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Toward an understanding of neural responses to emotion in recent onset and chronic psoriasis: A feasibility brain imaging study

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Psoriasis is linked to significant stigmatization. Prior research suggests that people with psoriasis demonstrate altered neurobiological responses to disgust. However, chronically affected patients may develop coping mechanisms to disgust-related social cues. We investigated whether the duration of psoriasis is associated with more attenuated responses to disgust. We used brain functional magnetic resonance imaging while conducting a covert facial recognition task, and a task involving emotionally stimulating pictures in patients with chronic psoriasis, patients with recent-onset psoriasis, and controls without skin disease. We found no differences in disgust processing between patients and healthy controls. Shorter duration of psoriasis was marginally associated with an attenuated brain response to disgust in the left fusiform gyrus within the inferior temporal cortex. An inverse relationship was observed between the age of onset and the hippocampus response when comparing the chronic psoriasis and recent-onset psoriasis patient groups. Our findings suggest that both the duration and the age of psoriasis onset may modulate disgust processing in patients, possibly reflecting evolved learned strategies and disease coping mechanisms. Timely pharmacological and psychosocial interventions for psoriasis may be beneficial for people diagnosed during life stages that may increase vulnerability to neurocognitive changes. Further studies are needed to replicate these results.

Keywords: Emotion, fMRI, Psoriasis, Psychodermatology

INTRODUCTION

The psychosocial burden of psoriasis, as well as the associated disability and life-changing impact are well recognized. Patients with psoriasis commonly experience stigmatization and overt public rejection because of the visibility of skin lesions (Germain et al, 2021) and have a high burden of psychiatric morbidity, primarily depression (Parisi et al, 2019). Patients demonstrate an attentional bias to words signaling threat, including disgust, which may be caused by stigmatization fear and is followed by social avoidance patterns (Etty et al, 2024; Fortune et al, 2003). However, the neurocognitive processes underlying the internalized stigma, self-image, and overall psychological consequences of psoriasis are not clear.

Kleyn et al (2009) previously demonstrated differences in the neural processing of disgust in 13 male patients with psoriasis compared to healthy controls, using a validated covert, face processing task implemented in functional magnetic resonance imaging (MRI). In functional MRI, local neural activity is associated with the blood-oxygen-level-dependent (BOLD) signal, which reflects changes in blood oxygenation. For example, when neural activity increases in a brain region, local blood flow typically increases, producing a measurable change in the BOLD signal. In the study by Kleyn et al (2009), patients showed a significantly reduced BOLD response to disgust in the insula cortex, which is considered a key brain region in disgust recognition and processing (Chapman and Anderson, 2012). Importantly, the

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Abbreviations: BOLD, blood oxygenation level dependent; MRI, magnetic resonance imaging; ROI, region of interest

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duration of psoriasis was proportional to the attenuated insular signal.

Psoriasis duration has previously been linked to less distress and higher acceptance (Hill and Kennedy, 2002). However, it is not clear if the neural responses found in this previous study reflect an isolated protective coping mechanism in psoriasis or a fundamental change in patients' emotional processing in the form of a trait. Such changes may be related to self-perception and contribute to psychiatric pathology and functional impairment. Furthermore, disgust processing in the human brain is not restricted to the insula, and it is not clear whether altered neural responses in psoriasis may extend to other areas, importantly, the fusiform cortex, the amygdala, and the orbitofrontal cortex, which have been linked to disgust and emotional face processing (Fusar-Poli et al, 2009; Habel et al, 2007; Harry et al, 2013; Schienle et al, 2002). Understanding these processes in psoriasis is critical in order to develop appropriate interventions for the psychosocial impact of psoriasis and tailor them for patients.

We developed a feasibility study to investigate whether emotional processing of disgust in psoriasis is a core marker of its psychosocial effect and reflects long-standing psychological processes over time. We therefore hypothesized that patients with long-standing moderate-to-severe psoriasis (disease duration $\geq$ 10 years) would show decreased brain responses to disgust compared to newly diagnosed patients (disease duration $\leq$ 6 years) and healthy volunteers. Secondarily, we aimed to explore synergistic effects of age of onset alongside disease duration on disgust processing, given evidence suggesting a negative association between age and coping difficulties in psoriasis (Hill and Kennedy, 2002).

RESULTS

Participants

Twenty patients with long-standing psoriasis (50% female; mean age: 34.7 $\pm$ 8.4 years, range: 21–50; female disease duration 20 years, range 10–42), 16 patients with a recent onset of psoriasis (69% female; mean age: 27.5 $\pm$ 8.3 years, range: 19–44; median disease duration 2.5 years, range 0.2–6) and 19 controls (42% female; mean age: 32.9 $\pm$ 8.1 years, range: 21–48) with no history of skin disease participated in the study (Table 1).

