18, 0.39]	0.98[0.97, 0.98]
Surprise^1 *vs. Neutral*	0.24[0.15, 0.33]	0.70[0.62, 0.81]	0.45[0.37, 0.54]	0.41[0.23, 0.65]	0.86[0.80, 0.90]
Surprise^2 *vs. Neutral*	0.05[0.03, 0.08]	0.93[0.88, 0.96]	0.72[0.66, 0.77]	0.29[0.19, 0.49]	0.95[0.93, 0.97]
Pain^1 *vs. Disgust*	0.18 [0.09, 0.30]	0.79[0.64, 0.90]	0.54[0.46, 0.60]	0.26[0.14, 0.48]	0.79[0.71, 0.86]
Pain^2 *vs. Disgust*	0.05[0.03, 0.08]	0.93[0.88, 0.96]	0.65[0.61, 0.68]	0.27[0.17, 0.45]	0.88[0.71, 0.95]
Pain^1 *vs. Surprise*^{1}	0.04[0.02, 0.72]	0.90[0.85, 0.94]	0.49[0.45, 0.54]	0.28[0.19, 0.44]	0.94[0.91, 0.97]
Pain^2 *vs. Surprise*^{2}	0.06[0.04, 0.09]	0.90[0.85, 0.93]	0.54[0.50, 0.57]	0.30[0.20, 0.48]	0.95[0.93, 0.97]
Disgust vs. Surprise^1	0.04[0.02, 0.08]	0.93[0.85, 0.96]	0.46[0.42, 0.50]	0.25[0.16, 0.43]	0.96[0.93, 0.98]
Disgust vs. Surprise^2	0.03[0.01, 0.05]	0.97[0.95, 0.99]	0.52[0.48, 0.58]	0.26[0.17, 0.43]	0.96[0.93, 0.98]

[1] *expressions fully reflective of CERT output*

[2] *expressions in which AU 26 data was recoded as AU 27*

Table S1 reports the average value of all four parameters (plus goodness of fit) in each of the 11 continua, revealing that the expressions were on overall well discriminated from one another. Interestingly however, the worst fitting was associated with pain and surprise expressions modelled with AU 26, especially in the Pain vs. Disgust, Surprise vs. Neutral continua. Indeed, in those two cases the intercept was reliably higher than zero, suggesting an amount of responses even in those stimuli in which the expression of interest was absent (see Table S1 and Figure S1, variant 1). This was not the case for those expressions obtained by recoding the AU 26 as AU 27 (variant 2). For this reason, we decided to use the latter template to build totally ambiguous stimuli, by adopting as weightings the estimated PSE. Table S2 reports the details of the selected models of pure pain, disgust and surprise as fed to the FACSGen software.

Table S2. *Indexes for facial expressions templates of Pain, Disgust and Surprise as fed in the FACSGen software. Each template is described by 21 AUs (20 from CERT software plus AU 27), each associated with an index ranging from 0 [neutral-like response] to 1 [the most pronounced response observed]. Omitted AUs are set to 0.*

	Pain	***Disgust***	***Surprise***
AU 1	0.11	0	0.55
AU 2	0	0	0.63
AU 4	0.69	0.67	0
AU 5	0	0.01	0.59
AU 6	1	0.53	0.01
AU 7	0.93	0.77	0
AU 9	0.38	0.63	0
AU 10	0.60	0.66	0.02
AU 12	0.58	0.12	0.02
AU 14	0.17	0.02	0
AU 15	0	0.33	0.06
AU 17	0	0.49	0
AU 18	0	0	0
AU 20	0.49	0.47	0.02
AU 23	0	0.34	0

