Effective connectivity reveals distinctive patterns in response to others' genuine affective experience of disgust as compared to pain

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Abstract

Empathy is significantly influenced by the identification of others' emotions. In a recent study, we have found increased activation in the anterior insular cortex (aIns) that could be attributed to affect sharing rather than perceptual saliency, when seeing another person genuinely experiencing pain as opposed to merely acting to be in pain. In that prior study, effective connectivity between aIns and the right supramarginal gyrus (rSMG) was revealed to track what another person really feels. In the present study, we used a similar paradigm to investigate the corresponding neural signatures in the domain of empathy for disgust - with participants seeing others genuinely sniffing unpleasant odors as compared to pretending to smell something disgusting. Consistent with the previous findings on pain, we found stronger activations in aIns associated with affect sharing for genuine disgust compared with pretended disgust. However, instead of rSMG we found engagement of the olfactory cortex. Using dynamic causal modeling (DCM), we estimated the neural dynamics of aIns and the olfactory cortex between the genuine and pretended conditions. This revealed an increased excitatory modulatory effect for genuine disgust compared to pretended disgust. For genuine disgust only, brain-to-behavior regression analyses highlighted a link between the observed modulatory effect and the perspective-taking empathic trait. Altogether, the current findings complement and expand our previous work, by showing that perceptual saliency alone does not explain responses in the insular cortex. Moreover, it reveals that different brain networks are implicated in a modality-specific way when sharing the affective experiences associated with pain vs. disgust.

Keywords

empathy; emotion; recognition; insular cortex

Introduction

Our affective states are remarkably affected by the perceived feelings of others. A theoretical framework of empathy proposed by Coll et al. (2017) states that identification of another's emotion crucially contributes to the consequential sharing of feelings with that person. A recent study by our group has revealed that when individuals witness another person genuinely experiencing pain as compared to merely acting to be in pain, they attribute more painful feelings to that person and report experiencing stronger self-unpleasantness in response to the other's genuine pain (Zhao et al., 2021b).

On the neural level, that study found increased brain activations for the genuine compared to the pretended pain in the anterior insular cortex (aIns) and the anterior mid-cingulate cortex (aMCC), i.e., a network that has been consistently associated with affective responding in studies on self-experienced pain as well as empathy for pain (Lamm et al., 2011; Rütgen et al., 2015; Jauniaux et al., 2019; Xiong et al., 2019; Feng Zhou et al., 2020; Fallon et al., 2020, for meta-analyses). One major contribution of our previous study is that we have shown aIns, a key node of this neural network, is indeed associated with affect sharing, rather than being driven by the perceptual saliency of the facial expressions of pain. Moreover, by means of dynamic causal modeling (DCM) analyses, distinctive effective connectivity of genuine pain vs. pretended pain has been found on the connection between aIns and the right supramarginal gyrus (rSMG), a region selectively related to affective self-other distinction, in the sense that it is distinct from a more posterior part centering more on the angular gyrus, the temporo-parietal junction, that is implicated in self-other distinction in the cognitive domain (Silani et al., 2013; Steinbeis et al., 2015; Hoffmann et al., 2016; Bukowski et al., 2020). This suggests that the interaction of aIns and rSMG tracks how we identify and share the actual feelings of another person, allowing an observer to engage in appropriate affect sharing rather than simply responding to salient, yet possibly non-genuine displays of pain.

What remains an open question is whether these findings are specific to pain or could be extended to other aversive experiences. Among the array of aversive experiences, the emotion of disgust partially overlaps with pain regarding its neural mechanisms (Corradi-Dell'Acqua et al., 2016). Also, disgust and pain share similarities with respect to their facial expression (Zhao et al., 2021a) and are similarly important for survival and somatic protection (Sharvit et al., 2015; Sharvit et al., 2020). Particularly, research using multi-voxel pattern analysis (MVPA) shows overlapping brain maps in aIns and aMCC not only for self-experienced but also vicarious experiences of pain and disgust, suggesting a modality-independent representation of the unpleasantness shared by self-experienced aversive affect and empathy for such affect (Corradi-Dell'Acqua et al., 2016).

The aim of the present study was, thus, to replicate and expand the findings of our previous study on pain (Zhao et al., 2021b), but targeting the emotion of disgust. Specifically, participants watched video clips either presenting a person showing a disgust expression when sniffing something unpleasant, or merely displaying a disgust expression without genuinely smelling any unpleasant odor. We expected to find that 1) on the behavioral level, genuine disgust would result in higher other-oriented disgust ratings and self-oriented unpleasantness ratings; 2) on the neural level, aIns, aMCC, and rSMG would show stronger responses to the genuine disgust, as compared to pretended disgust; and 3) distinct patterns of aIns' effective connectivity with rSMG would be found, and explain the different empathic responses to genuine vs. pretended disgust in a similar way as for pain.

Materials and Methods

To maximize comparability, data collection for the current study had been planned and performed together with the study focusing on pain (Zhao et al., 2021b). Thus, all procedures of both studies (i.e., creation and validation of stimuli, the pilot study, and the main fMRI experiment) were exactly conducted in the same sessions and with the identical participant sample. We decided to analyze

91 and report them separately for reasons of reporting complexity and as the two reports have a
92 different focus. While the details about all procedures are fully documented in (Zhao et al., 2021b),
93 for reasons of enhancing accessibility and reproducibility, we summarize the main points relevant to
94 the current study herein.

95 **Participants**

96 Forty-eight participants participated in this study. This sample size was estimated a priori using
97 Gpower 3.1 (Faul et al., 2007), for which a minimum sample size statistically required for this study
98 was 34 with a medium effect size of Cohen's d = 0.5 (α = 0.05, two-tailed, 1−β = 0.80). Three
99 participants (only for the current study) were excluded because of excessive head motion (> 15%
100 scans with the frame-wise displacement over 0.5 mm in one session; same criteria as the pain study).
101 Data of the remaining 45 participants (21 females; age: Mean = 26.76 years, S.D. = 4.58) were
102 entered into analyses. Participants had normal or corrected to normal vision and were pre-screened
103 by an MRI safety-check questionnaire to assure no presence or history of neurologic, psychiatric, or
104 major medical disorders. All participants reported being right-handed and signed the informed
105 consent. The study was approved by the ethics committee of the Medical University of Vienna and
106 was conducted in accordance with the latest revision of the Declaration of Helsinki (2013).

107 **Manipulation of facial expressions**

108 We created the stimuli for disgust with the same demonstrators who had also performed for the
109 pain stimuli. In strict analogy to the stimuli we created for pain, the stimuli we created for this study
110 consisted of video clips showing demonstrators ostensibly in four different situations: 1) Genuine
111 disgust: the demonstrator sniffed dog feces in an *opened* bottle with a picture depicting dog feces on
112 it; the demonstrator's facial expression changed from neutral to strongly disgusted. 2) Genuine no
113 disgust: the demonstrator sniffed cotton balls in an opened bottle with a picture depicting cotton
114 balls on it; the demonstrator's facial expression maintained neutral. 3) Pretended disgust: the
115 demonstrator sniffed dog feces in a *closed* bottle (covered by a cap) with a picture depicting dog

feces on it; the demonstrator's facial expression changed from neutral to strongly disgusted. 4) Pretended no disgust: the demonstrator sniffed cotton balls in an opened bottle with a picture depicting cotton balls on it; the demonstrator's facial expression maintained neutral. In fact, the genuine no disgust condition and pretended no disgust condition contained identical videos. We randomly labeled 50% of neutral videos as "genuine no disgust" when the same demonstrators appeared in the genuine disgust condition, and treated the other 50% neutral videos as "pretended no disgust" when the same demonstrators presented in the pretended disgust condition.

