Breaking the itch-scratch cycle

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The candidate confirms that the work submitted is her own and that appropriate credit has been given where reference has been made to the work of others.

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Dedication

In memory of

Peter Young

who was looking forward to saying his daughter is a doctor

Abstract

The itch-scratch cycle is a well-documented problem for people itchy skin conditions. Itching prompts scratching, which creates skin damage, which causes further itching. This physical exacerbation also has a psychological component, which this thesis aimed to examine using Visually-Evoked Itch (VEI). VEI is the phenomenon whereby itch-related images create sensations of itch in the absence of a physical pruritic stimulus. This effect was manipulated and combined with other methods to study the relationship between itch inducers, itches and scratches, and to elucidate how an itch develops across time.

This thesis comprises four experimental chapters. Chapter 3 investigated VEI directly, measuring itchiness, located itches, and observed scratches. This approach revealed complex interactions between patterns of itch and scratch responses. Chapter 4 isolated the visual element of VEI by removing additional itch cues from the procedure. Without this priming, participants scratched less than those who were asked to report their itch experiences. Chapter 5 examined VEI using psychophysics by combining it with the Somatic Signal Detection Task. This demonstrated that VEI corresponds with a slightly lowered response criterion and decreased overall perceptual thresholds. Chapter 6 compared whether VEI differences between healthy and clinical itch participants is reflected in an attentional bias to VEI-inducing images. Clinical participants showed implicit and explicit biases towards itch images, whereas healthy participants showed an implicit aversion and explicit indifference.

Knowledge from these studies and the wider literature has been synthesised into a new theoretical model. The Threshold Model proposes that the process of entering into the itch-scratch cycle via VEI consists of a set of perceptual thresholds, which use input from visual attention and interoceptive processes, and are modulated by threat detection mechanisms. It conceptualises itch as an interpreted experience, for which VEI provides the context and manipulates the interpretation. Developing our understanding of this will elucidate how psychological triggers can affect the development and persistence of pruritic skin conditions.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

EBA	Extrastriate Body Area
fMRI	Functional Magnetic Resonance Imaging
MUS	Medically Unexplained Symptoms
SSDT	Somatic Signal Detection Task
tDCS	Transcranial direct current stimulation
VEI	Visually-Evoked Itch

Chapter 1 : Introduction

1.1 Chronic itch and the itch-scratch cycle

Itch is a prominent feature in dermatology characterised by discomfort and the urge to scratch, or in more nuanced terms “Itching is a sensation that, if sufficiently strong, will provoke either conscious or reflex scratching or the desire to scratch” (Bernhard, 2005, p.289).

1.1.1 Chronic itch: prevalence and impact

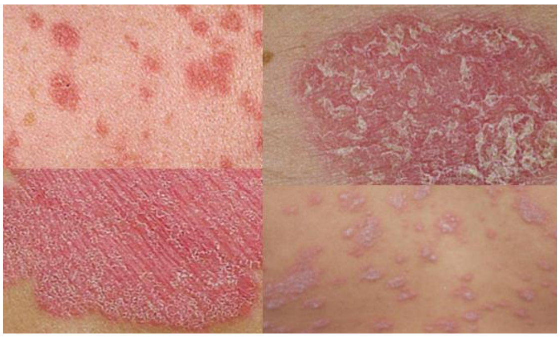
Itch is a highly prevalent symptom in skin disease worldwide (Weisshaar & Dalgard, 2009). Symptoms of the most common skin diseases are outlined in Figure 1.1. A survey by Dawn et al. (2009) found that 91% of people with atopic dermatitis experienced itch at least once per day, and a similar survey looking at people with chronic idiopathic urticaria found a 68% daily prevalence (Yosipovitch, Ansari, Goon, Chan, & Goh, 2002). For people with psoriasis, 89% reported itch during a psoriatic episode (Reich, Hrehorow, & Szepietowski, 2010). Even in the general population, it is estimated that 25% of people experience persistent or problematic itching at some point in their lives (Matterne, Apfelbacher, Vogelgsang, Loerbroks, & Weisshaar, 2013).

Chronic itch is reported to be one of the main factors impacting on an affected person’s quality of life (Finlay & Khan, 1994) comparable to that of chronic pain. The extent of this impact appears to be dependent on both the severity of itch and availability of support networks (Kini et al., 2011). In atopic dermatitis, itch impairs health-related quality of life (Blome, Radtke, Eissing, & Augustin, 2016), affecting not just the patient themselves but also their family due to the impact on social functioning and psychological well-being (Lifschitz, 2015).

Experiencing chronic itch has also been linked to deterioration of quality of life in patients with psoriasis across a range of measures, as reviewed by (Obradors, Blanch, Comellas, Figueras, & Lizan, 2016). Furthermore, Reich et al. (2010) found that the intensity of itch correlated with the severity of patients’ experiences of stress, stigmatisation, and depression. They concluded that pruritic symptoms in particular have a negative influence on patients’ psychosocial status. Augustin and Radtke (2014) also reported psoriasis patients suffering from stigmatization, embarrassment, and psychological strain. They considered improving these outcomes to be a crucial part of disease management.

Atopic dermatitis/Eczema

“Eczema (atopic dermatitis) is a condition that causes the skin to become itchy, red, dry and cracked. It's usually a long-term (chronic) condition, although it can improve significantly, or even clear completely, in some children as they get older. Atopic eczema causes the skin to become itchy, dry, cracked, sore and red. Some people only have small patches of dry skin, but others may experience widespread red, inflamed skin all over the body and constant itching. Although atopic eczema can affect any part of the body, it most often affects the hands (especially fingers), insides of the elbows, backs of the knees and the face and scalp in children. People with atopic eczema usually have periods when symptoms are less noticeable, as well as periods when symptoms become more severe (flare-ups). Flare-ups may occur as often as two or three times a month. Scratching can disrupt your sleep, make your skin bleed, and cause secondary infections. It can also make itching worse, and a cycle of itching and regular scratching may develop.” (“Atopic eczema - NHS,” 2016, para. 2)



Psoriasis

“Psoriasis is a skin condition that causes dry red, flaky, crusty patches of skin covered with silvery scales. These patches, known as plaques, normally appear on your elbows, knees, scalp and lower back, but can appear anywhere on your body. The plaques can be itchy or sore, or both. In severe cases, the skin around your joints may crack and bleed. Psoriasis is a long-lasting (chronic) disease that usually involves periods when you have no symptoms or mild symptoms, followed by periods when symptoms are more severe.” (“Psoriasis - NHS,” 2018, para. 1)

Other common forms of dermatitis

“Contact dermatitis is a type of eczema triggered by contact with an irritant or allergen, usually within a few hours or days of exposure. Contact dermatitis can cause skin to become red, inflamed (irritated), blistered, dry, thickened and cracked.” (“Contact dermatitis - NHS,” 2018, para. 1) “Discoid dermatitis is a long-term skin condition that causes skin to become itchy, reddened, swollen and cracked in circular or oval patches. They can affect any part of the body, although they don't usually affect the face or scalp. They tend to be very itchy, particularly at night.” (“Discoid eczema - NHS,” n.d., para. 1). “Stasis dermatitis, also known as venous, gravitational or Varicose eczema, is a long-term skin condition that affects the lower legs. It's common in people with varicose veins. The affected skin becomes itchy, red, swollen, dry, flaky, scaly or crusty.” (“Varicose eczema - NHS,” 2016, para. 1). “Lichen simplex, also known as Neurodermatitis, is a type of dermatitis. Patches of itchy thickened skin may develop most commonly on the nape of the neck, the legs and around the ankles. The patches may persist for many years and are very itchy. Repeated rubbing or scratching of the skin, causes lichen simplex which results in thickening of the skin and an itchy sensation, which triggers them to scratch more.” (“Lichen Simplex Patient Information,” n.d., para. 2,3)

Urticaria

“Urticaria, also known as hives, weals, welts or nettle rash, is a raised rash that appears on the skin. The rash is usually very itchy and sometimes feels like it's stinging or burning. It can range in size from a few millimetres to the size of a hand. The rash usually settles within a few days. Urticaria can be acute, if the rash clears completely within 6 weeks, or chronic, where the rash persists or comes and goes for more than 6 weeks, often over many years.” (“Hives - NHS,” 2018, para. 2)

Figure 1.1 Common forms of chronic skin conditions, for which itch is a prominent symptom.
Descriptions are abridged quotes from the NHS health A-Z and patient information leaflets.

1.1.2 Psychodermatology and disease progression

In recent years, research in the field of psychodermatology has gained momentum as the interaction between skin problems and psychological states has become a prominent issue. Negative quality of life outcomes are problematic not just because of their direct impact on the patient, but also because these same psychosocial issues can exacerbate and prolong chronic itch conditions (Mercan & Kivanç Altunay, 2006). Recent studies emphasise the importance of combining physical and behavioural management of skin problems to optimize treatment outcomes (Elmariah, 2017; Pavlis & Yosipovitch, 2017).

Psoriasis and eczema have been termed psychophysiological disorders as they are skin problems that flare up in reaction to emotional states (Koo & Lebwohl, 2001). Stress in particular has been highlighted as such a state (Szepietowski & Reszke, 2017) as it has been shown to induce itch and to exacerbate pre-existing itch. Verhoeven et al.'s (2008) review also found that stressful cognitive states such as helplessness and worrying exacerbate itch symptoms and worsen participants' skin conditions overall. Using their biopsychosocial model of itch, they determined anxiety and worrying to be clear predictors of disease severity and progression. As stress and anxiety are implicated as both causes and consequences of worsening itch, Sanders and Akiyama (2018) described this problem as a vicious cycle of itch and anxiety, reciprocally degrading disease prognosis and quality of life.

1.1.3 The itch-scratch cycle

The itch-scratch cycle is the process by which an itchy skin condition can become exacerbated by scratching the affected skin, irritating the wound, inducing the release of histamine, and consequently creating more itching (Gil Yosipovitch & Papoiu, 2008). Thus chronic itch patients inadvertently participate in the creation of the symptoms they suffer from by self-stimulation of the pruritic mechanism (Olek-Hrab, Hrab, Szyfter-Harris, & Adamski, 2016). Patients often feel they become trapped in this cycle as even when the underlying cause and other aggravating factors have been eliminated, the behavioural pattern contributes to the continuation of symptoms (Kaneko, 2018). Mochizuki, Schut, Nattkemper and Yosipovitch (2017) quote the phrase "the itch that rashes, rather than the rash that itches" (p.14) characterising the cyclical nature of atopic dermatitis.

This is infamous as a vicious cycle amongst sufferers of chronic itch conditions, yet there appears to be mixed views on what the cycle involves. Different conceptions include various physical aspects, such as inflammation (National Eczema Association, 2013), infection (Pavlis & Yosipovitch, 2017), exposure to allergens (Eucerin, 2015). Many others refer to psychological aspects such as frustration (Walter, 2011), stress (Szepietowski & Reszke, 2017), and temporary relief (Horne, 2015). Most versions agree upon the basic components as itching, scratching and skin irritation. As such, the cycle of these key aspects (Figure 1.2) will be the version referred to throughout this thesis.