AU 24	0.13	0.28	0
AU 25	0.81	0.32	0.50
AU 26	0	0	0
AU 27	0.43	0	0.41
AU 28	0	0	0
AU 45	0.51	0.31	0

Results S1. Respiration data

Respiration parameters were fed to the same ANOVA used for the other measures. This analysis revealed a significant main effect of Time ($F_{(19,513)}$ = 83.08, p < 0.001, η_p^2 = 0.75), and significant Unpleasantness*Time ($F_{(19,513)}$ = 3.98, p < 0.001, η_p^2 = 0.13) and Unpleasantness*Modality*Time interactions ($F_{(19,513)}$ = 5.76, p < 0.001, η_p^2 = 0.18). No other effect was found to be significant ($Fs \leq 2.87$). As visible in Figure S2, the main effect of Time is driven by the increased inspiration volume following the “breathe-in” instruction, for both thermal and olfactory events. Consistently with previous investigations (Sharvit et al., 2015, 2018), the inspired volume was reduced during the occurrence of disgusting odors. Indeed, paired-sample *t*-tests confirm larger values for Neutral > Unpleasant odors between 0-3 seconds from the “breathe-in” instruction onset (also ~12 sec – $ts_{(27)} \leq -2.19$, p < 0.038, d = -0.41). This was not the case for all other time-bins, during either thermal or olfactory stimulations ($ts_{(27)} \geq -2.04$, d = -0.38).

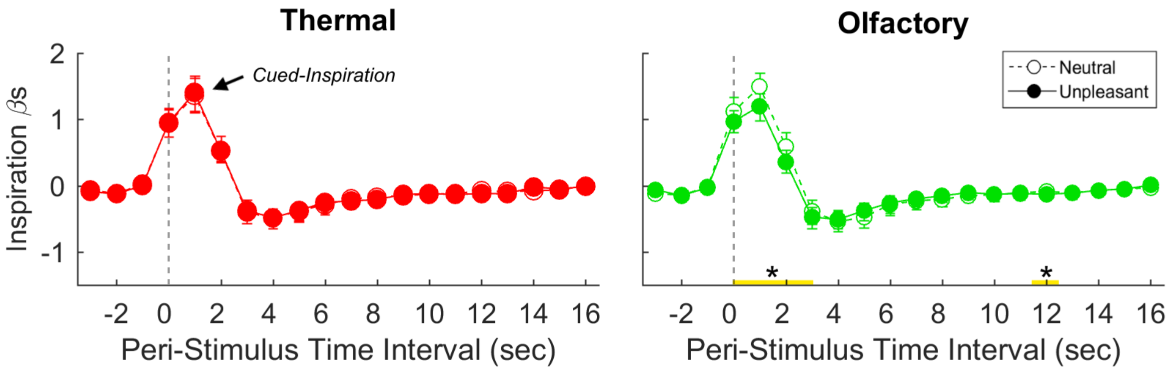

***Figure S2**. Inspiration volume associated with thermal (red lines) and olfactory (green lines) stimuli. Full circles refer to unpleasant events, whereas empty circles refer to neutral controls. Physiological responses are plotted within a time-window of 20 seconds, from the three seconds preceding the stimulus onsets (corresponding to the countdown – see methods), to 17 seconds following the presentation of the stimulus. Error bars refer to bootstrap-based 95% confidence intervals. “*” and horizontal yellow bars refer to time-bins associated with lower signal for Unpleasant < Neutral even at* $t_{(27)} \leq -2.05$, *corresponding to* $p < 0.05$.

Results S2. Gender Effects

We further explored whether the effects observed in the present manuscript were in turn modulated by the gender of the participants and, for the classification task, of the facial expressions.