Patients with recent-onset disease were younger than the patients with chronic disease and had a significantly higher mean age of onset. The patient groups did not differ for psoriasis severity (PASI: mean score 5.6 $\pm$ 3.2, range: 0.7–15.6 for the chronic disease group and 5.1 $\pm$ 2.8, range: 1.4–11.1 for the recent-onset disease group), psoriasis-related QOL or psychometric scores for depression, disgust sensitivity, or disgust propensity (Table 1).

Table 1. Baseline Characteristics

Baseline Characteristic	Healthy Controls (n = 19)	Patients with Chronic Psoriasis (n = 20)	Patients with Recent-Onset Psoriasis (n = 16)	*P*–value
Sex, female (%)	8 (42%)	10 (50%)	11 (69%)	.277
Age y, mean (SD)	32.9 (8.1)	34.7 (8.4)	27.5 (8.3)	**.036**
BMI, mean (SD)	23.1 (3.6)	27.3 (3.4)	25.0 (5.1)	**.009**
Disgust sensitivity, mean (SD)	9.5 (3.1)	8.9 (2.5)	10.3 (2.9)	.338
Disgust Propensity, mean (SD)	12.9 (4.5)	15.2 (3.1)	15.6 (3.9)	.088
BDI, median (IQR)	1 (1.5)	3.5 (7)	3.5 (11.3)	.414
PASI, mean (SD)		5.6 (3.2)	5.1 (2.8)	.598
DLQI, median (IQR)		5 (3.5)	5 (5.5)	.469
Age of onset, mean (SD)		12.6 (7.5)	24.7 (8.3)	**< .001**
Disease duration, median (IQR)		20 (11.25)	2.5 (3.1)	**< .001**
Treatment				.218
Topical		9 (45%)	8 (50%)	
Phototherapy		0 (0%)	2 (12.5%)	
Oral		6 (30%)	2 (12.5%)	
Biologics		2 (10%)	1 (6.2%)	
Other		2 (10%)	0 (0%)	
None		1 (5%)	3 (18.8%)	

Abbreviations: BDI, beck depression inventory; BMI, body mass index; DLQI, dermatology life quality index; IQR, interquartile range.

Chi-square tests were used for sex and treatment data. *t*-tests and Mann-Whitney *U* tests were used where means and medians, respectively, among patient groups were compared. ANOVA and the Kruskal-Wallis test were used, where means and medians, respectively, among all three groups were compared. *P*-values < .05 are presented in bold.

Functional MRI data

Whole brain analysis of BOLD responses to disgust-expressing faces compared with neutral faces across all three groups showed activations in regions within the bilateral middle occipital gyrus, the bilateral middle temporal and fusiform gyri, and in the left insula. The opposite contrast showed activations in the anterior cingulate and medial prefrontal cortex and the bilateral calcarine cortex. Table 2 presents these activations, reflecting the regions where the group-level analysis in the total sample indicates a significant difference between the disgust and neutral conditions in the faces task, along with the voxel counts representing the spatial extent of these significant activation clusters.

Whole-brain analysis of BOLD responses to disgust-inducing images, compared to neutral images, across all three groups revealed bilateral activations in the middle occipital cortex extending to the fusiform gyrus, the amygdala, the inferior frontal gyrus, the dorsal striatum, the thalamus, the right medial frontal gyrus, the cingulate gyrus, and the right supramarginal gyrus (Table 3). Conversely, the opposite contrast demonstrated activations in the right cuneus, insula, and superior motor cortex, as well as the left superior temporal gyrus (Table 3). Whole-brain analysis activations are summarized in Figure 1.

Overall, the findings of our whole-brain analysis across all three groups aligned with our a priori hypotheses and previous literature showing involvement of the insula, the fusiform gyrus, the amygdala, and inferior frontal areas in processing disgust.

