Attentional bias in psoriasis: The role of processing time and emotional valence

Short title: attentional hypervigilance in psoriasis

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Conflict of Interests

CEK has undertaken consultancy work and/or received grants and/or received honoraria from AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Janssen, La Roche-Posay, Leo Pharma, Novartis, Pfizer, UCB. The authors have no other conflicts of interest to declare.

Data availability statement

The study protocol was pre-registered (https://www.researchregistry.com/, Research Registry UIN: researchregistry5126). The raw data and all analysis scripts are available at https://osf.io/cu8de/. A preprint version of this manuscript has been submitted to https://psyarxiv.com/vpyf8.

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Abstract

Purpose: The present study explored whether people with psoriasis display an attentional bias towards disease-related threat words and whether this bias occurs relatively early during the phase of stimulus disengagement, or during a later maintained attention phase dominated by controlled strategic processes. We also explored the degree to which attentional bias is dependent on the emotional valence of control words.

Methods: Individuals with psoriasis and matched controls took part in 4 online experiments. Participants completed a spatial cueing paradigm using disease-related threat words and control words as cues, in order to obtain reaction time estimates of attentional bias.

Results: We did not observe evidence for attentional bias when control words were matched with threat words for emotional valence, regardless of whether processing time for the cues was limited (Experiment 1: SOA=250ms) or extended (Experiment 2: SOA=1050ms). We also did not observe evidence for attentional bias when control words of positive valence were used, but processing time was limited (Experiment 3). An attentional bias was only observed ($p=.012$, Cohen's $d=0.37$) when sufficient processing time was available and positively-valanced control words were used (Experiment 4).

Conclusion: Rather than showing large and generalized AB effects as predicted by previous accounts, our results tentatively suggest that AB in psoriasis is restricted to situations where participants have ample processing time and threat words are easily distinguishable from control words on the basis of emotional valence. The pattern of results suggests that attentional bias in psoriasis is best characterised as a relatively slow strategic process.

Keywords

psoriasis, hypervigilance, psychosocial impact, maintained attention, depression

Statement of Contribution

An information processing bias towards disease-related information has been proposed as a significant contributor to everyday stress in patients with psoriasis, however the direction of the effect (hypervigilance or attentional avoidance) and its potential automaticity are currently not well understood. The present study suggests that people with psoriasis show a hypervigilant attentional bias only during a relatively late time window. The bias and cognitive schemas related to it are thus likely to be accessible to cognitive behavioural interventions designed to reduce the psychosocial burden of the disease.

Introduction

Psoriasis is a currently incurable, chronic, immune-mediated skin disorder characterized by visible skin lesions, especially affecting the elbows, scalp, lower legs and knees although all body regions may be affected (Augustin et al., 2019; Lowes et al., 2007). It is among the most common immune-mediated diseases affecting almost 3% of people in the UK (Springate et al., 2017). The condition has a substantial negative impact on people's quality of life (Krueger et al., 2001) mainly related to the appearance of the skin, feelings of stigmatization and reduced mood (McKenna & Stern, 1997).

A considerable amount of variation in psychological distress in psoriasis can be explained by the way patients cognitively represent their disease (Fortune et al., 2003). According to illness perception models (Leventhal et al., 1992), patients are active processors of information about their disease and use this information to build up common-sense beliefs. These rich cognitive representations include perceived causes and consequences, beliefs about cure, control and duration as well as experienced symptoms (Fortune et al., 2002). The illness perception models held by patients with psoriasis may act as a schema (Beck & Clark, 1997) that guides information processing where stimuli that are consistent with a schema are elaborated upon whereas schema-inconsistent stimuli are ignored. For example, patients with psoriasis might have "stigma schema" or a "symptom schema" leading to an enhanced processing of disease-related stimuli in the environment (an attentional bias). Importantly, such an information processing account predicts that hypervigilance is not just the by-product of living with psoriasis, but plays a critical role in the maintenance of distress. A tendency for hypervigilant processing of psoriasis-related threats, such as sensory, visual or social aspects of the disease, may maintain and exacerbate psychological distress (Fortune et al., 2003).

Allocation of attention is a constant and necessary process during sensory perception, because the amount of incoming information far exceeds the bandwidth of conscious awareness (Raichle, 2010). Thus, rather than attending to all information to the same degree, attention is allocated based on relevance. A selective allocation of attention based on stimulus relevance, with more attentional resources allocated to potential threats, is an evolutionary advantageous trait of the human brain. However, an excessive amount of attentional allocation to threat-related stimuli, a so-called attentional bias, is dysfunctional, distressing and often elicits an anxiety-provoking cascade of maladaptive cognitions and emotions (Bar-Haim et al., 2011).

Attentional biases (AB) can occur at multiple processing stages (Posner, 1980; Posner & Petersen, 1990), either during the early phase of engagement with a stimulus, during the subsequent phase of stimulus disengagement, or during a late maintained attention phase dominated by controlled strategic processes. Experimentally manipulating the presentation time of threat stimuli allows to

specifically test during which stage an AB occurs (Cisler et al., 2009). Early ABs at the phase of early engagement with a stimulus are assumed to reflect automatic stimulus-driven bottom-up processes. Strong evidence for AB during the engagement phase can be obtained when stimuli are presented for very brief amounts of time (less than 100ms) followed by a visual mask as to preclude conscious processing (Becker et al., 2022; Bradley et al., 1997; Cisler et al., 2009), although it has been questioned whether such masking really prevents conscious processing (Phaf & Kan, 2007). Late attentional maintenance can be studied when long stimulus presentation times of more than 500ms are used. Such long presentation times allows multiple shifts of attention which are under strategic control (Liossi et al., 2011). Presentation times between 100 – 500ms (without visual masking) allow to study the intermediate period where both automatic and controlled processes are assumed to be operating on stimulus engagement and disengagement (Cisler et al., 2009; Fox et al., 2001).

In addition to when an AB is taking place, it is also important to determine the direction of that bias. Within each of the three processing stages, there are 3 possible patterns. First, people with psoriasis in relation to healthy controls could show an enhanced attentional processing of disease-related threats (i.e. hypervigilance); secondly, they could show attentional avoidance of threats; or thirdly, they could show an unbiased processing pattern.

There is already some evidence that people with psoriasis process disease-relevant information in an attentionally biased manner. Fortune et al. (2003) used a modified Stroop task to assess AB in patients with psoriasis and a control group. Groups were matched with respect to age and gender, but patients reported significantly higher levels of depression, anxiety and worrying than controls. Three different kinds of threat words were presented in that study, relating either to the self (e.g. *outcast*), others (e.g. *stare*) or the condition itself (e.g. *flaking*). Patients showed significantly longer reaction times for all 3 threat types, relative to controls. No such group difference was found for neutral words (e.g. *table*). This pattern of results was interpreted by the authors as reflecting a hypervigilant AB. Given that stimuli were not masked in the study, but remained on the screen until a response occurred, the bias cannot be characterized as an automatic engagement bias, but probably reflects a bias during the later disengagement phase. A more recent study by van Beugen et al. (2016) also used a Stroop task in a sample of psoriasis patients. They presented social threat and condition-specific threat words, in addition to neutral words. No evidence for an attentional bias was observed, which may be due to either a smaller sample size, the lower disease severity of psoriasis or because of the fact that in the van Beugen study, patients and controls were matched for levels of depression and anxiety. Very recently the same group (Nadinda et al., 2023) reported an additional task from the same sample where words related to itch (which is one important symptom

in psoriasis, Elewski et al., 2019) were compared with neutral words. Again, no evidence for an attentional bias was observed.

