Itch-related avoidance and attentional biases in patients with psoriasis?

Nadinda, P.G.; Laarhoven, A.I.M. van; Evers, A.W.M.; Maas, J.; Beugen, S. van

Manuel Pereira[1] and Konstantin Agelopoulos[1]

[1]Department of Dermatology and Center for Chronic Pruritus, University Hospital Münster, Münster, Germany; and [2]Moscow Scientific and Practical Center of Dermatovenerology and Cosmetology, Moscow, Russia
*Corresponding author e-mail: henning.wiegmann@ukmuenster.de

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at www.jidonline.org, and at https://doi.org/10.1016/j.jid.2023.02.022.

REFERENCES

Ádám D, Arany J, Tóth KF, Tóth BI, Szöllősi AG, Oláh A. Opioidergic signaling-A neglected, yet potentially important player in atopic dermatitis. Int J Mol Sci 2022;23:4140.

Bigliardi-Qi M, Gaveriaux-Ruff C, Pfaltz K, Bady P, Baumann T, Rufli T, et al. Deletion of μ- and κ-opioid receptors in mice changes epidermal hypertrophy, density of peripheral nerve endings, and itch behavior. J Invest Dermatol 2007;127:1479–88.

Chéret J, Gherardini J, Soeberdt M, Hundt JE, Abels C, Bertolini M, et al. Non-neuronal kappa-opioid receptor activation enhances epidermal keratinocyte proliferation, and modulates mast cell functions in human skin ex vivo. J Dermatol 2020;47:917–21.

Elliott G, Vanwersch R, Soeberdt M, Metze D, Lotts T, Ständer S, et al. Topical nalfurafine exhibits anti-inflammatory and anti-pruritic effects in a murine model of AD. J Dermatol Sci 2016;84:351–4.

Fishbane S, Jamal A, Munera C, Wen W, Menzaghi F. KALM-1 Trial Investigators. A phase 3 trial of difelikefalin in hemodialysis patients with pruritus. N Engl J Med 2020;382:222–32.

Gein SV. Dynorphins in regulation of immune system functions. Biochemistry (Mosc) 2014;79:397–405.

Inan S, Torres-Huerta A, Jensen LE, Dun NJ, Cowan A. Nalbuphine, a kappa opioid receptor agonist and mu opioid receptor antagonist attenuates pruritus, decreases IL-31, and increases IL-10 in mice with contact dermatitis. Eur J Pharmacol 2019;864:172702.

Kupczyk P, Reich A, Hołysz M, Gajda M, Wysokińska E, Kobuszewska A, et al. Opioid receptors in psoriatic skin: relationship with itch. Acta Derm Venereol 2017;97:564–70.

Lipman ZM, Yosipovitch G. An evaluation of difelikefalin as a treatment option for moderate-to-severe pruritus in end stage renal disease. Expert Opin Pharmacother 2021;22:549–55.

Parkhill AL, Bidlack JM. Reduction of lipopolysaccharide-induced interleukin-6 production by the kappa opioid U50,488 in a mouse monocyte-like cell line. Int Immunopharmacol 2006;6:1013–9.

Phan NQ, Lotts T, Antal A, Bernhard JD, Ständer S. Systemic kappa Opioid receptor agonists in the treatment of chronic pruritus: A literature review. Acta Derm Venereol 2012;92:555–60.

Rogers TJ. Bidirectional regulation of opioid and chemokine function. Front Immunol 2020;11:94.

Snyder LM, Chiang MC, Loeza-Alcocer E, Omori Y, Hachisuka J, Sheahan TD, et al. Kappa opioid receptor distribution and function in primary afferents. Neuron 2018;6(99):1274–1288.e6.

Taneda K, Tominaga M, Negi O, Tengara S, Kamo A, Ogawa H, et al. Evaluation of epidermal nerve density and opioid receptor levels in psoriatic itch. Br J Dermatol 2011;165:277–84.

Tominaga M, Ogawa H, Takamori K. Possible roles of epidermal opioid systems in pruritus of atopic dermatitis. J Invest Dermatol 2007;127:2228–35.

Itch-Related Avoidance and Attentional Biases in Patients with Psoriasis?

Journal of Investigative Dermatology (2023) **143,** 1848–1850; doi:10.1016/j.jid.2023.02.032

JID Open

TO THE EDITOR

Itch is a common symptom of skin conditions such as psoriasis (Elewski et al., 2019). The processing of itch-related information can be influenced by implicit processes such as biased avoidance tendencies (Silverberg et al., 2018; Verhoeven et al., 2006) and attentional biases (Evers et al., 2019; van Laarhoven et al., 2020), which can amplify the sensation of itch. These processes can especially affect those with chronic itch and their significant others (SOs), because they may be exposed to itch-related stimuli more often than the general public. However, little is known about the role of avoidance tendencies in itch as there are few to no studies that have experimentally investigated it. Furthermore, findings on attentional bias in itch are mixed (van Laarhoven et al., 2020). Thus, in this study, we aimed to investigate whether patients with psoriasis and their SOs tend to avoid and display more attention toward itch-related stimuli as opposed to neutral stimuli, than to controls. Exploratively, we investigated whether psoriasis, itch, and scratch severity correlate with behavioral and attentional biases. Understanding this may inform us further about the underlying mechanisms that can be targeted to reduce itch symptoms.

Participants consisted of patients with psoriasis ($N = 50$), the patients' SOs ($N = 50$), and controls from the general population ($N = 50$). For a summary of the participant characteristics, we refer to Supplementary Table S1. Those who met the inclusion criteria were invited to come into the research laboratory and provide written informed consent to participate. Next, they were asked to complete multiple tasks on a desktop computer, followed by a series of printed paper-and-pencil questionnaires that assessed psoriasis-related symptoms (such as itching and scratching). The approach-avoidance task (Rinck and Becker, 2007) was used to measure approach and avoidance tendencies in response to itch and neutral pictures, and a modified Stroop task (Williams et al., 1996) was used to assess attentional bias for itch-related words. Due to the noninvasive nature of the study, the METC Oost-Nederland determined that a formal ethical approval was not required. For a complete overview of the methods, we refer to the Supplementary Text and van Beugen et al. (2016) (see also preregistration: https://doi.org/10.17605/OSF.IO/MW6EA).