Table 2. Brain Responses During the Recognition of Facial Expressions of Disgust Compared to Neutral Expressions

L/R	Region	Voxels	BA	T-value	MNI coordinates (x y z)
Disgust > Neutral					
L	Middle occipital gyrus	118	19	5.60	−36 −91 6
L	Middle temporal gyrus and fusiform gyrus	87	22, 37	4.90	−48 -61 −2
R	Middle temporal gyrus and fusiform gyrus	92	37	4.49	45 −61 −2
R	Middle occipital gyrus	54	19	4.34	42 −82 18
L	Insula	22	13	4.34	−36 −25 26
Neutral > Disgust					
R	Anterior cingulate and medial orbitofrontal cortex	283	32	5.59	18 50 −10
R & L	Calcarine cortex and lingual gyrus	215	17, 18	4.99	15 −85 −2
R	Middle cingulate & superior medial frontal cortex	88	32	4.32	9 32 30

Voxels refer to the volume elements of the three-dimensional brain image, which are the basic spatial units of measurement in fMRI. The voxel numbers in the table represent the total number of contiguous voxels within each significant activation cluster identified in the group-level analysis. The reported activations reflect only regions where the BOLD response meets or exceeds the predefined statistical threshold, which was determined at an initial voxel-based level of $P < .001$ and cluster-corrected FWE $P < .05$. BA refers to the respective Brodmann Area of the cerebral cortex. MNI coordinates refer to the coordinates of each region according to the MNI template, a commonly used standardized brain atlas. The *t*-value indicates the *t*-statistic for each region for the disgust > neutral and neutral > disgust contrasts.

Abbreviations: BA, brodmann area; BOLD, blood oxygenation level dependent; FEW, family-wise error; fMRI, functional magnetic resonance imaging; MNI, montreal neurological institute.

Table 3. Brain Responses to Disgust-Inducing Images Compared to Neutral Images

L/R	Region	Voxels	BA	*t*-value	MNI coordinates (x y z)
Disgust > Neutral					
L	Middle occipital and fusiform gyrus	1424	19, 37	11.71	−51 −73 6 & −42 −52 −10
R	Middle occipital and fusiform gyrus	1595	19, 37	10.15	30 −76 22 & 48 −67 6
R	Inferior frontal gyrus, insula and amygdala	811	45, 47, 13	8.83	48 11 18 & 39 29 −2
L & R	Thalamus and dorsal striatum	526		8.01	−3 −31 −2 & 9 5 2
R	Superior medial frontal and middle cingulate gyrus	522	9, 32	7.72	6 50 26 & 6 26 42
L	Amygdala, insula, and inferior frontal gyrus	442	13, 47	6.98	−18 −4 −10 & −27 20 −10 & −48 2 26
L	Inferior parietal lobule (supramarginal gyrus)	69	40	4.72	−57 −28 30
Neutral > Disgust					
R	Insula	274	13	5.52	39 −19 14
R	Cuneus	97	18, 19	4.57	6 −82 26
R	Superior motor area	62	6	4.50	9 −19 54
L	Superior temporal gyrus	70	22	4.29	−57 −34 10

Voxels refer to the volume elements of the three-dimensional brain image, which are the basic spatial units of measurement in fMRI. The voxel numbers in the table represent the total number of contiguous voxels within each significant activation cluster identified in the group-level analysis. The reported activations reflect only regions where the BOLD response meets or exceeds the predefined statistical threshold, which was determined at an initial voxel-based level of $P < .001$ and cluster-corrected FWE $P < .05$. BA refers to the respective Brodmann Area of the cerebral cortex. MNI coordinates refer to the coordinates of each region according to the MNI template, a commonly used standardized brain atlas. The *t*-value indicates the t-statistic for each region for the disgust > neutral and neutral > disgust contrasts.

Abbreviations: BA, brodmann area; BOLD, blood oxygenation level dependent; FEW, family-wise error; fMRI, functional magnetic resonance imaging; MNI, montreal neurological institute.

We then performed region of interest (ROI) analyses to investigate differences among the three groups within these areas of interest and the hippocampus, which was identified in our a priori hypothesis. To compare disgust processing across groups, we measured the difference in BOLD responses when viewing facial expressions of disgust and disgust-provoking images in the two respective experimental paradigms. For comparative purposes, we also measured the difference in BOLD responses when viewing facial expressions of neutral and fearful/fear-provoking expressions and images.

During the covert emotion processing task, we found a group difference in the BOLD response to disgust in the left fusiform ($F [2, 49] = 3.36$, $P = .043$). Post-hoc analysis showed significantly higher signal values for the chronic disease group than the recent-onset disease group (estimated marginal means 0.48, 95% confidence interval = 0.34−0.62 vs. 0.18, 95% confidence interval 0.006−0.36; $P = .036$).

