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2	The role of auditory itch contagion in psoriasis: A link between				
3	susceptibility and symptom severity				
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18 Abstract

19 Itch and associated scratching is a common and distressing symptom of psoriasis. Here, we tested 20 whether people with psoriasis, relative to healthy controls, show an increased vulnerability to 21 auditory itch contagion when presented with sounds of itch-associated actions of scratching and 22 rubbing. We were also interested in whether manipulating the high frequency volume of these 23 sounds alters itch perception. Results show that both groups rated scratching sounds as more itch-24 inducing than rubbing sounds, and the amount of induced itch increased as a function of high 25 frequency volume. The amount of auditory itch contagion (i.e., difference of scratch - rub) was 26 positively linked with psoriatic symptom severity. These findings demonstrate the role of auditory 27 cues in eliciting sensations of itchiness in the absence of peripheral stimulation. Reducing the high 28 frequency volume of itch-associated sounds may offer a novel approach for targeted multisensory 29 itch interventions.

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31 Introduction

32	Psoriasis is a chronic s	ystemic inflammatory	disease predomina	ntly affecting the skin.
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Approximately 2% of the population are affected at any time with 85% of those experiencing itch (1,

2) which can have a detrimental effect on quality of life, sleep, mental wellbeing (3) and

35 concentration. Treatment goals for psoriasis tend to focus on measurement of area and severity and

36 assessment of quality of life (4, 5). Pruritus is a common symptom that is not always targeted

37 although many treatments will have anti-pruritic effects. Although there are treatments specifically

38 for pruritus, many have side-effects and limited impact in reducing psoriatic itch.

39 Itch is a multimodal experience. Scratching to alleviate an itch not only elicits a cutaneous

40 perception, but also visual (e.g., sight of scratching, reddened skin), auditory (e.g., sound of

41 scratching) and kinaesthetic (e.g., movement of the limbs) sensations. Each non-cutaneous sense

42 contributes to subjective feelings of itchiness. For example, watching itch-related stimuli in the

43 absence of peripheral stimulation (e.g., ants crawling on the ground) is sufficient to induce itch (6, 7).

44 Since itch can be amplified by concurrent non-cutaneous sensory information (8), this type of

45 sensory feedback might also provide a means to reduce itch intensity.

Here, we explore auditory modulation of itch in people with psoriasis and age-matched controls.
Jousmäki and Hari (9) demonstrated that modulating the sound of hands being rubbed together
changes the perception of skin roughness. When they increased the volume of high frequency
feedback, the skin started to feel smoother and drier (hence the name 'parchment skin illusion').

50 Conversely, when reducing the proportion of high frequencies, the skin started to feel rougher and

51 more moist.

52 The present study investigates whether itch perception can be selectively increased or decreased in 53 a similar way and whether people with psoriasis would show an increased susceptibility to auditory 54 itch contagion. Addressing these questions may begin to offer novel solutions to the challenging 55 issue of effectively treating psoriatic itch.

56 MATERIALS & METHODS

57 Aims

58 The aims of the study were two-fold. First, we wanted to establish whether auditory itch contagion 59 is essentially a normative response (i.e., experienced by most people). Such a susceptibility of 60 auditory itch conduction could either manifest itself in the form of higher itch ratings for scratching as comparing to rubbing sounds (which act as a high-level baseline), or in a linear increase of itch as 61 62 a function high frequency amplitude in the sound recordings (decreased by 10 dB, original, increased 63 by 10 dB). A second aim of the study was to investigate whether people with psoriasis, where itch 64 and associated scratching are a common problem, show an increased vulnerability to auditory itch 65 contagion.

66 Sample

Sixty four participants were recruited to each experimental group. This sample size was chosen 67 68 because it is sufficient to detect an effect in a between-group design that is at least of medium size 69 or greater (Cohen's $d \ge 0.5$) with a probability of 80%, as indicated by an a-priori power analysis (10). 70 Experimental group inclusion criteria were: (i) self-reported history of psoriasis, (ii) age \geq 18 years, 71 (iii) normal or corrected-to-normal hearing and (iv) access to an internet-enabled computer, with the 72 capability to play sound. Since this was an online study, we had no control over the volume setting 73 or particular sound setup participants were using on their computer. However, the experimental 74 manipulation was realized within subjects. Thus, the difference in sound intensity between 75 experimental conditions remains stable, regardless of the particular sound setup of each computer. 76 Inclusion criteria for the control group were identical except control participants had to be without 77 any history of psoriasis and not currently experiencing itch. Mean age did not differ significantly 78 between groups [psoriasis group: M = 39.42, SD = 10.6; control group: M = 39.89, SD = 10.6; t(126) = 79 0.25, p = 0.80], nor gender distribution (psoriasis group: females N=25, control group: N=31, χ 2=

1.14, p = 0.29). On average, participants in the psoriasis group had been living with the condition for
10.1 years (range 0 - 61 years, SD = 11.1).