Thermal and Olfactory Stimulations

Hence, for the analysis of the Reference Trials, we fed participants median ratings in a Repeated Measure ANOVA with Unpleasantness (low vs. high), Modality (thermal vs. olfactory) as within-subjects factor, and Participants' Gender (male vs. female) as between-subjects factor. The analysis confirmed the main effect of Unpleasantness reported in the main text ($F_{(1,26)} = 142.27$, $p < 0.001$, $\eta_p^2 = 0.85$). In addition, we found a Modality*Participants' Gender interaction ($F_{(1,26)} = 4.47$, $p = 0.044$, $\eta_p^2 = 0.02$), presumably reflecting stronger sensitivity of women to olfactory events (average pleasantness: -1.30, Confidence Intervals: [-1.87, -0.83]) as opposed to thermal (-0.73 [-1.34, 0.10]), but stronger sensitivity of men to thermal stimuli (-1.40 [-1.75,-0.97]) as opposed to olfactory (-1.13 [-1.53, -0.69]). No other effect was found to be significant ($Fs_{(1,26)} \leq 1.05$, $p \geq 0.316$, $\eta_p^2 \leq 0.04$).

We then extended the analysis of the physiological measures (electrodermal, cardiac and respiratory activity) associated with thermal and olfactory stimulations. For each of these measures we ran a Repeated Measure ANOVA with Unpleasantness (low vs. high), Modality (thermal vs. olfactory), Time (up to 20 seconds) as within-subjects factor, and Participants' Gender (male vs. female) as between-subjects factor. The analysis of electrodermal responses confirmed all main effects and interactions observed in the main text ($Fs \geq 4.65$, $ps \leq 0.040$, $\eta_p^2 \geq 0.16$). In addition, we found a significant main effect of Participants' Gender ($F_{(1,26)} = 5.69$, $p = 0.027$, $\eta_p^2 = 0.17$), and significant Time*Participants' Gender interaction ($F_{(19,494)} = 2.08$, $p = 0.005$, $\eta_p^2 = 0.07$), and Modality*Time*Participants' Gender ($F_{(19,494)} = 2.03$, $p = 0.006$, $\eta_p^2 = 0.07$). No other effects were found to be significant ($Fs \leq 3.56$, $ps \geq 0.071$, $\eta_p^2 \leq 0.12$). We further explored Modality*Time*Participants' Gender interaction by running Repeated Measure ANOVAs with Unpleasantness, Modality and Participants' Gender, per each time bin separately. We found a significant Modality*Participants'

Gender interaction at 11 seconds after the countdown ($F_{(1,26)}$ = 4.40, p = 0.046, η_p^2 = 0.14), presumably reflecting stronger galvanic modulation for thermal (βs = 0.19 [0.07, 0.33]) than olfactory stimulations (-0.03 [-0.15, 0.11]) in males, but no difference in females (Thermal: -0.17 [-0.48, 0.03]; Olfactory; -0.20 [-0.47, 0.01]). Hence, consistently with what found for the ratings, male participants seemed more sensitive to thermal events than females.

For the analyses of cardiac or respiratory responses, we confirmed the main effects as found without modeling Participants' Gender (Cardiac response: Unpleasantness*Time interaction [$F_{(19,494)}$ = 6.19, $p < 0.001$, η_p^2 = 0.19]; Respiration: Unpleasantness*Modality*Time interaction: [$F_{(19,494)}$ = 5.70, $p < 0.001$, η_p^2 = 0.18]), without these being further modulated by the grouping factor ($Fs \leq 1.54$, $ps \geq 0.067$, $\eta_p^2 \leq 0.06$). Interestingly (and unexpectedly), the analysis of cardiac responses revealed a significant main effect of Participants' Gender ($F_{(1,26)}$ = 7.22, p = 0.012, η_p^2 = 0.22), and significant effects of Time*Participants' Gender interaction ($F_{(19,494)}$ = 1.65, p = 0.041, η_p^2 = 0.060), reflecting enhanced heart rate in males between 4-8 sec (ts ≥ 2.11, ps ≤ 0.050, $ds \geq 0.40$) between and 12-14 sec (ts ≥ 2.23, ps ≤ 0.045 $ds \geq 0.42$; all other time-bins ts ≤ 2.04, ps ≥ 0.060, $ds \geq 0.39$).

