



Are sex and history of pruritic skin conditions factors which affect the phenomenon of visually evoked itch? An exploratory study

Donna M. Lloyd^a, Rebecca Dodd^a, Caroline Higgins^a, Melanie R. Burke^a, Francis McGlone^{b,c,*}

Introduction: We have previously shown that sensations of itch and the scratch response can be evoked using itch-related images. However, we did not determine whether individual differences in a person's experience of itch could moderate this effect. This exploratory study aimed to determine whether sex or a history of pruritic skin conditions (PSCs) could influence the effects of visually evoked itch and scratch.

Methods: Forty-one participants (19 males; 16 with a history of PSCs) viewed static images that could either be itch or nonitch related. These were further separated by picture type: "skin contact" (ants crawling on the hand vs. a butterfly on the finger); "skin response" (scratching an insect bite vs. washing the hands); "skin condition" (psoriasis vs. freckles) or "context only" (insects vs. birds). Images were rated using a 10-point scale by answering: "How itchy do you feel?" (Self-rating) and "How itchy do you think the person in the picture feels?" (Other-rating). Frequency and location of scratching was also recorded.

Results: The highest itch scores were to itch-related skin contact pictures. Females gave higher itch ratings than males, and people with a history of PSCs gave higher itch ratings when viewing images of people scratching. There was no correlation between itch ratings and scratch response, and no relationship between body site viewed and location of scratching.

Discussion: There is a heightened response to itch-related cues in females and those with PSCs, indicating a more centrally mediated pathway bringing subconscious itch sensations into conscious awareness in these populations. These findings could influence personalized treatment interventions aimed at reducing awareness of itch sensations in susceptible individuals.

Keywords: Visually evoked itch (VEI), Scratch response, Sex, Pruritic skin conditions (PSCs), Body location

Introduction

The reflexive itch-scratch cycle is both an addictive and rewarding behavioral response in healthy people and a highly debilitating symptom in pruritic dermatological conditions such as atopic dermatitis (AD). This cycle can be triggered by "contagious itch," that is an induced feeling of itch typically followed by a scratch response, resulting from viewing another person scratching^[1]. While several studies have explored this effect using different methods for triggering the phenomenon^[1-4], only 1 study has thus far compared the effectiveness of different visual stimuli to evoke itch and scratch^[5]. However, it did not assess the

impact of individual differences such as sex or history of pruritic dermatological conditions on visually evoked itch (VEI). The main aim of the present study was to explore the impact of these individual differences on itch sensations and the scratch response in order to determine whether these factors make some people more vulnerable to contagious itch.

One factor that could influence susceptibility to VEI is having a history of pruritic skin conditions (PSCs). Previous studies have demonstrated that a combination of watching videos of people scratching while participants received either histamine or saline administration caused self-reported itch intensity to increase in all participants, but resulted in a doubling of spontaneous scratching episodes in those with AD who also appeared to scratch a more widespread area for longer^[1]. Lloyd et al^[5] have shown that images containing itch-related stimuli in contact with the body (such as ants crawling on the skin) produce the highest ratings of itch intensity. However, it has yet to be established whether participants with a history of PSCs, and/or images of skin conditions (such as psoriasis), produce higher ratings, thereby confirming the importance of VEI in the itch-scratch cycle.

A second factor that can influence itch perception and the scratch response is sex. Although recent studies have shown sex-specific differences in the quality, localization and triggering of chronic pruritus, and in the underlying disease and scratching behavior^[6], studies from the experimental literature have typically found no sex differences in itch contagion^[3], itch ratings or scratch behavior^[1]. However, this may be due to limited sample sizes (eg, only 3 males and 8 females with AD were tested in Papouli et al^[1]) or biased samples that recruited twice as many

^aSchool of Psychology, University of Leeds, Leeds, ^bSchool of Natural Sciences & Psychology, Liverpool John Moores University and ^cInstitute of Psychology, Health & Society, University of Liverpool, Liverpool, UK

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*Corresponding author. Address: School of Natural Sciences & Psychology, Room 1.18, Life Sciences Building, Liverpool John Moores University, Byrom Street, Liverpool, L3 3AF, UK. Tel: +44-151-904-6332. E-mail address: F.P.McGlone@ljmu.ac.uk (F. McGlone).

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females to males^[3]. To address this bias, similar numbers of males and females were recruited in the current study.