Twenty demonstrators (10 females), with experience in acting, were recruited for creating the stimuli of the current study. Each demonstrator signed the agreement of using their videos clips and static images for scientific purposes. An experimenter who stood on the right side of the demonstrators, of whom only the right hand holding the bottle could be seen, moved the bottle from the demonstrator's right side and stopped it just below the demonstrator's nose. Unbeknownst to the participants, all disgusted expressions were acted and the so-called "dog feces" were actually an odor-neutral object that resembled dog feces. As soon as the bottle was close enough to the demonstrator's nose (just below the right nostril), the demonstrator started to make a disgusted facial expression along with a slightly avoidant movement of their head, as naturally and vividly as possible. In the neutral control conditions, demonstrators maintained a neutral facial expression during the whole process of the bottle movement. Note that, the reason for presenting the pictures and supposed content of dog feces in both disgust conditions was because we deemed it essential to match the conditions in terms of the presence and visibility of an aversive disgusting object approaching the other person's face. Otherwise, any difference between conditions could be confounded by responses of participants to the presence vs. absence of a disgusting object and its explicit photographic display. Note that the pain condition of our previous work also followed this logic, with a needle covered by a plastic cap approaching the cheek.

Stimulus validation and pilot study

To validate the stimuli, 110 participants (59 females; age: Mean = 29.32 years, S.D. =10.17) were recruited and asked to rate a total of 120 video clips of 2 s duration of the two conditions (60 of each condition) showing disgusted facial expressions (i.e., the genuine and pretended disgust conditions). The main aim of the validation study was to identify a set of demonstrators that expressed disgust with comparable intensity and quality, and whose expressions of disgust in the genuine and pretended conditions were comparable. After each video clip, participants rated three questions on a visual analog scale with 9 tick-marks and the two end-points marked as "almost not at all" to "unbearable": 1) How much disgust did the person *express* on his/her face? 2) How much disgust did the person *actually feel*? 3) How unpleasant *did you feel* to watch the person in this situation? These questions were presented in a pseudo-randomized order. Moreover, we set eight catch trials to test whether participants maintained attention to the stimuli, in which participants were required to correctly choose the demonstrator they had seen in the last video, from two static images showing either the correct demonstrator's or a distractor's neutral facial expression side by side.

Data collection was performed with the online survey platform SoSci Survey (https://www.soscisurvey.de), and participants got access to the survey through a participation invite published on Amazon Mechanical Turk (https://www.mturk.com/). Survey data of 62 out of 110 participants (34 females; age: Mean = 28.71 years, S.D. =10.11) were entered into the analysis (inclusion criteria: false rate for the test questions < 2/8, survey duration > 20 min and < 150 min, and the maximum number of continuous identical ratings < 5). According to the validation analysis, videos of 6 demonstrators (3 females) were excluded for which participants showed a significant difference in perceived disgust expressions in others between genuine disgust and pretended disgust. As a result of this validation, videos of 14 demonstrators (7 females) were selected for the subsequent pilot study.

In the pilot study, a separate group (N =47, 24 females; age: Mean = 26.28 years, S.D. = 8.80) were recruited for a behavioral experiment in the behavioral laboratory. All conditions including the

neutral conditions described above were presented to the participants to test the feasibility of the procedures that we intended to use in the following fMRI experiment. Participants were explicitly instructed that they would watch some persons' genuine expressions of disgust in some blocks, while in other blocks, they would see some other persons acting out disgust expressions (recall that in reality, all demonstrators had been actors). All demonstrators showed neutral expressions as well. The three questions mentioned above were required to be rated. According to the video screening, we excluded videos of two demonstrators (1 female) for whom participants showed a large difference in ratings of *expression* of disgust between pretended vs. genuine conditions. Three separate repeated-measures ANOVAs were respectively performed for the three rating questions regarding the remaining videos. For the disgusted expressions in others, the main effect of genuineness (genuine vs. pretended) was not significant and was low in effect size ($F_{genuineness}$ (1, 46) = 0.867, p = 0.357, η^2 = 0.018), but it was significant and showed high effect size for the disgusted feelings in others ($F_{genuineness}$ (1, 46) = 207.225, p < 0.001, η^2 = 0.818) as well as for the unpleasantness in self ($F_{genuineness}$ (1, 46) =21.360, p < 0.001, η^2 = 0.317). The main effects of disgust (disgust vs. no disgust) for all three ratings were significant with high effect size (the smallest effect size was for the rating of unpleasantness in self, $F_{disgust}$ (1, 46) = 44.489, p < 0.001, η^2 = 0.492). The findings of our pilot study for the domain of disgust were thus very much in line with the findings of the same pilot study for the domain of pain (see Zhao et al., 2021b). Finally, video clips of 12 demonstrators (6 females) were determined for the main fMRI experiment.

Experimental design and procedures of the fMRI study

The experimental design and procedures are sketched in Figure 1A and 1B. The fMRI experiment was performed in two runs, and each run consisted of two blocks showing genuine disgust and two blocks showing pretended disgust. The order of genuine ("G") blocks and pretended ("P") blocks was pseudo-randomized across participants; specifically, the block order was "G G P G P G P P" for one half of the participants and "P P G P G P G G" for the other half. In each block, participants watched

191 nine video clips containing both disgusted and neutral videos. The order of disgusted videos and
192 neutral videos was pseudo-randomized. Additionally, the order of disgust sessions and pain sessions
193 (with the latter being reported in Zhao et al., 2021b), was counterbalanced across participants.

194 After the scanner session, participants came on another day to complete three questionnaires in the
195 lab: the Empathy Components Questionnaire (ECQ), the Interpersonal Reactivity Index (IRI), and the
196 Toronto Alexithymia Scale (TAS). The ECQ is categorized into Five subscales with 27 items (i.e.,
197 cognitive ability, cognitive drive, affective ability, affective drive, and affective reactivity), using a 4-
198 point Likert scale ranging from 1 ("strongly disagree") to 4 ("strongly agree") (Batchelder, 2015;
199 Batchelder et al., 2017). The IRI is divided into four subscales with 28 items (i.e., perspective taking,
200 fantasy, empathic concern, and personal distress), using a 5-point Likert scale ranging from 0 ("does
201 not describe me well") to 4 ("describes me very well") (Davis, 1980). The TAS is composed of three
202 subscales with 20 items (i.e., difficulty describing feelings, difficulty identifying feelings, and
203 externally oriented thinking), using a 5-point Likert scale ranging from 1 ("strongly disagree") to 5
204 ("strongly agree") (Bagby et al., 1994). Participants were debriefed at the end of the whole study.

205 **Behavioral data analysis**

206 Repeated-measures ANOVAs were run in SPSS (version 26.0; IBM) to investigate the main effects
207 and the interaction of the two factors genuine vs. pretended and disgust vs. no disgust. Furthermore,
208 we conducted Pearson correlations to examine whether ratings of disgust feelings in others were
209 correlated with unpleasantness in self for the genuine disgust and the pretended disgust. The
210 comparison of the correlation coefficients was performed using a bootstrap approach with the R
211 package bootcorci (https://github.com/GRousselet/bootcorci).