There were no further significant differences between the groups for any emotion or ROI in either task (Tables 4 and 5). Interestingly, however, there was a marginal group effect on the response to fearful faces in the left fusiform ($F [2, 49] = 3.04$, $P = .057$). Similarly to disgust, this effect reflected higher BOLD signal values for the chronic disease group than the recent-onset disease group (estimated marginal means 0.45, 95% confidence interval = 0.31−0.59 vs. 0.18, 95% confidence interval = 0.004−0.36; $P = .053$).

We did not find any differences in the BOLD response to neutral faces among the groups.

Furthermore, we explored whether the onset of psoriasis may moderate emotional processing of disgust in the two groups. During the covert emotion processing task, we found a significant interaction between the patient group and the age of onset in the right hippocampus ($F [1,29] = 5.89$, $P = .02$). This suggested an inverse trend in the relationship between the age of onset and the BOLD response for the chronic disease and recent-onset disease groups. Following post-hoc tests, the association between the age of onset and the right hippocampus signal was not statistically significant for either of the groups (Figure 2). There were no significant

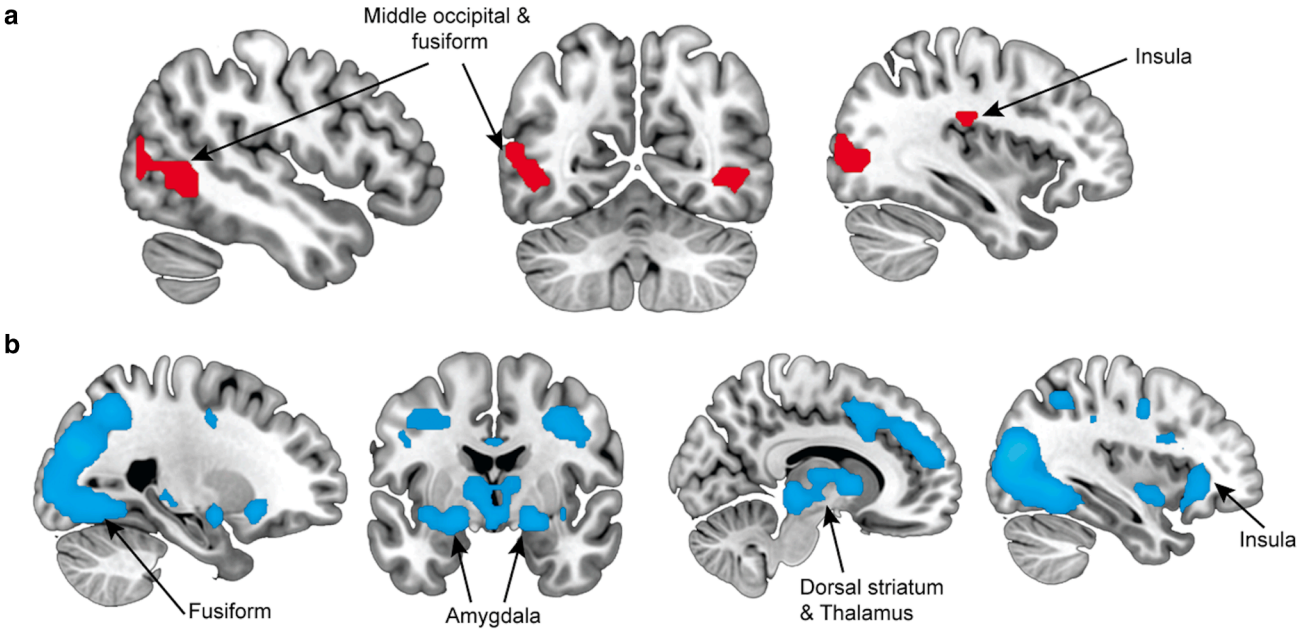

Figure 1. Whole-brain activations for disgust. (**a**) Whole-brain activations for disgust compared to neutral faces. **(b)** Whole-brain activations for disgust compared to neutral pictures.

Table 4. Faces Task — *P*-values From the Statistical Comparisons (ANOVAs) of BOLD Responses in ROIs Across the 3 Groups

ROI	Disgust	Fear	Neutral
Amygdala left	.610	.481	.633
Amygdala right	.693	.463	.897
Frontal inferior orbital cortex left	.277	.521	.147
Frontal inferior orbital cortex right	.156	.827	.608
Fusiform left	**.043**	.057[1]	.299
Fusiform right	.230	.311	.430
Hippocampus left	.319	.058	.404
Hippocampus right	.982	.376	.932
Insula anterior left	.627	.762	.964
Insula anterior right	.364	.436	.632

The BOLD response refers to the change in blood-oxygen-level–dependent signal measured during the faces fMRI task. All models were adjusted for age. Significant effects are presented in bold.

