

Predictive processing in depression: Increased prediction error following negative valence contexts and influence of recent mood-congruent yet irrelevant experiences

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ABSTRACT

Background: Novel theoretical models of depression have recently emerged based on an influential new perspective in neuroscience known as predictive processing. In these models, depression may be understood as an imbalance of predictive signals in the brain; more specifically, a dominance of predictions leading to a relative insensitivity to prediction error. Despite these important theoretical advances, empirical evidence remains limited, and how expectations are generated and used dynamically in individuals with depression remains largely unexplored.

Methods: In this study, we induced facial expression predictions using emotion contexts in 34 individuals with depression and 34 healthy controls.

Results: Compared to controls, individuals with depression perceived displayed facial expressions as less similar to their expectations (i.e., increased difference between expectations and actual sensory input) following contexts evoking negative valence emotions, indicating that depressed individuals have increased prediction error in such contexts. This effect was amplified by recent mood-congruent yet irrelevant experiences.

Limitations: The clinical sample included participants with comorbid psychopathology and taking medication. Additionally, the two groups were not evaluated in the same setting, and only three emotion categories (fear, sadness, and happiness) were explored.

Conclusions: Our results shed light on potential mechanisms underlying processing abnormalities regarding negative information, which has been consistently reported in depression, and may be a relevant point of departure for exploring transdiagnostic vulnerability to mental illness. Our data also has the potential to improve clinical practice through the implementation of novel diagnostic and therapeutic tools based on the assessment and modulation of predictive signals.

1. Introduction

In recent years, novel models of depression have been proposed using a relatively new approach to perception and action from the neurosciences known as predictive processing (Bar, 2009; Barrett et al., 2016;

Fabry, 2020; Kube et al., 2020; Paulus et al., 2019). According to predictive processing (see, e.g., Clark, 2013; Friston, 2005, 2010), the brain is not a passive stimulus-response organ but, rather, is active and constantly attempting to explain sensory input using an internal model of the world based on past experiences. Predictions about sensory input

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(exteroceptive and interoceptive) based on this internal model are issued and compared with actual sensory input. The difference between the two signals (predictions and incoming sensory input), which is called prediction error, is used to update the internal model to minimize future errors. Predictions and prediction error are balanced based on their ‘precision’, i.e., how reliable these different signals are, so that the most weight is given to the most reliable signal (for a recent primer on precision, see, [Yon and Frith, 2021](#); for discussions on the affective/interoceptive domains see [Barrett and Simmons, 2015](#); [Ferreira-Santos, 2016](#)). At the neural level, predictions and prediction errors have been proposed to flow hierarchically across cortical areas. More specifically, limbic cortices may issue high-level (highly abstract) predictions that cascade down the hierarchy to the rest of the cerebral cortex, becoming more specific as they reach lower-level (more specialized) cortical areas, such as sensory areas ([Chanes and Barrett, 2016](#)). Different brain-related conditions may be understood as specific disruptions of such hierarchical organization ([Chanes and Barrett, 2020](#)), which may contribute to a better understanding of cross-disorder vulnerability to illness.

Recent perspectives suggest that disturbances in interoceptive and exteroceptive predictive processing may be related to depressive symptomatology ([Barrett et al., 2016](#); [Clark et al., 2018](#); [Fabry, 2020](#); [Kube et al., 2019, 2020](#); [Paulus et al., 2019](#)). In the interoceptive domain, depressive symptoms have been proposed to emerge from individuals overly relying on priors (i.e., predictions) and being relatively insensitive to prediction error, resulting in inefficient energy regulation and an inability to update the internal model ([Barrett et al., 2016](#); [Paulus et al., 2019](#); [Seth and Friston, 2016](#)). It has also been proposed that such dominance of predictions and the tendency to disregard prediction errors may be particularly important for negatively-valenced expectations ([Kube et al., 2020](#)). Depression may lead to a dominance of negative priors about ongoing and future experiences, and a subjective feeling of confirmation resulting from ignoring opposite-valence (positive) information disconfirming them (prediction error) ([Kube et al., 2020](#)). Indeed, initial evidence at the behavioral level supports the hypothesis that predictive processing differs across individuals with depression and healthy controls. Deficits in implicit learning of predictive relationships ([Janacsek et al., 2018](#)) and impaired responses to feedback information in a gambling task ([Steele et al., 2007](#)) have been reported. Moreover, difficulties in abandoning negative expectations ([Kube et al., 2019](#)), and higher predictive pessimism and certainty about the future ([Andersen, 1990](#)) have also been observed. Along the same lines, individuals with depression have been shown to lack an optimistic bias in updating beliefs about future life events observed in healthy controls ([Korn et al., 2014](#)). Moreover, having inflexible negative interpretations of events, or failing to update initial negative interpretations of events when presented with disconfirming positive information, has also been shown to be associated with depression and anxiety symptom severity in a non-clinical sample ([Everaert et al., 2020](#)). Predictive processing disruptions at the neural level have also been reported in depression in the context of associative learning ([Gradin et al., 2011](#)), with a gambling task ([Steele et al., 2007](#)), as well as regarding the above-mentioned unbiased belief updating observed reported by [Korn et al. \(2014\)](#) ([Garrett et al., 2014](#)).