Previous studies have suggested that separate mechanisms may be responsible for the sensation of itch and subsequent scratching, which may not be body part specific^[1]. Ward et al^[7] found that participants used both hands equally often to scratch themselves, which was independent of the hand seen in the image. However, the visual stimuli depicted scratching only to the arms and chest, while the vast majority of the participants' directed scratching toward their head. Other studies have shown that, while itch was more intensely perceived at the ankle, scratching attenuated itch most effectively on the back^[8]. Although not one of our main aims, the current study further investigates the topographical differences in VEI and scratch by presenting images of 4 different body parts: head, arm, leg, and torso, and recorded whether the site depicted matched the area participants subsequently scratched.

Methods

Participants

Forty-one participants were opportunity sampled from the undergraduate cohort in the School of Psychology at the University of Leeds (22 females; mean age = 20 y, SD = 1.4) and agreed to take part in the study. They were not chosen on the basis of having an itchy skin condition; however, 7 males and 9 females self-reported having current/previous PSCs (eg, eczema, AD). The study received ethical approval from the School of Psychology Research Ethics Committee, University of Leeds (ref. no: 14-009) and was conducted in accordance with the Helsinki Declaration of 1975, as revised in 1983. Volunteers provided written informed consent and were free to withdraw from the study at any time.

Apparatus and materials

The visual stimuli consisted of 32 static images: 23 sourced from Google Images [Images were free to use at time of testing.], 8 taken from a previous study^[5] and 1 photograph taken by the experimenters (images available on request). These were divided into 16 itch and 16 non-itch-related images, which were further subdivided into 4 picture types (4 in each category): (i) "skin contact," including images of itch-related versus non-itch-related objects in contact with the skin (eg, insects crawling on the hand vs. marbles touching the skin); (ii) "skin response," which included images of human responses to itch (ie, scratching) or non-itch-related touching of the skin (ie, washing the hands or rubbing cream onto the face); (iii) "context," which included pictures where itchy or nonitchy stimuli were seen in the environment but not on the body (eg, ants crawling on the ground or butterflies flying); and (iv) "skin condition" (eg, hives or freckles). Finally, the images in each of these picture types were divided by body part depicting a person's head, torso, arm, or leg and displayed on a 17-inch Dell LCD monitor, using E-prime software version 2.0. For each picture, participants answered the following questions: (i) "How itchy do you think the person in the picture feels?" ("Other" rating) and (ii) "How itchy do you feel?" ("Self" rating). For pictures where no other person was present, only the self-rating question was asked. All images were presented randomly and participants recorded their responses using the number pads on the computer keyboard based on a numerical rating

scale ranging from 0 (not itchy at all) to 9 (intensely itchy). The McGill Pain Questionnaire (MPQ^[9]) was used to note the location and frequency of scratches on the body. A scratch was defined as any behavior where participants rubbed their fingertips over an area of skin in a forward and back motion^[2]. Any scratches made while answering the self/other itch questions were added to the frequency of scratches caused by that picture and the total number of scratches over the whole group of participants was used for the analysis.

Procedure

Participants completed the task individually seated in front of a computer monitor displaying the images. The experiment began with a fixation cross, after which a picture appeared. Participants examined each picture and were told to imagine placing themselves within the context of the picture to answer the questions "How itchy do you feel?" and "How itchy do you think the person in the picture feels?" They could view each picture for as long as they wanted and pressing the space bar on the keyboard caused the picture to disappear and the questions to appear. During testing the experimenter sat discretely in the corner of the room to observe scratching behaviors (unknown to the participant) and recorded these on the body outline of the MPQ. The task took ~30 minutes to complete. Participants were then debriefed on the nature of the study after completing the task and could withdraw their data if they so wished (none chose to do so).

Design and statistics

A 2 × 4 factorial within-group design was implemented for the self-itch ratings and analyzed using repeated measures analysis of variance (ANOVA). The independent variables were sensory category (itch vs. nonitch pictures) and picture type (skin response, skin contact and context, and skin condition). For the other-itch ratings a 2 × 3 within-group design was used (again analyzed with repeated measures ANOVA) with the independent variables sensory category (itch vs. nonitch) and picture type (skin response, skin contact, and skin condition; NB. The "context" category was omitted from this analysis as no person was depicted in the picture). The number of times participants scratched themselves during the task was also analyzed within a 2 × 4 repeated measures ANOVA. In addition, we included the between-subjects factors of sex and whether the participant currently had, or had ever had, a PSC. The Pearson bivariate correlations were used to assess whether self-itch and other-itch ratings correlated and whether itch ratings correlated with the scratch response. All data were analyzed using SPSS version 21.0 (SPSS Inc., Chicago, IL). Where Mauchly's test indicated the assumption of sphericity had been violated, the Greenhouse-Geisser correction was applied and *t* tests were corrected for multiple comparisons.