Abbreviation: SOs, Significant Others

Accepted manuscript published online 23 March 2023; corrected proof published online 12 June 2023

In terms of approach-avoidance tendencies, ANOVA results indicated that groups did not differ in approach-avoidance reaction times in response to itch and neutral pictures ($F(2,147) = 0.76$, $P = 0.47$, $\eta_p^2 = 0.01$, $BF_{01} = 2.65$). However, irrespective of groups, participants were generally faster to respond to neutral pictures than to itch pictures ($F(1,147) = 96.05$, $P < 0.001$, $\eta_p^2 = 0.40$, $BF_{10} = 2.83 \times 10^{+14}$) and were faster to push (avoid) than to pull (approach) pictures, regardless of picture type ($F(1,147) = 59.22$, $P < 0.001$, $\eta_p^2 = 0.29$, $BF_{10} = 5.39 \times 10^{+9}$). In terms of attentional bias, results also revealed that groups did not differ in reaction times in response to itch and neutral words ($F(2,144) = 0.52$, $P = 0.60$, $\eta_p^2 = 0.01$, $BF_{01} = 2.82$). However, participants were again generally slower in naming itch-related words than neutral words ($F(1,144) = 26,34$, $P < 0.001$, $\eta_p^2 = 0.16$, $BF_{10} = 16,113.98$). Finally, we found no significant correlation between clinical characteristics (psoriasis severity measures, itching and scratching intensity) and attention and avoidance biases (see Table 1). More details on the results can be found in the Supplementary Text.

Table 1. Correlation between Clinical Characteristics, AAT Effects, and Stroop Effects

	AAT[1] Effects		Stroop Effects[2]	
Pearson Correlation Coefficient				
Clinical Characteristics	*r*	*P*	*r*	*P*
SAPASI	-0.08	0.66	0.01	0.97
Psoriasis severity VAS Score	-0.15	0.39	0.20[3]	0.18[3]
ISDL Itch Subscale	-0.05[3]	0.73[3]	-0.04	0.84
ISDL Scratch Subscale	-0.03	0.88	0.01	0.94
Partial Correlation				
Clinical Characteristics	*r(33)*	*P*	*r(33)*	*P*
SAPASI	-0.10	0.56	0.02	0.90
Psoriasis severity VAS Score	-0.13	0.44	0.05	0.76
ISDL Itch Subscale	-0.05	0.78	-0.08	0.66
ISDL Scratch Subscale	-0.03	0.87	-0.04	0.80

Abbreviations: AAT, approach-avoidance task; SAPASI, self-administered psoriasis area and severity index; VAS, visual analog scale; ISDL, impact of chronic skin disease on daily life.

Partial correlations were calculated for all correlation coefficients to control for education as a covariate.

[1]AAT Effects were calculated by subtracting the AAT itch scores (push−pull responses on itch pictures) by AAT Neutral scores (push−pull responses on neutral words).

[2]Stroop Effects were calculated by subtracting the reaction time responses of naming the color of itch words by reaction time responses of naming the color of neutral words. Due to non-normality of the data, Pearson's correlation coefficients were calculated with 1000 sample bootstrapping to explore the relationship between psoriasis, itch, and scratch severity and attentional and avoidance biases.

[3]As the data revealed non-linearity, Spearman's Rho was computed to explore the relationship between AAT effects and ISDL Itch Subscale and Stroop Effects and Psoriasis VAS score.

The findings suggest that neither patients nor their SOs have a greater tendency to avoid or display more attention to itch-related stimuli than neutral stimuli, as compared to controls. Irrespective of group, a general effect of slower responding to itch-related stimuli than to neutral stimuli was found in all participants. Our findings could indicate that patients with chronic skin conditions and their SOs respond to visual itch stimuli the same way as controls, which may suggest that frequent exposure to itch or itch-related stimuli does not seem to affect itch-avoidance and -attentional tendencies. The current findings are in line with our previous publication in which we found no avoidance bias in patients with psoriasis in response to disease-related pictures, such as psoriasis affected skin (van Beugen et al., 2016). However, although our findings are also in line with previous itch-related attentional research in patients with chronic post-burn itch (van Laarhoven et al., 2016), they contradict the results of a study by Fortune and colleagues in patients with psoriasis (Fortune et al., 2003) and more recent studies in healthy participants (Becker et al., 2020; Etty et al., 2022; van Laarhoven et al., 2021[1]). The difference in findings between the current study and the previous studies may be due to various factors, including the type of stimuli used (words vs. pictures), the type of sample (patients vs. healthy controls), and the method used to assess attention (Stroop task vs. dot-probe task). However, it should be noted that we displayed various stimulus types in each of the tasks (e.g., itch-related, disease-related, positive, negative, and neutral stimuli). This could have led to confounded results, as responses could be influenced by previous responses to different stimuli. Nevertheless, the results add to the literature on avoidance and attentional biases in itch, which could help generate new treatment models that target these mechanisms (e.g., attentional bias training) in patients with psoriasis.

To our knowledge, this was the first study to experimentally evaluate itch-avoidance and -attentional biases in three different sample groups using reaction time tasks assessing implicit processes. Considering how itch and pain share similar properties (Yosipovitch et al., 2007), we would have expected to see stronger avoidance tendencies in patients with psoriasis and their SOs as opposed to controls. Yet, we only found a general avoidance effect among all participant groups. Although these tendencies may not always be reflected in observable behaviors, avoidance should be further explored in the context of itch. In addition, all participants tend to pay more attention to itch stimuli than to neutral stimuli, suggesting that (visual) itch stimuli may, in general, demand attention and subsequent action (van Beugen et al., 2022). Further studies are needed to fully understand the role of avoidance and attentional biases in itch and other chronic itch conditions.

Data availability statement

Datasets related to this article are available through a complete publication package in the DataverseNL

[1] van Laarhoven A, Veldhuijzen DS, Dijkerman HC. Itch evoked by the rubber hand illusion. ArXiv 2021, https://psyarxiv.com/b8tw3/.

repository through https://dataverse.nl/dataverse/leidenuniversity. These datasets can be accessed upon request at https://doi.org/10.34894/MCETBG.