Abbreviations: BOLD, blood oxygenation level dependent; fMRI, functional magnetic resonance imaging; ROIs, regions of interest.

[1]Trend to significance.

interactions or main effects of the age of onset on the BOLD response in any other ROIs in this task. Finally, in the picture viewing International Affective Picture System task, we did not find an interaction of age of onset with group and disgust processing in any ROI.

DISCUSSION

We found that a shorter duration of psoriasis was associated with an attenuated BOLD response to disgust in the left fusiform. However, there were no significant differences in disgust processing in any ROI between patients and healthy controls. This is in contrast to the previous study by Kleyn et al (2009), showing reduced insula response to disgust in patients with psoriasis compared to healthy controls. The reason for this discrepancy is not clear, but it may be related to scanner differences between the two studies, as well as different patient populations and sample sizes; for example, Kleyn et al (2009) included a smaller male-only sample (13 males), limiting the extrapolation of its findings.

The fusiform cortex is involved in facial recognition; however, growing evidence suggests an important role in emotional face processing (Harry et al, 2013). This is supported by our findings, where the activation trends in the left fusiform observed for disgust and, to a lesser extent, fear processing were not replicated for neutral faces. Furthermore, our findings align with a large meta-analysis of emotional processing studies in humans, which reported that activation in the left fusiform gyrus supports disgust processing (Fusar-Poli et al, 2009). Expressed disgust is perceived as a cue for violating social norms and is often experienced as shame, leading to social alienation (Giner-Sorolla and Espinosa, 2011). Patients with recent-onset psoriasis' attenuated processing of expressed disgust in the left fusiform gyrus may, therefore, also reflect a coping strategy to this aversive social cuing. The lack of group differences for the picture-viewing task may indicate differential processing of personal experiences of disgust versus recognizing others' disgust, further supporting the interpretation that psoriasis affects disgust processing in an interpersonal context.

Our secondary analysis indicated that the age of onset might play a role in how people with psoriasis recognize and process others expressed disgust. We found an inverse effect of the age of onset on the BOLD response in the right hippocampus for the chronic disease and recent-onset disease groups, with a positive correlation trend in the chronic disease group. It is not clear why this effect was only found for the hippocampus. Although our findings implicate the

Table 5. IAPS Task — *P*-values From the Statistical Comparisons (ANOVAs) of BOLD Responses in ROIs Across the 3 Groups

ROI	Disgust	Fear	Neutral
Amygdala left	.077	.229	.079
Amygdala right	.259	.515	.289
Frontal inferior orbital cortex right	.745	.571	.239
Frontal inferior orbital cortex left	.613	.682	.151
Fusiform left	.293	.266	.192
Fusiform right	.183	.163	.176
Hippocampus left	.298	.333	.193
Hippocampus right	.469	.654	.422
Insula anterior left	.103	.468	.458
Insula anterior right	.624	.858	.834

The BOLD response refers to the change in blood-oxygen-level –dependent signal measured during the IAPS fMRI task. All models were adjusted for age. Significant effects are presented in bold. Abbreviations: BOLD, blood oxygenation level dependent; fMRI, functional magnetic resonance imaging; IAPS, International Affective Picture System; ROIs, regions of interest.

hippocampus, one possibility requiring further investigation is that it regulates activity in the insula. Hippocampal connectivity with the insula has been linked to internally generated disgust, supported by memory retrieval and imagery, when viewing disgust-provoking images (Fitzgerald et al, 2004). In addition, hippocampus-insula connectivity has been found to increase with disgust-associated imagery (Jabbi et al, 2008). These changes may reflect the recall of disgust-associated autobiographical events and represent evolved strategies over time via learning and conditioning (Fitzgerald et al, 2004; Jabbi et al, 2008).

In psoriasis, neurocognitive restructuring may develop more effectively in individuals with early childhood disease onset, as well as in those who acquire psoriasis later in life, after completing their identity development and establishing their personal and social resources. Indeed, a number of studies have found an association between age and resilience in adults (Cohen et al, 2014; Portzky et al, 2010), with more frequent use of maladaptive mechanisms in adolescents and younger adults, including self-blame and hostile reaction (Irion and Blanchard-Fields, 1987). In adults with psoriasis, age has been negatively correlated with maladaptive coping and distress (Hill and Kennedy, 2002). People with adolescent and young adulthood onset of disease may, therefore, be less able to develop adequate emotional regulating defense mechanisms to cope with the consequences of psoriasis in the social context. Furthermore, recognition of others' facial expressions of disgust starts being shaped at around 9 years of age, which may also explain the differential processing we observed in the group with earlier childhood compared to late adolescence onset (Widen and Russell, 2013). People diagnosed in late adolescence and young adulthood could therefore benefit most from interventions offering psychosocial support and teaching adaptive coping skills, such as cognitive-behavioral therapy-based programs to improve their emotional well-being and psychological functioning (Sansom-Daly et al, 2012).