The starting point for the present series of experiments was to expand upon the study by Fortune et al (2003). Due to the type of AB task employed in that study (Stroop task), an alternative explanation unrelated to AB (e.g. threat words leading to greater emotional arousal which interferes with word processing) cannot be ruled out (Bar-Haim et al., 2007). A further limitation of the Stroop task is that it cannot distinguish between the two possible directions of an AB, hypervigilance and attentional avoidance. Another aspect that makes it difficult to ascertain whether the RT difference between threat and control words reported by Fortune reflects a true AB effect is that all threat words in that study were of emotionally negative valence and all control words of neutral valence. It therefore cannot be ruled out that people with psoriasis are not just attentionally biased towards threats related to physical, social and affective aspects of their disease, but may show a generalized bias towards negatively-valenced words, regardless whether they are disease-related or not. One way to rule out such an alternative explanation is to ensure that control words are matched with threat words with respect to their emotional valence. Finally, all previous studies have focused on tasks that tap into the phase of attentional disengagement, but no study so far has tested whether people with psoriasis show an AB during the subsequent phase of maintained attention (Bradley et al., 1997; Liossi et al., 2011).

The present study therefore employed an AB task (in the form an emotional spatial cueing task, Stormark et al., 1995) that allows distinguishing between hypervigilant and avoidant forms of AB. A total of 4 studies using this task were conducted, where patients and controls matched for age, gender, depression and anxiety were presented with threat words (e.g. *flaking*) and control words. To determine the temporal pattern of AB in psoriasis, words were either presented briefly (SOA 250ms, Experiments 1 and 3) or for longer periods of time (SOA: 1050ms, Experiments 2 and 4). To clarify whether there is still evidence for an AB in psoriasis when threat and control words are matched for valence, we used either negative (Experiments 1 & 2) or positive control words (Experiment 3 & 4). We predicted that people with psoriasis should show a larger AB than controls, in the form of a hypervigilant response pattern. The hypothesis and predictions of the 4 experiments were created in an iterative manner, where the result of one study led the next experiment.

General Methods

Transparency and Openness Promotion

In this article, we report how we determined our sample size, all data exclusions, all manipulations, and all measures that were included in the study, and we follow the STROBE guideline for reporting case – control studies. All data, analysis code, and research materials are available at https://osf.io/cu8de/. Data were analysed using R version 4.2.0 (R Core Team, 2022) as well as the packages *afex* (Singmann et al., 2022), *emmeans* (Lenth, 2022) and *splithalfr* (Pronk et al., 2021).

Participants

The study was originally planned to recruit patients from a local Dermatology clinic. We pre-registered the study protocol (https://www.researchregistry.com/, Research Registry UIN: researchregistry5126). We aimed to recruit 64 patients and the same number of control participants, providing sufficient power (80%, Cohen, 1992) to detect an effect that is at least of medium size or greater.

Shortly after recruitment started in January 2020, the Covid-19 pandemic began and we were no longer able to recruit face-to-face in a clinic context. Instead we decided to run the study online. Ethical approval for this online study was obtained from the Faculty of Health Sciences committee at the University of Hull. Participants were recruited via Prolific, an online participant recruitment platform, and a small number were directed to Prolific to enrol after responding to social media advertisements from the Psoriasis Association. Previously recruited participants from the dermatology department of Castle Hill Hospital were also invited to participate in the study, with 1 participant responding and continuing to enrol in the study via Prolific. Prolific is a large-scale online participant pool that allows researchers to connect with potential participants from all over the world. Studies are hosted on the platform, and pre-screening tools allow specific populations to be targeted, and participants sign up if they wish to take part. Prolific allows complete anonymity for participants in both data collection, compensation for participation, and follow up contact between participants and researchers. Participants were compensated at a rate of £9.00 per hour.

Compared to the pre-registered protocol, we made the following adaptions for the online studies: First, we increased the sample size to at least 80 participants in each arm of each study, to offset the potential increased variability when collecting data online as opposed to face to face. Second, we no longer used an inclusion criterion based on the Psoriasis Area and Severity Index (PASI), as this assessment is carried out by a dermatologist in a face-to-face situation. Instead, patients self-assessed their disease severity (see methods). Third, we used an online participant recruitment

platform (prolific.co) to identify and recruit patients and control participants. Fourth, only participants that passed all attention checks embedded into the online surveys were included in the analysis. All other details were as described in the initial registration.

For each of the 4 studies, we aimed to recruit a minimum of 100 patients and 100 controls. The demographic data for patient and controls, their anxiety and depression scores from the HADS, as well as the PASI and DLQI scores of the patients are summarised in Table 1. However, since not all patients who were originally enrolled in the study met all inclusion criteria, we had to exclude some patients in each study at the analysis stage bringing the total N for patients to below 100. Data were collected between June 2020 and October 2021. Participants were allowed to take part in more than one experiment. Overall, 51 patients took part in all 4 experiments, 44 in 3, 30 in 2 and 49 in 1 experiment. With respect to controls, 75 took part in all 4 experiments, 24 in 3, 25 in 2 and 13 in 1 experiment. When a participant took part in multiple experiments, there was a minimum gap of 7 days between successive experiments. For patients, the average time gap between Experiment 1 and 2 was 112 days (range 71 – 187), the average gap between Experiments 2 and 3 was 124 days (range 108 – 127) and the average gap between Experiment 3 and 4 was 16 days (range 13 – 27). For controls, the mean of the first gap was 22 days (range 7 to 81), the mean of the second gap was 123 days (range 66 – 132) and mean of the third gap was 16 days (range 8 – 37).

The demographic data for all participants included in the statistical analysis is shown in Table 1. In all 4 experiments, patients and controls were matched for age, gender as well as anxiety and depression scores (HADS-A, HADS-D). There were no significant group effects on any of these 4 variables across the 4 experiments (all $p > .23$, see Supplementary Table 2).

Materials

HADS

The HADS (Zigmond & Snaith, 1983) uses a single questionnaire to calculate 2 scores; one for anxiety (HADS-A, range 0-21) and one for depression (HADS-D, range 0-21), with scores > 8 in either category considered to be indicative of clinical anxiety or depression (Rishi et al., 2017). Both HADS-A and HADS-D show good concurrent validity (Bjelland et al., 2002; Snaith et al., 1982). In the present study, Cronbach's α was 0.8 and 0.85 for the HADS-D and HADS-A, respectively.

DLQI

The Dermatology Life Quality Index (DLQI, Finlay & Khan, 1994), a commonly used questionnaire in dermatology services, was used to measure the effect of skin condition on quality of life in the psoriasis group (range 0-30). In the present study, Cronbach's α of the DLQI was 0.85.

PASI

Psoriasis severity was evaluated using a modified self-assessed version of the PASI (Psoriasis Area and Severity Index, Fredriksson & Pettersson, 1978), rather than the usual practice of this being carried out by a qualified healthcare professional. The PASI is the recommended tool for the assessment of psoriasis in UK healthcare settings (NICE, 2012) and represents a score (range 0-72) based on the surface area of skin affected by psoriasis lesions and the appearance of those lesions.

The modified PASI questionnaire we used in our study asked participants to self-assess different elements of their psoriasis in each section of their body (head, arms, trunk, and legs). To assess area of skin affected by active lesions, participants were asked to use the rule of palm (Hettiaratchy & Papini, 2004). This involved using the palm of their hand as a measurement equal to approximately 1% of total body surface area. Participants then gave their answers in palm units, e.g., "3 palms worth of skin". Participants were also asked to rate the colour, thickness, and scaling of their psoriasis in each section of their body. Area scores and rating scores from each of the 4 body areas were then used to calculate an overall PASI score for each participant. In the present study, Cronbach's alpha of this self-assessed PASI was 0.71.