Results

Means and SDs for self-itch and other-itch ratings [The data from 4 conditions from the self-itch and other-itch ratings were positively skewed and attempts to transform (log, sqrt) did not normalize the data. Therefore, outlying scores with *z*-scores > 1.96 were changed to the next lowest score +0.01 for statistical analysis^[10].], scratch frequencies, and average display times for

Table 1
Means (\pm 1SD) for self-itch and other-itch ratings as measured on a continuum between 0 and 9 (where 0 = not itchy at all and 9 = intensely itchy), total number of scratches for both itch and non-itch-related pictures across each picture category and average display times for each picture (ms).

| | Itch-related Pictures | | | | Non-itch-related Pictures | | | |
|-------------------|-----------------------|-------------|-----------------|-------------|---------------------------|-------------|----------------|-------------|
| | Response | Contact | Context | Condition | Response | Contact | Context | Condition |
| Self-itch rating | 3.5 (1.8) | 5.4 (1.9) | 3.4 (1.8) | 4.6 (2.1) | 1.1 (1.0) | 1.0 (0.9) | 0.7 (0.8) | 2.5 (1.9) |
| Other-itch rating | 5.5 (2.0) | 7.4 (1.5) | — | 7.4 (1.3) | 2.0 (1.3) | 1.6 (0.9) | — | 4.2 (1.9) |
| Scratching | 14 | 14 | 18 | 10 | 8 | 5 | 5 | 16 |
| Display times | 4151 (1505) | 3851 (1690) | 4088 (1297) | 3668 (1423) | 3704 (1344) | 3743 (1415) | 3283 (1234) | 4288 (1777) |
| Collapsed means | | | | | | | | |
| | Itch related | | Nonitch related | | Skin response | | Skin condition | |
| Self-itch rating | 4.2 (1.0) | | 1.3 (0.8) | | 2.3 (1.7) | | 3.6 (1.5) | |
| Other itch | 6.8 (1.1) | | 2.6 (1.4) | | 3.8 (2.5) | | 5.8 (2.3) | |
| Scratching | 56 | | 34 | | 22 | | 26 | |

Overall means (and SD's) collapsed across all main conditions and picture types are also shown for self-itch and other-itch ratings and total frequency of scratch responses.

each picture type [As can be seen from Table 1 there is no consistent evidence that having longer display times increased the propensity to scratch or that the non-itch-related elements in the pictures could have drawn attention or the reflex to click away quickly. This was formally tested with an ANOVA where we found an interaction between itch condition and picture type ($F_{2,383,95,340} = 10.816$, $P < 0.001$, $\eta_p^2 = 0.213$) due to the fact that participants were slower to respond to the itch versus non-itch-related response pictures ($P = 0.006$) and context pictures ($P < 0.001$) but faster to respond to the itch-related versus non-itch-related skin condition pictures ($P < 0.001$). The scratch data correlated with display time only for the itch-related contact pictures but in a negative direction ($r = -0.365$, $P = 0.019$), ie, the longer the participant spent looking at this picture the less frequently they scratched. No other interactions or correlations were significant.] are given in Table 1.

Impact of sex and history of PSCs on self-itch ratings

We first established there was a significant main effect of sensory category ($F_{1,37} = 186.303$, $P < 0.001$, $\eta_p^2 = 0.834$) confirming that itch stimuli were rated higher than nonitch stimuli and a significant main effect of picture type ($F_{2,329,98,521} = 61.233$, $P < 0.001$, $\eta_p^2 = 0.623$). Pairwise comparisons revealed that skin condition pictures were rated higher than all others ($P \leq 0.001$). The interaction between sensory category and picture type was also significant ($F_{2,261,83,660} = 59.236$, $P < 0.001$, $\eta_p^2 = 0.616$), with participants giving higher self-itch ratings for itch-related skin contact pictures than all others (all P 's ≤ 0.001). However, there was no main effect of sex or history of PSCs. Examination of the means (Fig. 1A) shows females rate themselves as feeling "itchier" in response to itch-related pictures than males as confirmed by a significant interaction between sensory condition and sex ($F_{1,37} = 10.480$, $P = 0.003$, $\eta_p^2 = 0.221$). There was also a significant interaction between picture type and sex ($F_{3,111} = 3.011$, $P = 0.033$, $\eta_p^2 = 0.076$) with females rating themselves as feeling itchier in response to skin contact pictures ($P < 0.001$).