Over the past few decades, numerous studies have contributed to the characterization of sensory (interoceptive and exteroceptive), cognitive, and affective processing more generally in individuals diagnosed with depression, showing significant differences compared to healthy controls (for recent reviews, see, e.g., [Harshaw, 2015](#); [LeMoult and Gotlib, 2019](#)). One observation that has been consistently reported across studies is a bias toward negative stimuli. More specifically, depression has been associated with difficulties inhibiting and disengaging from negative stimuli in working memory ([Joormann, 2006](#)) as well as negative attentional ([Gotlib et al., 2004](#)) and long-term memory biases (see [Gaddy and Ingram, 2014](#); [LeMoult and Gotlib, 2019](#) for a review). Within the domain of social cognition, facial affect processing, key to social development and functioning, is particularly relevant to models of

depression, and research suggests that individuals with depression show differences in facial affect interpretation, attention, and memory compared to controls (for a review, see, [Bistricky et al., 2011](#)). Evidence of a negative attentional bias in individuals with depression has been reported consistently when faces are used as stimuli, suggesting a reduced orientation to positive stimuli (see [Armstrong and Olatunji, 2012](#), for a review). Similarly, even beyond facial expressions, negative bias has been widely observed in individuals with depression regarding perception of social information, most notably in the perception of body language and emotion expressed vocally ([Kupferberg et al., 2016](#)). These features may reflect underlying differences in predictive processing of emotion expressions or social information for individuals with depression vs. healthy individuals.

Despite initial studies on predictive coding and depression, how individuals with depression generate and use their expectations as well as recent experience dynamically, particularly in the domain of social perception, remains largely unexplored and requires novel designs. In the present study, we explored predictive processing at the behavioral level in individuals with depression and healthy controls using emotion contexts. We induced predictions about facial expressions dynamically across trials, which we were able to violate or confirm to a certain extent through the subsequent presentation of actual facial expressions. We asked participants to assess predictability, i.e., how similar actual facial expressions were to what they had predicted. Following the theoretical accounts of predictive processing in depression described above ([Barrett et al., 2016](#); [Clark et al., 2018](#); [Kube et al., 2020](#); [Seth and Friston, 2016](#)), we expected to observe group differences for individuals with depression vs. healthy controls, particularly for negative valence emotions. In addition, we explored the impact of previous trials on predictions and social perception in our task. This allowed us to examine whether individuals with depression, as compared to healthy controls, were more susceptible to the influence of recent, yet irrelevant negative emotional experiences. The present study contributes to a novel growing body of knowledge on depression and predictive coding, which could be a potential underlying mechanism for the consistently reported processing abnormalities particularly regarding negative information. This may become a relevant point of departure for the exploration of novel diagnostic and therapeutic strategies.

2. Methods

2.1. Participants

Thirty-four individuals diagnosed with depression (depression group) participated in the present study. This group included 10 (29.4%) men and 24 women (70.6%) aged 49 ± 12 (*Mean* \pm *SD*) who were outpatients at the Consorci Sanitari de Terrassa, a public healthcare center in the Barcelona area. The diagnosis of major depressive disorder and/or dysthymic disorder was made by clinical experts at the center according to the DSM-IV-TR ([American Psychiatric Association, 2000](#)) diagnostic criteria using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; [First et al., 2002](#)), which is routinely used at the healthcare center. The clinical version of the SCID-5 is not available in Spanish. The diagnostic criteria for major depressive disorder and dysthymic disorder/persistent depressive disorder are consistent across the DSM-IV-TR and DSM-5. Inclusion criteria for the clinical sample were as follows: diagnosis of major depressive disorder and/or persistent depressive disorder (dysthymia); aged ≥ 18 years; no prior history of brain injury; no history of acute or previous hypomanic, manic, or psychotic episodes; and no immediate need for hospitalization due to suicide risk or recent suicide attempt. The gender ratio of the sample roughly reflects the ratio observed in clinical practice ($\sim 2/1$ for women/men) ([American Psychiatric Association, 2013](#)). In this group, 47.1% of the participants exhibited comorbid psychopathology, mainly anxiety disorders, distributed as follows: panic disorder (8.8%), generalized anxiety disorder (5.9%), agoraphobia (2.9%), other unspecified anxiety

disorder (8.8%), and personality disorder (14.7%). Two participants had two of the above-mentioned comorbidities (5.9%). The mean age at the time of diagnosis for the depression group was 44 years old (± 12) and most individuals from this group were taking medications ($n = 32$; 94.1%) (Table 1). Thirty-four healthy individuals, reporting no history of mental disorder, matched in gender and approximate age with the individuals of the depression group, were recruited from the environment around the researchers in the Barcelona area as a control group. This group also included 10 men and 24 women, aged 46 ± 13 (Mean \pm SD). The sample size ($n = 34$ per group) was based on a previous study that had applied similar behavioral measures with similar sample sizes, which proved sufficient to reveal relevant behavioral effects (Chanes et al., 2018). Age did not differ significantly between the groups (Mann-Whitney two-tailed U test, $U = 484.00$, $p = .251$, $r_B = -0.163$, 95% CI $[-0.414, 0.112]$). All individuals reported normal or corrected-to-normal vision and were native Spanish speakers or bilingual Catalan-Spanish. All individuals participated voluntarily, provided written informed consent, and did not receive monetary compensation for their participation. The study was approved by the Consorci Sanitari de Terrassa ethics committee.

2.2. Experimental procedure and instruments

For the depression group, the experiment took place at the healthcare center (Consorci Sanitari de Terrassa). Due to space limitations and privacy issues the control group could not be run in the healthcare center. For that group, participants performed the experiment at home. General information was collected from all participants, which included age, gender, handedness, and education level, after which all participants performed a social perception task. Stimuli were presented using E-Prime 2 software (Psychology Software Tools, Inc., Pittsburgh, PA, USA) running on an HP ProBook 640 G4 (display size: 14"; resolution:

Table 1
Sociodemographic and clinical variables for the depression ($n = 34$) and control ($n = 34$) groups.