Selection and Validation of Verbal Stimuli for Emotional Spatial Cueing Task

85 psoriasis-related threat words were selected by identifying relevant words from previous research (Fortune et al., 2003; van Beugen et al., 2016), and from psoriasis related websites (NHS, 2017). These 85 words were then rated by people with psoriasis, along with 21 control words included as filler words. Participants volunteered to participate by responding to an advert describing this rating study by the Psoriasis Association. 28 participants with psoriasis rated each word from 0-10 on the following: Relatedness (0: not related to my psoriasis, 10: related to my psoriasis), Arousal (the level of emotional reaction the word provokes, 0-10), and Valence (how negative or positive the word is in terms of meaning, 0: negative, 10: positive). To assist in their ratings participants were presented with the Self-Assessment Manikin (Bradley & Lang, 1994) for valence and arousal at the beginning of the survey. The rating survey was created and distributed using JISC Online Surveys. A total of 24 threat words were then selected on the basis of the obtained ratings. Control words were then matched for arousal, lexical frequency and word length (± 1 letter) using published databases (van Heuven et al., 2014; Warriner et al., 2013). For Experiments 1 and 2, control words were additionally matched for valence, whereas for Experiments 3 and 4, positively valenced control words were used. The matching procedure resulted in 24 pairs of threat and control words for each study (for a full list of words, see Supplementary Table 1).

Emotional Spatial Cueing Task

AB was measured with the emotional spatial cueing task (Fox et al., 2001) which is an adaptation of Posner's spatial cueing task. A cue word on either the left- or right-hand side of a fixation cross was followed by a target which appeared either in the same location as the cue (so-called valid trial, 75% of trials) or on the opposite side of the screen (so-called invalid trial, 25% of trials). The participants' task was to indicate via button press, as quickly and as accurately as possible, on which side of the screen the target appeared. The keys 'F' and 'J' were used as response buttons, and participants were asked to use their left and right index fingers to make a response. The task was implemented for online testing using Psychopy (V 2020.1, psychopy.org) and the experiment was hosted on the online platform pavlovia (pavlovia.org). Since participants in an online study will use a variety of devices with different screen resolutions, the sizes of our stimuli were scaled relative to the height of that participant's screen.

Each trial began with a fixation cross in the centre of the screen along with two rectangles on either side (height=33%, width=22%, distance between rectangles: 22%). After 1000ms, the cue word appeared in one of the rectangles for a duration of either 200ms (Experiments 1 and 3) or 1000ms (Experiments 2 and 4). The cue then disappeared and after 50ms the circular target (size 3%) was presented (see Fig. 1). Thus, the stimulus onset asynchrony (SOA) between cue word onset and target was thus either 250ms (in Experiments 1 and 3) or 1050ms (in Experiments 2 and 4). Please see Supplementary Table 1 for an overview of all stimulus material.

Each block contained 32 trials, with 24 valid trials (12 control, 12 threat) and 8 invalid trials (4 control, 4 threat). Each block contained a total of 8 different word cues, with each threat word appearing with its matched control word in the same block (See Supplementary Table 1). Each participant completed 6 blocks. The experimental blocks were balanced with respect to the side on which a cue word appeared (left or right) and the experimental factors of Validity (valid vs invalid) and Cue_Type (threat vs control).

Reaction times (RTs) are typically faster for valid trials due to attention already being engaged with the cued location, and slower for invalid trials reflecting the cost of reorienting attention to the un-cued location. The latency difference between invalid and valid trials is referred to as the validity effect ($RT_{invalid} - RT_{valid}$). Larger validity effects for threat trials than for control word trials indicate an AB *toward* threat-related information (i.e. hypervigilance, Bar-Haim et al., 2007). The opposite pattern (larger validity effects for control cue trials) indicates an AB *away* from threat-related information (attentional avoidance). The difference between validity effects for threat and control cues can also be summarized numerically as $[(RT_{threat\_invalid} - RT_{threat\_valid}) - (RT_{control\_invalid} - RT_{control\_valid})]$.

This difference of differences is known as the bias score (Cisler & Olatunji, 2010; Etty et al., 2022; Koster et al., 2006), with positive bias scores indicating hypervigilance and negative scores indicating attentional avoidance.

Procedure

Patients were identified on the prolific platform through a series of screening surveys implemented using Jisc Online Survey (see Figure 2). Initially a 2 item-screening was distributed to all members of the prolific platform, where participants were asked to indicate whether they have a diagnosis of psoriasis, and whether their psoriasis is currently active with visible lesions. Those that said 'yes' to both questions (N = 601) where invited to take part in a second longer screening survey. This secondary screening assessed demographic data (age, gender), diagnosis of plaque psoriasis, current status of psoriasis (active or not), any other health condition with a larger perceived impact than their psoriasis and whether patients had any other skin condition apart from psoriasis. Additionally, the Hospital Anxiety and Depression scale was completed. Those patients (N = 246) that met inclusion criteria (currently active plaque psoriasis, no current psychological treatment, no other medical condition with larger self-perceived impact) were then invited to a third survey where PASI and DLQI were assessed. Attention checks were built into the surveys by asking participants to select a specific response option on a few questions (e.g. an attention check question might read 'please select sometimes' in a selection screen where multiple response options were given). These questions were used to calculate an attention score for each participant. This allowed exclusion of participants showing insufficient attention when giving their responses (see Figure 2). Patients for all 4 studies were recruited from this pool of 246 patients.

Controls were identified using a similar process of sequential screening surveys. All participants without a diagnosis of psoriasis (N= 2710, i.e. those that responded 'no' to the first question of the initial screening) were then invited to a secondary screening where demographic data, diagnosis of any skin conditions and the HADS were assessed. Following matching for age, gender, depression and anxiety scores, controls for all 4 experiments were recruited from this pool of 279 volunteers.

Participants were allowed to take part in more than one experiment (see participants section for details).

Data Analysis

Trials with very long (RT > 1250ms, 0.2% of data) and very short RTs (RT < 150ms, 1.6% of data) were excluded. RTs outside ± 2 SDs of a participant's mean (4.2% of data) as well as incorrect responses (1.8% of data) were also excluded. Participants with less than 75% of trials remaining after application of these criteria were excluded from the statistical analysis (see Figure 2). For each

experiment, we then conducted a 2 x 2 x 2 mixed ANOVA, using the within-subject factors Cue Type (threat, control), Validity (valid, invalid) as well as the between-subject factor Group (patients, controls). We also calculated the aforementioned bias score for each participant, and in those cases where there was a significant difference in bias scores between groups, we additionally tested via one-sample t-tests whether this bias reflects attentional hypervigilance (i.e. bias score significantly > 0) or attentional avoidance (bias score significantly < 0).

To analyse the reliability of the reaction time estimates of our experimental conditions, we performed a split-half analysis of the reaction time data for each of the 4 repeated measures conditions in the study (threat-valid, threat-invalid, control-valid, control-invalid). This analysis was performed using the R package splithalfr (Pronk et al., 2021), using a total of 1000 permutations. On each permutation, the split-half correlation between test halves was computed and the Spearman-Brown prophecy formula was used to correct for test length.

Results

We report the reliability of the data that formed the basis of our statistical analysis, i.e. the subject-level aggregated means from the four repeated measure conditions (threat-valid, threat-invalid, control-valid, control-invalid). Reliability of these scores was high across all 4 experiments, with all mean Spearman-Brown coefficients > 0.95 (see Supplementary Table 3a for details). We performed an additional reliability analysis, to estimate the degree to which the reaction scores remain reliable once the repeated measure aspect of our study is taken into account. For this analysis, we first subtracted each individual's mean reaction time from each split-half condition estimate. Reliability indices for these demeaned reaction time estimates were somewhat lower and ranged between 0.58 and 0.75 (see Supplementary Table 3b).