ORCIDs
Putu Gita Nadinda: https://orcid.org/0000-0002-9619-1977
Antoinette I.M. van Laarhoven: https://orcid.org/0000-0001-6932-9283
Andrea W.M. Evers: https://orcid.org/0000-0002-0090-5091
Joyce Maas: https://orcid.org/0000-0001-8049-8942
Sylvia van Beugen: https://orcid.org/0000-0001-8220-1807

CONFLICT OF INTEREST
The authors state no conflict of interest.

ACKNOWLEDGMENTS
We would like to thank everyone who contributed to the completion of this study. In particular, we thank Mike Rinck, Eni Becker, Peter van de Kerkhof, and Henriët van Middendorp for their help with designing the study. We thank Hannah Niermann, Elke Schoneveld, Tijn Mommers, and Nina Koch for their contributions in collecting and validating the stimuli and participant testing. The various word stimuli used in the Stroop task were selected from the Dutch Emotional List which was part of a PhD thesis by JFA. We thank Tessel Galesloot and the Nijmegen Biomedical Study (www.nijmegenbiomedischestudie.nl) for facilitating the data collection of participants from the general population. We also thank the Dutch Psoriasis Association for facilitating patient recruitment as well as Myrthe Veenman for her assistance in interpreting the Bayesian analyses.

AUTHOR CONTRIBUTIONS
Conceptualization: SvB, JM, AWME, AIMvL; Data Curation: SvB, JM; Formal Analysis: PGN; Investigation: SvB, JM; Methodology: JM, SvB; Project Administration: SvB; Supervision: AWME, AIMvL, SvB; Stimulus Validation: SvB; Visualization: PGN, AIMvL; Writing – Original Draft: PGN; Writing – Review and Editing: PGN, AIMvL, JM, SvB, AWME

Putu Gita Nadinda[1,*], Antoinette I.M. van Laarhoven[1], Andrea W.M. Evers[1,2], Joyce Maas[3,4] and Sylvia van Beugen[1]

[1]Department of Health, Medical and Neuropsychology Unit, Leiden University, The Netherlands; [2]Medical Delta, Leiden University, Technical University Delft and Erasmus University, The Netherlands; [3]GGZ Oost Brabant, Centre for Eating Disorders, Helmond, The Netherlands; and [4]Department of Medical and Clinical Psychology, Tilburg University, The Netherlands
[*]Corresponding author e-mail: p.g.nadinda@fsw.leidenuniv.nl

SUPPLEMENTARY MATERIAL
Supplementary material is linked to the online version of the paper at www.jidonline.org, and at https://doi.org/10.1016/j.jid.2023.02.032

REFERENCES
Becker JM, Vreijling SR, Dobbinga S, Giesbers JJJ, Evers AWM, Veldhuijzen DS, et al. Attentional bias towards visual itch and pain stimuli in itch- and pain-free individuals? Acta Derm Venereol 2020;100:adv00199.

Elewski B, Alexis AF, Lebwohl M, Stein Gold L, Pariser D, Del Rosso J, et al. Itch: an under-recognized problem in psoriasis. J Eur Acad Dermatol Venereol 2019;33:1465–76.

Etty S, George DN, Van Laarhoven AIM, Holle H. Acute itch induces attentional avoidance of itch-related information. Acta Derm Venereol 2022;102:adv00691.

Evers AWM, Peerdeman KJ, Laarhoven AIM. What is new in the psychology of chronic itch? Exp Dermatol 2019;28:1442–7.

Fortune DG, Richards HL, Corrin A, Taylor RJ, Griffiths CEM, Main CJ. Attentional bias for psoriasis-specific and psychosocial threat in patients with psoriasis. J Behav Med 2003;26:211–24.

Rinck M, Becker ES. Approach and avoidance in fear of spiders. J Behav Ther Exp Psychiatry 2007;38:105–20.

Silverberg JI, Kantor RW, Dalal P, Hickey C, Shaunfield S, Kaiser K, et al. A comprehensive conceptual model of the experience of chronic itch in adults. Am J Clin Dermatol 2018;19:759–69.

van Beugen S, Maas J, van Laarhoven AIM, Galesloot TE, Rinck M, Becker ES, et al. Implicit stigmatization-related biases in individuals with skin conditions and their significant others. Health Psychol 2016;35:861–5.

van Beugen S, van Laarhoven AIM, Spillekom-van Koulil S, Evers AWM. The psychology of itch: current evidence and future directions. Amsterdam: Elsevier; 2021. Ref Module Neurosci Biobehav Psychol 2022;(8):486–500.

van Laarhoven A, Peerdeman K, Van Ryckeghem D, Evers A. Cognitive processing of itch and pain: the role of attention and expectations. In: Yosipovitch G, Arendt-Nielsen L, Andersen H, editors. Itch and pain: similarities, interactions, and differences. Wolters Kluwer; 2020. p. 289–99.

van Laarhoven AI, Ulrich DJ, Wilder-Smith OH, van Loey NE, Nieuwenhuis M, van der Wee NJ, et al. Psychophysiological processing of itch in patients with chronic post-burn itch: an exploratory study. Acta Derm Venereol 2016;96:613–8.

Verhoeven L, Kraaimaat F, Duller P. Kerkhof P van de, Evers A. Cognitive, behavioral, and physiological reactivity to chronic itching: analogies to chronic pain. Int J Behav Med 2006;13:237–43.

Williams JMG, Mathews A, MacLeod C. The emotional Stroop task and psychopathology. Psychol Bull 1996;120:3–24.

Yosipovitch G, Carstens E, McGlone F. Chronic itch and chronic pain: analogous mechanisms. Pain 2007;131:4–7.