212 **fMRI data acquisition**

213 We used a Siemens Magnetom Skyra 3T MRI scanner (Siemens, Erlangen, Germany) with a 32-
214 channel head coil to collect fMRI data. A multiband-accelerated T2*-weighted echoplanar imaging

215 (EPI) sequence was applied to collect functional whole-brain scans (TR = 1200 ms, TE = 34 ms,
216 acquisition matrix = 96 × 96 voxels, FOV = 210 × 210 mm^2, flip angle = 66°, inter-slice gap = 0.4 mm,
217 voxel size = 2.2 × 2.2 × 2 mm^3, multiband acceleration factor = 4, interleaved ascending acquisition in
218 multi-slice mode, 52 slices co-planar to the connecting line between anterior and posterior
219 commissure). Each of the two functional imaging runs lasted around 16 min (~800 images per run). A
220 magnetization-prepared rapid gradient-echo (MPRAGE) sequence was implemented to acquire
221 structural images (TE/TR = 2.43/2300 ms, FOV= 240 × 240 mm^2, flip angle = 8°, voxel size =
222 0.8×0.8×0.8 mm^3, slice thickness = 0.8 mm, ascending acquisition, 208 sagittal slices, single-shot
223 multi-slice mode).

224 **fMRI data processing and mass-univariate functional segregation analyses**

225 Imaging data preprocessing was performed with a combination of Nipype (Gorgolewski et al., 2011)
226 and MATLAB (version R2018b 9.5.0; MathWorks) with Statistical Parametric Mapping (SPM12;
227 https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). Raw data were arranged into BIDS format
228 (http://bids.neuroimaging.io/; Gorgolewski et al., 2016). Functional data were 1) slice time corrected
229 to the middle slice (Sladky et al., 2011), 2) realigned to the first image of each session, 3) co-
230 registered to the T1 image, 4) segmented between grey matter, white matter, and cerebrospinal
231 fluid (CSF), 5) normalized to MNI template space using Diffeomorphic Anatomical Registration
232 Through Exponentiated Lie Algebra (DARTEL) toolbox (Ashburner, 2007), and 6) smoothed using a 6
233 mm full width at half-maximum (FWHM) of the Gaussian kernel. To improve data quality, scrubbing
234 was performed when the frame-wise displacement (FD) of a scan was larger than 0.5 mm (Power et
235 al., 2012; Power et al., 2014).

236 In order to perform mass-univariate functional segregation analyses, we created a first-level GLM
237 design matrix composed of two identically modeled runs for each participant. Seven regressors of
238 interest were entered in each model: stimulation phase of the four conditions (i.e., genuine disgust,
239 genuine no disgust, pretended disgust, pretended no disgust; 2000 ms), rating phase of the three

240 questions (i.e., disgusted expressions in others, disgusted feelings in others, and unpleasantness in
241 self; 12000 ms). Six head motion parameters and the scrubbing regressors (FD > 0.5 mm; if
242 applicable) were additionally entered as nuisance regressors.

243 On the second level, we used a flexible factorial design for the group-level analysis. Three factors
244 were included: a between-subject factor (i.e., subject) that was specified independent and with
245 equal variance, a within-subject factor (i.e., genuine or pretended) that was specified dependent and
246 with equal variance, and a second within-subject factor (i.e., disgust or no disgust) that was specified
247 dependent and with equal variance were included in the design (Gläscher & Gitelman, 2008). Four
248 contrasts were computed: 1) genuine: disgust – no disgust, 2) pretended: disgust – no disgust, 3)
249 genuine disgust – pretended disgust, and 4) genuine (disgust – no disgust) – pretended (disgust – no
250 disgust).

251 An initial threshold of $p < 0.001$ (uncorrected) at the voxel level and a family-wise error (FWE)
252 correction ($p < 0.05$) at the cluster level were applied. The cluster extent threshold was determined
253 by the SPM extension "cp_cluster_Pthresh.m" (https://goo.gl/kjVydz).

254 **Brain-behavior relationships**

255 We built a multiple regression model on the group level to investigate the relationship between
256 specific brain activations and behavioral ratings. In this model, the contrast genuine disgust –
257 pretended disgust was set as the dependent variable, and differences between conditions for three
258 behavioral ratings were specified as independent variables. The reason that we entered the
259 condition differences for both brain signals and behavioral ratings into the analyses was to control
260 for the potential effects of perceptual salience. Moreover, we used the contrast genuine disgust –
261 pretended disgust instead of the more exhaustive contrast genuine (disgust – no disgust) –
262 pretended (disgust – no disgust), because our aim was to focus on the genuine and pretended
263 disgust conditions rather than the neutral conditions. In addition, the disgust contrast showed more
264 robust (in terms of statistical effect size) and widespread activations across the brain, making it more

265 likely to pick up possible brain-behavior relationships. The same threshold as above (i.e., cluster-wise
266 FWE correction, $p < 0.05$) was applied in this analysis. All covariates were mean-centered. An
267 intercept was added to the model.

268 **Analyses using dynamic causal modeling (DCM)**

269 We considered the following regions of interest (ROI) for the DCM model space: the right aIns and
270 rSMG according to the previous study of pain (Zhao et al., 2021b) and the left (primary) olfactory
271 cortex according to the exploratory analyses. As for the latter, the results showed no evidence that
272 effective connectivity between aIns and rSMG for genuine disgust vs. pretended disgust was distinct.
273 Therefore, we extended the analysis to the primary olfactory cortex, which was not hypothesized
274 when planning this study but highly plausible given the employed task and the specific link between
275 olfaction and disgust. In fact, previous studies indeed demonstrated the olfactory cortex was not
276 only engaged in perceptual processes (e.g., odor perception and recognition), but also in affective
277 processing of disgust-related experiences (Gottfried et al., 2002; Zelano et al., 2011; Alessandrini et
278 al., 2016; Schulze et al., 2017; Schienle et al., 2020). We additionally defined an ROI of the right
279 olfactory cortex as a comparison to the left olfactory cortex. The ROI masks were defined as the
280 anatomical masks created by the Wake Forest University (WFU) Pick Atlas SPM toolbox
281 (http://fmri.wfubmc.edu) with the automated anatomical atlas (AAL). Note that the olfactory cortex
282 mask defined in AAL largely overlaps with the primary olfactory cortex that we were interested in
283 (Desikan et al., 2006).

284 Three DCM analyses were performed based on different considerations. Firstly, to investigate if the
285 distinct effective connectivity between aIns and rSMG we have found between genuine pain and
286 pretend pain could be observed in disgust as well, we performed a DCM analysis between the right
287 aIns and rSMG under the manipulation of genuine disgust and pretended disgust. Secondly, to
288 explore if other brain patterns could dissociate genuine disgust and pretended disgust, we
289 performed a second DCM analysis between the right aIns and the left olfactory cortex. Finally, to test

290 the robustness of the second DCM model, we performed a third DCM analysis between the right
291 aIns and the right olfactory cortex.