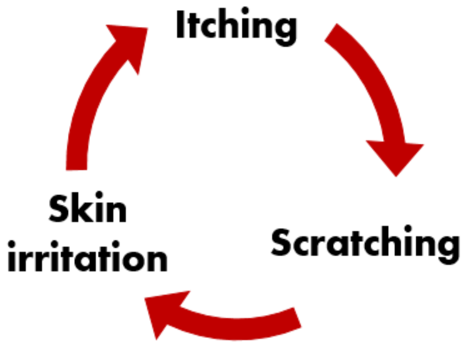


Figure 1.2 The itch-scratch cycle

Patients are trapped in the itch-scratch cycle by more complex factors than simply the inflammatory response. Zhao et al. (2014) found that serotonin, a neurotransmitter associated with pleasure and reward, was released as a result of scratching and was consequently influential in forming an itch-scratch cycle in mice. When serotonin was reduced, scratching behaviour decreased. They suggested that the rewarding aspects of scratching served to reinforce a damaging behaviour. Mochizuki et al. (2014) found results consistent with this in humans using functional magnetic resonance imaging (fMRI): scratching proximal to an itch site, but not distal, activated the striatum and midbrain, which are considered key reward centres in the brain. In a subsequent study they also found scratching to activate the caudate nucleus, from which they concluded that overactivity in the reward system may be associated with hypersensitisation and the addictive aspects of scratching (Mochizuki et al., 2015). Itch is inherently an unpleasant experience, but fulfilling the desire to scratch can be experienced as pleasurable relief (Mochizuki et al., 2014), reinforcing the cycle. It is clear that the itch-scratch cycle contains a substantive cognitive element that requires a psychological intervention to break.

1.2 Manipulating psychological influences on itch

In addition to itches that arise due to irritation or allergic responses it is possible for a perceptual stimulus in a different modality to induce or increase itch sensations through psychological suggestion, with no physical stimulation of the skin. These effects can be created or manipulated in an experimental setting.

1.2.1 Placebo and nocebo effects

Itch is modulated by psychological influences from both naturally occurring emotional states such as stress and anxiety, but also from deliberate manipulation and intervention using placebo and nocebo effects. Placebos occur when psychological influences result in a beneficial effect separate from any physical or pharmacological intervention and conversely nocebo effects create a detrimental effect separate from any physical harm. Itch is susceptible to both effects, with suggestion able to alter participants expectations of itch severity, which then alters their experience of it accordingly. Verbal suggestions of what a physical itch stimulus will feel like are able to do this to a greater extent than the equivalent for a pain stimulus (van Laarhoven, Kraaimaat, Wilder-Smith, van de Kerkhof, & Evers, 2010). Furthermore, the effect is more pronounced when verbal suggestions are combined with visual cues (Bartels et al., 2014), indicating that multisensory itch triggers particularly salient.

The enhanced itch produced by a nocebo has been shown to increase activity in the caudate, dorsolateral prefrontal cortex, and intraparietal sulcus (Napadow et al., 2015). This indicates that noceboes are able to replicate the neural response to allergen-induced itch, as well as comparable subjective reports of itchiness. It has even been shown to induce physical worsening of symptoms from psychological suggestion. Stumpf et al. (2016) used verbal suggestions to induce higher itch intensity ratings alongside stronger cutaneous responses, resulting in a greater wheal and flare in response to histamine and sodium chloride. Thus, we can be confident that psychological itch induction is not limited to a change in the judgement and reporting of an itch experience, but a change in the sensory quality and intensity of that experience.

1.2.2 Psychological suggestion and contagious itch

The creation or exacerbation of itch symptoms through psychological suggestion has often been suggested anecdotally. For example, it is frequently mentioned in descriptions of “medical students’ disease” whereby medical students tend to find themselves experiencing the symptoms they are studying (Woods, Natterson, & Silverman, 1966, p785; Mechanic, 1962). Itch has similarly been implicated in mass psychogenic illness (Mazzoni, Foan, Hyland, & Kirsch, 2010) where participants who took a nocebo drug and observed an actor displaying the expected side effects also reported experiencing those symptoms, inclusive of itching.

Rechenberger (1981) first noted contagious itch as a distinct phenomenon in terms of a form of pruritus “triggered psychically and have[ing] a physical substrate as a consequence” (p.1005). Skelton and Pennebaker (1982) subsequently observed that people scratched themselves if they were sat near a confederate who was deliberately scratching. They further commented that it did not appear to matter whether the confederate attributed their itch to a contagious or benign cause, so the likelihood of physical contagion did not appear to be the driving force influencing participants’ behaviour.

While contagious itch is most often visually-mediated, it has also been investigated in the auditory domain by Swithenbank, Cowdell and Holle (2016) who found that the scratching sounds, particularly at higher frequencies, elicited more itching in both psoriatic and healthy participants compared to rubbing sounds. The neutrality of this as a control condition is debatable though: rubbing skin is also a means of relieving itch albeit a less common one. Nonetheless, this study demonstrates that itch contagion can be induced by both visual or verbal cues, and thus is a multimodal effect.

1.2.3 Defining psychological itch triggers

At this point it is useful to clarify the distinction between terms in psychological itch induction. There is currently no standardised consensus on these terms, so more than one term may apply to the studies cited despite the terminology chosen by the authors.

- ***Visually-evoked itch (VEI)*** is the specific effect of inducing itch by viewing itch related visual images (including both static images and videos). It overlaps with contagious itch in visual form, but also incorporates itch triggers that do not depict another person experiencing them, such as images of itch-inducing plants and insects.
- ***Contagious itch*** refers to the phenomenon of itch being triggered by exposure to another person's itch, in any modality. The itch transmission is considered to be socially contagious between people.
- ***Nocebo itch*** is itch that arises from or is amplified by psychological suggestion in any form. Contagious itch and VEI are specific forms of nocebo itch.

1.3 Key studies on visually-evoked itch

Although the effect of inducing itch by viewing another person's itch experience has been noted and commented on, it has only been systematically studied a small number of times. The approaches taken and their findings are summarised below.

1.3.1 'Observations during an Itch-Inducing Lecture'

The ability to induce itching through purely psychological means was first demonstrated by Niemeier, Kupfer and Gieler (2000) who presented a short lecture on itching accompanied by slides with relevant images, followed by a session on relaxation. They observed that the audience scratched significantly more frequently during the itch lecture than the relaxation lecture and thus inferred that itching had been induced by the audiovisual stimuli. They also asked participants to rate their itchiness at 3 timepoints, before and after each lecture session. They found that the itch ratings were highest after the itch lecture, for both healthy participants and those with self-reported skin conditions. This study provided a clear demonstration of itch outcomes corresponding with visual and verbal suggestions of itch, but the lack of counterbalancing between itch and non-itch stimuli greatly weakens its explanatory power and it is not possible to separate the influence of itch from the potential order effects in this experimental set up.

1.3.2 ‘Generating physical symptoms from visual cues: An experimental study’

In another investigation of audiovisual itch induction, Ogden & Zoukas, (2009) used video clips of people scratching and lice crawling through hair to generate itch symptoms. They found that healthy participants with little reported experience of itching scratched more and reported higher levels of itchiness during these videos, than similar participants who viewed videos relating to pain and cold. This method, however, meant that there were no baseline measures of itch within subjects, and no overall neutral control condition. They chose this design to avoid priming effects from reading the symptom checklist prior to watching the videos, but this was at the cost of knowing how these participants would have responded without viewing symptom-inducing content.

1.3.3 ‘Contagious itch in humans: A study of visual 'transmission' of itch in atopic dermatitis and healthy subjects’

The first study to directly compare the effects of VEI on healthy and clinical (atopic dermatitis) participants was untaken by Papoiu et al. (2011). They administered either histamine to induce itching or a saline control solution to the forearms of their participants, then showed them videos of people scratching their forearms or sitting still. They found that the scratching videos increased the amount of itch reported and scratching observed for both the clinical and healthy participants, with the former showing a larger effect. This was the case when histamine was used, but also to a lesser extent when the control solution was used. They also noted that despite the localised focus on the forearm in both the video content and the histamine stimulation site, the scratching behaviour displayed by participants was scattered across the whole body.

Overall, they concluded that psychologically contagious itch is the product of a built-in mechanism in the healthy population, which is amplified in people with atopic dermatitis. While this does appear to be consistent with the findings from purely audiovisual induction of itch, the use of histamine prevents this from being a directly comparable effect. It is arguably visually exacerbated itch though, which may be a realistic model for how such images affect people with existing itchy skin conditions.

1.3.4 'Can itch-related visual stimuli alone provoke a scratch response in healthy individuals?'

Lloyd et al. (2013) expanded on these findings by using static visual images instead of dynamic audiovisual stimuli and by comparing the effects of different types of itch content on healthy participants. They used three types of image: skin-contact, featuring either itchy insects on skin or non-itchy creatures on skin; skin-response, featuring either scratching or washing the skin; and context-only featuring either insects or non-itchy creatures in the environment. In contrast to previous studies, participants were asked to rate both how itchy they felt themselves when viewing these images and how itchy they thought the person in the picture felt. These results correlated with one another, indicating that empathy and identification with another person's itch experience may be influential in creating the effect.

As expected, they found that itch images elicited higher itchiness ratings and more scratching than non-itch images. They also found an interaction between the three stimulus conditions with higher ratings for skin-contact images, indicating that the more visceral imagery of irritants on a person's skin produced the strongest reaction. Scratching, however, was found to be more frequent when viewing skin response (scratching) images, further suggesting that identification with the person in the image was influential on how the effect was experienced. This indicates that self-reported itch and observed scratch are not governed by the same mechanism as different aspects of the stimulus can influence them. Accordingly, they did not find a correlation between itchiness ratings and scratch frequency, indicating that these measures reflected different components of VEI.

1.3.5 'Neural basis of contagious itch and why some people are more prone to it'

The first attempt to identify the neural correlates of contagious itch was carried out by Holle et al. (2012) using fMRI while showing healthy participants videos of a person scratching (or as a control, tapping) their arms and chest. They found that viewing scratching activated the 'itch matrix' in a similar way to somatosensory itch stimuli; specifically, the anterior insular, primary somatosensory, prefrontal and premotor cortices. This fundamentally indicates that scratching induced by VEI is indicative of an experience of itch rather than an imitation of scratching as activation it is not limited to motor regions. The areas involved are associated with mirroring and simulation of actions (premotor cortex), sensory aspects of itch (primary somatosensory cortex), which correlated with itchiness ratings, and top-down predictions of interoceptive signals which may enable simulation of the feeling of itching (anterior insular).