Experiment 1 (Negative Control Stimuli, SOA 250ms): Results & Discussion

The ANOVA yielded a significant main effect of Validity ($F(1, 183) = 619.03$, $p < 0.001$) with invalid trials showing longer RTs (M = 371, 95% CI [364, 379]) than valid trials (M = 328, 95% CI [322, 334]) across both groups (see Table 2, Figure 3, Supplementary Table 4). However, the critical 3-way interaction of Group × Validity × Cue Type was not significant ($F(1, 183) = .39$, $p = .599$) suggesting that the attentional bias score did not differ significantly between groups.

Experiment 1 presented threat words and valence-matched control words briefly (SOA: 250ms). The design of the task closely followed Fox et al. (2001), who observed robust AB effects with a similar SOA, interpreted as reflecting a bias during the stimulus disengagement phase. In Experiment 1, we

observed no evidence for people allocating their attention preferentially towards threat words during the stimulus disengagement period, relative to controls.

One possible explanation of this negative finding is insufficient processing time. At an SOA of 250ms, there is only a limited time for controlled/strategic processes to influence attentional allocation. Since we observed no evidence for AB in Experiment 1 with a short SOA, it might be the case that AB in psoriasis is primarily a consequence of strategic processing and thus only observable when participants have more time to process each cue before the target appears. This possibility was tested in Experiment 2, where participants had roughly 4 times as much time to process each word cue (SOA of 1050m instead of 250ms).

Experiment 2 (Negative Control Stimuli, SOA 1050ms): Results and Discussion

The ANOVA for Experiment 2 yielded significant main effects of Group ($F(1, 183) = 7.00$, $p = .009$) and Validity ($F(1, 183) = 321.08$, $p < .001$). As in Experiment 1, the main effect of Validity reflected longer RTs for invalid ($M = 373$, 95% CI [367, 380]) as compared to valid trials ($M = 348$, 95% CI [341, 354]). The main effect of Group was due to longer RTs for patients ($M = 369$, 95% CI [360, 379]) as compared to controls ($M = 352$, 95% CI [343, 360]). No other main effects or interactions of the ANOVA were significant.

In Experiment 2 participants had roughly 4 times as much time to process each word cue as compared to Experiment 1 (SOA of 1050m instead of 250ms). Again, we observed no evidence for an AB, suggesting that people with psoriasis do not preferentially allocate their attention to threat words, relative to valence-matched control words, even when there is ample processing time available. This second negative finding in Experiment 2 caused us to reconsider our earlier decision to use valence-matched control words. Fortune et al. (2003) detected an AB effect using threat and control words that were not matched for valence whereas the present study failed to detect an AB effect in two well-powered studies (Experiments 1 and 2) using valence-matched threat and control words. It might the case that a clear valence contrast between threat and control stimuli is a necessary requirement for an AB effect to occur because it amplifies the distinctiveness between the two cue types. Without a valence contrast, as in Experiments 1 and 2 of the present study, threat words may not stand out as clearly against the background of control words, thus limiting the sensitivity of a study to detect an AB. We empirically tested this possibility in Experiments 3. This experiment was identical to Experiment 1, except that the negatively-valenced control words were replaced with positive ones, to maximize the valence contrast between threat and control words.

Experiment 3 (Positive Control Stimuli, SOA 250ms): Results & Discussion

The ANOVA for Experiment 3 revealed significant main effects of Group ($F(1, 197) = 5.76$, $p = .017$) and Validity ($F(1, 197) = 826.17$, $p < .001$), as well as a significant Cue Type × Validity interaction ($F(1, 197) = 7.74$, $p = .006$). The main effect of Validity again reflected longer RTs for invalid (M = 374, 95% CI [367, 380]) than valid trials (M = 328, 95% CI [322, 334]), whereas the main effect of Group was due to longer RTs for patients (M = 358, 95% CI [349, 367]) relative to controls (M = 343, 95% CI [335, 352]). The Cue Type × Validity interaction was driven by significantly larger validity effects ($t(197) = 2.78$, $p = .006$) for threat trials (M = 47.2, 95% CI [43.8 50.2]) relative to control word trials (M = 45.0, 95% CI [41.8 48.1]). No other main effects or interactions of the ANOVA were significant.

Experiment 3 (short SOA, positive control words) again provided no evidence for a difference in AB scores between groups suggesting that even when there is a clear valence contrast between threat and control words, people with psoriasis do not automatically allocate their attention to threats during the stimulus disengagement phase. As a final possibility, we considered the case that AB in psoriasis is primarily a consequence of strategic processing and thus only observable when participants have more time to process each cue before the target appear, in addition to having the benefit of a clear valence contrast between threat and control words. This possibility was tested in Experiment 4, where participants had both the benefit of more processing time (long SOA) and of a clear valence contrast (positive control words).

Experiment 4 (Positive Control Stimuli, SOA 1050ms): Results

In Experiment 4, the ANOVA indicated a significant main effect of Validity ($F(1, 191) = 321.11$, $p < .001$). The main effect of Validity reflected longer RTs for invalid (M = 372, 95% CI [365, 379]) as compared to valid trials (M = 342, 95% CI [336, 349]). Additionally, the critical three-way interaction Group × Cue Type × Validity ($F(1, 191) = 6.41$, $p = .012$) was significant. The three-way interaction reflected that the bias score in the patient group (M = 3.53, 95% CI [0.67 6.39] was significantly larger ($t(191) = 2.53$, $p = .012$, Cohen's $d = 0.37$) than the bias score in the control group (M = -1.42, 95% CI [-4.00 1.17], see Table 2. Since bias scores greater than 0 indicate a pattern of hypervigilance, we additionally tested whether the bias score differed significantly from 0 using one-sample t-tests. This was the case in the patient group ($t(86) = 2.36$, $p = .020$), but not in the control group ($t(105) = 1.11$, $p = .269$).

General Discussion

It has been suggested that vigilance for threat may be an important contributor to the everyday stress experienced by many patients with psoriasis (Fortune et al., 2003). Such an account would

predict strong attentional biases, possibly spanning multiple stages of attention. The results of the present series of experiments provide a more nuanced view. Instead of a generalized AB across several stages of attention, we observed that AB in psoriasis is restricted to situations where participants have sufficient processing time for each stimulus, whereas no AB occurs when processing time is very limited. Furthermore, disease-related threat words do not draw more attention than negatively-valenced words unrelated to the disease experience. Instead, it seems that a clear valence contrast is a second pre-condition for an AB, in addition to sufficient processing time.

The evidence for a hypervigilant bias we observed for a long SOA of 1050ms in Experiment 4 may indicate enhanced or sustained processing of a disease-related stimulus once it has been detected. It has been suggested that biases at this later stage are characteristic of depression (Bradley et al., 1997; Gotlib et al., 2004; Mathews & MacLeod, 1994) and may be linked to rumination (Bradley et al., 1997; Siegle et al., 2002). A somewhat speculative way to interpret the pattern of results could be that mood, rather than anxiety, is the key driver for altered attentional allocation in people with psoriasis. Such an account would predict that depression but not anxiety is correlated with AB in patients. Unfortunately, our study was not designed to perform a meaningful test for this relationship because of the considerable time gap between the self-report assessments and the reaction time assessment of AB.