Dietary Fiber Improves Skin Wound Healing and Scar Formation through the Metabolite-Sensing Receptor GPR43

Journal of Investigative Dermatology (2023) **143,** 1850–1854; doi:10.1016/j.jid.2022.07.036

TO THE EDITOR
Wound healing is a dynamic process that involves a complex sequence of cellular and biochemical events. It is characterized by an early inflammatory stage, followed by the formation of a fibroproliferative tissue rich in immature collagen bundles and newly formed blood vessels. The recruitment of inflammatory leukocytes to a wound is also a critical process for tissue repair owing to the broad spectrum of mediators released and the influence they exert over other cells during tissue

Abbreviations: HF, high-fiber; LF, low-fiber; SCFA, short-chain fatty acid; WT, wild type

Accepted manuscript published online 23 March 2023; corrected proof published online 21 April 2023

SUPPLEMENTARY MATERIALS AND METHODS

Participants

Participants consisted of patients with psoriasis, the patients' SOs, and controls from the general population. Patients who were at least 18 years of age were recruited through the Dutch Psoriasis Association and were asked to invite a significant other (e.g., partner, relative, or friend) to participate in the study alongside them. A general population was invited to participate through the subsample of the Nijmegen Biomedical Study (www.nijmegenbiomedischestudie.nl). Exclusion criteria were self-reported severe psychiatric and/or physical (co-)morbidity, psoriatic arthritis, and visual and/or physical impairments that can interfere with task performance. In addition, any significant others (SOs) or controls with self-reported chronic skin conditions were also excluded from the study. All participants provided written informed consent to participate in the study. Formal ethical approval of the current study was not required by the regional medical research ethics committee (METC Oost-Nederland formerly known as CMO Regio Arnhem-Nijmegen) due to the noninvasive nature of the study.

Experimental tasks and stimuli

Approach-avoidance tedencies. The approach-avoidance task (AAT) (Rinck and Becker, 2007) was used to measure approach and avoidance tendencies in response to itch and neutral stimuli. For this task, participants were seated in front of a 19-inch computer screen (resolution: 1024 × 786 pixels) and a joystick that was tightly fastened to the table approximately 20 cm from the edge of the table. Starting from an upright joystick position, participants were asked to push or pull a joystick as quickly and accurately as possible depending on the angle of the picture (tilting left or right) presented on the screen. The push and pull responses that participants had to perform in response to the left or right tilt were randomized between participants. When the correct response was performed (by pushing or pulling the joystick by approximately 30 degrees), the picture disappeared and a new picture was presented. Starting from the middle position (picture dimension 338 × 261), pulling the joystick resulted in the picture size increasing by three sizes (up to 799 × 618), thus creating a visual impression of pulling the object closer, while pushing the joystick, resulted in a decrease in picture size by three sizes (as small as 136 × 105), thus creating a visual impression of pushing the object away. Participants were able to practice the task over 10 practice trials with empty frames. The experimental task consisted of 80 trials distributed across two blocks. The pictures presented were related to two categories (20 pictures for each category): itch/scratching and neutral pictures. A series of itch-related pictures were developed and validated through experts that have worked with patients with a chronic skin condition, as well as a randomly selected group of individuals that represented the target population (i.e., individuals with psoriasis and/or their significant other). Of the 90 developed pictures, the ones that scored at least a 3.5 (out of 5) rating on itching were used as the itch/scratch stimuli. On the other hand, pictures of fabric resembling skin were used as the neutral stimuli (van Beugen et al., 2016; Schuck et al., 2012).

Attentional bias. A modified Stroop task (Williams et al., 1996) was used to assess attentional bias for itch-related words. In this task, participants were asked to name the color of the words presented as fast as possible. However, unlike the original Stroop task, the following word categories were used: negative words, positive words, neutral words, psoriasis-related words (skin-related words), itch scratch/related words, and social stigma-related words. The positive, negative, and neutral words were selected from the Dutch Emotional Word list. For the current study, only itch-related and neutral words were assessed. All other word categories have been described in our previous publication (see van Beugen et al., 2016).

Words within a category (e.g., itch-related words or neutral words) were presented on the screen in a block design. For each block, a standard card for each word category containing 8 words (see Dutch and English translated words in Supplementary Table S2) that were repeated five times in random order were displayed on a black background. The words presented per block were matched with each other based on the total number of letters per block; however, the itch block (64 letters) was 8 letters shorter than the neutral block (72 letters), as the neutral words were taken from the Dutch Emotional Word list, thus there were no perfectly matching words. Participants were seated in front of a computer screen and asked to say out loud the colors of the words that were presented on the screen. Reaction times as well as errors in naming the word colors were measured for the different word categories. The errors were scored manually by an experimenter who was blind to the word category, and the response times were recorded through a mouse click at the start and end of each word category.

Questionnaires

Self-report questionnaires regarding participants' health status, as well as demographics such as gender, age, education level, and marital status were administered. In addition, all participants were asked about their level of itch over the past week using an 11-point visual analog scale (VAS), with 0 indicating no itching and 10 indicating the worst itching ever, as part of the Dutch version of the impact of chronic skin disease on daily life (ISDL) itch subscale (Evers et al., 2008).

For patients with psoriasis, questions pertaining to their psoriasis severity and their itch and scratch intensity were also asked. Psoriasis severity was assessed using two measures: one was the self-administered psoriasis area and severity index (Feldman et al., 1996), in which patients were able to mark their affected skin areas as well as rate the redness, thickness, and scaliness of their affected areas. An overall score was calculated for the self-administered psoriasis area and severity index to assess psoriasis severity with the highest score of 72 indicating most severe psoriasis. The other psoriasis measure was assessed using an 11-point VAS in which patients indicated their psoriasis severity on a scale of no active psoriasis to worst active psoriasis. Furthermore, in addition to the itch VAS, the patients' itch intensity over the past four weeks was also measured using the ISDL itch subscale. Patients had to rate their itch intensity using a Likert scale on a scale of 1 (almost never) to 4 (almost always) in response to the items: “My skin condition was accompanied by itching during the past four weeks”, “I had itching attacks over the past four weeks”, and “I suffered from itching continuously during the past four weeks.” Furthermore, scratch intensity was measured using the ISDL scratch subscale, in which patients had to rate their scratching behavior using the same Likert scale as the itch subscale. Patients had to respond to items such as “I scratched during the past four weeks” and “I scratch while I’m asleep”. Additional questionnaires were also administered, which have been discussed in a previous publication (see van Beugen et al., 2016).