Similarly, while there was no main effect of having a history of PSCs, examination of the means (Fig. 1B) indicates that these participants report higher self-itch ratings when viewing images of people scratching as confirmed by a significant interaction

between sensory category, picture type, and history of skin disorder ($F_{3,111} = 2.716$, $P = 0.048$, $\eta_p^2 = 0.068$).

The data for body part location was heavily skewed; therefore, a nonparametric Friedman test of differences among repeated measures was conducted. There was no main effect of viewing itch-related body parts (mean of head = 4.7; torso = 4.3; arm = 4.7; leg = 4.4); however, the relationship between body part and viewing itch-related response images was significant [$\chi^2(3, N = 41) = 8.235$, $P = 0.041$] with higher self-itch ratings to images of people scratching the torso versus leg ($P = 0.003$) and arm

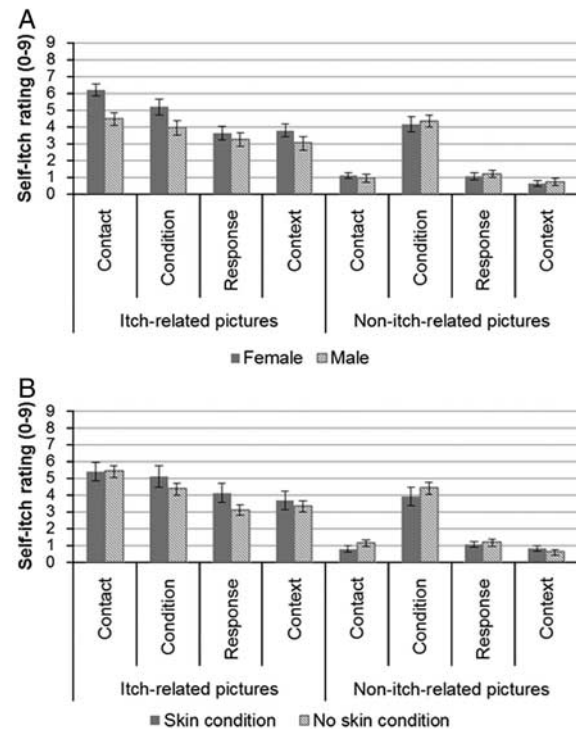


Figure 1. Mean self-itch ratings (\pm 1 SEM) for males and females (A) and participants with a history of PSCs and without across the 4 picture types (skin contact, skin condition, skin response, and context only) (B) for both the itch and nonitch sensory categories in response to the question "How itchy do you feel?"

versus leg ($P=0.011$). Paired comparisons indicated that the response to skin contact images (head, torso, arm, and leg), and skin condition images (of the torso) was greater in females than males (all P 's < 0.05). However, only images of people scratching their arm produced higher self-itch ratings in those with PSCs ($P=0.005$).

Impact of sex and history of PSCs on other-itch ratings

Again, we first established there was a significant main effect of sensory category ($F_{1,37}=691.826$, $P<0.001$, $\eta_p^2=0.949$) with higher other-itch ratings to itch-related versus non-itch-related pictures and a significant main effect of picture type ($F_{2,74}=37.835$, $P<0.001$, $\eta_p^2=0.506$). Participants rated the people in the pictures feeling "itchier" in the skin condition pictures than any other picture type ($P<0.001$). The interaction between sensory category and picture type was also significant ($F_{1,680,62.169}=38.911$, $P<0.001$, $\eta_p^2=0.513$), with participants giving higher other-itch ratings for itch-related skin contact and skin condition pictures versus skin response (all P 's ≤ 0.001).

However, there was no significant main effect of sex (Fig. 2A) or history of PSCs (Fig. 2B), but females rated the person in the itch-related picture as feeling "itchier" than males as confirmed by a significant interaction between sensory condition and sex ($F_{1,37}=9.823$, $P=0.003$, $\eta_p^2=0.210$).