Variables	Depression group		Control group	
	<i>n</i> / <i>mean</i>	%/[SD]	<i>n</i> / <i>mean</i>	%/[SD]
Gender				
Women	24	70.6%	24	70.6%
Men	10	29.4%	10	29.4%
Age (years)	49	[12]	46	[13]
Educational level				
Primary or lower	10	29.4%	6	17.6%
High school	17	50.0%	6	17.6%
University	7	20.6%	22	64.7%
Age at the time of diagnosis	44.5	[12.4]		
Patient Health Questionnaire-9 score	16.5	[5.3]	4.6	[2.5]
Principal diagnostic category (DSM-IV-TR)				
Major depressive disorder	20	58.8%		
Persistent depressive disorder (dysthymia)	14	41.2%		
Pharmacological treatment				
Benzodiazepines	20	58.8%		
Selective serotonin reuptake inhibitor	17	50.0%		
Serotonin-norepinephrine reuptake inhibitors	10	29.4%		
Norepinephrine-dopamine reuptake inhibitor	1	2.9%		
Serotonin agonist and reuptake inhibitor	3	8.8%		
Norepinephrine reuptake inhibitor	2	5.9%		
Noradrenergic and specific serotonergic antidepressant	1	2.9%		
Tetracyclic antidepressants	3	8.8%		
Tricyclic antidepressants	1	2.9%		
Agomelatine	2	5.9%		
Vortioxetine	2	5.9%		

1920×1080). Participants' eyes were placed approximately 57 cm away from the screen, although this distance was not systematically measured. After the social perception task, participants completed the Patient Health Questionnaire 9 (PHQ-9) (Spitzer et al., 1999, Kroenke et al., 2001; Spanish version used: Diez-Quevedo et al., 2001), among other questionnaires not used for this study (Positive and Negative Affect Scale, Watson et al., 1988; Emotion Regulation Questionnaire, Gross and John, 2003; short version of the UPPS-P impulsive behavior scale, Billieux et al., 2012). The patients' diagnoses (including comorbidities), age at the time of diagnosis, and medications at the time of study participation were collected from their medical records.

2.2.1. Social perception task

The social perception task was based on a task developed previously by Chanes et al. (2018). Each trial (Fig. 1a) started with a black fixation screen (4 s). Next, a photograph of a target person exhibiting a neutral facial expression was displayed ($11.5^\circ \times 17.5^\circ$; Fig. 1b) at the center of the screen (5 s). A written short story (scenario; $15.5^\circ \times 3-6^\circ$) was then displayed for 20 s in white font. Each scenario, describing a situation that the target person was currently experiencing, was designed to evoke one of three emotions (fear, happiness, or sadness). Participants were asked to imagine, while reading, how the target person would appear in the given scenario. Following the scenario, a second photograph of the same target person, this time exhibiting a stereotypical facial expression (Fig. 1b) for one of the three possible evoked emotions (fear, happiness, or sadness), was displayed for 5 s. On some trials, the stereotypical expression matched the emotion evoked by the scenario (matched trials) and on some trials it did not (nonmatched trials) (Fig. 1c). Next, participants were asked to make two ratings on 4-point scales without a response time limit. First, they rated how similar the target person looked compared to what they had imagined while reading the scenario (predictability rating) from 1 = "not at all similar" to 4 = "very similar". Finally, participants were asked to rate how likable the target person was (likability rating) on a scale from 1 = "very unlikable" to 4 = "very likable".

The task included 3 practice trials followed by 45 experimental trials divided into 5 blocks. Each block consisted of 9 trials and participants were allowed to take a short break after completing each block if they wished. The 45 experimental trials included 15 scenarios evoking each of the three emotions (i.e., 15 fear scenarios, 15 happiness scenarios, and 15 sadness scenarios). Within each set of 15 scenarios for a given emotion, 9 scenarios were followed by the stereotypical facial expression for the evoked emotion (e.g., a happiness scenario followed by a happy facial expression [matched trials]; Fig. 1c) and 6 were followed by a stereotypical facial expression for a different emotion than the one evoked by the scenario, 3 from each of the other two emotion conditions (e.g., a happiness scenario followed by a sad facial expression, 3 trials, or a fearful facial expression, 3 trials, [nonmatched trials]; Fig. 1c). The order of the trials, pairing of target faces with scenarios, and which scenarios were matched or nonmatched, were all pseudorandomized within each subject.

2.2.2. Photographs of faces

We used color photographs (400×600 pixels) of human faces with closed mouths and a direct gaze, which belong to the Interdisciplinary Affective Science Laboratory² (www.affective-science.org) (for more details see Chanes et al., 2018). A different target person (identity) was used for each of the 48 trials (3 practice trials: 2 female, 1 male; 45 experimental trials: 28 female, 17 male). Sample face stimuli can be found in Supplementary Material, along with a list of the specific

² Development of the Interdisciplinary Affective Science Laboratory (IASLab) Face Set was supported by the National Institutes of Health Director's Pioneer Award (DP1OD003312) to Lisa Feldman Barrett. More information is available online at www.affective-science.org.