82 Materials

Stimuli were recordings of scratching or rubbing. Different targets were scratched or rubbed for 20
seconds, including three body (beard, hand, leg) and three non-body (polyester, denim, leather)
targets. High Frequencies (HF) above 1000 Hz were then either increased or decreased in amplitude
by 10 dB using PRAAT (version 5.3.52, www.praat.org) resulting in 3 different versions of each sound
file: Original, HF increased and HF decreased.

88 To assess the amount of experienced itch within the last 14 days, all 128 participants completed the 89 5D itch scale (11) which provides estimates for 5 dimensions of itch (degree, duration, direction, 90 disability, and distribution), as well as an overall score. The overall 5D score can vary between 5 (no 91 itch) and 25 (most severe itch). Finally, participants in the psoriasis group assessed their symptom 92 severity using the Self-assessed Psoriasis Area and Severity Index (SAPASI) (12). This instrument 93 requires participants to indicate the body surface area affected by psoriasis, followed by a severity 94 rating of a typical psoriatic lesion with respect to colour, thickness and scaliness. The resulting 95 overall SAPASI index varies between 0 (no psoriasis on the body) and 72 (the most severe case of 96 psoriasis).

97 Procedure

The experiment was conducted using a secure website. Healthy participants and people with psoriasis listened to sound recordings of either scratching or rubbing sounds. After each sound, participants were asked to rate the intensity of itchiness (if any) induced by the preceding sound. The rating scale ranged from 1 (not at all) to 7 (extremely), with 4 indicating moderate itchiness. The 36 sound stimuli were divided into 3 blocks, with the constraints that (a) each block contained an equal number of sounds from each condition, and (b) each block contained only one of the 3 variants of each particular sound (e.g., Block A would contain 'leg_rub_orig', Block B 'leg_rub_incr' and Block C 'leg_rub_decr'). Sound order within each block was randomized. Participants completed
all 3 blocks, with block order counterbalanced across participants. Participants had the opportunity
to complete the study one block at a time, and could take a break if they wished. Most participants
(60 out 64 in the psoriasis group, 58 out 64 in the control group) chose to complete the study on a
single day.

110 Design and Data Analysis

The study used a 2 x 2 x 3 factorial design, using Movement Type (rub, scratch) and HF volume (original, HF_inc and HF_decr) as within-subject factors, as well as group (psoriasis, control) as a between-subject factor. Data were analysed using a mixed 2 x 2 x 3 ANOVA. For all main comparisons, Cohen's d is given as an effect size measure, using the pooled variance between conditions as a standardizer(13).

116 RESULTS

117 Questionnaires

118 The overall 5D itch score was higher in the psoriasis group than in the control group (see Table 1). 119 Similarly, the dimension scores for Degree, Duration, Disability and Distribution were significantly 120 higher in the psoriasis group. The direction (i.e., amount of change in itch during the last 14 days, 121 relative to the previous month) did not differ significantly between groups (t(126) = 0.74, p = 0.46). 122 However, the lack of a group effect for the direction scale should be interpreted with caution. The 123 relevant question "Over the past 2 weeks has your itching gotten better or worse compared to the 124 previous month?" is difficult to answer for someone not currently experiencing itch (which was an 125 inclusion criterion for the control group), and a response of 'unchanged' is scored with 4 points in 126 the 5D questionnaire. This may also explain the relatively high overall 5D itch score of the control 127 group, which is largely driven by the direction sub-scale.

- The mean SAPASI score of the psoriasis group was 13.26 (range: 2.6 52.4, SD = 9.83) indicating that
 on average, symptom severity was moderate, although there were considerable differences
 between individuals.
- 131 Itch response in the control group
- 132 In the control group (Figure 1), there was a main effect of Movement Type (F(1,63) = 42.78, p <
- 133 0.001, d = 0.61), indicating that scratching sounds (M = 2.94, SD = 0.92) were perceived as more itch-
- inducing than rubbing sounds (M = 2.40, SD = 0.82). There was also a main effect of HF volume
- 135 (F(2,126) = 16.59, p < 0.001, ε = 0.80). Two post-hoc t-tests indicated that relative to the unmodified
- 136 original sounds (M = 2.66, SD = 0.84), accentuating the HF volume was associated with increased itch
- 137 (M = 2.90, SD = 1.02; t(63) = 3.10, p = 0.003, d = 0.25). In contrast, dampening HF volume was
- associated with reduced itch (M = 2.46, SD = 0.76), relative to unmodified sounds (t(63) = 3.54, p =
- 139 0.001, d = 0.25). The interaction between Movement Type and HF Volume was not significant in the
- 140 control group (F(2,126) = 1.12, p = 0.33).