Classification of Facial Expressions

For the analyses of the pure facial expressions, we fed the rates of accuracy and response time in a Repeated Measure ANOVA with Unpleasantness (high vs. low), Modality (thermal vs. olfactory), Expression (Neutral, Pain, Disgust, Surprise) and Expressions' Gender (male vs. female) as within-subjects factor, and Participants' Gender (male vs. female) as between-subjects factor. The analysis confirmed the Modality*Expression interaction as reported in the main text (Accuracy: [$F_{(19,494)}$ = 3.53, p = 0.018, η_p^2 = 0.12] Response Times: [$F_{(3,78)}$ = 3.29, p = 0.025, η_p^2 = 0.11]), without these effects being further modulated by either Participants' or Expressions' Gender ($Fs \leq 4.01$, $ps \geq 0.056$, $\eta_p^2 \leq 0.13$). Unexpectedly, the analysis of the accuracy revealed a Participants' Gender*Expressions' Gender interaction ($F_{(1,26)}$ = 6.12, p = 0.020, η_p^2 = 0.19), reflecting higher proficiency at classifying a face of the same gender as one's own: i.e. women were slightly more accurate for the female expressions (accuracy: 0.90 [0.81, 0.96]), as opposed to male expressions (0.86 [0.77, 0.92]), whereas men were more accurate for male expressions (0.93 [0.89, 0.96]), as opposed to female expressions (0.91 [0.88, 0.94]). Furthermore, we found a Modality*Expressions' Gender interaction ($F_{(1,26)} = 5.08$, $p = 0.033$, $\eta_p^2 = 0.16$) presumably reflecting slightly higher proficiency at classifying female expressions following thermal events (average: 0.92, Confidence Intervals: [0.89, 0.95]) as opposed to male expressions (0.90 [0.85, 0.94]), but better the accuracy of male expressions following olfactory stimuli (0.91 [0.88, 0.94]) as opposed to female expressions (0.89 [0.85, 0.93]). Finally, for the Response Times, we observed a significant Expression*Expressions' Gender interaction ($F_{(3,78)} = 2.90$, $p = 0.040$, $\eta_p^2 = 0.10$), showing faster responses to male (relative to female) expressions for both disgust (differential response times = -255.30 msec, [-523.18, -17.42]) and surprise (-143.42 msec, [-331.09, -38.38]), as opposed to neutral (-74.58 msec, [-224.34, 66.51]) and pain expressions (86.92 msec, [-47.79, 219.86]). No other effect was found to be significant ($Fs \leq 4.01$, $ps \geq 0.056$, $\eta_p^2 \leq 0.13$).

Finally, we tested the role of both Participants' Gender and Expressions' Gender in the analysis of classification errors. As error counts data cannot be analyzed in a standard ANOVA, we conducted an exploratory analysis focusing exclusively on the conditions of interest from the main analysis: i.e., misclassifications between pain and disgust, following either thermal or olfactory events. No significant effect was found (Participants' Gender: Mann Whitney rank-sum test: $|Z|$s ≤ 1.00, ps ≥ 0.32, rs ≤ 0.19 – Expressions' Gender: Wilcoxon sign-rank test; $|Z|$s ≤ 1.44, ps ≥ 0.230, rs ≤ 0.27).

The same logic was applied to the analysis of hybrid expressions, for which we focused on the conditions in which PD, PS and DS hybrids were classified as either pain or disgust. Also in this case no significant effect of Participants' Gender was observed ($|Z|$s ≤ 1.14, ps ≥ 0.252, rs ≤ 0.22). However, Expressions' Gender influenced the classification of PS hybrids, as they led to higher pain classification both following thermal ($Z = 2.40$, $p = 0.015$, $r = 0.45$) and olfactory events ($Z = 2.40$, $p = 0.018$, $r = 0.45$), with consequent decrease of surprise classifications (following thermal: $Z = -2.25$, $p = 0.026$, $r = -0.43$;

olfactory: $Z = -2.70$, $p = 0.006$, $r = -0.51$). No other condition was associated with a significant effect ($|Z|$s ≤ 1.41, ps ≥ 0.17, rs ≤ 0.27).

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