292 All DCM analyses were performed with DCM12.5 implemented in SPM12 (v. 7771). As a first step,
293 individual time series were extracted separately for each ROI. The voxels were determined both on a
294 group-level and an individual-level threshold to ensure the selected voxel were indeed engaged in a
295 task-relevant activity instead of random signal fluctuations (Holmes et al., 2020). The initial
296 threshold was set as $p < 0.05$, uncorrected. The significant voxels in the main effect of genuine
297 disgust and pretended disgust were further selected by an individual threshold. An individual peak
298 coordinate within the ROI mask was searched for each participant and an individual mask was
299 consequently defined using a sphere of the 6 mm radius around the peak. The individual time series
300 for each ROI was subsequently extracted from the significant voxels of the individual mask and
301 summarized by the first eigenvariate. For the second and third DCM analyses, seven participants
302 were excluded as no voxels survived significance testing in either the left or right olfactory cortex. In
303 the next step, three regressors of interest were specified: genuine disgust, pretended disgust, and
304 the video input condition (the combination of genuine disgust and pretended disgust). The reasons
305 for not specifying the no-disgust conditions were that 1) disgust conditions were our main focus, and
306 2) adding effects of non-interest would inevitably increase the model complexity. In DCM, three sets
307 of parameters were estimated: bidirectional connections between the regions and their self-
308 connections (matrix A), modulatory effects (i.e., genuine disgust and pretended disgust) on the
309 between-region connections (matrix B), and driving inputs (i.e., the video input condition) on both
310 regions (matrix C) (Zeidman et al., 2019a). Finally, we performed group-level DCM inference using
311 parametric empirical Bayes (Zeidman et al., 2019b). An automatic search was conducted over the
312 entire model space (max. n =256) using Bayesian model reduction (BMR) and random-effects
313 Bayesian model averaging (BMA), resulting in a final group model that takes accuracy, complexity,
314 and uncertainty into account (Zeidman et al., 2019b). This procedure was similarly performed for all
315 three DCM analyses. We reported all parameters with positive evidence on the posterior probability

316 (*pp* > 0.75). Finally, modulatory effects of the genuine and pretended disgust conditions were
317 compared using a paired sample t-test for each group-averaged model.

318 To probe whether task-related modulatory effects were associated with behavioral measurements,
319 we performed multiple linear regression analyses of modulatory parameters with, 1) the three
320 behavioral ratings, and 2) the empathy-related questionnaires (i.e., IRI, ECQ, and TAS). We set up
321 two regression models for the genuine and pretended disgust conditions, respectively, in which the
322 DCM parameters of modulatory effects were determined as dependent variables and the three
323 ratings as independent variables. Considering that interactions between behavioral ratings might
324 contribute to the regression model, five regression models (with and without interaction) were
325 tested for both conditions. Results (Supplementary Table 1) showed the model without any
326 interaction outperformed the other models for both genuine disgust and pretended disgust. We
327 thus reported the results of the winning multiple regression model in the results section. We
328 performed two additional regression models for both conditions in which DCM modulatory effects
329 were set as dependent variables and scores of each questionnaire subscale were set as independent
330 variables, respectively. Given the number of independent variables was considerable (>10), we used
331 a stepwise regression approach to perform the analyses for questionnaires. As two participants did
332 not complete all three questionnaires, we excluded their data from the regression analyses. The
333 statistical significance of the regression analysis was set to $p < 0.05$. The multicollinearity for
334 independent variables was diagnosed using the variance inflation factor (VIF) that measures the
335 correlation among independent variables, in the R package car (https://cran.r-
336 project.org/web/packages/car/index.html). Here a rather conservative threshold of *VIF* < 5 was
337 adapted as an indication of no severe multicollinearity (Menard, 2002; James et al., 2013).

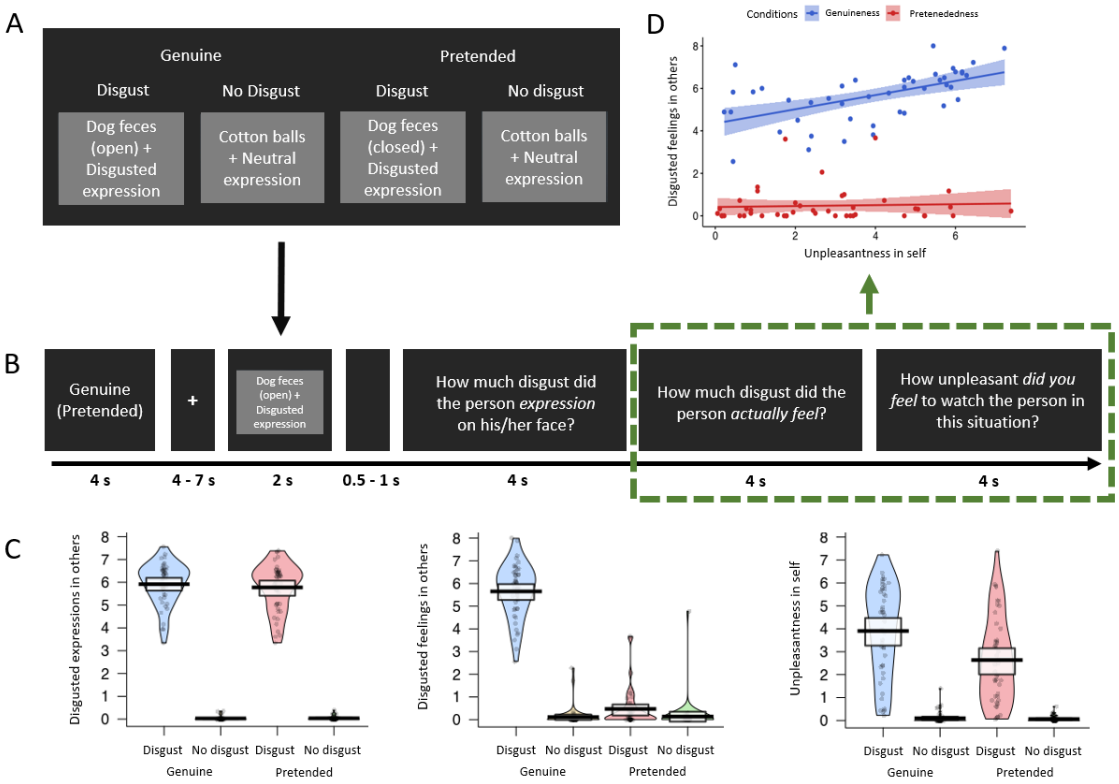
338

339 **Results**

340 **Behavioral results**

We performed three repeated-measures ANOVAs with the factors *genuineness* (genuine vs. pretended) and *disgust* (disgust vs. no disgust), for each of the three behavioral ratings. For ratings of disgusted *expressions* in others (Figure 1C, left), the main effect of the factor genuineness was not significant: $F_{genuineness}$ (1, 44) = 1.861, p = 0.179, η^2 = 0.041. There was a main effect of disgust: participants showed higher ratings for the disgust vs. no disgust conditions, $F_{disgust}$ (1, 44) = 1769.396, p < 0.001, η^2 = 0.976. The interaction term was not significant, $F_{interaction}$ (1, 44) = 2.270, p = 0.139, η^2 = 0.049. For ratings of disgusted feelings in others (Figure 1C, middle), there was a main effect of genuineness: participants showed higher ratings for the genuine vs. pretended conditions, $F_{genuineness}$ (1, 44) = 510.686, p < 0.001, η^2 = 0.921. There was also a main effect of disgust, as participants showed higher ratings for the disgust vs. no disgust conditions, $F_{disgust}$ (1, 44) = 854.136, p < 0.001, η^2 = 0.951. The interaction was significant as well, $F_{interaction}$ (1, 44) = 360.516, p < 0.001, η^2 = 0.891, and this was related to higher ratings of disgusted feelings in others for the genuine disgust compared to the pretended disgust condition. For ratings of unpleasantness in self (Figure 1C, right), there was a main effect of genuineness: participants showed higher ratings for the genuine vs. pretended conditions, $F_{genuineness}$ (1, 44) = 37.694, p < 0.001, η^2 = 0.461. There was also a main effect of disgust: participants showed higher ratings for the disgust vs. no disgust conditions, $F_{disgust}$ (1, 44) = 141.277, p < 0.001, η^2 = 0.763. The interaction was significant as well, $F_{interaction}$ (1, 44) = 32.341, p < 0.001, η^2 = 0.424, and this was related to higher ratings of unpleasantness in self for the genuine disgust compared to the pretended disgust condition. In sum, the behavioral data indicated that there was no difference in ratings of disgusted expression in others between the genuine and pretended disgust conditions, while higher ratings and large effect sizes of disgusted feelings in others and unpleasantness in self for the genuine disgust condition as compared to the pretended disgust condition. Moreover, results showed that participants rated expressions of disgust as more unpleasant than neutral expressions, regardless of whether they were genuine or not. These results were perfectly in line with our hypotheses and what we found in the pilot study.