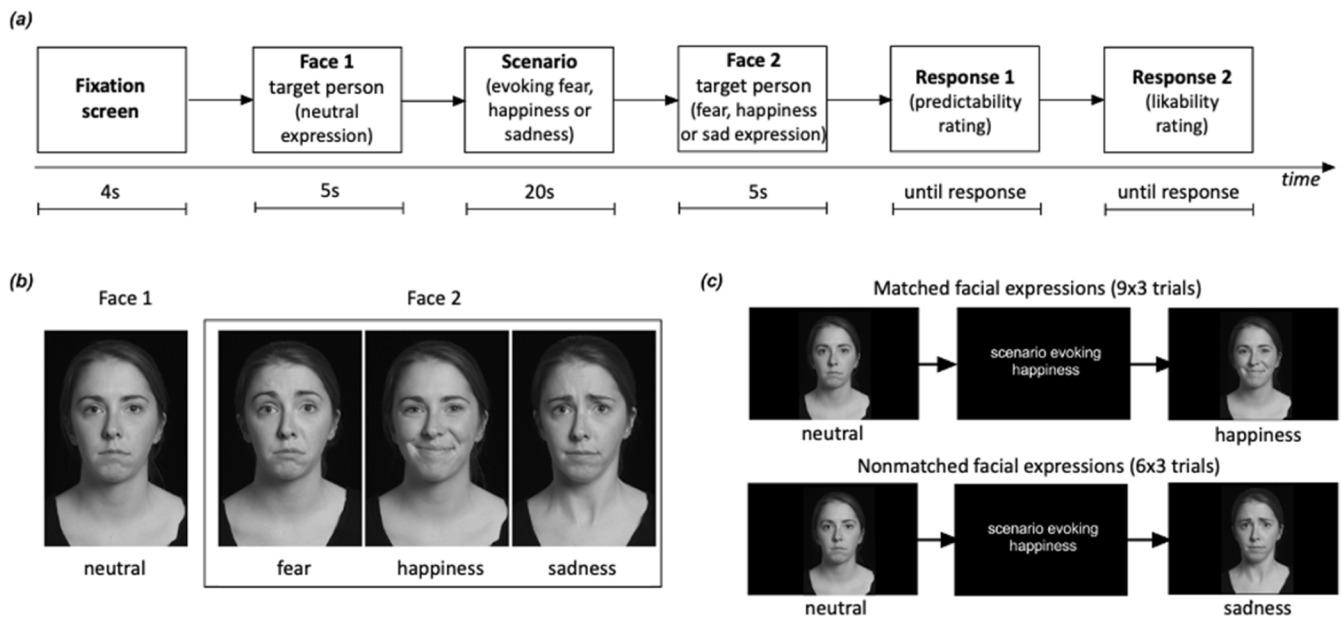


Fig. 1. Social perception task. (a) Schematic representation of an experimental trial. Each trial began with a black fixation screen followed by a photograph of a target person exhibiting a neutral facial expression. A scenario was then presented, which described a situation about the target person and was designed to evoke one of three emotions: fear, happiness, or sadness. While reading the scenario, participants were asked to imagine how the target person would look in that scenario. Afterwards, a second photograph of the target person was displayed, this time exhibiting a stereotypical facial expression for one of the three emotions evoked by the scenario (fear, happiness, or sadness), either matching the scenario emotion (matched trial) or not matching it (nonmatched trial). Participants were then asked to perform two ratings: 1) how similar the facial expression was to what they had imagined while reading the scenario (predictability rating) and 2) how likable the target person was (likability rating). (b) Example of a target person with a neutral facial expression (Face 1) and expressions of fear, happiness, and sadness (Face 2). (c) Example of a matched and a nonmatched trial.

identities used (Fig. S1). Norming information (intensity, attractiveness, stereotypicality/emotion categorization) for American and Spanish samples can be found in Supplementary Material (Table S1).

2.2.3. Scenarios

We used a Spanish translation of the scenarios used in Chanes et al. (2018), which were based on the scenarios developed by Wilson-Mendenhall et al. (2013). Sample scenarios for both original English and Spanish translated versions can be found in Supplementary Material, along with a link to full Spanish scenarios (Table S2). The scenarios described a situation that matched the target person's gender (see Chanes et al., 2018 for details) and sampled from the four quadrants of the affective circumplex, meaning they evoked either positive (happiness) or negative (sadness or fear) valence emotions with either high or low arousal for each emotion.

2.2.4. Questionnaire

We used the Spanish version of the Patient Health Questionnaire 9 (PHQ-9) (Spitzer et al., 1999; Spanish version used: Diez-Quevedo et al., 2001; the operating characteristics of this translation of the PHQ are comparable to those of the original English version, see Diez-Quevedo et al., 2001 for more details) to assess depressive symptom severity at the time of the experimental session. The PHQ-9 consists of 9 self-reported items, including items such as “feeling down, depressed or hopeless” and “poor appetite or overeating”, with responses on a 4-point scale (ranging from 0, “not at all” to 3, “nearly every day”). Responses are summed to provide a single index of depressive symptom severity over the prior 2 weeks. Reliability scores obtained for the depression and control groups were 0.82 and 0.61, respectively.

2.3. Data analysis

Non-aggregated data from individual trials were analyzed using hierarchical linear modeling (HLM 7.0; Scientific Software International,

Inc., Skokie, IL, USA) with trials nested within individual participants. For these analyses, we used a continuous sampling model with participants treated as a random factor, and a restricted maximum likelihood method of estimation for model parameters (Raudenbush and Bryk, 2002). Continuous trial-level predictor variables (e.g., ratings of predictability) were centered around each participant's mean (Enders and Tofghi, 2007). All models had random intercepts. Additionally, all predictor variables had random slopes unless the model specified failed to converge, indicating a lack of between-level variance. In this case, individual random slopes were dropped from the model until it successfully converged. The full specifications and syntax are available online (https://osf.io/n8jsf/?view_only=aff91de9ce6943a0b0fd9e41129ad781). Additional statistical analyses were performed using JASP (JASP Team 2019; version 0.9.2.0). We used Mann-Whitney *U* tests when normality assumptions were not met. Prism 8.3.0 (GraphPad Software, San Diego, CA, USA) was used for data visualization.