Compared to the previous studies by Fortune et al, who observed large reaction time differences between patients and controls, the magnitude of the AB we observed in Experiment 4 is smaller. One possible reason for this might be the choice of threat words. Fortune et al. used 3 categories of threat words (related to self, others and the condition itself). Descriptively, they observed the largest AB for social threat words related to negative reactions of others (e.g. disgust, stare), and a smaller AB for threat words related to visual or sensory aspects of psoriasis (e.g. itching, scaling). The stimulus pool of the present study (see Supplementary Table 1) predominantly contained words related to the sensory or affective aspect of psoriasis, but fewer social threat words, which may have reduced the magnitude of the AB observed in the present study. Another factor that might explain the difference in effect sizes between studies could be the degree to which participant variables were controlled for. The present study, as well as the two studies from the Netherlands (Nadinda et al., 2023; van Beugen et al., 2016) matched patients and controls for age, gender, depression and anxiety. In these studies, either no AB (Experiment 1-3 of present study, as well as Nadinda et al., 2023; van Beugen et al., 2016), or an AB of small magnitude (Exp. 4 of the present study) were observed. In contrast, the study by Fortune et al reported a large AB effect, but only matched for age and gender, with patients showing significantly higher depression, anxiety and worrying scores. Disease severity might be another factor contributing to the differential outcomes of experiments.

Patients in the study by Fortune (mean PASI of 9.8) had more extensive psoriasis than the patients of the current study (mean PASI between 5.1 and 5.6) or the studies from the Leiden group (mean PASI: 4.56).

From a clinical perspective, the results of the present study could be of interest for psychological interventions for people with psoriasis. Unlike early pre-attentive ABs, which are difficult to address with typical psychological interventions, late ABs as identified in the present study are much more accessible to introspection. AB may provide diagnostic value in identifying attentional biases in people with psoriasis. The underlying schema can then be explored with the help of a psychological practitioner. This could allow identifying relevant thought patterns for a mindfulness cognitive therapy (Segal et al., 2018) or acceptance and commitment therapy (Hayes et al., 2012), but may also be useful for identifying and altering irrational beliefs (e.g. self-stigma) as part of a rational emotive therapy (Ellis, 1987).

The present study raises a number of interesting questions for future research. At higher disease intensities, patients are more likely to experience a significant negative impact of psoriasis on their quality of life and this relationship might be mediated by AB. Van Ryckeghem and colleagues (Van Ryckeghem et al., 2013) conducted a diary study with chronic pain patients, a condition where AB has been researched quite intensively. They found that daily pain intensity was positively reed with disability. AB moderated this relationship such that a large AB strengthened the relationship between pain and disability. It would be interesting to probe whether a similar relationship exists in patients with psoriasis. Another interesting question for future research is the degree to which people with psoriasis show an automatic early AB. Strong evidence for an automatic AB can only be obtained when stimuli are presented in a way that precludes conscious processing, such as using a very short SOA of < 100ms, followed by a visual mask (Bradley et al., 1997; Cisler et al., 2009). None of the existing studies have used such a way to present their stimuli, thus a strong test of the potential automaticity of AB in psoriasis is still outstanding. A systematic comparison of different categories (sensory, affective, stigma) would also be of great interest. There is evidence from pain that a sensory AB predicts current pain levels (Haggman et al., 2010; Sharpe et al., 2014), whereas an affective AB is a better predictor of future pain and chronicity (Sharpe et al., 2014). Since attending to affective vs attending to sensory pain differently affects AB in pain (Boston & Sharpe, 2005), a similar dissociation may exist for psoriasis as well, where itch is a very frequent symptom.

Like all studies, the current one is not without limitations. Due to impact of COVID, we switched towards an online recruitment form where patients self-reported that they had a diagnosis of psoriasis. Another limitation is that number of words relating to social threats in the stimulus pool

(which may be an important driver of AB) was too small for an analysis that separates out different groups of threat stimuli (e.g. sensory threat words, affective threat words, social threat words). A further limitation is the unequal number of patients and controls in the 4 experiments. Although an equal number of patients and controls were recruited in each experiment, subsequent analysis indicated that some patients did not meet all inclusion and exclusion criteria, which recued the number of patients available for the statistical analysis. Another limitation is that there was a considerable time gap between the initial self-report assessments (e.g. HADS, DLQI) and the subsequent reaction time assessments. Furthermore, we did not systematically assess medication or fatigue in our participants. We acknowledge that the pattern of results obtained in the present study may not generalize to patient populations with more extensive psoriasis. Furthermore, since convergent validity of different AB measures seems to be limited (Cisler et al., 2009; Van Bockstaele et al., 2020), it cannot be taken for granted that the current result of late hypervigilance towards threat in people with psoriasis generalizes to other AB measures.

In conclusion, our results tentatively suggest that AB in psoriasis is restricted to situations where participants have ample processing time and threat words are easily distinguishable from control words on the basis of emotional valence. The pattern of results suggests that AB in psoriasis is best characterised as a relatively slow strategic process possibly related to rumination.

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Tables

Table 1 Demographic data of participants included in the statistical analysis

Exp.	Group	N	Female	Male	Non-binary	Age (*SD*)	Other health condition (N, %)	HADS-A (*SD*)	HADS-D (*SD*)	DLQI (*SD*)	PASI (*SD*)
Exp. 1	Control	101	40	60	1	31.4 (10.2)	0 (0%)	8.5 (4.4)	6 (3.7)		
	Patient	84	33	51	0	30.9 (9.9)	6 (7.1%)[a]	8.3 (4)	6.2 (3.9)	8 (5.4)	5.6 (4.6)
Exp. 2	Control	102	38	63	1	31.5 (10.4)	0 (0%)	8.5 (4.3)	5.8 (3.2)		
	Patient	83	33	49	1	32.2 (9.9)	7 (8.4%) [a]	8.1 (4.1)	5.9 (3.8)	7.2 (5.1)	5.3 (4.1)
Exp. 3	Control	107	39	67	1	31.3 (10.7)	0 (0%)	8 (4.5)	5.5 (3.4)		
	Patient	92	38	53	1	32.8 (9.8)	9 (9.8%) [a]	8.1 (4.3)	5.8 (3.9)	6.9 (5.2)	5.3 (4.1)
Exp. 4	Control	106	36	69	1	31.8 (10.9)	0 (0%)	8 (4.4)	5.7 (3.7)		
	Patient	87	39	47	1	33.5 (9.9)	7 (8.1%) [a]	8.1 (4.3)	5.6 (3.8)	6.8 (4.7)	5.1 (4)

[a] List of other major health conditions reported by patients: Patient 1: Hypothyroidism; Patient 2: Kyphosis & lordosis, Patient 3: Heart disease; Patient 4: Insulin resistance; Patient 5: Type 2 diabetes & hypertension; Patient 6: Asthma; Patient 7: Hypertension; Patient 8: Diabetes; Patient 9: HIV; Patient 10: Ulcerative colitis. HADS-A & HADS-D: Hospital Anxiety and Depression Scale, anxiety and depression scores, respectively. DLQI: Dermatology LIfe Quality Index. PASI: Psoriasis Area and Severity Index.