366 We also found significant correlations between behavioral ratings of disgusted feelings in others and
367 unpleasantness in self for the genuine disgust condition, $r = 0.548$, $p < 0.001$; while for the
368 pretended disgust condition, the correlation was not significant, $r = 0.051$, $p = 0.740$ (Figure 1D). A
369 bootstrapping comparison showed a significant difference between the two correlation coefficients,
370 $p = 0.025$, 95% Confidence Interval (CI) = [0.073, 0.860].



371

372 **Figure 1. fMRI experimental design and behavioral results.** (A) Overview of the experimental design
373 with the four conditions genuine vs. pretended, disgust vs. no disgust. Examples show static images,
374 while in the experiment, participants were shown video clips. (B) Overview of experimental timeline.
375 At the outset of each block, a reminder of "genuine" or "pretended" was shown (both terms are
376 shown here for illustrative purposes, in the experiment either genuine or pretended was displayed).
377 After a fixation cross, a video in the corresponding condition appeared on the screen. Followed by a
378 short jitter, three questions about the video were separately presented and had to be rated on a
379 visual analog scale. These would then be followed by the next video clip and questions (not shown).
380 (C) Violin plots of the three types of ratings for all conditions. No difference was found for the rating
381 of disgusted expressions in others between the genuine disgust condition and the pretended disgust

condition. For the ratings of disgusted feelings in others and unpleasantness in self, participants demonstrated higher ratings for genuine disgust than pretended disgust. Ratings of all three questions were higher in the disgusted situation than in the neutral situation, regardless of whether in the genuine or pretended condition. The thick black lines illustrate mean values, and the white boxes indicate a 95% CI. The dots are individual data, and the "violin" outlines illustrate their estimated density at different points of the scale. (D) Correlations of disgusted feelings in others and unpleasantness in self for the genuine disgust and the pretended disgust (the relevant questions were highlighted with a green rectangle). Results revealed a significant Pearson correlation between the two questions for the genuine disgust condition, but no correlation in the pretended disgust condition. The lines represent the fitted regression lines, bands indicate a 95% CI.

fMRI results: mass-univariate analysis

We computed four contrasts: 1) genuine: disgust – no disgust, 2) pretended: disgust – no disgust, 3) genuine disgust – pretended disgust, and 4) genuine (disgust – no disgust) – pretended (disgust – no disgust). In the first two contrasts, we found the predicted activations in bilateral aIns, aMCC, and rSMG, as well as significant (not originally predicted) activation in the olfactory cortex; in the third contrast, we found significant activation in the right aIns, as well as strong activation (k = 255) in the left olfactory cortex; in the last contrast, the only significant activation was found in the right cerebellum (Figure 2A and Table 1).

To identify whether or which brain activity was selectively related to the behavioral ratings described above, we performed a multiple regression analysis on the whole brain level where we explored the relationship of activation in the contrast genuine disgust – pretended disgust with the three behavioral ratings. The only significant cluster we found encompassed the right aIns, extending into the right inferior frontal gyrus, and this was selectively related to ratings of self-unpleasantness (Figure 2B) rather than the ratings of disgusted expressions in others or the disgusted feelings in others.

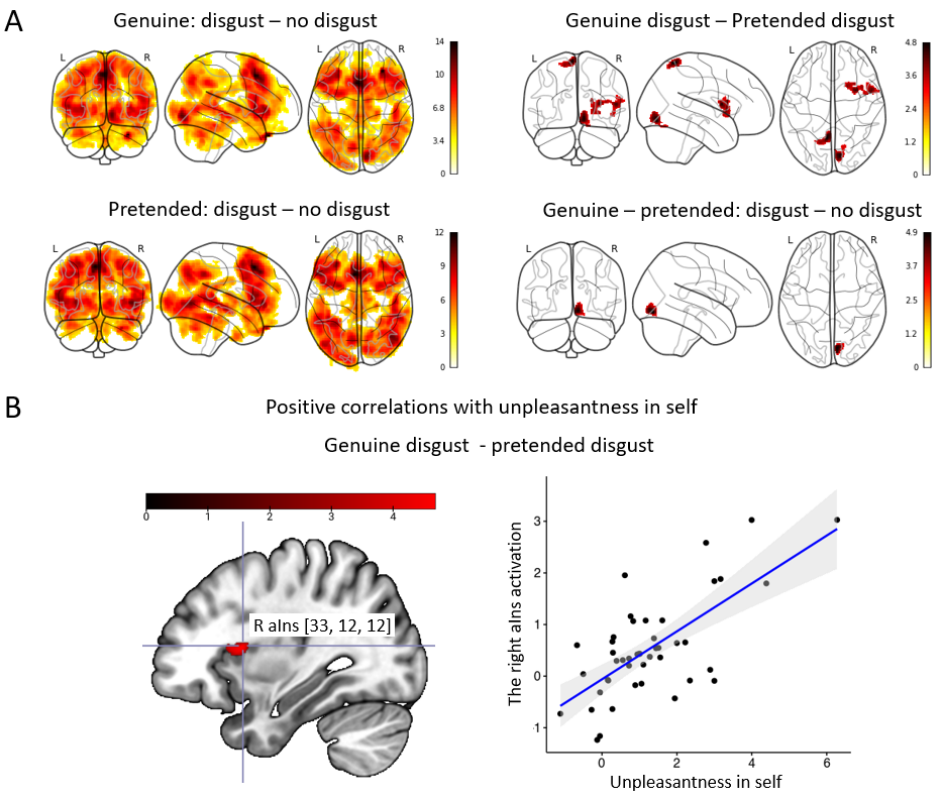


Figure 2. Neuroimaging results: Mass-univariate analyses. (A) Activation maps of genuine: disgust – no disgust (top left), pretended: disgust - no disgust (bottom left), genuine disgust – pretended disgust (top right), and genuine (disgust – no disgust) – pretended (disgust – no disgust) (bottom right). For contrasts of disgust –no disgust in both genuine and pretended conditions, we found expected brain activations in bilateral aIns, aMCC, and rSMG, and significant activation in the olfactory cortex; for the contrast of genuine disgust vs. pretended disgust, we found significant activation in the right aIns and strong activation in the left olfactory cortex (a cluster of k=255, though not pass the threshold); for the contrast of genuine (disgust – no disgust) vs. pretended (disgust – no disgust), the only significant activation was in the right cerebellum. (B) The multiple regression analysis demonstrated a significant cluster in the right aIns (peak: [33, 12, 12]) that was positively associated with the ratings of unpleasantness in self but not associated with the ratings of either disgusted expressions in others or disgusted feelings in others when comparing genuine disgust vs. pretended disgust. All activations are thresholded with cluster-level FWE correction, $p < 0.05$ ($p < 0.001$ uncorrected initial selection threshold). The lines of the scatterplots represent the fitted regression lines, bands indicate a 95% CI.

434 **Table 1.** Results of mass-univariate functional segregation analyses in the MNI space. Region names
435 were labeled with the AAL atlas and thresholded with cluster-wise FWE correction, $p < 0.05$ (initial
436 selection threshold $p < 0.001$, uncorrected). BA = Brodmann area, L = left hemisphere, R = right
437 hemisphere.