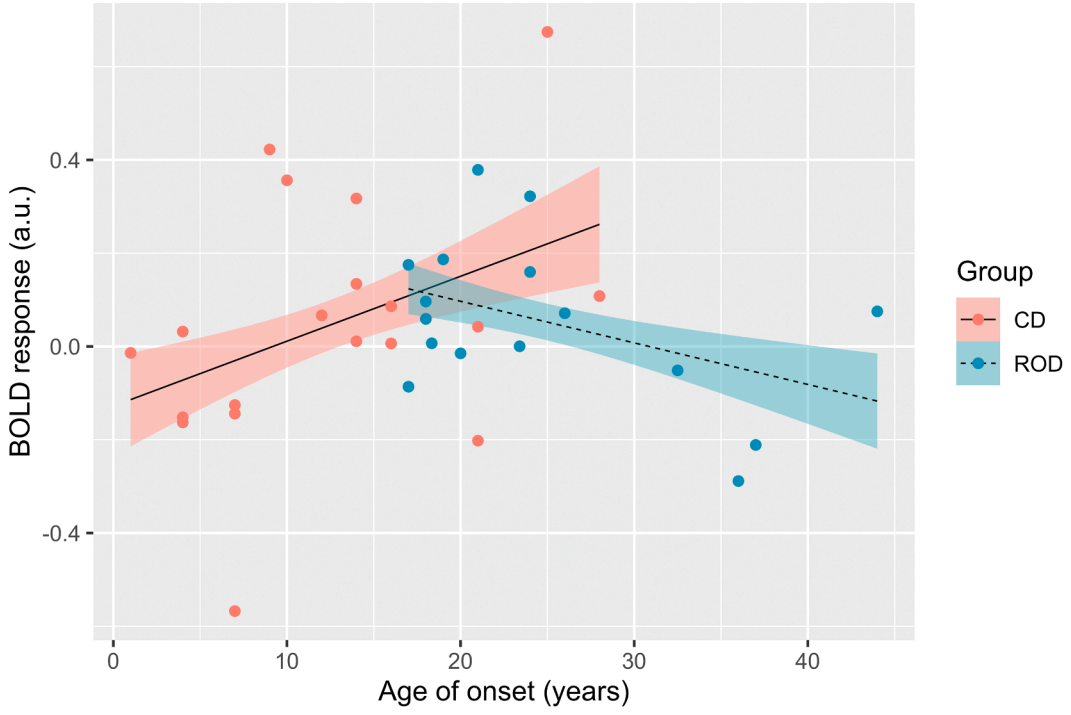

Figure 2. BOLD signal effects of disgust in the right hippocampus in the covert emotion processing task in patients with chronic disease (CD) and patients with recent onset disease (ROD), depending on the age of psoriasis onset. These effects are expressed as AUs of GLM-estimated beta values. The shaded area around the estimated trend line represents confidence intervals. There was a significant interaction between the patient group and the age of onset (F [1,29] = 5.89, $P = .02$), suggesting an inverse trend in the relationship between the age of onset and the BOLD response for the chronic disease and recent-onset disease groups. The association between the age of onset and the right hippocampus signal was not statistically significant for either of the groups. AUs, arbitrary units; BOLD, Blood oxygenation level dependent; GLM, general linear model

Our study has some limitations. Although larger than the previous pilot sample of Kleyn et al (2009), the present study sample remains relatively small, and smaller effects of psoriasis on emotional processing may not be detectable. As a result, non-significant findings should be interpreted with caution and not as definitive evidence of no effect. Furthermore, given the exploratory nature of the ROI analysis, no correction for multiple comparisons was applied on the ROI analysis. This may increase the risk of type I error, and the reported *P*-values should be interpreted as exploratory rather than confirmatory. However, it is of note that both effects that were around the uncorrected significance level were in the fusiform gyrus. Replication in larger cohorts will be important to confirm these findings. Finally, we have tested for several demographic and disease characteristics among groups and controlled for age differences. However, it is possible that unmeasured confounding factors, such as other subclinical psychopathology, may have affected our findings.