Statistical analysis

Analyses were performed using both frequentist and Bayesian approaches. For all frequentist analyses, data were prepared and analyses were computed using SPSS version 27.0 for Windows (SPSS, Chicago, IL). To test for baseline differences between groups, a one-way ANOVA was performed on age, as well as two chi-square tests on gender and education level. As three of the education level cells contained an expected count of less than five, Fisher’s exact test results were reported. To prepare the AAT data, extreme reaction times of less than 300 ms or more than 2000 ms were removed before aggregation (e.g., Lansu et al., 2013; van Beugen et al., 2016). No additional outliers were removed to keep the analyses as close to the unaltered data as possible. Upon removal of extreme outliers, participants’ median reaction times were calculated for all picture categories. To prepare the Stroop data, participants with extreme reaction times across all Stroop categories were excluded.

For both AAT and Stroop data, the normality of the residuals was checked by calculating a z-score of the skewness and kurtosis. The data was also checked for sphericity using Mauchly’s test and checked for homogeneity using Levene’s test. All assumptions were met except for the assumption of normality. To adjust for normality, all reaction time data, including the push and pull responses for the itch and neutral pictures and reaction times for the itch and neutral words, were transformed using a natural log transformation.

To assess whether patients with psoriasis and their SOs showed an avoidance bias to itch-related pictures compared to controls, we performed a 2 × 2 × 3 mixed ANOVA with stimulus category (itch and neutral structure) and response direction (push and pull) as the within-subject factor, and group (psoriasis, SOs, and control subjects) as the between-subjects factor. We also calculated an AAT effect score by subtracting the participants’ push (avoidance) reaction times by their pull (approach) reaction times. A positive score would indicate a stronger approach, whereas a negative score indicated stronger avoidance. Planned contrasts were carried out using the AAT effect scores, comparing the control group with either the patients with psoriasis or the SOs using a Sidak adjustment for multiple comparisons.

To assess whether patients with psoriasis and their SOs showed an attentional bias toward itch-related words compared to controls, we performed a 2 × 3 mixed ANOVA with word category (itch and neutral) as the within-subjects factor and group (psoriasis, SOs, and controls) as the between-subjects factor. Attentional bias can be detected by the longer response times in naming the colors of the words owing to the saliency of the itch words than the neutral words. Again, planned contrasts using Sidak adjustment for multiple comparisons were used to compare the control group with either patients with psoriasis or their SOs.

Although we initially planned to analyze all participant data as stated in the preregistration, correlations between AAT and Stroop responses, and self-reported measures of itch and scratching were only calculated in patients with psoriasis as they were the only participant group in which all self-reported measures (i.e., self-administered psoriasis area and severity index, VAS scores for psoriasis, and ISDL) were measured. The total score for the self-administered psoriasis area and severity index and the VAS scores for psoriasis severity were used in the correlation analysis. In addition, contrary to the analysis plan, which states that itch would be calculated using two separate measures (see preregistration: https://doi.org/10.17605/OSF.IO/MW6EA), a total itch score was computed by combining the VAS itch score (divided by 10, multiplied by 4) with the first three ISDL itch subscale items to follow the correct scoring procedure as described in (Evers et al., 2008). Furthermore, level of scratch was calculated by adding all but one (final question regarding scratching duration over the past week) of the items in the ISDL subscale for scratch, again to follow the correct scoring procedure as described in Evers et al. (2008).

Finally, Bayesian analyses were calculated using JASP (JASP Team, The Netherlands) version 0.17.0. For this, Bayes factors were calculated. The Bayes factor assesses the magnitude of evidence in favor of either the null or alternative hypothesis. Evidence in favor of the alternative hypothesis as opposed to the null hypothesis is indicated by BF_{10}, and evidence in favor of the null hypothesis as opposed to the alternative hypothesis is indicated by BF_{01}. BF_{10} was reported in cases of statistically significant findings based on frequentist ANOVAs, and BF_{01} was reported in cases of nonsignificant findings. Higher Bayes factors showed signify stronger evidence in favor of one of the two hypotheses. For example, $BF_{10} = 5$ indicates that the data supporting the alternative hypothesis is five times more likely than the null hypothesis. To interpret the strength of the evidence, the following categories have been suggested: BF_{10} of 3 to 20 suggests positive evidence, 20 to 150 suggests strong evidence, and >150 suggests very strong evidence for the alternative hypothesis (Kass and Raftery, 1995). For the current study, Bayesian MRE-ANOVAs were conducted as described in van den Bergh et al. (2022)[2] using default settings.

RESULTS

The main findings of the study, such as the approach-avoidance reaction times, attentional bias, and correlations, have been reported in the main text. Below are the additional findings that we found to supplement the main results.

Participant characteristics

The characteristics of the sample are described in Supplementary Table S1. The test for baseline differences revealed no significant difference for age ($P = 0.32$) and gender ($P = 0.65$) between groups. However, there was a significant difference in education levels between patients with psoriasis and their SOs ($P = 0.002$).

Approach-avoidance tendencies

The average AAT effects and the descriptive statistics of the reaction times are presented in Supplementary Figure S1 and Supplementary Table S3. Results indicated no significant interaction between type of picture stimuli (itch vs. neutral), response direction (push vs. pull), and group (patients vs. SOs vs. controls) ($F(2,147) = 0.39$, $P = 0.68$, $\eta_p^2 = 0.01$). This is supported by Bayesian analyses, which suggest that there is inconclusive evidence for a three-way interaction effect (see Supplementary Table S4). Our planned contrasts on the AAT effects revealed that there was again no significant difference in avoidance effects when comparing controls with patients with psoriasis or SOs for both itch (mean difference 12.26 ± 23.03; $P = 0.93$, vs. 28.16 ± 23.03; $P = 0.53$, respectively) and neutral stimuli (mean difference 5.88 ± 21.70: $P = 0.99$, vs. 8.09 ± 21.70: $P = 0.98$, respectively).