Ward, Burckhardt and Holle (2013) added further analysis from this study based on their observations of participants videotaped outside of the scanner. They recorded participants scratching or touching themselves, noting the location on the body and the hand used. It emerged that participants used both hands equally and regardless of the hand featured in the stimuli. Similarly, the location of scratches did not match the arms and chest scratched in the stimuli, but was instead directed towards the face and hair. They interpreted this to mean that the experience of itch was not vicariously shared via contagious transmission and that the mechanism behind it is more related to affective and sensory processing.

1.3.6 ‘Brain Processing of Contagious Itch in Patients with Atopic Dermatitis’

Building upon Holle et al.'s (2012) findings from healthy participants, Schut et al. (2017) used fMRI to investigate the brain processing of contagious itch in participants with atopic dermatitis. They used a video of people scratching (and of them doing nothing as a control) to induce itch, which they found outside of the scanner led to higher itch ratings and more scratching. They also found a notable difference from Holle et al. (2012) in the activation of the supplementary motor area, left ventral striatum and right orbitofrontal cortex. These areas are part of the fronto-striatal circuit which is, in terms of itch perception, associated with the urge to scratch. They suggest this network is heightened in atopic dermatitis and thus should be the target of interventions to reduce scratching.

However, they did need to remove 6 (out of 19 screened) participants from the sample who did not experience VEI strongly enough, to ensure a clear result distinct from effects purely due to the observation of actions. As they did not also test healthy controls it is unclear whether their results depict a response that is characteristic of having atopic dermatitis or simply of being someone who experiences VEI vividly. Also, their experiences of VEI may have been different during the fMRI procedure as they would have been required to suppress the urge to scratch during scanning, which may have contributed to the activation found.

1.3.7 ‘Contagious itch: what we know and what we would like to know’

Schut et al. (2015) compiled a review of the existing literature on contagious itch and explored explanations involving empathy, mirror neurons and associative learning (which are discussed further in section 4 below). They concluded that contagious itch is not location-specific and that negative affect resulting from viewing itch experiences is more important than what is seen, with regard to how influential a stimulus is.

They suggested that future research should focus on how the effect is created in physiological terms, such as whether contagious itch triggers the release of histamine and other such pruritogens or whether it is purely a cortical response. Furthermore, they wanted to know what brain areas are involved in this response and specifically whether the mirror neuron system is activated, especially in chronic itch patients. They also suggested that more research was needed on what correlates with induced itch and whether it is affected by age, gender or other demographic variables. In addition, it is important to know whether chronic itch patients show a greater empathic reaction to another person scratching than healthy controls. Lastly, they recommended further investigation into the efficacy of interventions based on reducing the effect of visual itch cues.

1.4 Explanations of visually-evoked itch

As Schut et al.’s (2015) review summarised, there is currently little consensus on what mechanisms underlie the effects of visually-evoked itch. Within the literature, the following interpretations have been suggested.

1.4.1 Personality characteristics

There have been mixed findings for personality traits that correspond with susceptibility to contagious and visually-evoked itch. Based on Lloyd et al.’s

(2013) findings that participants' self-ratings of itchiness correlated with their other-ratings of the photo subjects' itchiness, Schut et al. (2015) have suggested that empathy may have a role in itch contagion. Holle et al. (2012), however, found no link between trait empathy and the level of contagion experienced by their participants. They did find that itch intensity was more clearly linked with neuroticism, although this was contradicted by Bartels et al. (2014), who found neuroticism had no relationship with psychological modulation of itch using the nocebo effect. Various other states and traits have been found to correspond with VEI, such as anxiety (Ogden & Zoukas, 2009), low extraversion (Bartels et al., 2014), and low agreeableness combined with self-consciousness (Schut et al., 2014).

Although there are noted gender and age differences in these traits themselves, Holle et al. (2012) found no gender differences in susceptibility to itch contagion, and neither did Niemeier et al. (2000). Also, previous findings (Lloyd, Dodd, Higgins, Burke, & McGlone, 2017) have specifically shown gender or age differences to have no significant impact on VEI. As a result, gender and age will not be considered further.

Holle et al. (2012) and Schut et al. (2014) in particular argue in favour of individual differences and associated personality traits modulating the intensity of psychologically-induced itch, and recommend these as screenable traits in chronic itch. However, given the disagreement between studies as to which personality traits might be involved in contagious itch, it seems most reasonable to view personality traits as covariates with susceptibility to VEI rather than predictors or active variables until further investigation can uncover what, if any, role they play in the effect.

1.4.2 Mirror neurons

Mirror neurons have been suggested as a possible explanation for VEI (Holle et al., 2012; Schut et al., 2015), as a means of transmitting an action to an observer in a similar way to contagious yawning (Akihiko Ikoma, Steinhoff, Ständer, Yosipovitch, & Schmelz, 2006). Holle et al. (2012) inferred this because of brain regions such as the premotor cortex, which they found were activated during visually-evoked itch, are associated with motor mirror systems (although they are also activated when observing actions regardless of mirroring). Mueller et al. (2017) has speculated that overactivity of the mirror neuron system may play a role in delusional infestation via VEI. This explanation is particularly relevant for socially contagious itch when VEI is based on seeing another person scratching.

Lloyd et al. (2013) provides the strongest evidence for this explanation, as they found that participants scratched most frequently when viewing images of people scratching, which implies that the mirroring of actions increased scratching beyond that induced by the itchiness of the image. They also found that participants' ratings of their own itchiness correlated with their ratings of the photo subject's itchiness, implying that they were experiencing itch similarly to how they perceived another's experience, which may involve perceptual mirroring.

Papoiu et al. (2011) found that participants with atopic dermatitis (AD) scratched body locations distal to the ones viewed, whereas healthy controls scratched more proximal locations. This implies that they were not experiencing VEI in the same way. It may be the case that the AD patients had a predisposition towards itch and thus experienced it more and targeted their scratching accordingly. On the other hand, controls may have experienced less itching and so mirroring the behaviour seen in the video may have had a stronger influence on how their scratching behaviour manifested.

Contrary to this idea, when Feneran et al. (2013) investigated visually-evoked itch with monkeys instead of humans, they observed that subjects scratched different locations on the body to the monkey in the video. They claimed that this indicated the monkeys were genuinely experiencing itch rather than simply mirroring behaviour, as mirroring tends to match the actions and body location being viewed. Furthermore, contagious itch has also been observed in mice (Yu, Barry, Hao, Liu, & Chen, 2017), so it is not necessarily a product of primate neurology from which the motor mirror system is primarily associated.

This explanation is still plausible, but it is important to note that although mirroring mechanisms have been inferred and suggested from behavioural data, at present there is no information on whether or not perceptual or motor mirror neuron systems are active when experiencing VEI. Furthermore, even if mirror neurons are involved, this can only explain a limited segment of psychologically-induced itching; scratch behaviour may be mirrored, but then how do verbal suggestions and images of irritants produce the effect in such a similar way when they require semantic interpretation and inference of cause and effect? It appears more likely that another mechanism governs the overall effect, possibly with motor mirror neurons enabling or enhancing the scratching component.

1.4.3 Classical conditioning

It is possible that visual images are able to elicit an itch sensation as a conditioned sensory response. For example, if the presence of insects as an unconditioned stimulus in real life consistently results in itching as an unconditioned response, then visual appearance of insects could become conditioned as a conditioned stimulus to evoke an itch as a conditioned response. Evidence in favour of this comes from Jordan and Whitlock (1974) who demonstrated that both atopic dermatitis patients and healthy controls could be conditioned to associate a tone with an itch stimulus, leading to scratching upon presentation of the tone. Support for this representing a physiological process was provided by Russell et al. (1984) who demonstrated that conditioning a histamine response was possible in guinea pigs by pairing an allergen with a neutral odour. The odour alone was subsequently sufficient to produce an increase in histamine production.

However, just because itch can be conditioned does not mean it is; these findings alone cannot be used to conclude that conditioning is the active mechanism behind VEI rather than merely a sufficient one. Instead, further investigation would be required to provide evidence that this process is happening organically. Despite this limitation, conditioning explanations have been supported by Schut et al.'s (2015) review of the literature as they claim people with chronic itch encounter more instances of itch being paired with the visual cues of scratching and damaged skin.

Whilst this seems reasonable as an explanation, it is limited in its explanatory power. Based on these principles, it could be predicted that whilst insect-related images would produce a strong effect, skin based images might not as scratching is paired more with the extinction of an itch, especially for the healthy population. In addition, classical conditioning cannot account for how simply talking about itchiness can induce an itch sensation (Mitchell, 1995). As with the mirror neuron explanation, conditioning is more likely to play a reinforcing role within a wider VEI mechanism.

1.4.4 Threat detection

Expanding on the conditioning explanation, it has been suggested that rather than being individually conditioned in most people's experiences, VEI might be the product of an evolved mechanism that has established the connection. Itch itself is claimed to have an evolutionary basis as a defence against harm to the skin from irritants (Stante, Hanna & Lotti, 2005). Indeed, initiating the scratch reflex is principally a defensive reaction (Olek-Hrab et al., 2016), so it is plausible that contagious itch may be a by-product of this defence.

Threat detection mechanisms have been shown to orient visual attention towards a range of threatening stimuli, such as angry faces (Karin Mogg et al., 2000), dangerous animals (Ohman, Flykt, & Esteves, 2001), the subjects of phobias (Rinck & Becker, 2005) etc. In these studies, participants have been shown to detect threatening stimuli faster than neutral targets indicating an attentional bias towards it, and a hypervigilance when there is a possibility of encountering it.

Dey, Landrum and Oaklander (2005) claimed that pain and itch are complementary responses in that pain provokes withdrawal of the body from a threat, and itch provokes the removal of a threat from the body. This is supported by Mochizuki et al.'s (2013) findings that itch and pain imagery activate the same brain regions and thus differences between them are functional rather than neurological. If this premise is accepted, then it is reasonable to theorise that itch may involve threat detection mechanisms similar to those involved in pain. In evolutionary terms, it is plausible that itch-inducers such as venomous insects could have posed a sufficient level of threat for a threat detection mechanism to have evolved to detect and avoid them.

Kupfer and Fessler (2018) argued that humans have adapted such itch generation and scratch grooming mechanisms as a defence against ectoparasites (insects which live on the skin). They proposed that such mechanisms would involve detecting ectoparasites, increasing bodily vigilance, potentiating itch sensations, and activating defensive scratch behaviours. These features are rendered maladaptive in chronic itch disorders, which they suggest can, in some cases, be considered pathologies or dysfunctions of the ectoparasite defence system. Furthermore, they describe this system as overlapping with the disgust system, resulting in a complementary mechanism to remove organisms that threaten the body either via skin irritation or ingestion, respectively. In addition, the behavioural response for disgust is withdrawal and avoidance, which links to the withdrawal pain response, suggesting a network of responses for managing a range of threats.