In conclusion, we found no significant differences in the processing of expressed disgust between patients with psoriasis and controls. However, our results suggest that the duration of psoriasis and age of psoriasis onset may contribute to how patients process and cope with social reactions to their skin, which may consequently affect their experience of internalized stigma, feelings of shame, and the severe psychosocial consequences of psoriasis. These effects warrant further research and could have implications on treatment decisions, particularly since stress from others' reactions and stress-perpetuating avoidance behaviors have been shown to be the most important markers of disability in psoriasis (Fortune et al, 1997). Early intervention and psychological support may be of most benefit for patients who experience psoriasis during their formative years (adolescence and early adulthood), particularly in the first years after diagnosis, as they may present with higher vulnerability, experience more severe distress, and less resilience in their social interactions due to their skin.

MATERIALS AND METHODS

Recruitment

Patients were recruited from our weekly tertiary psoriasis clinic, local general practices, and a database of patients with declared interest in research. Healthy volunteers responded to the advertisement.

We included patients with a dermatologist-confirmed diagnosis of moderate-to-severe chronic plaque psoriasis. Healthy volunteers had no history of skin disease or significant disfigurement in their family. Inclusion criteria for all participants were: (i) aged between 18 and 50 years; (ii) right-handed; (iii) not taking psychotropic medication; (iv) no contraindications to functional MRI scanning; (v) no history of severe, enduring mental or neurological illness; and (vi) not pregnant.

Clinical assessment

Following informed consent, all participants underwent clinical assessment on the day of the scan. This included full medical history, physical examination, PASI, where appropriate, and, for women, a urine pregnancy test. PASI is a widely used physician-rated measure of psoriasis severity, providing a composite score (range 0–72) (Fredriksson and Pettersson, 1978). The dermatology life quality index (Finlay and Khan, 1994) was used to assess the impact of psoriasis on QOL.

Experimental design

Each participant was presented with a series of pictures, while brain scans were acquired. Participants were first presented with facial expressions of emotion, including disgusted, fearful, and neutral expressions, as part of the covert recognition of faces task (Ekman and Friesen, 1976). We describe the protocol for this paradigm in detail elsewhere (Kleyn et al, 2009). In summary, participants were shown face stimuli (expressing emotions and neutral faces, with each face shown for 3 seconds) and were asked to determine the sex of the face. Covert brain responses to emotions could therefore be studied. In order to derive baseline measures for the BOLD signal-based analysis, blocks of rest periods were also included.

In a separate task, each participant viewed a set of color photographs, selected from the International Affective Picture System (Lang et al, 1997), which provides normative ratings for a set of photographs for investigations of emotion and attention. Participants were shown randomly 21 disgust-inducing pictures, 21 fear-inducing pictures, and 21 pictures with neutral content (4 seconds for each picture).

Both tasks were included because, although limited evidence suggests shared substrates between the experience of disgust and identification of expressions of disgust in others (Wicker et al, 2003), it is currently unclear whether facial expressions of disgust and disgust-inducing pictures are processed differently and engage distinct neural networks.

Neuroimaging parameters

Brain images were acquired in a Philips 3.0 Tesla MRI scanner. T2*-weighted/echo-planar imaging data were acquired separately from each task (for the faces task: 3 × 3 × 4 mm voxel size; 80 × 80 matrix size; repetition time = 2.3; echo time = dual echo of 12 and 30; total volumes = 192; for the International Affective Picture System task: 3 × 3 × 4 mm voxel size; 80 × 80 matrix size; repetition time = 2.5; echo time = dual echo of 12 and 30, total volumes = 290). A T1-weighted structural image was also acquired for each participant (1 mm voxel size isotropic) to exclude structural abnormalities and for use in spatial pre-processing of functional images. A healthy control with an abnormal scan was excluded from the analysis.

Imaging analysis

Imaging data were analyzed using statistical parametric mapping (SPM5) (Penny et al, 2011), with a random effects model. We used the same imaging analysis methods for the two tasks (faces and International Affective Picture System) and analyzed the data from them separately.

Echo-planar imaging data were realigned to the first image using a standard 6-parameter rigid body transformation and reslicing using sinc interpolation, coregistered to the individual T1-weighted images, and spatially normalized to Montreal Neurological Institute space. The data were then spatially smoothed using an 8 mm isotropic full width half maximum Gaussian kernel.

Following preprocessing, data were analyzed using the general linear model at the first-level analysis for each participant. The onset and duration of each block of interest (neutral, disgust, fear) were convolved with the canonical hemodynamic response function. The 6 movement parameters produced at realignment for each participant were used as regressors of no interest to account for residual

effects of movement artefacts. A high-pass filter of 128 seconds was applied to the data.