Region label	BA	Cluster size	*x*	*y*	*z*	*t*-value
1) Genuine: disgust - no disgust						
Temporal_Pole_Sup_R	38	164988	32	33	-33	13.57
Supp_Motor_Area_L	8		-3	16	50	13.31
Lingual_R	18		9	-84	-6	11.89
Frontal_Sup_Medial_R	8		6	21	45	10.95
Insula_L	45		-32	27	4	10.81
Frontal_Inf_Oper_L	44		-50	15	6	10.80
Insula_R	13		33	27	4	10.17
Frontal_Inf_Tri_L	45		-30	32	0	10.12
Frontal_Inf_Oper_R	44		52	15	15	9.80
Frontal_Inf_Orb_R	47		32	32	-3	9.69
Lingual_L	17	422	-21	-66	4	5.10
2) Pretended: disgust - no disgust						
Supp_Motor_Area_L	8	137060	-4	16	50	11.95
Frontal_Sup_Medial_L	8		-8	26	44	10.69
Temporal_Mid_R	19		44	-68	2	10.35
Frontal_Inf_Oper_L	44		-51	16	6	10.01
Insula_L	45		-30	30	2	9.77
Frontal_Inf_Tri_L	45		-56	20	12	9.68
Cingulum_Mid_R	8		8	20	45	9.47
Parietal_Inf_L	39		-32	-51	40	9.37
Temporal_Pole_Sup_R	38		32	34	-33	9.35
Frontal_Mid_L	6		-27	2	54	9.26
Cingulate_Post_L	23	1821	-4	-42	22	5.71
Cingulate_Mid_R	23		-3	-26	27	5.58
Cingulate_Post_R	23		8	-39	22	5.33
Cingulate_Mid_L	24		-3	-12	30	5.23
Vermis_9	37	522	2	-57	-39	5.27
Cerebelum_9_L	18		-2	-60	-46	4.55
Cerebelum_9_R	37		10	-57	-51	3.96
Temporal_Inf_L	20	517	-40	-9	-38	4.80
Temporal_Pole_Mid_L	38		-28	8	-39	3.62

Cerebelum_Crus2_L	18	487	-8	-76	-34	5.15
Cerebelum_Crus1_L	18		-18	-80	-27	3.21
3) Genuine disgust – pretended disgust						
Insula_R	44	976	32	8	12	4.56
Rolandic_Oper_R	44		54	8	10	4.38
Caudate_R	48		21	14	15	4.05
Putamen_R	49		30	16	-2	3.89
Frontal_Inf_Oper_R	44		40	12	14	3.85
Lingual_R	18	550	10	-81	-9	4.72
Cerebelum_6_R	18		15	-70	-18	3.35
Precuneus_L	7	474	-6	-56	69	4.85
Parietal_Sup_L	7		-16	-63	64	3.95
4) Genuine (disgust – no disgust) – pretended (disgust – no disgust)						
Lingual_R	18	431	8	-81	-10	4.90

DCM results

We first performed a DCM analysis of the effective connectivity between the right aIns and rSMG to examine if the group-averaged model replicated what we found in our previous study on pain (Zhao et al., 2021b). Specifically, we focused on the modulatory effect of genuineness, namely, whether the experimental manipulation of genuine disgust vs. pretended disgust tuned the bidirectional neural dynamics from aIns to rSMG and *vice versa*, in terms of both directionality (sign of the DCM posterior parameter) and intensity (magnitude of the DCM posterior parameter). If the experimental manipulation modulated the effective connectivity, we would observe a positive posterior probability ($p_p > 0.75$) of the modulatory effect. The reasons that we did not include aMCC in this analysis were that 1) unlike aIns, in aMCC we did not find strong evidence for the task involvement (in the univariate and multiple regression analyses), 2) for comparability of the present model with the previous model on pain, where aMCC had not been included either.

Similar to what we found in the pain study, strong evidence ($pp > 0.95$; $pp = 1.00$) of inhibitory modulatory effects on the aIns-to-rSMG connection was shown for both the genuine disgust condition and the pretended disgust condition (see Figure 3A). However, we did not find a significant

difference when comparing the strength of these two modulatory effects, t_{44} = -1.045, p = 0.302 (Mean $_{genuine\ disgust}$ = -1.214, 95% CI = [-1.462, -0.927]; Mean $_{pretended\ disgust}$ = -1.095, 95% CI = [-1.361, -0.799]. Note that the mean values in the test could slightly differ from those shown in the DCM models of Figure 3, since we used frequentist statistics for comparison analysis rather than the Bayesian approach that was implemented to compute the parameters for the DCM model. We did not find robust evidence on the intrinsic connectivity either from aIns to rSMG or *vice versa*. Moreover, there was no evidence of a modulatory effect on the rSMG to aIns connection, which was in line with what we had found for pain. Taken together, the DCM analysis between aIns and rSMG partially replicated the results of the pain study, namely the inhibitory modulatory effect from aIns to rSMG for both genuine and pretended conditions; however, this inhibitory modulatory effect failed to dissociate the experimental manipulation of genuine disgust and pretended disgust, suggesting that a distinctive pattern or set of brain regions underpins how the genuineness of disgust is processed.

We therefore performed an exploratory DCM analysis to test whether distinct modulatory effects could be found for genuine and pretend disgust on the connection between the right aIns and the left olfactory cortex (see Figure 3B). As mentioned in the methods sections, while the involvement of the left olfactory cortex was mainly exploratory and data-driven, it was also plausible on theoretical grounds. Results showed a significant excitatory effect for both genuine disgust (strong evidence, *pp* = 1.00) and pretended disgust (positive evidence, *pp* = 0.93) on the connection of the left olfactory cortex to the right aIns. A further comparison analysis on the modulatory effect between conditions revealed a stronger excitatory modulatory effect for genuine disgust as opposed to pretended disgust, t_{37} = 4.450, p < 0.001 (Mean $_{genuine\ disgust}$ = 0.805, 95% CI = [0.755, 0.851]; Mean $_{pretended\ disgust}$ = 0.573, 95% CI = [0.517, 0.628]. We did not find any modulatory effect on the reverse connection of the right aIns to the left olfactory cortex.

478 Finally, to justify whether lateralization of the olfactory cortex largely influenced the robustness of
479 the modulatory effect we found in the DCM model above, we performed an additional DCM analysis
480 on the connection between the right aIns and the right olfactory cortex (see Supplementary Figure
481 1). Results showed a similar group-average model to that of the right aIns and the left olfactory
482 cortex. Importantly, we replicated the excitatory modulatory effect on the connection of the
483 olfactory cortex to aIns in the sense of significant evidence for both conditions (genuine disgust:
484 positive evidence, *pp* = 0.91; pretended disgust: positive evidence, *pp* = 0.88). No evidence of the
485 modulatory effect on the connection of aIns to the right olfactory cortex was found, which was
486 consistent with the group-average model with the left olfactory cortex. A further comparison
487 analysis did not find significant difference on the strength of the two modulatory effects, $t_{37} = 0.595$,
488 $p = 0.556$ (Mean $_{\text{genuine disgust}} = 0.624$, 95% CI = [0.503, 0.738]; Mean $_{\text{pretended disgust}} = 0.577$, 95% CI =
489 [0.488, 0.678]).

490 **Individual associations between modulatory effects, behavioral ratings, and questionnaires**

491 Two linear regression models were computed to examine how the excitatory modulatory effect on
492 the connection of the (left) olfactory cortex to aIns was related to behavioral ratings respectively for
493 genuine disgust and pretended disgust. Results showed that none of the ratings was significant for
494 either the genuine disgust model or the pretended disgust model. No severe collinearity problem
495 was detected for either regression model (all *VIFs* < 4.500; the smallest *VIF* =1.229 and the largest
496 *VIF* = 4.410).