1.4.5 Itch and pain

As an understudied effect, itch is often compared to pain as the closest sensory phenomena with a much larger body of literature. At the physiological level, itch and pain utilise separate yet overlapping peripheral and central afferent pathways (Ikoma et al., 2003; Liu & Ji, 2013; Ständer & Schmelz, 2006; Yosipovitch, Carstens, & McGlone, 2007) therefore research in this field often compares the two responses. In terms of psychology, as mentioned above, itch and pain have been considered comparable forms of physical threat and have been suggested to have evolved as complementary threat-avoidance mechanisms (Dey, Landrum, & Oaklander, 2005; Ikoma, et al., 2005; Kupfer & Fessler, 2018). These parallels combined with the relative paucity of direct studies of contagious itch in certain contexts (attention, nocebos, and tactile sensitivity being prime examples) means that explanations often rely on analogy with pain as a comparable effect.

While comparison with pain provides an acceptable foundation for constructing hypotheses for itch effects, itch and pain do have some clear differences that prevent inferences being made directly from one modality to another. The overlap in physiology leads to one major distinction: Pain inhibits itch which thus enables scratching to provide relief (Bautista, Wilson, & Hoon, 2014). In terms of psychological influences, Vandenbroucke et al., (2013) has demonstrated that while itch can be visually evoked, pain cannot.

They found that people do not tend to experience vicarious pain sensations when viewing visual images depicting painful experiences. This indicates that itch is unique in the extent and prevalence of its social transmission, and so requires direct investigation as a distinct phenomena.

1.5 Questions to address

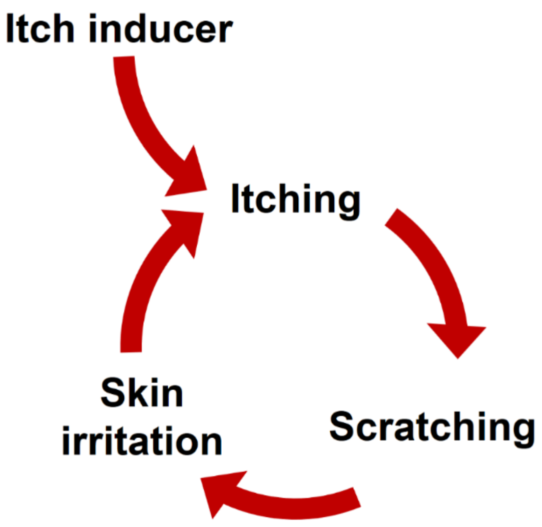


Figure 1.3 The itch-scratch cycle modelled with visually-evoked itch as an itch inducer leading into the cycle.

Visually-evoked itch is clearly established as a method of inducing itch without stimulation of the skin; therefore, it is considered a psychological itch trigger. In terms of the itch-scratch cycle, VEI can be conceptualised as an external inducer, which feeds into the cycle. This can be modelled as a version of the itch-scratch cycle shown in Figure 1.3, derived from the version outlined in section 1.3.

As VEI has a top-down effect on perception, it can be utilised to explore how psychological influences can create and modulate itching. Examining VEI in terms of the itch-scratch cycle provides a conceptual framework to systematically study the cyclical progression of chronic itch from itch-inducer to itch to scratch. It also allows us to develop an understanding of the psychological variables that affect this progression. Therefore, using this model as a basis, this thesis will attempt to address the questions that remain unaccounted for by previous explanations of VEI in order to investigate the mechanisms behind the effect and its role in propagating the itch-scratch cycle.

The overall goal of this project is to find ways of breaking the itch-scratch cycle by isolating factors which influence the entry to the cycle via VEI. As we currently lack an overarching theory for how VEI operates, areas for further investigation will focus on making it possible to synthesise an explanation of VEI within the itch-scratch cycle. For this reason, the research questions that form each experimental study are considered in terms of their location on the proposed model of the cycle.

1.5.1 What is the relationship between itch and scratch?

The scratch responses measured in previous VEI studies tend not to correspond closely to the content of the stimuli (Feneran et al, 2013; Ward et al., 2013), nor has there been much consistency between self-reported itch and observed scratch (Lloyd et al., 2013; Niemeier, Kupfer & Gieler, 2000). This raises the question of what the relationship between itch and scratch actually is. Itch is defined in terms of the desire to scratch so it is odd that such a discrepancy would exist between the two measures. It would seem that they are either measuring two distinct concepts, or that they are modulated by other psychological variables, which disrupt the appearance of a direct relationship. It is crucial to identify what the connection between induced itch and eventual scratch is, in order to extract meaningful conclusions from the VEI literature.

Chapter 3 addresses this issue by comparing the effects of different body locations and itch contents in the stimuli. It uses an itch location measure to identify distinct itches experienced by participants, as well as observing scratching. From this it is possible to draw out patterns in the itch locations, scratch locations, and the contents of the images. It is fundamentally an attempt to clarify the process of VEI from inducer to itch to scratch, providing an overview of how the effect occurs. Therefore it is situated across the whole path into the cycle covering all the elements of VEI, as shown in Figure 1.4.

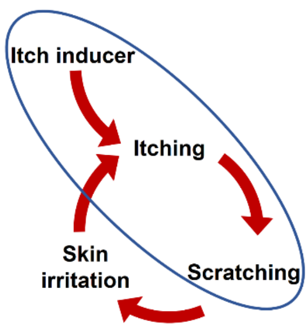


Figure 1.4 The location of Chapter 3 on the itch-scratch cycle

1.5.2 To what extent is VEI a visual effect?

If VEI is purely visually-evoked as opposed to merely visually-influenced, it should be possible to create itch simply by passively viewing itchy images. To date, no study of VEI has used a purely observational method to test this; all have chosen to question participants on what they experienced. Studies of 'placebo itch' demonstrate that suggestion and expectation can influence the intensity of itch (Bartels et al., 2014; Schut, Radel, Frey, Gieler, & Kupfer, 2016; Van Laarhoven et al., 2011), so it is currently unknown whether such effects influence the findings of VEI experiments. This has previously been raised as a possible problem of using symptom questionnaires (Ogden, 2003), so it is crucial to disentangle VEI from the potential suggestion effects of asking itch-related questions to isolate the effect of the visual itch content of the images.

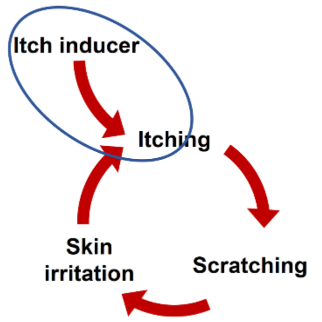


Figure 1.5 The location of Chapter 4 on the itch-scratch cycle

Chapter 4 examines the extent to which passive viewing of itch images produces scratching by replicating the design used in Chapter 3 with non-itch related questions, then comparing the scratch observations between them. It addresses the question of whether VEI is a purely visual effect, or whether the way it is investigated contributes additional itch suggestion. This is an attempt to isolate the visual element of VEI from contamination by other forms of psychologically-induced itch. Therefore it is situated on the path between the inducer and the itch, as shown in Figure 1.5.

1.5.3 Does VEI affect sensory tactile sensitivity?

VEI has previously been examined in terms of behaviour, self-report, and neural correlates, but there is little information on what changes in perception and cognition occur during psychological itch induction. Van Laarhoven et al. (2007; 2013) found that chronic itch patients have lower sensory thresholds for perceiving physical itch stimuli than healthy controls, and it has been suggested in other modalities that this sensitisation may be a product of psychological factors (Curatolo, Arendt-Nielsen, & Petersen-Felix, 2006; Smith et al., 2008). This raises the question of whether sensory thresholds are altered during VEI either by the psychological induction or by the induced itch itself. It is possible that VEI involves detecting itch signals in somatosensory noise either by increasing sensitivity or overinterpreting potential signals. Therefore, investigating changes in tactile sensitivity can allow us to gain a greater understanding of the mechanisms underlying the effect.

Chapter 5 used psychophysics to investigate whether VEI involves a change in tactile sensitivity. The somatic signal detection task (SSDT; Lloyd et al., 2008) was employed to explore participants' ability to detect faint sensation and their likelihood of reporting it. As this is measured during the physiological reaction to the stimuli, these questions are situated on the cycle around the point where itch is created and experienced as shown in Figure 1.6.

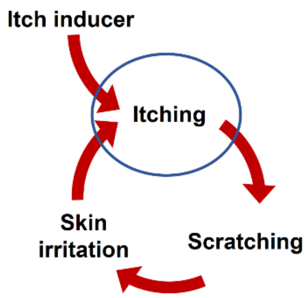


Figure 1.6 The location of Chapter 5 on the itch-scratch cycle

1.5.4 What role does visual attention play in susceptibility to VEI?

Attention has been explored in various ways as a mechanism in somatosensory effects and appears likely to play an important role in VEI. Tihanyi and Köteles (2017) have shown that various bodily sensations can be induced by focusing attention on the body, supposedly as a result of top–down sensory mechanisms. It is possible that VEI is partially a result of similar interoceptive attentional effects, as Van Laarhoven, Kraaimaat, Wilder-Smith and Evers (2010) found that higher levels of experienced itch corresponded with greater attentional focus on bodily sensations. It is clear that attentional effects overall require more in-depth investigation.

Visual attention in particular is an important aspect to consider in understanding VEI, in terms of whether itch-inducing images capture visual attention, drawing the person towards them and/or sustaining a focus on them. Attentional bias to itch has previously been found in both healthy (van Laarhoven et al., 2017) and clinical itch (Fortune et al., 2003) populations, although both studies have methodological limitations. Given that Papoiu et al. (2011) found differences in how clinical itch and healthy participants experience VEI, the next step in understanding these differences is to investigate whether these groups are inclined to allot attention differently when an itch inducer is present. Attentional bias may provide an answer to why some people are more susceptible to VEI as whether a person is drawn into the itch-scratch cycle may be linked to their ability to filter attention to itch triggers in the environment. These questions warrant the use of both behavioural reaction time measures and eye-tracking to examine which images participants look at first and most often, in order to gain a detailed understanding of how an itch inducer initiates VEI.

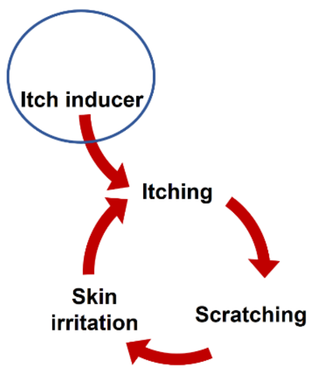


Figure 1.7 The location of Chapter 6 on the itch-scratch cycle

Chapter 6 investigates the role of visual attention, comparing how clinical itch and healthy participants' attention is drawn to itch images prior to VEI in order to investigate whether people with itchy skin conditions are predisposed to experience VEI differently. This was done using a reaction time based visual probe paradigm combined with eye-tracking, to examine implicit (fast and instinctive) and explicit (slower and considered) attentional biases to VEI inducing images. Attentional bias occurs very early on in the process of viewing an itch inducer, prior to cognitive appraisal or interpretation of the image content and certainly before the creation of an itch sensation. Therefore, within the itch-scratch cycle model, Chapter 6 is located at the point of first perceiving the potential itch inducer, as shown in Figure 1.7.