141 Itch response in the psoriasis group

142	The pattern across the six experimental conditions was similar in the psoriasis group. There was a
143	main effect of Movement Type (F(1,63) = 15.18, p < 0.001, d = 0.27), indicating that scratching
144	sounds (M = 4.21, SD = 1.40) were more itch-inducing than rubbing sounds (M = 3.81, SD = 1.51).
145	There was also a main effect of HF volume (F(2,126) = 29.68, p < 0.001, ϵ = 0.74). Two post-hoc tests
146	showed that accentuating HF volume (M = 4.40, SD = 1.58) increased itch (t(63) = 5.19, p < 0.001, d =
147	0.31), relative to unmodified sounds (M = 3.94, SD = 1.37), whereas dampening HF volume (M =
148	3.68, SD = 1.44) decreased itch (t(63) = 3.68, $p < 0.001$, $d = 0.19$). There was an interaction between
149	Movement Type and HF Volume in the psoriasis group (F(2,126) = 6.61, p = 0.002, ϵ = 0.82) which
150	was driven by the fact that the antipruritic effect of dampening the HF volume was significantly
151	more pronounced for rubbing than scratching. That is, (rub_orig – rub_decr) was significantly greater
152	than (scratch_orig – scratch_decr) in the psoriasis group, t(63) = 2.31, p = 0.02, d = 0.30. In contrast,

- (rub_orig rub_incr) was not significantly different from (scratch_orig scratch_incr), t(63) = 1.67, p
 = 0.10. However,
- 155 In an exploratory data analysis, we also looked at whether psoriatic symptom severity, as measured
- by the SAPASI, is linked with auditory itch contagion. These analyses indicated that the amount to
- 157 which participants perceive the scratching sounds as more itch-inducing than the rubbing sounds
- 158 (scratch rub) was positively linked with the overall SAPASI score, r(62) = 0.29, p = 0.02. In contrast,
- the SAPASI score was not significantly correlated with the effect of HF accentuation (incr original;
- 160 r(62) = -0.19, p = 0.13), or the effect of HF dampening (decr orig; r(62) = -0.17, p = 0.19).

161 Differences between groups in the itch response

162 Group comparisons indicated that the effect of accentuating HFs (HF incr. vs. unmodified sounds) 163 tended to be more pronounced in the psoriasis group (M = 0.46, SD = 0.71) than in the control group 164 (M = 0.23, SD = 0.6, t(126) = 1.96, p = 0.05, d = 0.35). Further analysis revealed that this group effect 165 was primarily driven by the rubbing sounds. The effect of accentuating HFs of rubbing sounds was 166 significantly more pronounced in the psoriasis group (M = 0.57, SD = 0.89) than in the Control group 167 (M = 0.25, SD = 0.80, t(126) = 2.16, p = 0.03, d = 0.38). No such group difference was observed for 168 scratching sounds (t(126) = 0.92, p = 0.36). The effect of dampening HFs (HF decr – orig) was not 169 significantly different between groups (t(126) = 0.64, p = 0.52), neither was the effect of Movement 170 Type (scratch – rub; t(126) = 1.05, p = 0.30). Finally, there was a main effect of group (F(1,126) = 171 43.74, p < 0.001, d = 1.17), indicating that across all six experimental conditions, participants in the 172 psoriasis group (M = 4.01, SD = 1.14) generally perceived the sounds as more itch-inducing than 173 participants in the control group (M = 2.67, SD = 1.14).

174 DISCUSSION

The present study demonstrates, for the first time, that itch-associated sounds of scratching andrubbing can induce feelings of itchiness in the absence of peripheral stimulation. Both healthy

volunteers and psoriatic patients were found to be susceptible to such auditory itch contagion.
These findings further our understanding of the psychological factors involved in the induction of
itch and could provide the basis for novel multimodal itch interventions.

180 A first important finding of our study is that auditory stimuli can be powerful inducers of itch.

181 Scratching sounds were perceived as significantly more itch-inducing than rubbing sounds in both

182 healthy controls and people with psoriasis. The magnitude of this effect was positively linked with

183 psoriatic symptom severity suggesting it may play a role in perpetuating chronic itch in psoriasis.