3. Results

As expected, the PHQ-9 scores differed significantly across groups (Mann-Whitney *U* test: $U = 50.50$, $p < .001$, $r_B = -0.910$, 95% CI $[-0.947, -0.848]$), such that participants in the depression group reported more depressive symptom severity than controls (depression group: $Mean \pm SD$: 16.5 ± 5.3 ; control group: $Mean \pm SD$: 4.6 ± 2.5) (Table 1). Scores were missing for 1 individual with depression due to incorrectly filling out the questionnaire. In this scale, a score between 0 and 4 is considered absence of symptoms, between 5 and 9 minimal symptoms, between 10 and 14 mild symptoms, between 15 and 19 moderate symptoms, and between 20 and 27 severe symptoms. Among patients, 1 (3%) exhibited no symptoms, 2 (6%) minimal symptoms, 6 (18%) mild symptoms, 15 (45%) moderate symptoms, and 9 severe symptoms (27%). Among individuals in the control group, 19 (56%) exhibited no symptoms, 14 (41%) minimal symptoms, 1 (3%) mild symptoms, and no individuals exhibited either moderate or severe

symptoms.

3.1. Effect of match condition on predictability ratings

To investigate the effect of match condition on predictability ratings, we conducted HLM analyses with trial-level predictability ratings as the outcome variable, match condition (matched and nonmatched) as a dummy-coded trial-level predictor variable, and group (depression and control) as a dummy-coded subject-level predictor variable, with the two-way interaction term included in the model. Consistent with our previous study (Chanes et al., 2018), these analyses revealed that matched facial expressions were rated as significantly more predictable ($Mean \pm SE: 3.05 \pm 0.05$) than nonmatched facial expressions ($Mean \pm SE: 1.76 \pm 0.04$) for the control group ($B = 1.28, SE = 0.07, t(66) = 19.34, p < .001$) (Fig. 2a). Similarly, participants in the depression group also rated matched facial expressions as significantly more predictable ($Mean \pm SE: 2.88 \pm 0.08$) than nonmatched ($Mean \pm SE: 1.65 \pm 0.06$) facial expressions ($B = 1.23, SE = 0.07, t(66) = 18.94, p < .001$) (Fig. 2a). The difference in predictability ratings between matched and nonmatched trials did not differ significantly across groups ($B = -0.05, SE = 0.09, t(66) = 0.53, p = .596$).

3.2. Association between predictability and likability ratings

To investigate the association between predictability and likability ratings, we conducted HLM analyses with trial-level likability ratings as the outcome variable, predictability ratings as a trial-level predictor variable, and group (depression and control) as a dummy-coded subject-level predictor variable, with the two-way interaction term included in the model. Also consistent with our previous study (Chanes et al., 2018), we observed a positive relationship between predictability and likability ratings. Faces that were rated as more predictable were also rated as more likable for the control group ($B = 0.25, SE = 0.04, t(66) = 6.77, p < .001$), and this relationship did not differ significantly across groups ($B = 0.01, SE = 0.05, t(66) = 0.30, p = .766$) (Fig. 2b). To confirm that the association between predictions and likability ratings was not driven only by nonmatched trials, in which blatant stereotype/norm violations occurred, we also assessed this relationship separately for matched and

nonmatched trials, by running separate models, with only matched trials included and with only nonmatched trials included. The relationship between predictability and likability ratings remained significant even when assessed separately within matched and nonmatched trials. Faces that were rated as more predictable were also rated as more likable in the control group for both matched ($B = 0.30, SE = 0.04, t(66) = 7.30, p < .001$) and nonmatched ($B = 0.18, SE = 0.05, t(66) = 3.48, p < .001$) trials. Consistent with the findings across all trials, the relationship between predictability and likability ratings did not differ significantly between groups when examining matched trials only ($B = 0.03, SE = 0.05, t(66) = 0.46, p = .644$) or nonmatched trials only ($B = -0.01, SE = 0.08, t(66) = -0.18, p = .860$). This pattern of results indicates that perceived likability is strongly associated with perceived predictability of facial expressions, and that this relationship is not significantly influenced by depression.

3.3. Predictability ratings by group and emotion scenario condition

Next, we investigated whether predictability ratings differed across the three evoked (scenario) emotion conditions (fear, happiness, sadness). In addition, we explored whether healthy controls and individuals with depression differed in terms of their predictability ratings across the three scenario emotion conditions. Given the strong evidence for negative bias in depression and associations between negative valence emotions and depression symptomatology (Armstrong and Olatunji, 2012; Kupferberg et al., 2016; LeMoult and Gotlib, 2019), we expected that we would see differences across groups when evoking negative valence emotions in particular (i.e., following fear and sadness scenarios).

To investigate this, we conducted HLM analyses with trial-level predictability ratings as the outcome variable, scenario emotion (fear, happiness, and sadness) as a dummy-coded trial-level predictor variable and group (depression and control) as a dummy-coded subject-level predictor variable, with all two-way interaction terms included in the model. Individuals with depression rated facial expressions following scenarios evoking sadness and fear as significantly less predictable than did healthy controls (sadness: $B = -0.21, SE = 0.10, t(66) = 2.10, p = .039$; fear: $B = -0.23, SE = 0.08, t(66) = 2.69, p = .009$), but their