Table 2 Mean (standard deviation) reaction times (RTs) in milliseconds (threat valid and invalid as well control word valid and invalid), and for both groups (control and patient). Also included are validity effects and overall bias score

		Threat Stimuli			Control Stimuli			
Exp.	Group	Invalid (Ti)	Valid (Tv)	Validity Effect (Ti-Tn)	Invalid (Ci)	Valid (Cv)	Validity Effect (Ci-Cv)	Bias Score [(Ti-Tv)-(Ci-Cv)]
Exp. 1	Control	368 (52)	328 (44)	41 (24)	368 (51)	328 (43)	40 (24)	0.1 (15)
	Patient	374 (48)	327 (44)	47 (26)	375 (52)	329 (44)	46 (26)	1.2 (14)
Exp. 2	Control	364 (45)	339 (48)	25 (21)	363 (44)	340 (48)	23 (20)	1.6 (16)
	Patient	384 (49)	356 (46)	28 (21)	382 (49)	355 (46)	27 (22)	1.3 (16)
Exp. 3	Control	366 (44)	320 (39)	46 (22)	365 (44)	321 (39)	43 (20)	3 (11)
	Patient	382 (52)	334 (48)	48 (25)	382 (52)	335 (48)	46 (26)	1.5 (12)
Exp. 4	Control	365 (47)	335 (41)	31 (22)	367 (46)	335 (39)	32 (23)	-1.4 (13)
	Patient	378 (54)	349 (52)	29 (26)	376 (52)	350 (52)	26 (25)	3.5 (14)

Figures

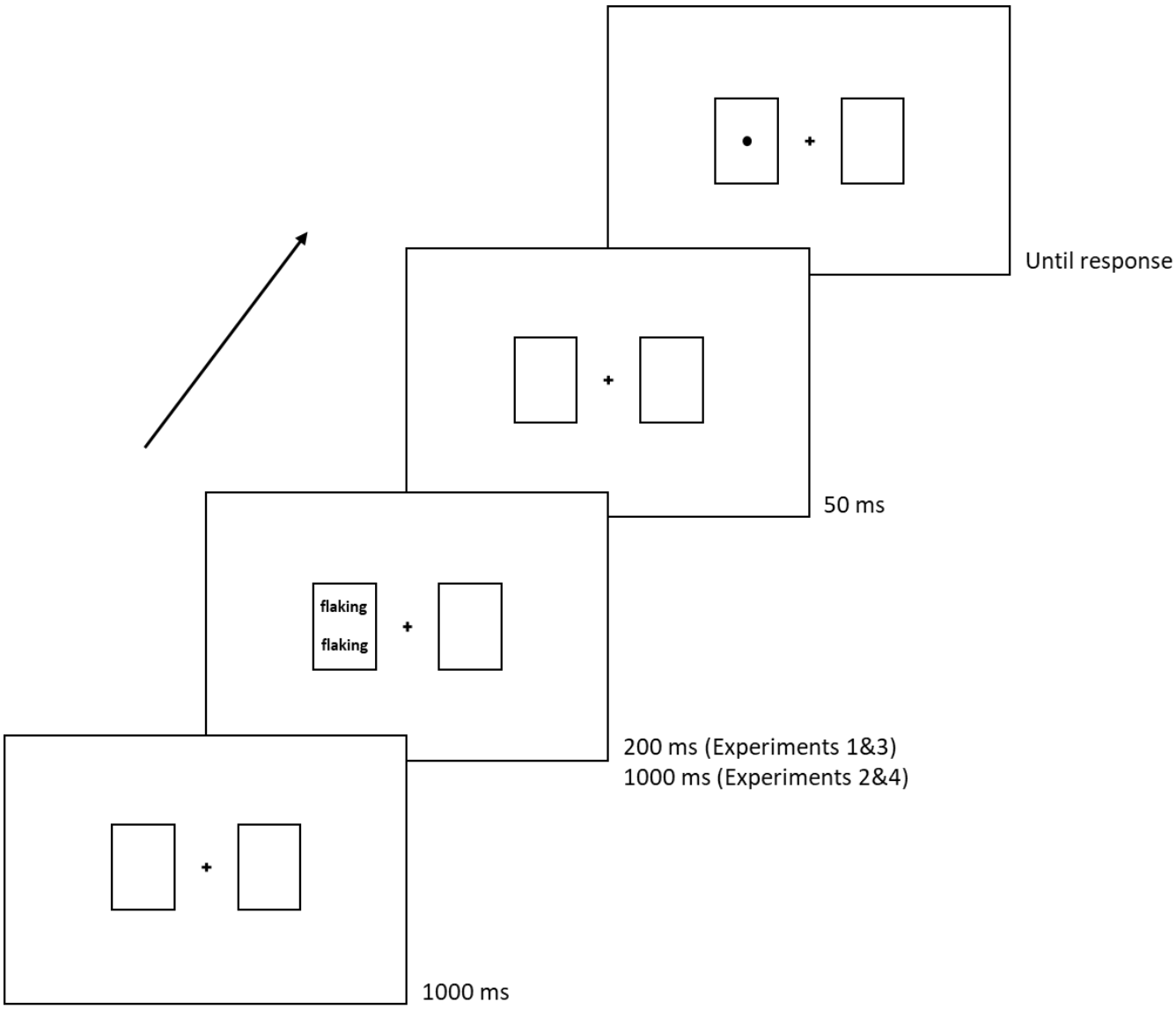


Figure 1 Example of a valid threat trial where word cue and subsequent target appeared in the same location. In invalid trials, the target appeared on the opposite side of screen in the uncued position. The task of the participant was to identify the position of the target as quickly and as accurately as possible. The latency of that response in milliseconds was the key outcome variable of the study.