1.6 Breaking the itch-scratch cycle

At present, the available advice on breaking the itch-scratch cycle focuses on using medicated creams and avoiding scratching, but the latter is easier said than done for many sufferers. Medication can be beneficial in reducing itching and accelerating healing, but it cannot eliminate the urge to scratch. Habit reversal training encourages patients to avoid or replace the harmful scratching behaviour (Grillo, Long, & Long, 2007; Nilsson, Levinsson, &

Schouenborg, 1997), but the urge to scratch still remains. The reward gained from scratching creates a cognitive dissonance that impedes the ability to change behaviour. This means that for many the cycle will repeat indefinitely unless behavioural and cognitive patterns change.

The overarching goal of this project is to provide an account of how VEI operates within the itch-scratch cycle, which can be used to inform psychological interventions. As most interventions target the physical aspects in the scratching and skin irritation stages, the avenues explored in this project will be based on the cognitive and perceptual aspects occurring prior to scratching. The intention is to create a theoretical model, which identifies how a psychological trigger creates an itch sensation and what then creates the urge to scratch. It is hoped that this model can be used to develop interventions that interrupt these processes and allow prevention at an early stage, before the cycle is able to propagate.

It is apparent that the cycle has complex mechanisms underlying it, and so simply addressing the physical manifestations is not sufficient to help patients avoid it. A cognitive solution is required to counteract the psychological triggers that perpetually induce further itching, and thus enable people to escape the itch-scratch cycle.

Chapter 2 : Development of Stimuli and Methods

2.1 Creation of the VEI stimulus set

An experimental stimulus set comprising 64 images was created for use in this project, drawing on elements found to be successful for evoking itch in previous studies (Lloyd et al., 2013; Niemeier et al., 2000; Ogden & Zoukas, 2009; C. Schut, Grossman, Gieler, Kupfer, & Yosipovitch, 2015). It was designed with the aim of creating a large set of well-matched itch and non-itch images, covering a range of itch contents, and eliminating extraneous details as much as possible. This set was then used in all 4 studies, enabling a consistent and validated induction of itch across these experiments.

2.1.1 Process for selecting stimuli

Potential images were sourced from the internet and assessed on their suitability to become stimuli. Unsuitable images were rejected for the following reasons:

- Visible ‘water marks’ or other indications of copyrighted content.
- Distracting elements such as recognisable celebrities or people in humorous situations.
- Obtrusive clothing or other objects that would be difficult to remove in editing.
- Mixed itch content such as insects biting skin, insects on irritated skin, scratching an existing rash, etc.
- Featuring people who were visibly dissimilar to the expected participant group (predominantly young adults, female, light-skinned).
- Unable to pair-match with another image to an acceptable standard.

A small selection of suitable images were shortlisted for each condition. From these, the images selected for inclusion in the stimulus set were the most clear and strong depictions of itch and those with the closest matched non-itch pairings.

2.1.2 Composition of stimuli

The stimulus set was designed to represent an even spread of three main attributes: (i) itch and non-itch images, (ii) type of itch content, and (iii) parts of the body. The full final stimulus set can be viewed in appendix A.

The type of itch content featured was selected based on Lloyd et al.'s (2013, p.107) study, which used three image content conditions: insects ("context"), insects touching skin ("skin contact"), and people scratching ("skin response"). The first two conditions were replicated and 'skin response' was sub-divided into two separate categories to differentiate between the act of scratching and the result of skin irritation. Thus, the itch content categories in the final stimulus set were:

- Action: the subject scratching their skin (itch) or touching their skin (non-itch)
- Skin response: rashes (itch) or bruises (non-itch) on the subject's skin
- Irritant contact: insects (itch) or innocuous objects (non-itch) touching the subject's skin
- Irritant context: insects not in contact with a person (itch) or objects which are visually similar to these insects (non-itch)

The decision to balance the body parts featured across the images was based on Holle et al. (2012), who noted differences in what parts of the arm people found itchiest. No previous study has fully examined or controlled for this aspect though, nor have they compared locations across the body as a whole, so its inclusion allows for systematic investigation of body location differences, with the full body represented in the stimuli. The body part categories in the final stimulus set were:

- Arms and hands
- Legs and feet
- Head and neck
- Torso
- Irritant context images which did not feature body parts.

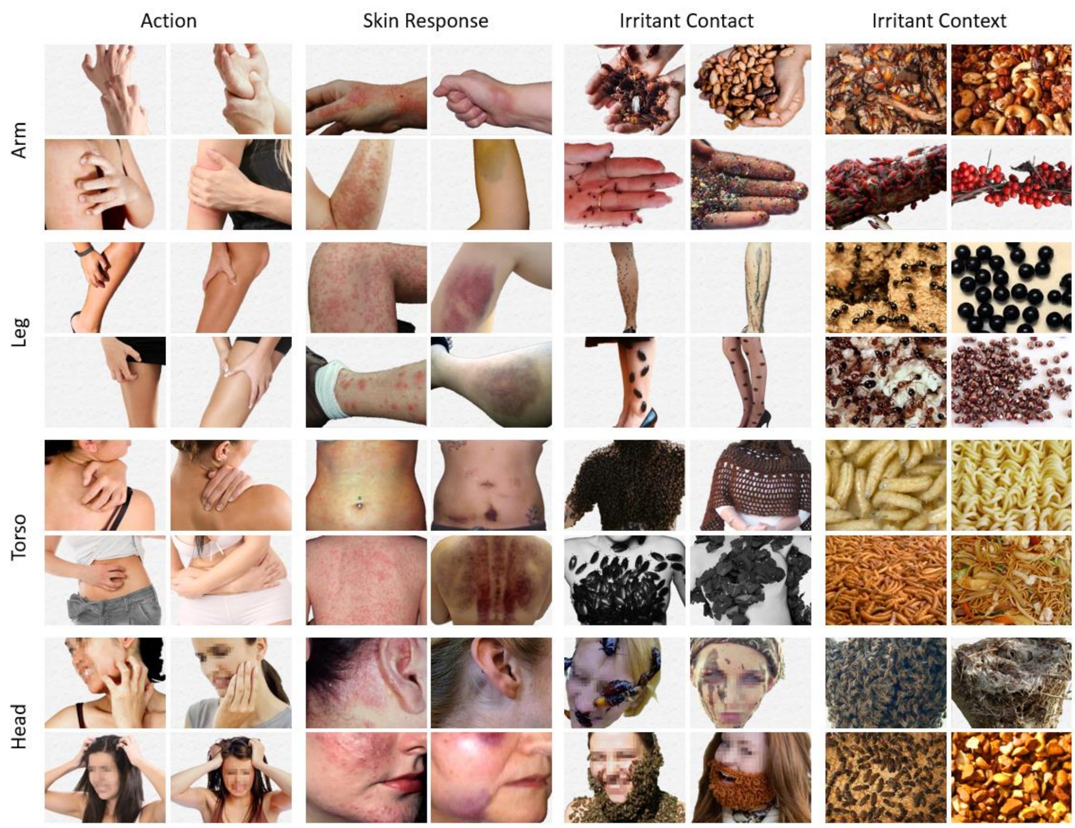


Figure 2.1 The full stimulus set presented in itch and non-itch pairs, grouped by itch content and body part.
Larger copies of these images can be viewed in appendix A.

The categories overlapped such that there were two pairs of images for every combination of content and body conditions, totalling 64 images: 4 itch contents x 4 body parts x 2 versions = 32 pairs of itch and non-itch images. As the irritant context images did not contain body parts, they instead featured 4 types of insect (ants, bees, maggots and roaches) so that there were still 2 closely related pairs for each. Figure 2.1 shows the full stimulus set, grouped by content and body part. The images were created in two sizes for use in different experiments: 600x600 pixels and 320x240 pixels. Both versions have a resolution of 72dpi, which is the recommended resolution for viewing on a computer screen.

2.1.3 Image matching

The itch and non-itch image pairs were matched on appearance and composition. The brightness and colour saturation were adjusted to make the images appear visually similar. All models were light skinned to match the majority of the participant pool available (Azevedo et al., 2013), all were adults and most were female. Their positions, the angle of view and the exact body locations featured were matched as closely as possible. The contents covered approximately the same proportion of the image area. Any additional itch-relevant details were removed (e.g., scratch marks or redness of the skin) from the images and facial expressions were pixelated to obscure the subjects' emotional reactions. To increase the overall uniformity of the stimuli, clothing was altered to feature only plain neutral colours and a textured white background was added to remove context.

Within the itch content categories, itch and non-itch images were paired in such a way as to be conceptually, as well as visually, similar in order to isolate the itch element. For the action category, scratching the skin was paired with neutral touching in the same place so the suggestion of touch is present in both. For skin response, rashes were paired with bruises as a comparable form of visible skin damage covering a similar area, with similar levels of unpleasantness. For irritant contact, insects touching the skin were paired with visually similar inanimate objects touching the skin in the same locations. For irritant context, insects were paired with inanimate objects that look as visually similar as possible, for example cockroaches and mixed nuts.

2.2 Image pair matching survey

A preliminary survey was carried out to test the new experimental stimulus set and measure how well matched the itch and non-itch pairs were. Ethical approval was given for this study by the School of Psychology at the University of Leeds, reference number:15-0029 (5/2/2015).

2.2.1 Methods

Twenty-nine participants completed a short survey via the internet. Fourteen participants were female, 6 were male and 9 were non-binary or declined to answer. Six were in the18-24 age bracket, 19 were 25-34, 2 were 35-44, and 2 declined to answer. Nine were located in London, 6 in Yorkshire, 8 in the East Midlands, 1 in the South East, 1 in the South West, 1 in the East of England, 1 in Sweden, and 2 who declined to answer. They came from a range of social backgrounds and ethnicities, but were all native English speakers.

In the survey, they were presented with every image in the stimulus set in a fully randomised order. For each image, they were simply asked to rate how stimulating the image appeared to them, using a seven-point scale illustrated with Self-Assessment Manikin pictograms (Bradley & Lang, 1994) as shown in Figure 2.2, to assist with the interpretation of 'stimulating'. They were not asked about the itchiness of the images and itch was not mentioned with regard to the purpose of the study. Participants generally took approximately 10 minutes to complete the survey.

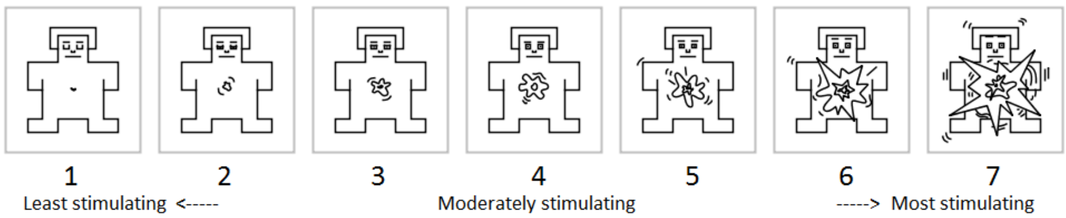


Figure 2.2 The rating scale used in the survey, featuring Self-Assessment Manikins to illustrate the scale.