To explore whole-brain responses to disgust, first-level *t* contrasts were created contrasting brain responses to disgust compared with neutral blocks (ie, disgust > neutral and neutral > disgust) across the whole sample. In more detail, in the first-level (within-subject) analysis, a contrast map was created for each participant, representing the magnitude and direction of the difference in BOLD activation between disgust and neutral stimuli at each voxel. The BOLD signal is measured separately within each voxel, which is the basic three-dimensional unit of the brain image. Multiple neighboring voxels showing a statistically significant BOLD response form an activation cluster, and the number of voxels in the cluster reflects the spatial extent of the activation.

The individual contrast maps from the first-level analysis were then entered into the second-level (group-level) analysis. Second-level group analyses were implemented as one-sample *t*-tests, exploring the group responses to disgust and neutral blocks and testing whether the BOLD signal is significantly greater for one condition relative to the other at each voxel across the sample. Significance in all analyses was determined at a cluster-corrected family-wise error $P < .05$, from an initial voxel-based level of $P < .001$ (Flandin and Novak, 2020; Friston et al, 1994).

To explore group differences, we performed ROI analysis in areas found to be activated in the whole sample that were also a priori hypothesized to play a role in disgust based on existing evidence. These include the bilateral anterior insula, fusiform gyrus, frontal inferior orbital cortex, and amygdala (Fusar-Poli et al, 2009; Kleyn et al, 2009; Schienle et al, 2002). We also included the hippocampus in the analysis based on a priori hypotheses regarding its role in learning and retrieval (Kafkas et al, 2024). For the ROI analysis, activation data (parameter estimates) were extracted using 6 mm spheres around the general linear model local maxima from the whole-brain analysis.

Statistical analysis

Statistical analysis was carried out in RStudio. Participant characteristics are reported as mean ± SD unless stated otherwise. We compared groups for baseline characteristics, including potentially confounding measured variables such as depression scores, using classical statistical tests as appropriate for the type of data, including chi-square tests, *t*-tests, and Mann-Whitney U tests; one-way ANOVA, or the Kruskal-Wallis test were used where means or medians, respectively, among all three groups were compared.

To compare the BOLD signal (parameter estimates) across the three groups, we performed ANOVAs for each ROI, adjusting for age to control for age effects on the hemodynamic response to emotional faces (Iidaka et al, 2002). For significant group effects in ANOVAs, we performed post-hoc comparisons using Tukey's method to adjust for multiple comparisons. To test the effects of age of psoriasis onset on the BOLD response to disgust among patients, we performed ANOVAs using interaction terms between the age of onset and the patient group (dichotomous variable). All models were age-adjusted and checked for multicollinearity using the variance inflation factor < 5. The level of statistical significance was set at 0.05 for all analyses.

ETHICS STATEMENT

The study was approved by the National Research Ethics Service (Ref: 13/NW/0549). Written informed consent was obtained from all participants.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

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CONFLICT OF INTEREST

GL received speaker honoraria from Janssen, Lilly, Leo, and Novartis. CEMG received honoraria and/or research grants from AbbVie, Almirall, Amgen, AnaptysBio, Artax, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Eli Lilly and Company, Evelo Bioscience, Galderma, GlaxoSmithKline Pharmaceuticals, Inmagene, Kyowa Kerin, Janssen Pharmaceuticals, ONO Pharmaceuticals, Novartis, Pfizer, Sun Pharma, and UCB Pharma. CEK conflicts of interest include consulting fees, research or institutional support, and educational grants for Almirall, Amgen, Celgene, Eli Lilly and Company, Janssen Pharmaceuticals, La Roche-Posay, LEO Pharma, Novartis, Pfizer, and UCB. CEK is also a Visiting Professor at the University of Bolton. The remaining authors state no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization: RE, CEK; Data Curation: SM, EM; Formal Analysis: GL, AK, SM, EM; Investigation: EM, CEK; Methodology: GL, AK, SM, EM, RE, CEK; Resources: CEMG, RE, CEK; Software: GL, AK, SM, EM; Supervision: RE, CEK; Visualization: GL, AK; Writing — Original Draft Preparation: GL; Writing — Review and Editing: GL, AK, SM, EM, CEMG, RE, CEK

DECLARATION OF GENERATIVE ARTIFICIAL INTELLIGENCE (AI) OR LARGE LANGUAGE MODELS (LLMs)

The author(s) did not use AI/LLM in any part of the research process and/or manuscript preparation.

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