184 Furthermore, our results suggest that manipulating the high frequency of action sounds typically 185 associated with itching (i.e., rubbing and scratching) modulates itch perception. Dampening the high 186 frequency was found to have an anti-pruritic effect in both groups. In contrast, accentuating high 187 frequencies increased the amount of induced itch, with the psoriatic group showing an increased 188 vulnerability to such auditory itch contagion. In our study, non-diseased skin was scratched during 189 the recording of the sounds. However, psoriatic skin is particularly dry, which likely increases the 190 high frequency volume of the scratching sound. Thus, the present study may be considered as a 191 lower bound estimate of the amount of auditory itch amplification in psoriasis. These findings could 192 have important clinical implications as pruritus is a common and troublesome symptom in many 193 psoriatic patients, which may or may not be controlled by conventional therapies some of which will 194 have unwanted side effects.

Looking ahead, the present study opens up a new perspective on the study of itch. While we used
pre-recorded scratching and rubbing sounds, future studies could ask whether the *concurrent*physical perception of itch (e.g., after a histamine prick test) is also influenced by auditory feedback.
Such studies could pave the way for targeted interventions designed to eliminate auditory
amplification of chronic itch.

200 More investigation is needed to discover what brain systems are involved when itch is induced by
 201 non-cutaneous sensory information. Most accounts of contagious itch assume that it involves some

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202 form of vicarious perception(6, 14). It is, however, currently unclear what specifically is being shared 203 between the scratching person and the perceiver. The first possibility is that it is the motor act of 204 scratching and associated somatosensory sensations of specific bodily locations that are being 205 simulated in the perceiver's brain, recruiting the auditory mirror neuron system(15). The second 206 possibility is that insular-mediated sharing of affect (in this case the unpleasantness of itch), rather 207 than vicarious perception of motor act and bodily target, gives rise to contagious itch. This account is 208 based on evidence from the related phenomenon of empathy for pain(16). In the present study, 209 participants were not able to perceive the bodily target of scratching. Nonetheless, listening to these 210 sounds induced itch. Furthermore, sounds where a non-body target was scratched/rubbed (denim, 211 polyester, leather) were perceived as equally itch-inducing as sounds associated with a body target 212 (beard, hand, leg). This is difficult to reconcile with a motor/somatosensory explanation, but in line 213 with the idea that sharing of affect might give rise to contagious itching(17).

A limitation of the current study is that diagnosis of psoriasis was based on self-report data.

215 Although 5D and SAPASI have been validated in clinical populations, it would be of interest to see if 216 our findings are replicable when diagnoses of psoriasis are verified by a clinician. Another question 217 for future research is whether auditory itch contagion affects only subjective itch, or whether it 218 generalizes to behavioural (e.g., scratching frequency)(6, 14, 18) and brain-based markers of itch 219 intensity (e.g., activity in itch-associated areas of the brain)(19). A final limitation is that we had no 220 control over the volume settings of the computers of our participants, creating an additional source 221 of variability compared to a lab-based experiment. However, the data pattern obtained from our control group was highly similar to that of previous group of healthy volunteers tested in a 222 223 controlled lab setting (20) suggesting that the mode of data acquisition (online vs. lab-based) does 224 not systematically influence the response.

In conclusion, the current study represents an important development in understanding auditoryitch contagion. Further research is needed to meet the ultimate aim of identifying a new non-

- 227 pharmacological approach to the management of itch, a frequent and distressing symptom of
- 228 psoriasis.

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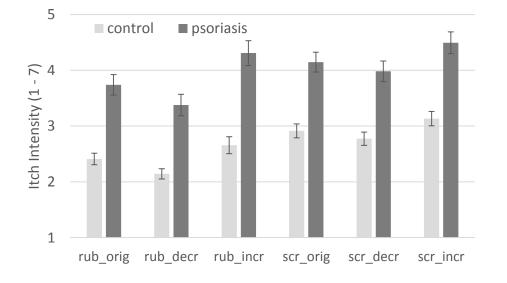
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Table 1 Means (+ SD) of the 5D Itch score and its underlying dimensions for each experimental group. Columns 3 and 4
 provide the t and associated p values of the corresponding two-tailed independent samples t-test.

	CONTROL GROUP	PSORIASIS GROUP	т	Ρ
5D ITCH SCORE	10.14 (3.21)	13.98 (3.43)	6.4	< .001
DEGREE	2.16 (0.98)	2.81 (0.69)	4.4	< .001
DURATION	1.45 (0.73)	2.11 (1.10)	4.0	< .001
DIRECTION	3.13 (1.18)	3.27 (0.96)	0.74	.46
DISABILITY	1.89 (0.89)	3.20 (0.95)	8.1	< .001
DISTRIBUTION	1.58 (0.61)	2.58 (0.89)	7.4	< .001



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