2.2.2 Survey results

Matched pairs were rated on average 0.7 points (SD=0.57) different from each other, with the largest difference being 1.66 and the smallest difference being 0.12. Twelve out of the 32 pairs were rated significantly differently at the $p<.05$ level, with the itch image rated as more stimulating in all cases. Of these, 4 were irritant contact images, 3 were irritant context images, and 5 were skin response images. As none were action images, this suggests action was the most well matched image category. The average ratings for each pair grouped by condition are displayed in Table 2.1. These results confirm that the majority of itch and non-itch images are well matched on the saliency of their content. Most itch images are generally no more stimulating than their non-itch counterparts, and so can be considered to differ only on their itch-related content. Further to this, there was little difference between the itch content groups, which indicates that the stimulus set was reasonably well balanced on image saliency across types of itch inducer.

Table 2.1 Average ratings of how stimulating the images are, grouped by itch category. Significant differences (p<.05) are marked with *.

	Itch		Non-itch		
	Mean	SD	Mean	SD	Difference
Action	2.3	1.21	1.8	1.18	0.4
	2.1	0.95	2	1.33	0.9
	2.3	1.32	1.9	1.19	0.4
	2.5	1.43	2.3	1.36	0.2
	2.2	1.6	2	1.39	0.2
	2.1	1.33	2	1.19	0.2
	2.4	1.39	2.3	1.46	0.1
	2.3	1.26	2.5	1.36	-0.2
Irritant contact	3.6	1.80	3.1	1.78	0.4
	4	1.88	2.3	1.63	1.7*
	3.9	2.09	2.9	1.75	0.9
	4.3	2.21	2.8	1.77	1.5*
	3.2	1.62	2.8	1.39	0.5
	3.7	2.21	2.5	1.57	1.2*
	4	2.26	3.1	2.15	0.9
	3.8	2.24	2.1	1.57	1.7*
Irritant context	3.6	1.88	2.2	1.54	1.4*
	3.5	1.84	2.4	1.76	1.1
	3.3	1.79	2	1.26	1.3*
	3.2	1.68	3	1.82	0.2
	3.3	1.87	2.5	1.35	0.8
	3.3	1.39	2.4	1.74	0.9
	3.9	2.36	3.2	2.09	0.7
	3.2	1.57	2.2	1.53	1*
Skin Response	3.1	1.65	2.0	1.26	1.1*
	3.4	1.88	1.8	1.1	1.6*
	2.7	1.52	1.8	0.89	0.9*
	3.3	1.92	3	1.81	0.3
	3.5	1.77	2.3	1.54	1.2*
	3	1.68	2.2	1.22	0.8*
	2.6	1.45	2.9	1.71	-0.3
	2.9	1.53	3.4	1.85	-0.5

2.3 Contact image content

To add an additional insight into what stimuli are most effective, data collected whilst demonstrating VEI at public engagement events were utilised to explore what elements of an image enhance or diminish its itch-inducing power. This data was collected at three events: Science Uncovered in Manchester (25th September 2015), Be Curious Festival in Leeds (19th March 2016), and Bradford Science Festival Super Senses Exhibition (14th July 2017). On the first two occasions, 41 itch images were rated in terms of how itchy they made people feel, via a laptop. At the Bradford event a paper version was used instead with a limited selection of 16 images. All ratings were given on a scale from 1 (not itchy at all) to 9 (very itchy).

The images selected all represent the irritant contact condition based on Lloyd et al’s (2013) findings that these are the strongest inducers of VEI. The aim of selection was to create the most impressive and salient effect to illustrate the science, rather than stringent experimental standards. Therefore, the images were unedited and unbalanced, and the participants responded in an ad hoc manner. Since this data was collected at various events throughout the PhD, it was not able to inform stimulus development or selection of images. Instead it is presented as a supplemental comment on the potency of different itch contents. The trends found in a rough selection of people’s reactions can further illuminate what elements of an image affect its VEI inducing power and consequently suggest what aspects may account for variability within the experimental stimuli set.

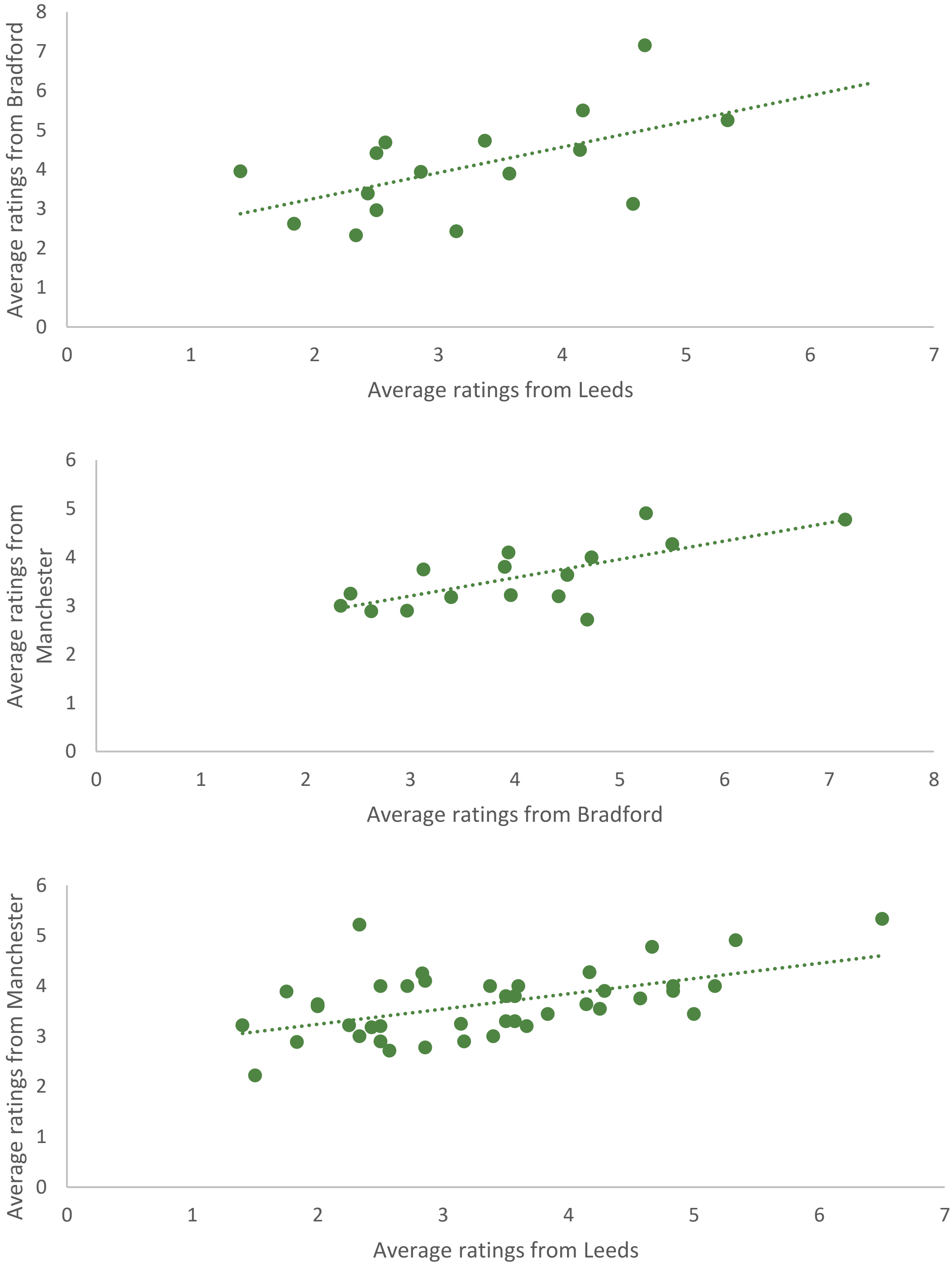


Figure 2.3 Correlations between ratings from a. Bradford and Leeds; b. Manchester and Bradford; and c. Manchester and Leeds.

2.3.1 Correlation between ratings from each event

Figure 3 depicts the correlations between the ratings. All comparisons showed significant moderate positive correlations, as measured non-parametrically using Spearman’s rho due to the differences and variability in the samples. Ratings from Leeds and Bradford correlated, as seen in Figure 2.3a, with rho=.580, $p<.05$; ratings from Bradford and Manchester also correlated, as seen in Figure 2.3b, with rho=.609, $p<.05$; and ratings from Leeds and Manchester correlated as seen in Figure 2.3c, with rho=.466, $p<.01$. This indicates that people's reactions to itch images are fairly consistent across different populations at different times and so using static images to create VEI in this format is a reasonably robust and replicable effect. Furthermore it suggests that the effects found with predominantly undergraduate samples the in lab-based experiments are roughly generalisable to the wider population. This validates the approach taken in this thesis of using the experimental stimulus set to assess various aspects of VEI in a range of experiments.

2.3.2 Thematic analysis

Thematic analysis was conducted on this data based on the procedure outlined by Komori and Keene (n.d.). First, attributes were assigned to each image: Insect type (ants, bees, mosquitos, roaches, cricket); location of insect (hands, feet, head, torso, arms, legs); quantity of insects featured (many or few), and size of insect (small or large). Images were then ranked from highest to lowest total average rating from all three events. This ranking of images along with their attributes is shown in Figure 2.4. This allows us to visualise the commonalities between high and low ranking images and draw out the themes among them.

In terms of insect size, it is clear that smaller insects feature more in the higher rated images and larger insects more in the lower rated images. For the quantity of insects, there is a tendency towards images with many insects featuring more in the higher-rated images. No particular pattern seemed to emerge in the insect location attribute, but the highest rated image was of a leg and the lowest was of a head. In terms of the type of insect, however, there was a distinct trend towards mosquitos featuring at the higher end of the scale, followed by ants. Bees seem to be spread across the full range, and roaches are a more common feature at the lower end.