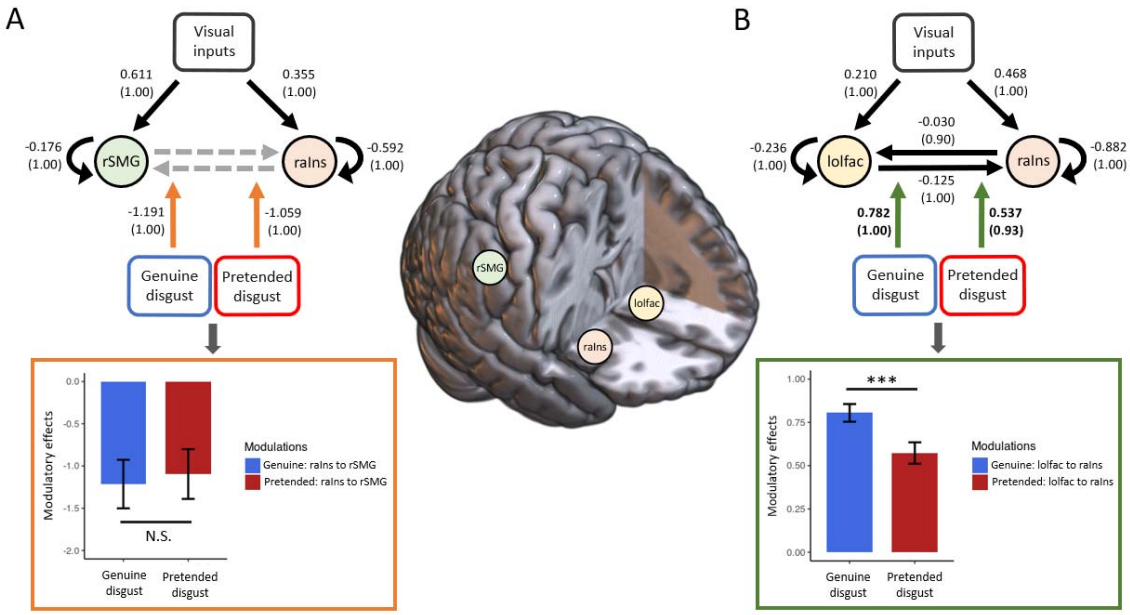
497 Another two linear regression models were tested to investigate whether subscales of all three
498 questionnaires could explain the excitatory modulatory effect for genuine disgust and pretended
499 disgust. For the genuine disgust condition, we found that the modulatory effect was significantly
500 explained by scores of the perspective-taking subscale of the IRI: $F_{\text{model}}(1, 35) = 4.177$, $p = 0.049$, $R^2 =$
501 0.109; $B = 0.011$, *beta* = 0.331, $p = 0.049$. No significant predictor was found with any subscale in the
502 other two questionnaires (i.e., ECQ and TAS). None of the three questionnaires significantly

503 explained variations of the modulatory effect for the pretended disgust condition. No severe

504 collinearity problem was detected for either regression model (all *VIFs* < 2.500; the smallest *VIF*

505 =1.000 and the largest *VIF* = 2.198).

506



507 **Figure 3. DCM results and brain-behavior analyses.** Three-dimensional visualization of ROIs involved

508 in the two DCM analyses is shown in the upper middle. (A) The group-average DCM model of the

509 right anterior insula and the right supramarginal gyrus (rSMG) for genuine disgust and pretended

510 disgust. We found inhibitory modulatory effects (orange arrows) for both conditions. All DCM

511 parameters of the optimal model showed greater than a 99% posterior probability (very strong

512 evidence) except the bi-directionally intrinsic connectivity between the right aIns (raIns) and rSMG

513 (grey dashed arrow; no evidence of existence, *pp* < 0.50). Paired sample *t*-test showed no difference

514 in the inhibitory modulatory effects on the raIns-to-rSMG connection between genuine disgust and

515 pretended disgust. This result is highlighted with an orange rectangle. Data are mean ± 95% CI. (B)

516 The group-average DCM model of the raIns and the left olfactory cortex (lolfac) for genuine disgust

517 and pretended disgust. We found the excitatory modulatory effect (green arrows) for both

518 conditions. All DCM parameters of the optimal model showed greater than or equal to a 90%

519 posterior probability (*pp* > 0.75, positive evidence). Paired sample *t*-test showed a stronger

520 excitatory modulatory effect of the lolfac-to-raIns connection for genuine disgust as compared to

521 pretended disgust (*** *p* < 0.001). This result is highlighted with a green rectangle. Data are mean ±

522 95% CI. For the DCM models, values without the bracket quantify the strength of connections;

523 positive values indicate neural excitation and negative values indicate neural excitation. Values in
524 the parentheses indicate the posterior probability of connections.
525

526 **Discussion**

527 Using a paradigm matched to our previously published study on pain (Zhao et al., 2021b), and in the
528 same sample and experimental session, we here report how participants responded to video clips
529 presenting people who supposedly either genuinely experienced disgust or merely pretended to feel
530 disgusted. Combining mass-univariate analysis with effective connectivity (DCM) analyses, we aimed
531 to clarify two main questions: 1) whether neural responses in areas such as aIns and aMCC to the
532 disgust of others were indeed related to a veridical sharing of affect, as opposed to simply tracking
533 sensory-driven responses to salient affective displays, and 2) whether the effective connectivity
534 between aIns and rSMG that we previously found to disentangle genuine pain from pretended pain
535 also enabled the dissociation of genuine disgust vs. pretended disgust.

536 We found increased activations in the right aIns for genuine disgust as compared to pretended
537 disgust that was selectively associated with the unpleasantness in self. These findings are in line with
538 what we have found in pain (Zhao et al., 2021b), implying an essential role of aIns in the processing
539 of shared feelings with others for both pain and disgust. However, an intriguing question is if the
540 aIns activation we observed in these two aversive states reflects a form of cross-modal affective
541 processing, or rather modality-dependent affective experiences? A study using multi-voxel pattern
542 analysis (MVPA) has shown both cross-modal and modality-specific evidence in terms of the
543 subfields of aIns for pain and disgust: in the left aIns (and aMCC), the shared encoding was detected
544 for first-hand and vicarious pain and disgust, regardless of the same or different modality; while in
545 the right aIns, sensory-specific rather than modality-independent patterns were more plausible for
546 processing first-hand and vicarious pain and disgust (Corradi-Dell'Acqua et al., 2016). Taken together,
547 the aIns activation we found suggests the engagement of affective processing that was related to

548 others' pain and disgust, while future research that explicitly matches pain and disgust salience is
549 required to further investigate whether this activation indicates cross-modal or modality-dependent
550 affective experiences.

551 We found significant inhibitory modulatory effects on the connection of aIns to rSMG for both
552 genuine and pretended disgust, but these effects did not differ significantly. This implies that we
553 only partially replicate the findings of the pain study: while we reproduce a role of the aIns and
554 rSMG connectivity, their crosstalk does not explain the distinction between genuine and pretended
555 expressions of disgust, as is the case for pain (Zhao et al., 2021b). We speculate that the absence of
556 differences between two conditions in rSMG activation as well as the inhibitory modulatory effect
557 could be related to generally lower salience of aversive experiences in the disgust task compared to
558 that of pain. Further investigation is required to test this assumption.