The data for body part location was again heavily skewed so nonparametric tests were conducted. Again, there was no main effect of viewing itch-related body parts (mean of head = 6.6; torso = 6.8; arm = 6.9; leg = 6.8); however, the relationship

between body part and viewing itch-related response images was significant [$\chi^2(3, N=41)=21.280$, $P\leq 0.001$] with higher other-itch ratings to images of the torso versus head ($P=0.03$), arm versus head ($P\leq 0.001$), and arm versus leg ($P=0.004$). Paired comparisons indicated that the response to skin contact images (of the torso, arm, and leg) and skin condition images (of the torso) was greater in females than males (all P 's < 0.05). There were no interactions with PSCs.

Scratch observations

Thirty-three of the 41 participants scratched at least once during the experiment resulting in a total of 105 scratches [Table 1 and Fig. 3 (One male participant scratched himself 15 times, > 2 SDs away from the group mean, and so their data was subsequently removed from further analysis.)]. The majority of scratches were directed toward the participants head/face (79%) followed by the arm (10%), torso (6%), and legs (5%). The data were again heavily skewed and so nonparametric tests were conducted. A Wilcoxon test reveal people scratched more when viewing itch versus non-itch-related images ($Z=2.553$, $P=0.011$) but this only interacted with picture type for the nonitch images [$\chi^2(3, N=40)=13.353$, $P=0.004$]. Paired comparisons revealed that people scratched more in response to skin condition versus skin contact ($P=0.005$) or context images ($P=0.008$). There was no main effect of body part, sex (Fig. 3A), or the effect of having a PSC (Fig. 3B). In response to both itch and non-itch-related pictures, participants mainly scratched their heads and the location of scratching had no relationship to the body part viewed.

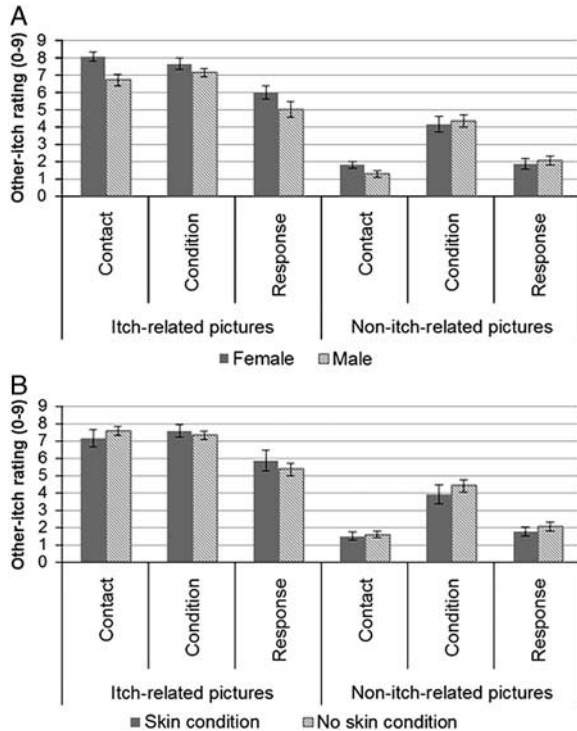


Figure 2. Mean other-itch ratings (± 1 SEM) for males and females (A) and participants with a history of PSCs and without across the 3 picture types (skin contact, skin condition, and skin response) (B) for both the itch and nonitch sensory categories in response to the question "How itchy do you think the person in the picture feels?"