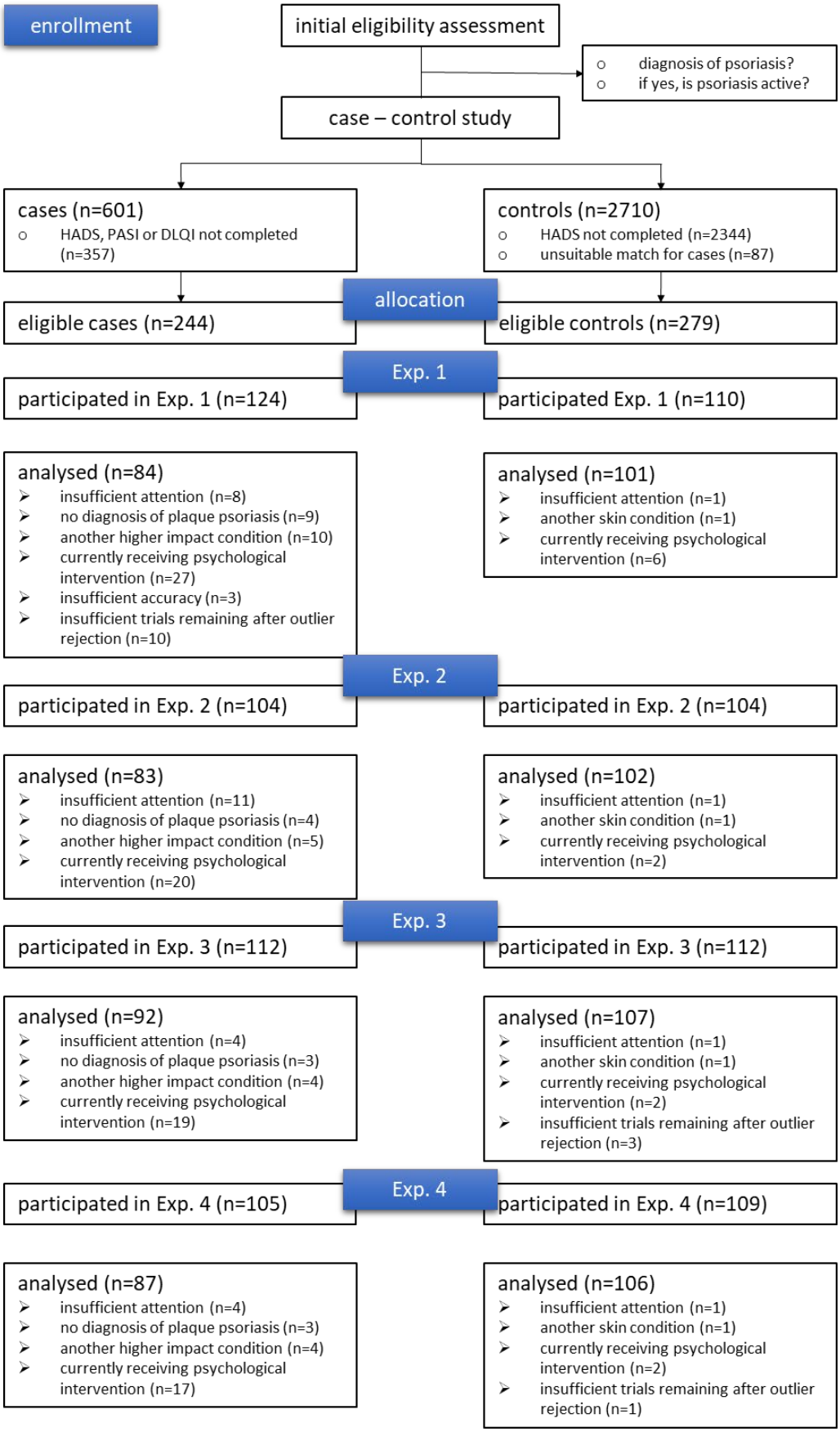


Figure 2 CONSORT flow diagram of present study

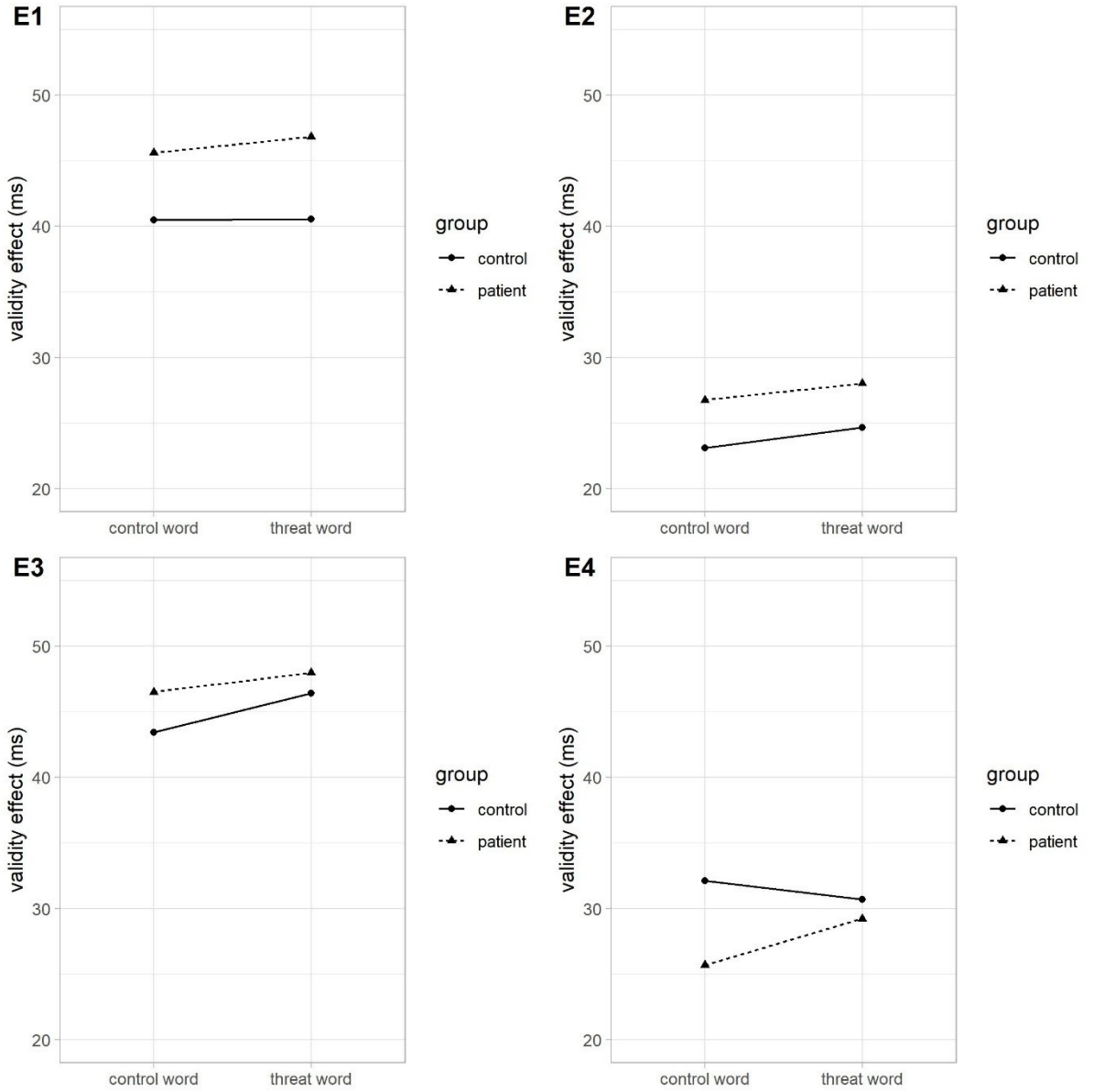


Figure 3 Mean validity effect (i.e. difference of invalid – valid) for control word and threat word trials, and both groups, for all 4 experiments (E1-E4).

Supplementary Tables

Supplementary Table 1 Overview of stimulus materials

Threat word	Word Pair	Arousal	Valence (reverse scored)	Relatedness	Control word (negative)	Control word (positive)
itching	1	7.50	8.71	9.18	intrude	charming
flare-up	2	7.32	8.64	9.07	paradox	ambition
flaking	3	6.93	8.25	9.21	disable	fluffy
scaly	4	6.79	7.75	8.68	chuck	safety
sore	5	6.79	7.96	8.32	spoil	neat
scaling	6	6.75	7.96	8.32	vacancy	pudding
scalp	7	6.50	7.54	8.75	dump	cuddle
inflamed	8	6.61	7.79	8.18	stricken	sunlight
scabby	9	6.54	8.25	7.54	nappy	gentle
pain	10	6.68	7.93	7.46	fatal	fun
irritated	11	6.61	7.64	7.57	deadline	limitless
raw	12	6.18	7.54	7.57	ram	new
lesion	13	6.29	7.68	7.25	warlord	jackpot
bleeding	14	6.11	7.50	7.57	outbreak	delighted
unhappy	15	6.36	8.39	6.32	seasick	amusing
insecure	16	6.61	7.89	6.50	sewage	talented
ugly	17	6.68	7.93	6.36	greed	wise
messy	18	6.54	7.29	6.68	dread	merry
burning	19	6.29	7.46	6.75	drinker	lovable
disgust	20	6.68	7.93	5.57	grouchy	courage
stinging	21	6.21	7.46	6.43	zombie	winnings
gross	22	6.36	7.71	6	noisy	enjoy
repulsive	23	6.21	7.71	5.75	pollution	romantic
stare	24	6.18	7.04	5.82	blast	smile

The same set of 24 threat words were used in all 4 experiments. Negative control words were used in Experiments 1 and 2, positive control words in Experiments 3 and 4.

Supplementary Table 2 Inferential tests to see whether patient and control groups are matched on key variables

Experiment	Variable	Statistical result for group effect	*p*
Exp. 1	HADS-A	$t(180.81) = 0.32$	.75
	HADS-D	$t(173.09) = -.26$	.79
	age	$t(178.48) = 0.37$	.71
	gender	$\chi^2(2) = 0.85$	.99
Exp. 2	HADS-A	$t(177.85) = 0.61$	.54
	HADS-D	$t(160.15) = -0.19$	.85
	age	$t(178.12) = -0.45$	.66
	gender	$\chi^2(2) = 0.15$	.88
Exp. 3	HADS-A	$t(194.92) = -0.12$	.90
	HADS-D	$t(183.12) = -0.55$	.58
	age	$t(196.27) = -0.98$	.33
	gender	$\chi^2(2) = 0.52$	.78
Exp. 4	HADS-A	$t(185.29) = -0.20$	.84
	HADS-D	$t(182.62) = 0.22$	.83
	age	$t(189.06) = -1.17$	.24
	gender	$\chi^2(2) = 2.45$	.23

Numerical outcomes were compared using Welch t-tests, the categorical outcome was evaluated using Fisher's exact test.