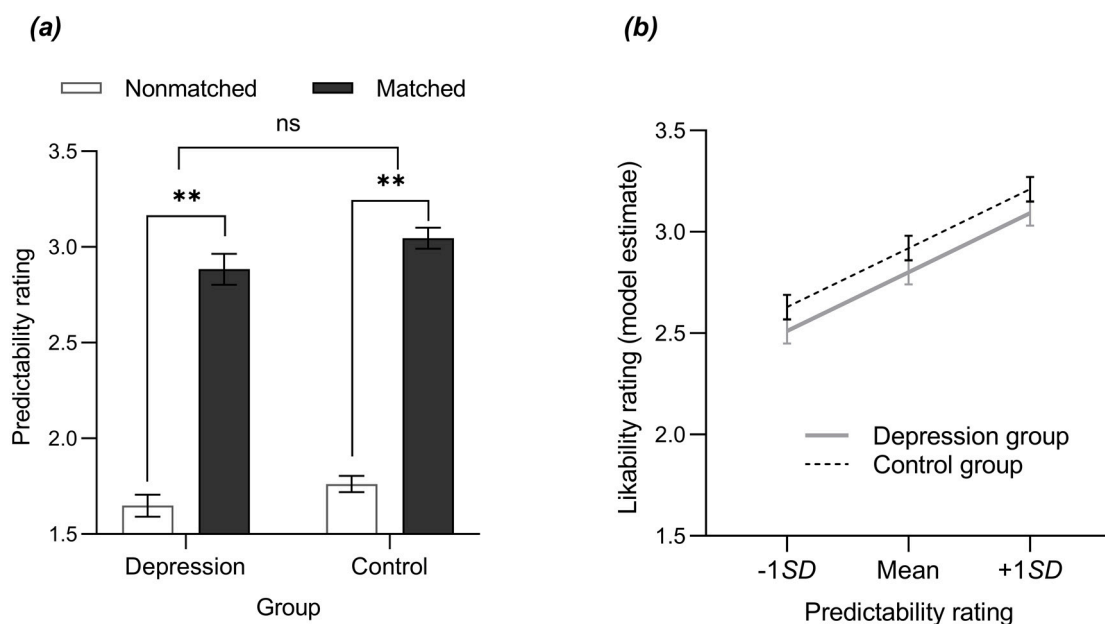


Fig. 2. Predictability ratings based on match condition (a) and the relationship between predictability and likability ratings (b) for the depression and control groups presented as means and standard errors. (a) Both groups rated matched facial expressions as more similar to what they expected than nonmatched facial expressions, indicating that both groups had stereotypical expectations about facial expressions. (b) Both groups rated more favorably (i.e., as more likable) those individuals exhibiting more predictable facial expressions. Two asterisks indicate $p < .005$.

predictability ratings did not differ from healthy controls for facial expressions following scenarios evoking happiness ($B = 0.01$, $SE = 0.08$, $t(66) = 0.15$, $p = .882$) (see Fig. 3). Analyses also revealed that relative differences in predictability ratings across scenario emotions differed by group, such that compared to healthy controls, individuals with depression showed greater differences in predictability ratings for expressions following scenarios evoking happiness vs. sadness ($B = 0.23$, $SE = 0.09$, $t(2988) = 2.60$, $p = .009$) and scenarios evoking happiness vs. fear ($B = 0.24$, $SE = 0.08$, $t(2988) = 3.00$, $p = .003$). However, differences in predictability ratings for expressions following scenarios evoking fear vs. sadness did not differ significantly by group ($B = -0.01$, $SE = 0.08$, $t(2988) = 0.16$, $p = .876$). Taken together, this pattern of results suggests that controls had significantly more stable ratings of predictability for facial expressions across all emotion scenarios, while individuals with depression showed significantly lower predictability ratings for facial expressions following fear and sadness scenarios compared to happiness scenarios (see Fig. 3).

Moreover, we further confirmed that match condition was not a relevant factor for revealing differences between groups in terms of their predictability ratings. To do this, we conducted HLM analyses with trial-level predictability ratings as the outcome variable, match condition (matched and nonmatched) as a dummy-coded trial-level predictor variable, scenario emotion (fear, happiness, and sadness) as a dummy-coded trial-level predictor variable, and group (depression and control) as a dummy-coded subject-level predictor variable, with all 2- and 3-way interaction terms included in the model. None of the interactions involving group and match condition were significant, i.e., the interaction between match condition and group across scenario emotion conditions (sadness: $B = -0.05$, $SE = 0.14$, $t(66) = 0.39$, $p = .701$; happiness: $B = -0.11$, $SE = 0.12$, $t(66) = 0.90$, $p = .372$; fear: $B = 0.02$, $SE = 0.14$, $t(66) = 0.12$, $p = .904$), and three-way interaction between match condition, group, and scenario emotion (fear vs. sadness: $B = 0.07$, $SE = 0.18$, $t(2916) = 0.40$, $p = .689$; happiness vs. sadness: $B = -0.06$, $SE = 0.16$, $t(2916) = 0.36$, $p = .717$; happiness vs. fear: $B = -0.13$, $SE = 0.16$, $t(2916) = 0.80$, $p = .427$) were not significant.

The association between predictability ratings and depression for negative valence emotions was also observed when considering depressive symptomatology as a continuum (using PHQ-9 scores) rather than a discrete diagnostic category. We performed HLM analyses for each evoked emotion with trial-level predictability ratings as the outcome variable and PHQ-9 scores as a subject-level predictor variable to examine the relationship between the PHQ-9 scores and predictability ratings across all participants, regardless of group ($n = 67$). This analysis

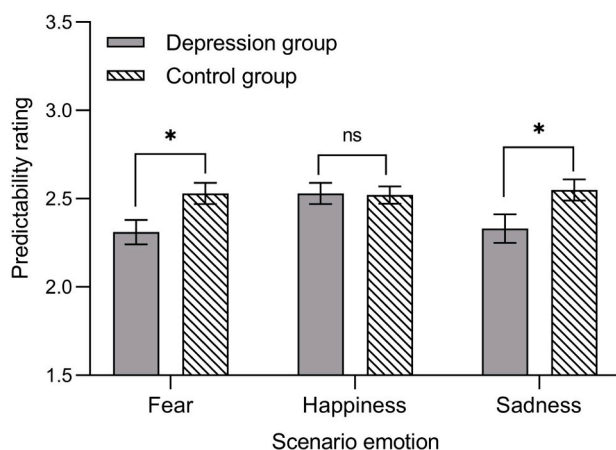


Fig. 3. Predictability ratings based on scenario emotion condition. Predictability ratings for trials with scenarios evoking fear, happiness, or sadness in the depression and control groups. For trials with scenarios evoking negative valence emotions (fear and sadness), individuals with depression rated the facial expressions as less similar to what they expected compared to controls.

revealed that facial expressions following scenarios evoking negative valence emotions were rated as significantly less predictable as symptoms increased (fear: $B = -0.02$, $SE = 0.01$, $t(65) = 2.44$, $p = .017$; sadness: $B = -0.02$, $SE = 0.01$, $t(65) = 2.07$, $p = .042$). This effect was not observed for facial expressions following scenarios evoking happiness ($B = -0.00$, $SE = 0.01$, $t(65) = 0.38$, $p = .705$).