As baseline differences revealed a significant effect of education, analyses were computed again while including education as a covariate. Results again indicated no significant interaction between type of picture, response direction, and group when controlling for education ($F(2,142) = 0.34$, $P = 0.71$, $\eta_p^2 = 0.005$). Again, when including education as a covariate, Bayesian analysis suggests inconclusive evidence for a three-way interaction effect (see Supplementary Table S5). However, while there was a significant main effect of stimulus type in which participants were still generally faster at responding to neutral pictures ($F(1,142) = 7.49$, $P = 0.007$, $\eta_p^2 = 0.50$, $BF_{10} = 1.14 \times 10^{+17}$), the main effect of response direction was no longer significant ($F(1,142) = 1.36$, $P = 0.25$, $\eta_p^2 = 0.009$, $BF_{01} = 2.86 \times 10^{-13}$).

Attentional bias

Data from the modified Stroop task was missing from three participants due to technical errors: one from the control group and two from patients with psoriasis. The analyses were carried out as planned without imputations. Mean reaction times from the modified Stroop task are presented in Supplementary Figure S1 and Supplementary Table S6.

Results revealed no significant interaction between type of word stimuli (itch vs. neutral) and group (patients vs. SOs vs. controls) ($F(2,144) = 0.40$, $P = 0.67$, $\eta_p^2 = 0.01$). This is in line with Bayesian analyses, which suggest inconclusive evidence for a two-way interaction effect (see Supplementary Table S7). Again, the results of our planned contrasts also showed that there was no significant difference in reaction times when comparing patients and controls, or SOs with controls for both itch (mean difference -0.004 ± 0.05: $P = 1.0$, vs. -0.05 ± 0.05: $P = 0.65$, respectively) and neutral stimuli (mean difference -0.01 ± 0.05: $P = 0.99$, vs. -0.04 ± 0.05; $P = 0.80$, respectively).

When controlling for education, results again revealed no significant interaction between type of stimuli and group ($F(2,139) = 0.36$, $P = 0.70$, $\eta_p^2 = 0.005$). Again, when including education as a covariate, Bayesian analyses suggest that there is inconclusive evidence for a two-way interaction (see Supplementary Table S8). Additionally, the main effect of stimulus type was no longer significant when controlling for education ($F(1,139) = 2.50$, $P = 0.12$, $\eta_p^2 = 0.02$, $BF_{01} = 3.42 \times 10^{-7}$).

Exploratory analyses

Results from the correlation analyses are reported in Table 1. Repeating analyses with education as a covariate did not change the statistical significance of the results.

REFERENCES

Evers AWM, Duller P, Van De Kerkhof PCM, Van der Valk PGM, De Jong EM, Gerritsen MJP, et al. The Impact of Chronic Skin Disease on Daily Life (ISDL): a generic and dermatology-specific health instrument. Br J Dermatol 2008;158:101–8.

Feldman SR, Fleischer AB, Reboussin DM, Rapp SR, Exum ML, Clark AR, et al. The self-administered psoriasis area and severity index is valid and reliable. J Invest Dermatol 1996;106:183–6.

JASP Team. JASP. Version 0.17.0; 2023 [computer software]. https://jasp-stats.org/. (accessed January 30, 2023).

Kass RE, Raftery AE. Bayes factors. J Am Stat Assoc 1995a;90:773–95.

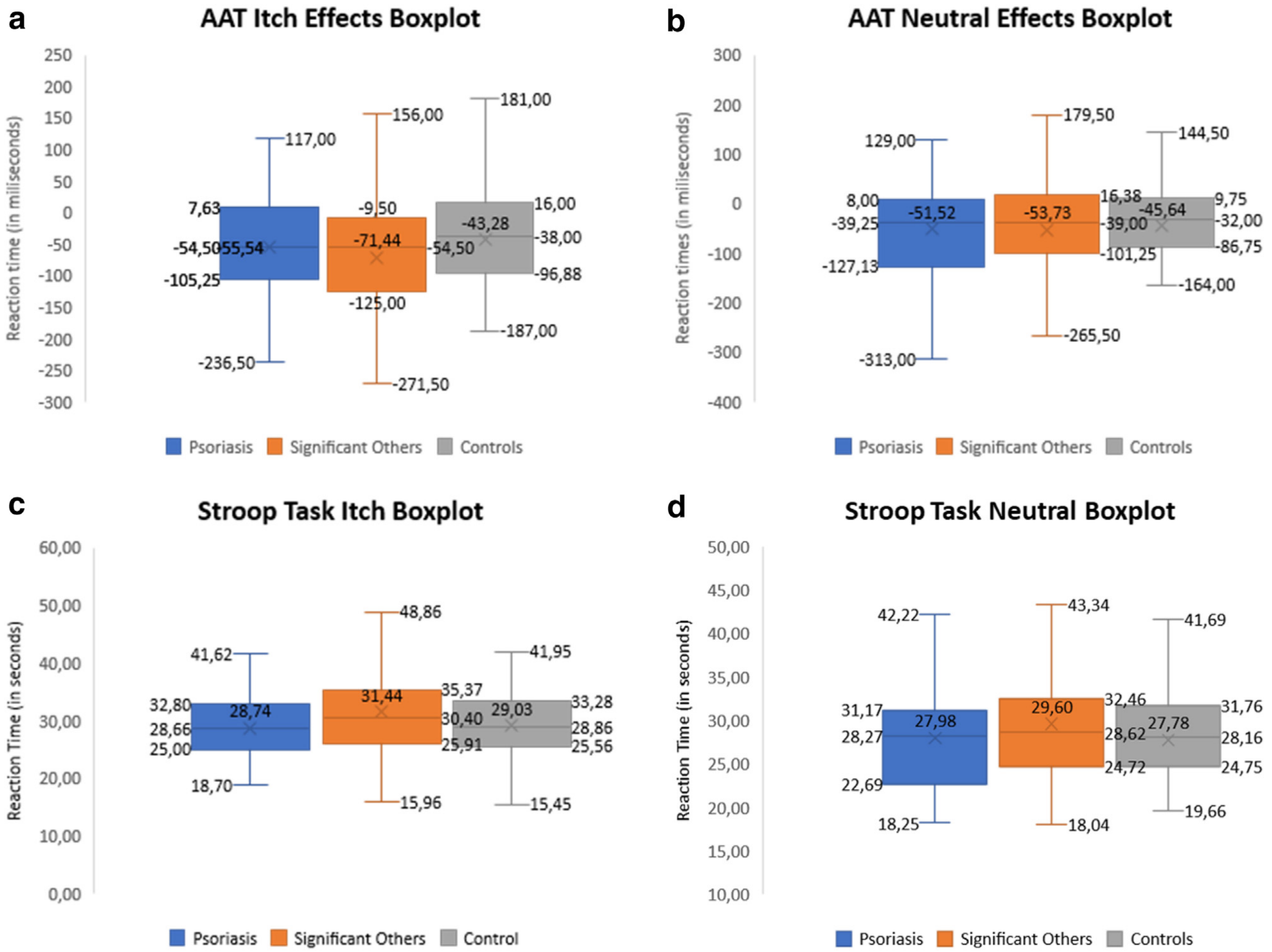
Lansu TAM, Cillessen AHN, Bukowski WM. Implicit and explicit peer evaluation: associations with early adolescents' prosociality, aggression, and bullying. J Res Adolesc 2013;23:762–71.