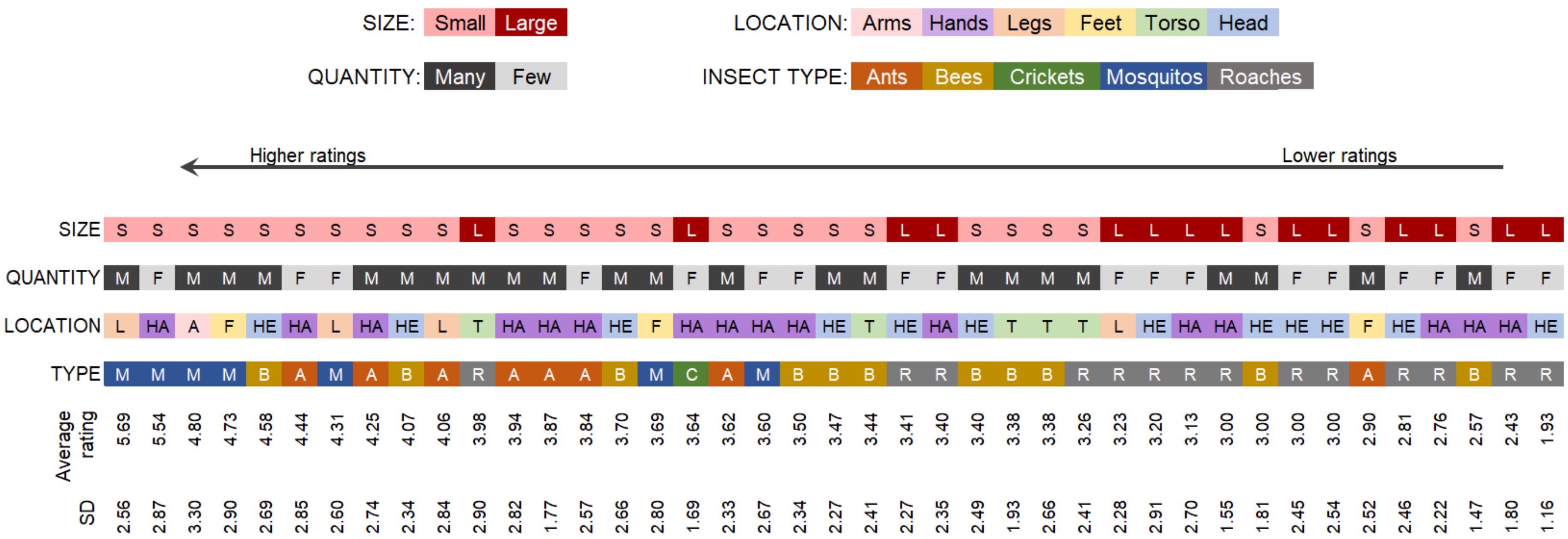


Figure 2.4 The distribution of attributes associated with each image, with images ranked in order of their ratings to enable themes to be inferred.

It appears that the most efficacious images feature lots of small mosquitos or ants on any part of a person’s skin. Most, although not all, of the contact images in the experimental stimulus set resembled this picture. Therefore, we can conclude that at least part of the experimental stimulus set is maximumly efficient at inducing VEI.

2.4 Basic VEI paradigm

The experiments in the following chapters use versions of the VEI paradigm adapted from the following default parameters. Stimulus presentation followed by an itch rating is deemed to be the basic paradigm, to which further measures can be added and incorporated.

2.4.1 Blocks

Stimuli are grouped into blocks of 4 trials which are either all itch or all non-itch, with image content and body part conditions equally represented. The blocks are presented in a random order and trials within each block are also randomised. There are no gaps between blocks.

2.4.2 Procedure

To begin, there are three non-itch practice trials to familiarise participants with the task. This is then followed by 64 experimental trials, with no repetition of images. Figure 2.5 shows the procedure of a trial. Within each trial the stimulus image is presented for 8 seconds. Participants are then presented with a scale from 1 (not itchy at all) to 9 (very itchy) and asked to rate how itchy they feel at that moment.

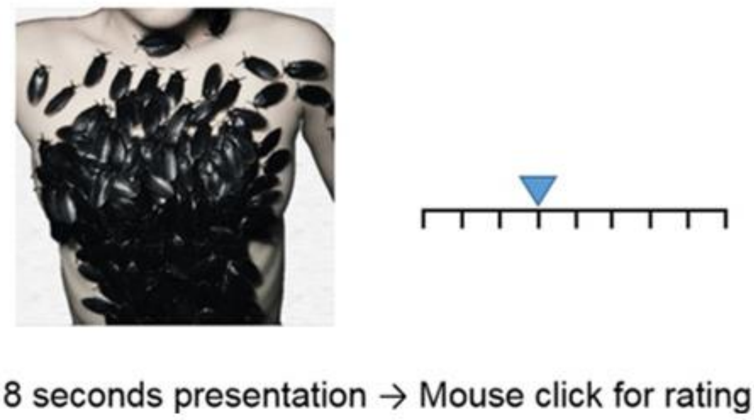


Figure 2.5 Basic VEI experimental procedure.

2.5 Scratch observation procedure

Multiple studies in the forthcoming chapters involve the identification and categorisation of participants' scratching behaviour. Therefore, it was important to develop a systematic approach to these measures.

2.5.1 Set up

The observation procedure was used in two ways. In Chapters 5 and 6 which only required a total sum of scratches, participants were observed by the experimenter and their scratches were recorded in real time during the experiment. This took the form of a tally, using the criteria outlined below, with no additional details regarding locations or timings recorded. In Chapters 3 and 4, which used a scratch location measure, a more precise method was employed. Participants' behaviour was recorded via a webcam, which was unobtrusively positioned above head-height facing the participant. The camera was angled to capture almost their entire seated body in the shot and the participants' chair was fixed at a precise location on the floor so that the view captured by the camera was the same for every participant. This view is depicted in Figure 2.6.

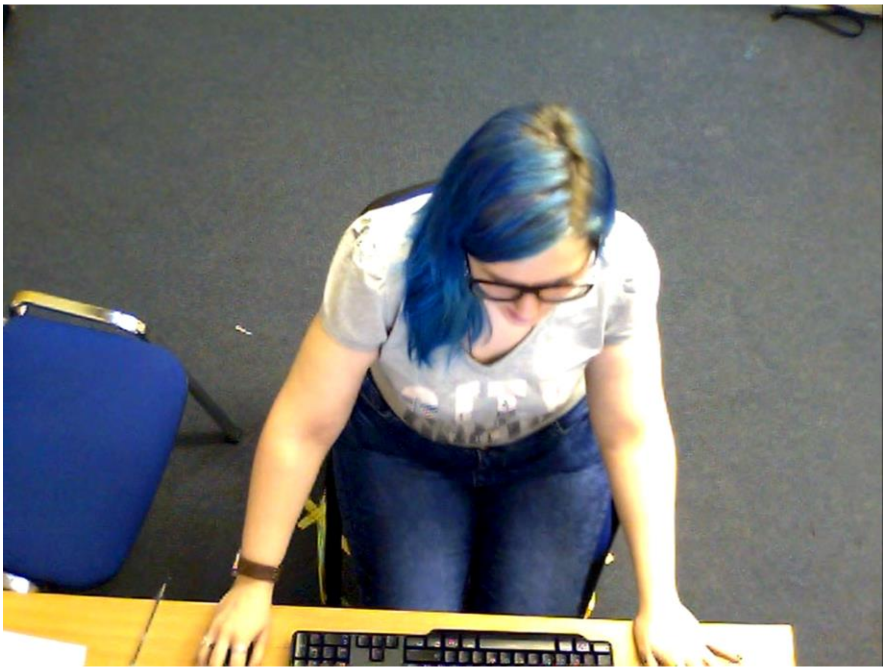


Figure 2.6 The view of participants captured by the camera in chapters 3 and 4.

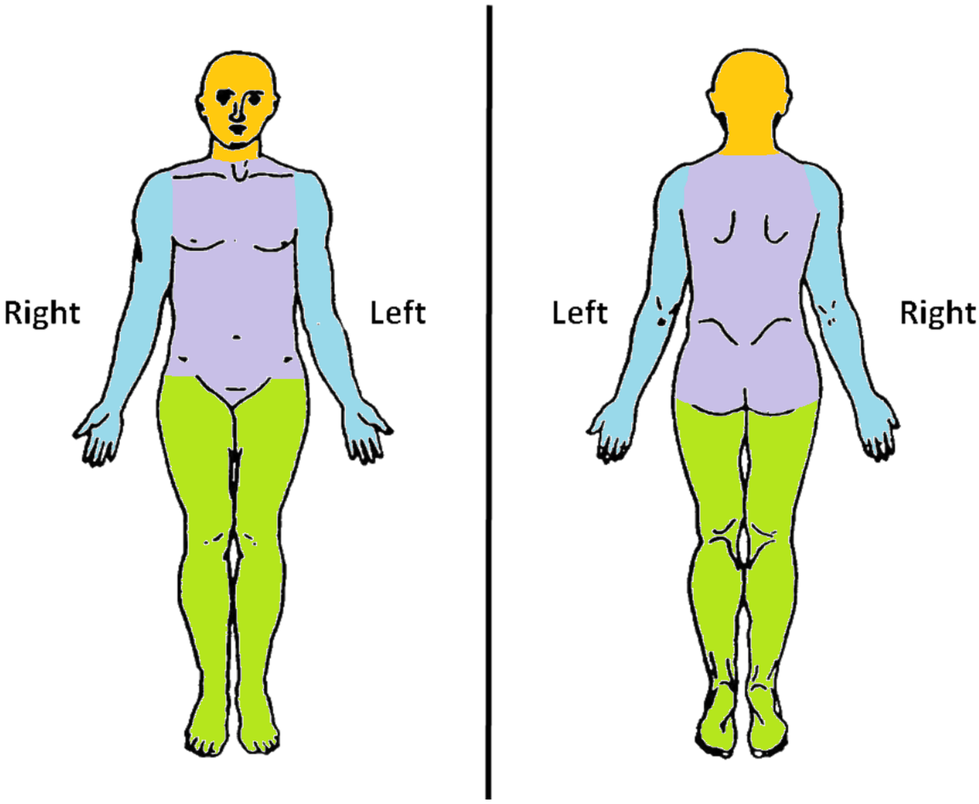


Figure 2.7 the boundaries between body locations defined on the body map: arms, legs, torso, and head.

The footage was used to transcribe scratches according to the criteria listed below and record the locations of scratches as either points on the body map or body part categories as described in Figure 2.7. Scratches were recorded in terms of the experimental trial they occurred within, which was visually delineated by observing the space bar keypress which triggered the start of each new trial. As Figure 2.6 shows, the experimenter was not able to see the computer screen so was blinded to whether the participants were completing an itch or non-itch trial at any given time.

2.5.2 Criteria for recording a scratch

The following criteria were determined prior to transcribing scratches from the videos. They account for the decisions made in every instance of ambiguity in the observations.

What actions *are* recorded as a scratch:

- Scraping with fingernails on the skin surface
- Rubbing either skin directly or clothing against skin in a way that causes friction on the skin surface. This can be either using a hand or another body part (foot, elbow, etc.)

What actions *are not* recorded as a scratch:

- Rubbing that would move the skin and massage the underlying tissue
- Tucking hair back or adjusting clothing, even if they could incidentally scratch the skin.

What distinguishes each individual scratch:

- Each targeted action is counted as 1 scratch
- A prolonged scratch in one place is still only counted as 1 scratch
- If the participant briefly stops and then resumes scratching in the same place it is counted as two scratches
- If they move their scratch location during an uninterrupted bout of scratching, any areas they pause on are counted as distinct scratches

Which scratches are associated with which images:

- Scratches are categorised by the trial the take place within
- A trial is defined by the period between each time the participant presses the space bar
- The precise latency between viewing a stimulus image and scratching is not recorded as it is not possible to determine accurately

Chapter 3 : What is the relationship between itch and scratch?