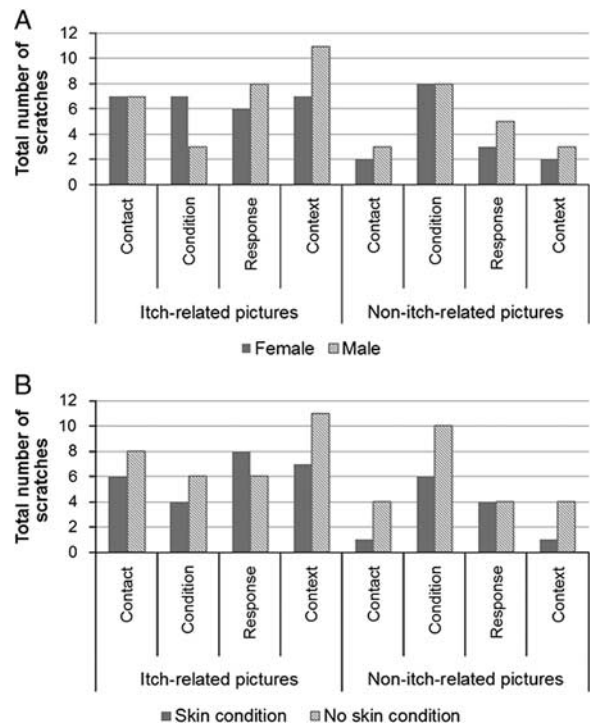


Figure 3. Frequency of scratch responses for males and females (A) and participants with a history of PSCs and without across the 4 picture types (skin contact, skin condition, skin response, and context only) (B) for both the itch and nonitch sensory categories.

Correlations between “self” and “other” itch ratings and the scratch response

There was a significant relationship between self and other itch ratings for the itch-related skin contact ($r=0.684$, $P<0.001$), skin condition ($r=0.763$, $P<0.001$), and skin response picture types [$r=0.787$, $P<0.001$ (Context only pictures were removed from this analysis because of a lack of person in the picture.)]. However, there was no relationship between self-itch or other-itch ratings and scratch response for any picture type.

Discussion

The current study replicated previous findings showing that feelings of itch and the scratch response can be induced visually (ie, without delivery of a pruritogen) in response to itch-related images^[5]. The highest self and other itch ratings were again given for skin contact pictures; however, a new category containing images of skin conditions also produced high levels of self and other itch ratings. We also replicated our previous finding that self and other itch ratings correlated but there were no correlations between these and the scratch response. While it seems logical to assume that people scratch themselves when they feel “itchy” previous studies have identified only a weak correlation between itch perception and the scratch response^[3] (see revised definition of itch proposed by Savin^[11] in which the “threshold to scratch” is implemented), which suggests that the itch-scratch cycle is not absolute in that not all scratches are triggered by feelings of itch and not all feelings of itch result in scratching behavior. Although it seems subjective feeling states can be shared between the self and others, this occurs without obligatory motor stimulation^[12,13], reflecting the automatic and autonomous nature of scratching.

While some studies have found no effect of sex on itch perception^[1,3-4], others have suggested that females may be more prone to itch-related skin conditions because of unique epithelial/hormonal shifts leading to cyclical changes across the age spectrum in the skin’s basic composition^[14]. Women also have more neuropathic and somatic symptom disorders (DSM V), underlying their chronic pruritus than males^[6]. We found that females’ itch ratings were higher than males for itch-related pictures, particularly in response to skin contact (torso, arms, and legs) and skin condition (torso only) images indicating possible sex differences in empathic judgements^[15]. However, we found no difference in the frequency of scratches between males and females, suggesting that any differences in VEI do not translate into scratching behavior.

People with AD give higher self-itch ratings when viewing videos of people scratching than those without^[1]. Our results support this as participants with a history of PSCs report higher self-itch ratings when viewing images of people scratching than those without a history of PSCs. In the study by Papoiu et al^[1] participants only saw videos of people scratching their left forearm; however, the sensation of itch extended beyond the local itch induction site to the face, neck, and contralateral forearm. They also spontaneously scratched the contralateral forearm, back, face, and neck and scalp the most [and the skin areas targeted for scratching by atopics were not eczematous (The experimenter was not blinded to the picture category when making their observations about scratching behavior. Although unlikely, this may have influenced the results.)]. The current study found static images of

people scratching their arm produced higher self-itch ratings in those with PSCs with scratching focussed mainly on the head and arm. Importantly, the frequency of scratching did not differ in those with and without PSCs, making VEI a safe method to use to explore the mechanisms of the itch-scratch cycle without aggravating/exacerbating the underlying condition. Unfortunately, we cannot comment on whether people with for example AD versus eczema, show more of this behavior as we did not ask people the specific nature of their PSC other than to give them examples (eg, eczema, AD). We also did not explicitly ask participants whether they had other itch conditions than skin-conditions^[16]. This study was exploratory in nature and designed to assess whether having a history of any itchy skin disease would interact with the phenomena of VEI. Furthermore, the participants were opportunity sampled and therefore we did not recruit on the basis of having a particular skin condition. Now we have established there is an interaction between VEI and itchy skin conditions, future studies will specifically recruit a sample of people with various types of disease, ensuring there are enough of each type on which to perform a meaningful analysis.