Rinck M, Becker ES. Approach and avoidance in fear of spiders. J Behav Ther Exp Psychiatry 2007;38:105–20.

Schuck K, Keijsers G, Rinck M. Implicit processes in pathological skin picking: responses to skin irregularities predict symptom severity and treatment susceptibility. J Behav Ther Exp Psychiatry 2012;43:685–91.

Williams JM, Mathews A, MacLeod C. The emotional Stroop task and psychopathology. Psychol Bull 1996;120:3–24.

van Beugen S, Maas J, van Laarhoven AIM, Galesloot TE, Rinck M, Becker ES, et al. Implicit stigmatization-related biases in individuals with skin conditions and their significant others. Health Psychol 2016;35:861–5.



Supplementary Figure S1. Descriptive statistics of AAT and Stroop effects of itch and neutral words based on means. (**a**) Shows the boxplot for AAT itch effects reaction times, and (**b**) shows the boxplot for AAT neutral effects reaction times. AAT effects were calculated by subtracting the push reaction times in response to itch-related pictures from the pull reaction times in response to itch-related pictures. (**c**) Shows the boxplot for Stroop itch reaction times and (**d**) shows the boxplot for the Stroop neutral reaction times. AAT, approach-avoidance task.

Supplementary Table S1. Sociodemographic and Clinical Characteristics of Patients with Psoriasis, Significant Others, and Controls

Demographic Variables	Psoriasis N = 50	Significant Others N = 50	Controls N = 50
Age (M (SD))	56.9 (12.9)	53.3 (15.5)	56.8 (12.1)
Gender female (N (%))	23 (46)	27 (54)	23 (46)
Education level (N (%))			
Primary education	1 (2)	1 (2)	0 (0)
Secondary education	36 (72)	29 (58)	18 (36)
Tertiary education	12 (24)	20 (40)	29 (58)
Missing	*1 (2)*	-	*3 (6)*
[1]**SAPASI (M (SD))**	4.5 (2.3)	-	-
[2]**Psoriasis VAS score (M (SD))**	4.1 (2.3)	-	-
[3]**ISDL itch subscale (M (SD))**	7.5 (3.1)	-	-
[4]**ISDL scratch subscale (M (SD))**	14.3 (3.8)	-	-

Abbreviations: M, Mean; SD, standard deviation; N, number of participants; SAPASI, self-administered psoriasis and severity index; VAS, visual analog scale; ISDL, impact of chronic skin disease on daily life.

[1]Scores range from 0—72 with higher scores indicating more severe psoriasis severity.

[2]Scores range from 0 (no active psoriasis) to 10 (most severe psoriasis).

[3]Scores range from 3—16 with higher scores indicating more itch.

[4]Scores range from 7—28 with higher scores indicating more scratching.

Supplementary Table S2. English Translation of Words Used in the Modified Stroop Task

Itch Words[1]		Neutral Words[1]	
English	**Dutch**	**English**	**Dutch**
Itchy	Jeukend	Tablecloth	Tafelkleed
Mosquito bite	Muggenbult	Doorknob	Deurknop
Flea bite	Vlooienbeet	Lightbulb	Gloeilamp
Stinging nettle	Brandnetel	Drinking mug	Drinkbeker
Head lice	Hoofdluis	Refrigerator	Koelkast
Itch	Jeuk	Kettle	Fluitketel
Scratch	Krabben	Kitchen	Keuken
Lice	Luizen	Nutcracker	Notenkraker

[1]Itch and neutral words were matched together in terms of length and contain single words in Dutch.

Supplementary Table S3. Descriptive Statistics of Participants' Reaction Times (in milliseconds) in the Approach-Avoidance Task in Response to Itch-Related and Neutral Pictures and AAT (Push−Pull) Effects Displayed Per Group

Picture Type	Response Direction		Group: Psoriasis *N* = *50*	Group: Significant Others *N* = *50*	Group: Controls *N* = *50*
Itch	**Pull**	*Mean (SD)*	894.17 (213.62)	964.60 (278.83)	886.34 (217.75)
	Push	*Mean (SD)*	838.63 (214.07)	893.16 (248.52)	843.06 (206.00)
	[1]AAT effect	*Mean (SD)*	-55.54 (110.90)	-71.44 (132.50)	-43.28 (99.60)
		Min	-360.00	-617.00	-348.00
		Max	241.50	224.50	181.00
		25th Percentile	-105.25	-125.00	-96.88
		Median	-54.50	-54.50	-38.00
		75th Percentile	7.63	-9.50	16.00
Neutral	**Pull**	*Mean (SD)*	848.59 (218.16)	873.72 (221.75)	837.37 (195.23)
	Push	*Mean (SD)*	797.07 (205.19)	819.99 (201.76)	791.73 (193.15)
	[1]AAT effect	*Mean (SD)*	-51.52 (103.22)	-53.73 (122.47)	-45.64 (98.22)
		Min	-313.00	-556.00	-422.00
		Max	258.00	179.50	144.50
		25th Percentile	-127.13	-101.25	-86.75
		Median	-39.25	-39.00	-32.00
		75th Percentile	8.00	16.38	9.75

Abbreviation: AAT, approach-avoidance task.

[1]AAT effects were calculated by subtracting push by pull responses from each stimulus category.