Supplementary Table 3a Reliability of reaction times [95% CI] for the all 4 experimental conditions across all 4 experiments

Experiment	Threat-valid	Threat-invalid	Control-valid	Control-invalid
Exp. 1	0.98 [0.98 0.99]	0.96 [0.96 0.97]	0.98 [0.98 0.99]	0.96 [0.94 0.97]
Exp. 2	0.98 [0.97 0.99]	0.95 [0.94 0.96]	0.98 [0.98 0.99]	0.95 [0.94 0.96]
Exp. 3	0.98 [0.98 0.99]	0.97 [0.96 0.97]	0.98 [0.98 0.99]	0.96 [0.96 0.97]
Exp. 4	0.98 [0.98 0.99]	0.96 [0.94 0.97]	0.98 [0.98 0.99]	0.96 [0.95 0.97]

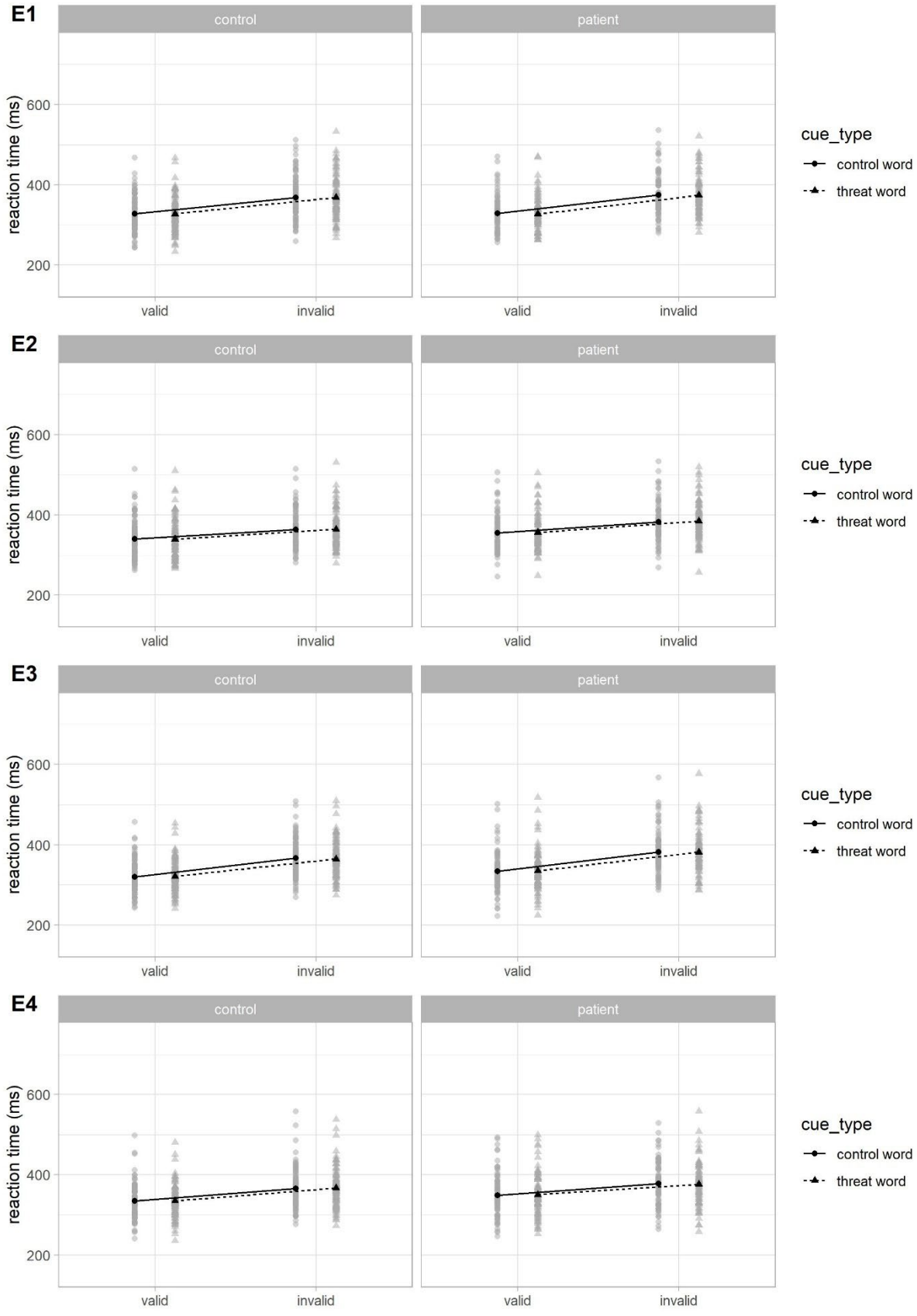
Supplementary Table 3b Reliability of reaction times [95% CI] for the all 4 experimental conditions after removing each participants mean RT

Experiment	Threat-valid	Threat-invalid	Control-valid	Control-invalid
Exp. 1	0.6 [0.46 0.72]	0.76 [0.7 0.8]	0.66 [0.54 0.75]	0.75 [0.6 0.8]
Exp. 2	0.58 [0.44 0.73]	0.66 [0.53 0.74]	0.62 [0.45 0.8]	0.7 [0.63 0.76]
Exp. 3	0.68 [0.56 0.79]	0.76 [0.69 0.81]	0.64 [0.54 0.72]	0.75 [0.66 0.81]
Exp. 4	0.71 [0.63 0.78]	0.72 [0.63 0.78]	0.66 [0.58 0.73]	0.72 [0.65 0.78]

Supplementary Table 4 *Full ANOVA results for all 4 experiments*

Experiment	Effect	df	MSE	F	p
Exp. 1	group	1, 183	8281.60	0.24	.628
	cue_type	1, 183	47.66	1.67	.198
	group:cue_type	1, 183	47.66	0.84	.361
	validity	1, 183	557.17	619.03	<.001
	group:validity	1, 183	557.17	2.67	.104
	cue_type:validity	1, 183	53.03	0.38	.539
	group:cue_type:validity	1, 183	53.03	0.28	.599
Exp. 2	group	1, 183	8220.72	7.00	.009
	cue_type	1, 183	70.57	1.30	.256
	group:cue_type	1, 183	70.57	0.50	.479
	validity	1, 183	375.00	321.08	<.001
	group:validity	1, 183	375.00	1.49	.223
	cue_type:validity	1, 183	63.12	1.44	.231
	group:cue_type:validity	1, 183	63.12	0.02	.899
Exp. 3	group	1, 197	7764.18	5.76	.017
	cue_type	1, 197	46.44	0.01	.931
	group:cue_type	1, 197	46.44	0.36	.551
	validity	1, 197	508.48	826.17	<.001
	group:validity	1, 197	508.48	0.52	.471
	cue_type:validity	1, 197	31.49	7.74	.006
	group:cue_type:validity	1, 197	31.49	0.87	.352
Exp. 4	group	1, 191	8462.38	3.74	.055
	cue_type	1, 191	79.55	0.01	.908
	group:cue_type	1, 191	79.55	0.88	.349
	validity	1, 191	516.05	321.11	<.001
	group:validity	1, 191	516.05	1.45	.230
	cue_type:validity	1, 191	45.61	1.17	.280
	group:cue_type:validity	1, 191	45.61	6.41	.012

Supplementary Figures



Supplementary Figure 1 *Mean reaction times for all experimental conditions across all 4 experiments*