3.4. Impact of recent yet irrelevant experience

Since prolonged processing of negative information (e.g., sad faces) has been observed in a previous study of emotive facial processing in depressed patients vs. healthy controls (Jaworska et al., 2012) we assessed the impact of recent yet irrelevant emotion information on predictability ratings, hypothesizing that recent past experience would have an impact despite being irrelevant to the task. During the task, the emotion evoked by the scenario from the previous trial was not relevant to the current trial since condition order was pseudorandomized for each participant. Thus, we assessed whether the lower predictability ratings observed for individuals with depression (relative to controls) on trials evoking negative valence emotions were impacted by the emotion evoked by the previous trial. To investigate this, we divided trials with negative valence emotion scenarios into three groups based on the emotion evoked in the previous trial: (i) those that were preceded by a trial with a scenario evoking fear, (ii) those that were preceded by a trial with a scenario evoking happiness, and (iii) those that were preceded by a trial with a scenario evoking sadness. For each of the three groups of trials we ran HLM analyses with trial-level predictability ratings as the outcome variable, and group (depression and control) as a dummy-coded subject-level predictor variable. These analyses revealed that trials with negative valence scenario emotions that were preceded by trials with scenarios evoking sadness were rated lower in predictability by participants in the depression group than by participants in the control group (control group: $Mean \pm SE$, 2.62 ± 0.06 ; depression group: $Mean \pm SE$, 2.31 ± 0.09 ; group difference: $B = -0.31$, $SE = 0.11$, $t(66) = 2.88$, $p = .005$) (Fig. 4). Conversely, predictability ratings did not differ significantly between the groups for trials with negative valence scenario emotions preceded by trials with scenarios evoking either happiness (control group: $Mean \pm SE$, 2.51 ± 0.06 ; depression group: $Mean \pm SE$, 2.37 ± 0.08 ; group difference: $B = -0.14$, $SE = 0.10$, $t(66) = 1.34$, $p = .184$) or fear (control group: $Mean \pm SE$, 2.49 ± 0.06 ;

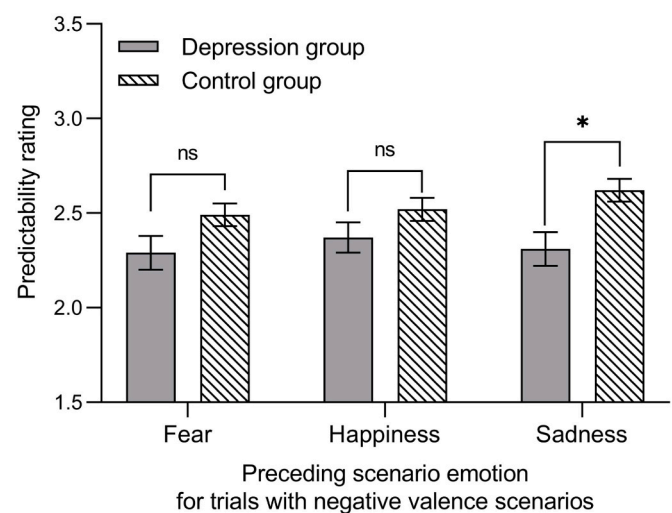


Fig. 4. Predictability ratings based on recent yet irrelevant experience. Predictability ratings for trials evoking negative valence emotions preceded by trials evoking fear, happiness, and sadness in the depression and control groups. Individuals with depression rated facial expressions lower than controls in trials with scenarios evoking negative valence emotions when they were preceded by trials evoking sadness but not fear or happiness. One asterisk indicates $p < .05$.

depression group: $Mean \pm SE$, 2.29 ± 0.09 ; group difference: $B = -0.20$, $SE = 0.11$, $t(66) = 1.81$, $p = .075$ (Fig. 4). These results suggest that the difference in predictability ratings between the depression and control groups for trials evoking negative valence emotions may be amplified by recent yet irrelevant prior evocations of sadness.

4. Discussion

In this study, we used a social perception task grounded in the predictive processing framework to assess a group of individuals diagnosed with unipolar depression (major depressive disorder or dysthymia/persistent depressive disorder) compared to a group of healthy controls at the behavioral level. Our findings replicate the observation from prior work that stereotypical facial expressions are rated as significantly more predictable when they match a previously evoked emotion than when they do not match a previously evoked emotion, suggesting that predictions about facial expressions are fairly stereotypical (Chanes et al., 2018). We also replicated the observation that individuals are evaluated more favorably (as more likable) when their facial expressions are rated as more predictable (Chanes et al., 2018). These effects were similarly observed for both individuals with depression and healthy controls.