Supplementary Table S4. Bayes Factors and Model Comparison of the Approach-Avoidance Task Data Interaction Effects

Models[1]	P (M)	P (M | data)	BF_M	BF_{10}	Error %
Null model (incl. Subject and random slopes)	0.053	3.286×10^{-25}	5.914×10^{-24}	1.000	
Group + Direction + Stimulus Type + Group ✻ Direction + Group ✻ Stimulus Type + Direction ✻ Stimulus Type	0.053	0.001	0.020	$3.344 \times 10^{+21}$	34.864
Group + Direction + Stimulus Type + Group ✻ Direction + Group ✻ Stimulus Type + Direction ✻ Stimulus Type + Group ✻ Direction ✻ Stimulus Type	0.053	4.698×10^{-5}	8.458×10^{-4}	$1.430 \times 10^{+20}$	59.342

Abbreviations: P(M), prior model probability; P(M|data), posterior model probability; BF_M, posterior model odds; BF_{10}, Bayes factor that shows the evidence in favor of the alternative hypothesis.

[1]All models include subject and random slopes for all repeated measurement factors. Bayes factors in favor of interaction effects can be calculated by dividing the BF_{10} of the model with the three-way interaction (i.e., $BF_{10} = 1.430 \times 10^{+20}$) by the BF_{10} of the model without the three-way interaction (i.e., $BF_{10} = 3.344 \times 10^{+21}$). In this case, the BF_{10} of the interaction effect is equal to 0.04 indicating little to no evidence.

Supplementary Table S5. Bayes Factors and Model Comparison of the Approach-Avoidance Task Data Interaction Effects when Including Education as a Covariate

Models[1]	P (M)	P (M|data)	BF_M	BF_{10}	Error %
Null model (incl. subject and random slopes)	0.026	1.377×10^{-27}	5.096×10^{-26}	1.000	
Group + Direction + Stimulus Type + Education + Group ✻ Direction + Group ✻ Stimulus Type + Direction ✻ Stimulus Type	0.026	0.001	0.052	$1.025 \times 10^{+24}$	17.937
Group + Direction + Stimulus Type + Education + Group ✻ Direction + Group ✻ Stimulus Type + Direction ✻ Stimulus Type + Group ✻ Direction ✻ Stimulus Type	0.026	8.031×10^{-5}	0.003	$5.831 \times 10^{+22}$	11.395

Abbreviations: P(M), prior model probability; P(M|data), posterior model probability; BF_M, posterior model odds; BF_{10}, Bayes factor that shows the evidence in favor of the alternative hypothesis.

[1]All models include subject, and random slopes for all repeated measurement factors. Bayes factors in favor of interaction effects can be calculated by dividing the BF_{10} of the model with the three-way interaction (i.e., $BF_{10} = 5.831 \times 10^{+22}$) by the BF_{10} of the model without the three-way interaction (i.e., $BF_{10} = 1.025 \times 10^{+24}$). In this case, the BF_{10} of the interaction effect is equal to 0.06 indicating little to no evidence.

Supplementary Table S6. Descriptive Statistics of the Participants' Reaction Times (in Seconds) During the Modified Stroop Task Per Group

		Group		
Word Type		Psoriasis [1]*N* = *48*	Significant Others *N* = *50*	Controls [1]*N* = *49*
Itch	*Mean (SD)*	29.94 (7.11)	31.44 (8.06)	29.62 (5.80)
	Min	18.70	15.96	15.45
	Max	52.89	53.67	47.83
	25th Percentile	25.25	25.91	25.83
	Median	28.75	30.40	28.99
	75th Percentile	33.33	35.37	33.36
Neutral	*Mean (SD)*	29.14 (8.39)	29.60 (6.99)	28.34 (5.41)
	Min	18.25	18.04	13.59
	Max	63.80	50.35	41.69
	25th Percentile	23.13	24.72	24.79
	Median	28.55	28.62	28.32
	75th Percentile	31.19	32.46	31.81

[1]Data was missing from three participants due to technical error.

Supplementary Table S7. Bayes Factors and Model Comparison of the Stroop Data Interaction Effect

Models[1]	P (M)	P (M | data)	BF_M	BF_{10}	Error %
Null model (incl. subject and random slopes)	0.200	4.349×10^{-5}	1.740×10^{-4}	1.000	
Group + Stimulus Type	0.200	0.276	1.526	6350.254	4.619
Group + Stimulus Type + Group ✻ Stimulus Type	0.200	0.023	0.094	529.565	7.215

Abbreviations: P(M), prior model probability; P(M|data), posterior model probability; BF_M, posterior model odds; BF_{10}, Bayes factor that shows the evidence in favor of the alternative hypothesis.

[1]All models include subject, and random slopes for all repeated measurement factors. Bayes factors in favor of interaction effects can be calculated by dividing the BF_{10} of the model with the interaction (i.e., $BF_{10} = 529.565$) by the BF_{10} of the model without the interaction (i.e., $BF_{10} = 6350.254$). In this case, the BF_{10} of the interaction effect is equal to 0.08 indicating inconclusive evidence.

Supplementary Table S8. Bayes Factors and Model Comparison of the Stroop Data Interaction Effect When Including Education as a Covariate

Models[1]	P (M)	P (M | data)	BF_M	BF_{10}	Error %
Null model (incl. subject and random slopes)	0.100	2.270×10^{-7}	2.043×10^{-6}	1.000	
Group + Stimulus Type + Education	0.100	0.306	3.965	$1.347 \times 10^{+6}$	5.447
Group + Stimulus Type + Education + Group ✻ Stimulus Type	0.100	0.027	0.245	116887.403	7.932

Abbreviations: P(M), prior model probability; P(M|data), posterior model probability; BF_M, posterior model odds; BF_{10}, Bayes factor that shows the evidence in favor of the alternative hypothesis.

[1]All models include subject, and random slopes for all repeated measurement factors. Bayes factors in favor of interaction effects can be calculated by dividing the BF_{10} of the model with the interaction (i.e., $BF_{10} = 116887.403$) by the BF_{10} of the model without the interaction (i.e., $BF_{10} = 1.347 \times 10^{+6}$). In this case, the BF_{10} of the interaction effect is equal to 0.09 indicating little to no evidence.