The highest self-itch and other-itch ratings were given to itch-related images of the head, torso, and arms. This partially agrees with a previous study where participants rated videos depicting scratching of the upper arm significantly itchier than the forearm and chest^[3]. Of the 21 (64%) participants who produced spontaneous scratches in response to these videos, the majority were directed to the face and hair^[7], but there were no differences between males and females. We also found that the vast majority of scratches (79%) were directed toward the participant’s head regardless of the body part depicted in the image. This may be an evolutionary response as nonhuman primates are also susceptible to contagious itch and show the same pattern of scratching body parts different to the ones observed, with the head scratched the most (over 70%) for each picture^[2]. Of course it must be remembered that the sensation of itch (like pain) cannot be perceived directly by an observer and can only be inferred from the subsequent behavioral response, that is, scratching, facial grimacing, guarding the damaged body part, etc. Previous studies have shown that movies depicting scratching activated many of the regions associated with physically induced itch (via histamine administration) and not motor regions of the brain associated with contagious scratching (although people were prevented from scratching in the scanner, which may have inhibited this response^[3]). Therefore, we would agree with^[7] that “contagious itchiness may be more driven by vicarious perception of the feeling state (itchiness/unpleasantness) than contagion of the motor act or bodily target.” In other words, people do not observe itch, they observe the subsequent scratch and from this infer that the person who is scratching is itchy. This can then trigger the sensation of itch in the observer, which subsequently leads to them scratching (so called “contagious itching”). Future studies should aim to disentangle the mechanisms behind the sequence of events that leads from VEI to the sensation of itch and why some itches result in scratches.

Results from the present and previous studies^[5,17] suggest that itch perception and the scratch response are not as closely correlated as first assumed and must be explained by other factors. Behavioral interventions for skin conditions (such as habit reversal, which aims to modify/prevent unhelpful scratching behaviors by encouraging people to focus on an alternative action to scratching in response to itch such as clenching the fists or

pinching the itchy spot^[18]) may be an important focus for therapeutic interventions, as this is the part of the itch-scratch cycle that seems to have the most damaging effect. This is an exciting change of focus given that, thus far, only histamine-related PSC have an established treatment^[19], to which chronic itch is usually resistant^[20]. These psychological interventions seem to have medium effect sizes for treating both AD and psoriasis, and seem equally effective in short-term group interventions, showing their cost effectiveness^[18]. The clinical application of VEI may have most impact on such psychological interventions. For example, people with psychogenic pruritus (where individuals experience abnormal tactile sensations such as itching, crawling, pricking, and stinging, or delusions of parasitosis) could be trained to disambiguate their perceptions of itch using a VEI-based training paradigm implemented within a psychological intervention such as autogenic training, cognitive behavioral therapy, or habit reversal behavioral training (for a review see Lavda et al^[18]), which have been shown to significantly decrease eczema severity, itching intensity, and scratching in AD patients^[21]. Comorbid factors such as stress, anxiety, and depression, which can increase the perception of itch in long-term sufferers, should also be assessed and considered when developing and tailoring an effective VEI-based intervention for individuals. The clinical application of VEI also lends itself to studying the central nervous system mediators of itch. For example, studies have suggested that patients with AD, when exposed to environmental stressors, respond with blunted production of cortisol, which may explain flare in the presence of stressors^[22]. The impact of such environmental stressors on the brain can be safely and easily explored with functional magnetic resonance imaging and a VEI-based paradigm and may provide targets for noninvasive brain stimulation methods such as transcranial direct current stimulation^[23].

Further applications of VEI could investigate how “social behavioral learning” and “suggestion” play a role in contagiously transferred itch. Anyone who has children will know the powerful effect that the word “nits” has on increasing sensations of itch. The effect of verbal suggestion on itch can be similarly explored in the same way as VEI by written or audio delivery of itch-evoking stimuli to explore the mechanisms of socially transferred itch and whether patients with chronic itch may have altered cognitive schemas that make them more prone to contagious itch versus the general population, as a consequence of suffering from long-term itch. VEI-based paradigms could also be used to evaluate AD itch-scratch triggers (eg, irritants, environmental allergens, food, and contact allergens) within a multidisciplinary intervention approach^[24]. The use of such adjunctive psychological interventions that target the habitual scratching may be of help to reduce and attenuate the itch-scratch cycle in particular in patients with chronic itch^[25].

Conflicts of interest

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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