Importantly, our results revealed predictive processing related differences across individuals with depression and healthy controls as a function of emotional valence. Compared to controls, individuals with depression showed lower predictability ratings, i.e., an increased difference between expected facial expressions and displayed facial expressions (which may be interpreted as a rough trial-by-trial measure of prediction error), for negative (both sadness and fear) but not positive (happiness) evoked emotions. These results are consistent with an increasing body of literature on predictive models and depression (Barrett et al., 2016; Clark et al., 2018; Fabry, 2020; Kube et al., 2020; Paulus et al., 2019; Seth and Friston, 2016), which suggest that depressive symptoms may be associated with a relatively inflexible “locked-in” brain strongly driven by priors that appears relatively insensitive to discrepancy or error. The specificity of this effect to negative valence emotion predictions suggests that negative valence emotions (notably fear and sadness assessed here) are emotion categories for which predictive processing disruptions in depression may be particularly important. One possible interpretation is that a characteristic “predictive style” with precise hyperpriors that the world is uncertain (Clark et al., 2018), are particularly relevant for negative valence emotions, leading to constant error that is not used to update the model because of its predicted low precision. Another related potential interpretation could be that, because individuals with depression have numerous, diverse, nuanced experiences of negative affect, they hold a “predictive style” dominated by self-relevant, fine-grained, negative valence priors, which would lead to prediction error due to a ‘dysfunctional’ high level of detail.

The specificity of the effect observed for negative valence emotions is consistent with prior work (Kube et al., 2020) and negative bias and impaired orientation to pleasant stimuli that has been consistently reported in individuals with depression (Armstrong and Olatunji, 2012; Kupferberg et al., 2016; LeMoult and Gotlib, 2019). A tendency to dwell on dysphoric stimuli may play a role both in the etiology and maintenance of depression. In the short term, dwelling on dysphoric stimuli could increase negative affect, while in the long term, altered allostatic regulation (with dominant priors and attentional bias) could lead to distorted beliefs and assumptions about the world (Armstrong and Olatunji, 2012; see also Barrett et al., 2016). Furthermore, the interpretations of precise hyperpriors about an uncertain world, particularly for negative valence contexts, and fine-grained negative-valence predictions may be consistent with the association between depressive symptoms and the tendency to present greater certainty about their own expectations when predicting negative events (Andersen, 1990) and the difficulty in abandoning negative expectations in the face of positive prediction error (Kube et al., 2019). Likewise, they would be also in line

with previous studies on belief updating regarding future life events, reporting the presence of an optimistic bias in healthy subjects but not individuals with depression (Garrett et al., 2014; Korn et al., 2014), pointing at a tendency to hold to less positive possibilities. Moreover, our observations are consistent with inflexible negative interpretations of social situations previously observed associated with depression and anxiety symptom severity in a non-clinical sample (Everaert et al., 2020), and they may provide a potential explanation based on the presence of increased prediction error observed in clinically depressed individuals for negative-valence contexts, which may be disregarded, thus, preventing dynamic updates to more positive expectations.

Our data revealed that mood-congruent recent, yet irrelevant past experiences amplified the effect observed. Evoked sadness from a previous trial was associated with lower predictability ratings for facial expressions following negative valence evoked emotions on the next trial for those in the depression group vs. those in the control group. More specifically, this group difference was observed for trials evoking negative valence emotions (fear or sadness) that were preceded by trials evoking sadness, thus, inducing sad priors or sad expectations. However, it is important to note that, in the social perception task used, previous trials were irrelevant to the current trial, and, thus, would not be expected to impact current trial ratings. This observation suggests an amplification of the effect observed by recent irrelevant past experiences (priors) that are mood-congruent, as sustained sadness is a core symptom of depression (American Psychiatric Association, 2013). Moreover, this may explain previous evidence suggesting that deficits in cognitive control over mood-congruent material underlie negative biases in attention and memory in individuals with depression (LeMoult and Gotlib, 2019).

The present study has some limitations and opens several avenues for further exploration. First, the clinical sample included participants with comorbid psychopathology, and most were taking one or more medications. While we reported a comprehensive description of the socio-demographic and clinical variables of individuals with depression and controls, we did not systematically exclude individuals taking medications or those with comorbidities, something that may be taken into account in future studies. In particular, the use of benzodiazepines was high ($n = 20$). At the level of severity of illness studied, however, investigations in an unmedicated state should be subjected to ethical considerations and the possibility of establishing subgroups within a larger sample may be considered. Second, the groups were not evaluated in the same setting; however, all materials and procedures used were exactly the same for both groups. Third, we only explored three emotion categories: two with negative valence (fear and sadness) and one with positive valence (happiness). Other emotions may be explored in the future in order to better characterize the observed effects. Additionally, our scenarios included both high and low arousal. The role of arousal may be systematically assessed in future studies. Moreover, the effects observed here would benefit from an exploration beyond the domain of social perception, for example, assessing self-related predictions.

In conclusion, the present study assessed predictive processing in patients with depression compared to controls in the domain of emotion and social perception using a well-controlled behavioral paradigm. Given the heterogeneous nature of depression, the present results have important implications for research and clinical practice by providing empirical evidence for a potential common underlying mechanism observed across individuals with depression; namely, increased discrepancy between expectations and sensory input in negative-valence contexts, possibly amplified by mood-congruent recent irrelevant experience. These findings may guide further research to characterize the neurobiological mechanisms underlying this phenomenon and provide insights into circuit-level pathophysiology in mood disorders. This behavioral phenotype may indeed represent a biomarker of potential clinical relevance, including as a therapeutic target for behavioral, pharmacological or device-based interventions. Further characterization of predictive processing both at the group and individual levels may

inform individual treatment programs leading to better clinical outcomes. Additionally, the present approach could be implemented cross-diagnostically for other brain-related conditions for which predictive processing accounts are emerging (e.g., autism, psychosis; see Chanes and Barrett, 2020 for a review).

Author statement contributors

Lorena Chanes and Irene Ramos-Grille designed the study and wrote the protocol.

Jennifer Weyant, Irene Ramos-Grille, Jolie Wormwood, and Marta Robles, performed data analyses.

Irene Ramos-Grille, Jennifer Weyant and Lorena Chanes wrote the first draft of the manuscript.

All authors contributed to and approved the final manuscript.

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Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jad.2022.05.030>.

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