559 Contrary to our expectations, we did not find any significant activation in rSMG for genuine disgust
560 as compared to pretended disgust; instead, we showed a relatively stronger engagement of the
561 primary olfactory cortex between conditions. As we mentioned beforehand, we did not target the
562 latter area when planning the study but later included it inspired by the exploratory analysis. The
563 (primary) olfactory cortex has been considered to mainly comprise the anterior olfactory nucleus,
564 the olfactory tubercle, piriform cortices, and subregions of amygdala and entorhinal cortex (Savic et
565 al., 2000; Tzourio-Mazoyer et al., 2002; G. Zhou et al., 2019). Studies have found that this region is
566 recruited not only for direct olfactory sensations but also for the indirect experience of olfactory
567 processing, such as odor imagery (Djordjevic et al., 2005; Bensafi et al., 2007) and odor prediction
568 (Zelano et al., 2011). Olfactory priming could facilitate the identification of the emotion of disgust
569 (Seubert et al., 2010a; Seubert et al., 2010b); in turn, priming with a disgusted face compared to a
570 happy face enhanced activation in the olfactory cortex when processing pleasant odors (Schulze et
571 al., 2017). These findings imply the engagement of the olfactory cortex in integrating olfactory
572 processes with visually conveyed affective information. Furthermore, the primary olfactory cortex

573 has been suggested to participate in processing the emotion of disgust, without necessarily
574 experiencing sensory-related disgust. Compared with healthy controls, patients with reduced
575 olfactory function (e.g., anosmia and hyposmia) have been found to identify less disgust for facial
576 expressions of disgust and show greater activations in the primary olfactory cortex, suggestive of a
577 compensatory effect, for disgusting scenes (Schienle et al., 2020). Altogether, the stronger
578 engagement of the olfactory cortex might be related to a higher level of identified disgust in others
579 when individuals observed others genuinely experiencing disgust compared with pretending
580 disgusted.

581 The exploratory DCM analysis of the right aIns and the left olfactory cortex demonstrated a stronger
582 excitatory modulatory effect on the olfactory cortex to aIns connection for genuine disgust as
583 opposed to pretended disgust. Studies from nonhuman primates and humans using tractography
584 have shown structural connections (for human: functional connectivity as well, see Deen et al., 2010)
585 between the olfactory cortex and a partial region of aIns (Mufson & Mesulam, 1982; Carmichael et
586 al., 1994; Ghaziri et al., 2015; Ghaziri et al., 2018). Specifically, as an important part of the secondary
587 olfactory cortex, aIns is considered to engage in receiving and integrating the primary olfactory-
588 affective information conveyed by the primary olfactory cortex. Moreover, the external sensory and
589 affective messages seem to be already preprocessed in the primary olfactory cortex before they are
590 conveyed to the secondary cortices (Soudry et al., 2011, for review; Seubert et al., 2013, for meta-
591 analyses). Together with the evidence of higher brain activation in the right aIns and left olfactory
592 cortex for genuine disgust compared to pretended disgust, we speculate that the increased
593 excitatory modulatory effect on the olfactory-to-aIns connection may be related to the processing of
594 passing messages of higher disgust emotion identified in others to activations related to affect
595 processing, which may constitute the neural underpinning of the increased shared unpleasantness
596 with others. This idea would also be in line with the theoretical framework proposed by Coll et al.
597 (2017), that higher identified emotion in others contributes to stronger shared affect, and that the
598 fully-fledged empathic response may be an integrated consequence of (at least) these two processes.

599 We performed another DCM analysis between the right aIns and the right olfactory cortex to test
600 whether lateralization of the olfactory cortex had a large impact on the reliability of the modulatory
601 effect we detected in DCM model with the left olfactory cortex. Results showed a very similar
602 pattern to the DCM model with the left olfactory cortex, in the sense of replicating the excitatory
603 modulatory effect on the connection of the olfactory cortex to aIns for both conditions and absence
604 of any condition-dependent modulatory effect on the connection of the opposite direction. Even
605 though for this model we did not find a significant difference in the modulatory effects between
606 genuine disgust and pretended disgust, these results at least attest to the robustness of the
607 modulatory effect from the olfactory cortex, regardless of the left or right hemisphere, to the right
608 aIns.

609 We found the excitatory modulatory effect for genuine disgust was positively related to individual
610 perspective-taking scores. This finding demonstrated that the connection of the olfactory cortex to
611 aIns for genuine disgust was related to the tendency of adopting the psychological point of view of
612 others, which would finally contribute to the level of one's own affective responses to the emotion
613 felt by another person. This view is supported by the evidence that aIns, especially the right aIns, is
614 implicated in distinct neural patterns of representing self- and other-related aversive states for
615 disgust as well as pain (Corradi-Dell'Acqua et al., 2016). No association with any questionnaire was
616 found for pretended disgust. Taking all these results together, we would speculate that for the
617 genuine disgust condition, the olfactory cortex interacts with aIns to achieve genuine identification
618 of disgust in others. This would call for a higher demand to take the other's perspective, and in this
619 way may contribute to the higher shared affect. For the pretended pain condition, sensory-driven
620 ("automatic") emotion processing induced by the saliency of disgust expression interacts with the
621 cognitive processes (i.e., knowing this person was merely acting out and did not feel any disgust at
622 all), resulting in both a low level of identified disgust and shared affect. In this case, it may be less
623 important to recruit the function of perspective-taking to share the emotions of others. However,
624 further investigation is required to test these interpretations.

625 Note that, the aim of the current study, in relation to our previous work (Zhao et al., 2021b), was to
626 investigate similar but parallel research questions in two closely related yet distinct modalities (i.e.,
627 disgust and pain). In this, we abstained from a quantitative comparison within an analysis framework
628 that included data from both tasks for the following reasons. First, direct comparison would have
629 required the saliency of the stimuli in the two modalities to be identical. Yet in an exploratory
630 analysis, we found that the genuine pain always evoked higher ratings on all three behavioral
631 measurements and stronger activations in regions that we were interested in, i.e., aIns, aMCC, and
632 rSMG, as opposed to genuine disgust (results of this exploratory analysis are not reported in detail
633 here; public links to the behavioral and functional data for disgust and pain can be found in the data
634 availability statement and Zhao et al., 2021b). In this sense, any conclusion or inference drawn from
635 directly comparing these two modalities could arguably be attributed to the difference in stimuli
636 salience or the responses to that salience, rather than the essential emotional properties in pain and
637 disgust. Second, incorporating all data into one large analysis model would have resulted in a very
638 complex analysis approach, especially when considering the many different factors of our
639 experimental design, the regions we were interested in, and the behavioral data we wanted to
640 incorporate. While the rationale to analyze the tasks separately thus resulted in more robust
641 evidence regarding each task, one limitation of the current study is that comparison across and
642 replication across tasks allows insights into similarity and differences in principles and brain function
643 rather in a descriptive way. Future research should thus better match the saliency (Sharvit et al.,
644 2015), on both perceptual and affective levels, between pain and disgust to allow direct quantitative
645 comparisons across modalities, while also keeping in mind the complexity of the experimental
646 design.

647 In conclusion, the current study largely replicates, as well as expands our previously reported
648 findings on pain. Firstly, and similar to what we have shown for empathy for pain using the same
649 experimental approach and within the same study, we provide evidence that responses related to
650 empathy for disgust in aIns can indeed be linked to the affective sharing rather than merely

651 perceptual saliency. Secondly, we show how aIns and the olfactory cortex, instead of aIns and rSMG
652 that we previously found in pain, orchestrate the tracking of disgust felt by another person. Taken
653 together, these findings indicate that similar as well as distinct brain networks are engaged in
654 processing different affective experiences, in this case pain and disgust, experienced by others. This
655 refines and expands our understanding of the neural bases of empathy, from a dynamic and multi-
656 modal perspective.

657

658

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