3.1 Introduction

Visually-evoked itch is a phenomenon whereby a visual stimulus can induce an itch sensation through psychological suggestion, with no physical stimulation of the skin. It was first demonstrated by Niemeier et al. (2000) who observed that an audience scratched more frequently during a lecture on itch than one on relaxation, and thus inferred that itching had been induced by the itch-related audiovisual stimuli. A similar effect was found by Papoiu et al. (2011) using histamine-induced itch. They found that videos of people scratching increased the amount of itch experienced and scratching observed for both atopic dermatitis (AD) and healthy control participants, with the former showing a larger effect. They also found that that the healthy participants scratched closer to the location seen in the stimuli than AD participants did. This finding, however, disagrees with Ward et al. (2013) findings that participants' scratches did not match the stimuli and also that they showed an overall preference for scratching their heads. Feneran et al. (2013) found a similar lack of connection between the locations shown in their stimuli and locations scratched by macaques who viewed it.

Lloyd et al. (2013) found that static images elicited higher itchiness ratings and more scratching for itch compared to non-itch contents in a healthy sample. They also compared different types of image content and found higher ratings for skin-contact images (e.g. insects on human skin), but more frequent scratching for skin-response images (e.g. people scratching). They did not find a correlation between itchiness ratings and scratch frequency however, which suggests that there may be other variables modulating the process leading from itch to scratch.

In this study we compared the itch-inducing potency of images featuring different body locations and itch contents. We hypothesised that there would be a difference between itch content conditions and that skin-contact images would be rated itchiest, as found by Lloyd et al. (2013). We predicted that a difference in body locations would be found, as was in Holle et al. (2012). They reported that people rated images of the left upper arm as the itchiest body location; however, we used a different range of body parts so did not expect to find similar results. Thus we hypothesised that there would be a difference between body location conditions but we did not make predictions as to what body part would be rated itchiest. Previous research has provided little indication of a link between the body locations of image content and subsequent scratches (Feneran et al., 2013; Ward et al., 2013). Nor has there been evidence of a connection between self-reported itch and observed scratch (Lloyd et al., 2013). Thus, measures of itch and scratch locations were analysed to provide previously unaccessed information, in order to elucidate the relationship between contagious itching and scratching. We hypothesised that there would be a relationship between itchiness ratings and number of itches identified and a relationship between the locations of identified itches and the locations of observed scratches, but no direct relationship between ratings of itchiness and observed scratches.

3.2 Methods

3.2.1 Participants

Thirty participants (plus one who was excluded due to problems with the video recording) without pruritic skin conditions were recruited from the University of Leeds and gave their informed consent to take part. 25 were female, 4 were male, and 2 were non-binary genders, with an average age of 23 years (SD 5.56). All participants had normal or corrected to normal vision with no known neurological, visual or motor deficits. Ethical approval was given for this study by the School of Psychology at the University of Leeds, reference number:15-0029 (5/2/2015).

3.2.2 Materials

The experiment was conducted using PsychoPy version 1.82.01 (Peirce, 2007) and displayed on a 21 inch, 1366x768 resolution computer screen. Data was analysed using SPSS.

The itch location measure used computerized body outlines adapted from the McGill Pain Questionnaire (Melzack, 1975). Scratch location was recorded via a webcam, which was unobtrusively positioned above head height facing the participant, angled to capture their entire seated body in the shot (see Figure 3.1).

Stimulus images were 600x600 pixels in size. The matched pairs of itch and non-itch images were divided into four image content conditions: action (scratching skin or touching skin), skin response (rashes or bruises), contact (insects on skin or innocuous objects on skin) and context (insects alone or visually similar objects). The stimuli were further categorised into four body conditions: arm, leg, head, and torso (context images were excluded from this classification as they did not feature body parts). The categories overlapped such that there were two pairs of images for every combination of content and body conditions, totalling 64 images (see Figure 3.2a for examples).

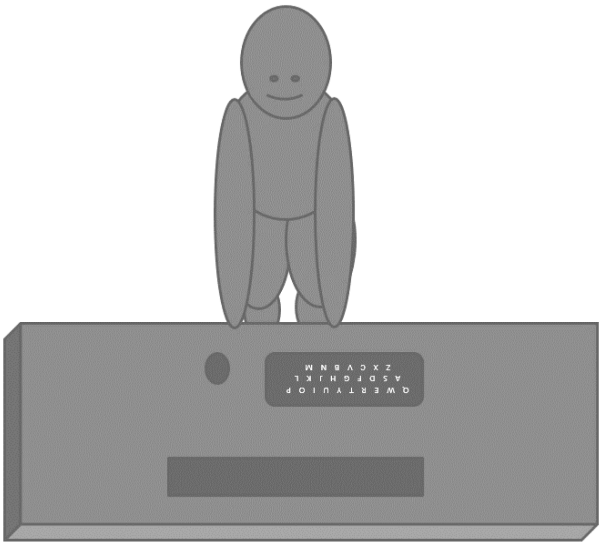


Figure 3.1 Depiction of a participant as viewed on the video recordings.

3.2.3 Design

A 2x4x4 factorial within-groups design was used. The independent variables were: Sensory Condition (itch or non-itch), Image Content (action, contact, context, or response), and Body Part (arm, leg, torso, or head). There were three measures used to collect three dependent variables:(i) Itchiness rating, self-reported on a 9-point scale from 1 (not itchy at all) to 9 (very itchy), (ii) itch location, self-reported by marking locations on a body map, and (iii) scratch behaviour, observed by the experimenter via video recordings, coded as body locations (arm, leg, head, torso) and marked on a separate body map.

There were 64 trials in total, with no repetition of images. Stimuli were grouped into blocks of 4 trials that were either all itch or all non-itch, with image content and body part conditions equally represented. The blocks were presented in a random order between participants, and trials within each block were also randomised. This reduced order effects whilst still allowing time for itch sensations to build across 4 consecutive trials. Additionally, blocking trials in this way enabled a hysteresis analysis to be carried out between trials in a block and across blocks.

3.2.4 Procedure

Participants were seated 70cm from the screen with unrestricted arm and leg movements. There were three non-itch practice trials to familiarise participants with the task, followed by 64 experimental trials. The experimenter remained in the room during the practice trials only.

Figure 3.2b shows the procedure of a trial. In each trial the image was presented for 8 seconds. Participants were then presented with a scale from 1 (not itchy at all) to 9 (very itchy) and asked to rate how itchy they felt at that moment. The next screen displayed two body outlines (front and back) in which participants clicked locations on the body map to indicate any itches they felt. These were marked with a red circle upon each click. Participants were knowingly yet unobtrusively filmed throughout the experiment, as depicted in Figure 3.1. Observed scratches were marked on a body map and then categorised by body location (arm, leg, head, torso) recorded with the trial they occurred in. The criteria outlined in the development chapter (see page 53) for determining what constitutes an individual scratch were used to classify the actions observed.

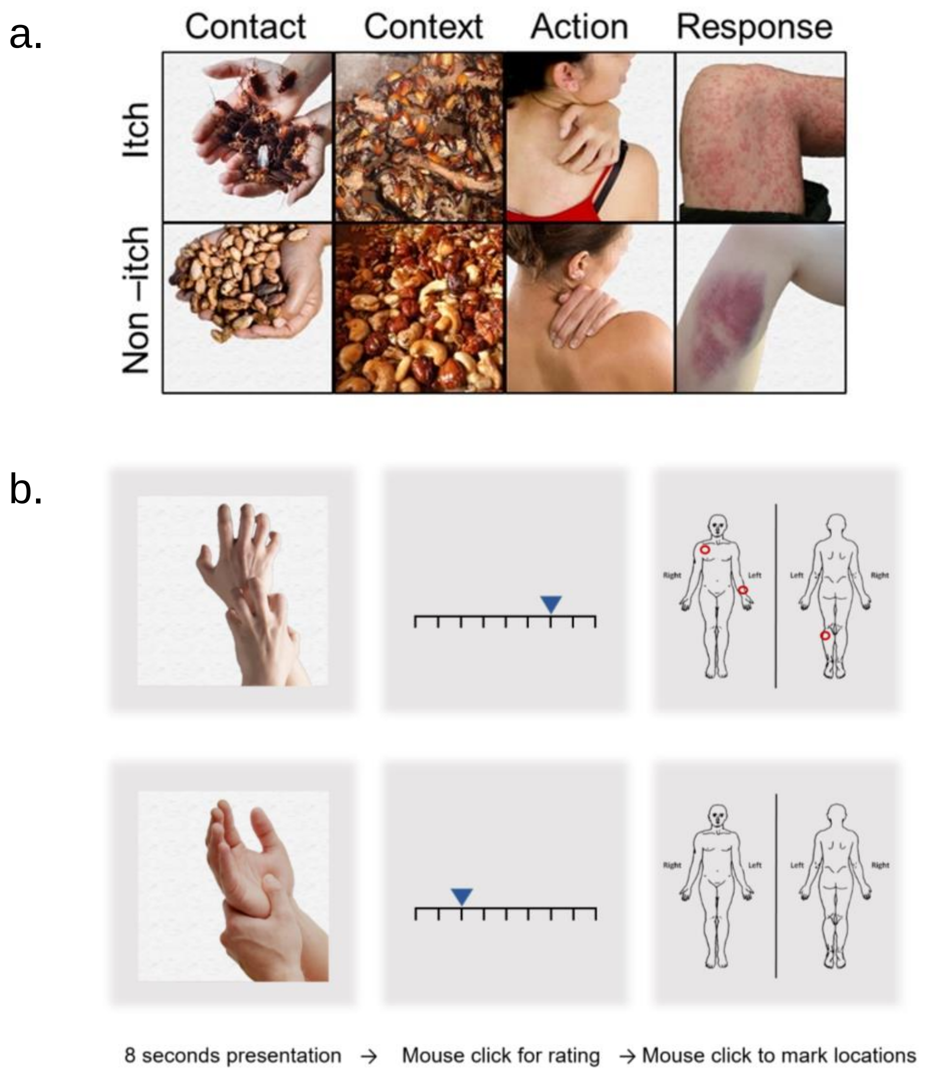


Figure 3.2 a. Examples of stimuli for each combination of body location and image content conditions, and b. the procedure of a trial, illustrated with an itch trial above and a non-itch trial below.

3.3 Image ratings

A log transformation was applied to the ratings to normalise the positively skewed distributions. Figure 3.3 shows the average itchiness ratings for Sensory Condition (itch vs. non-itch), Image Content (action, response, contact, context), and Body Part (arm, leg, torso, head). In line with previous studies (Holle et al., 2012; Niemeier et al., 2000; Ogden and Zoukas, 2009) a significant main effect of Sensory Condition [$F_{(1,90)}$=68.12, p<.001] was found, with itch stimuli rated itchier than non-itch stimuli confirming a VEI effect.

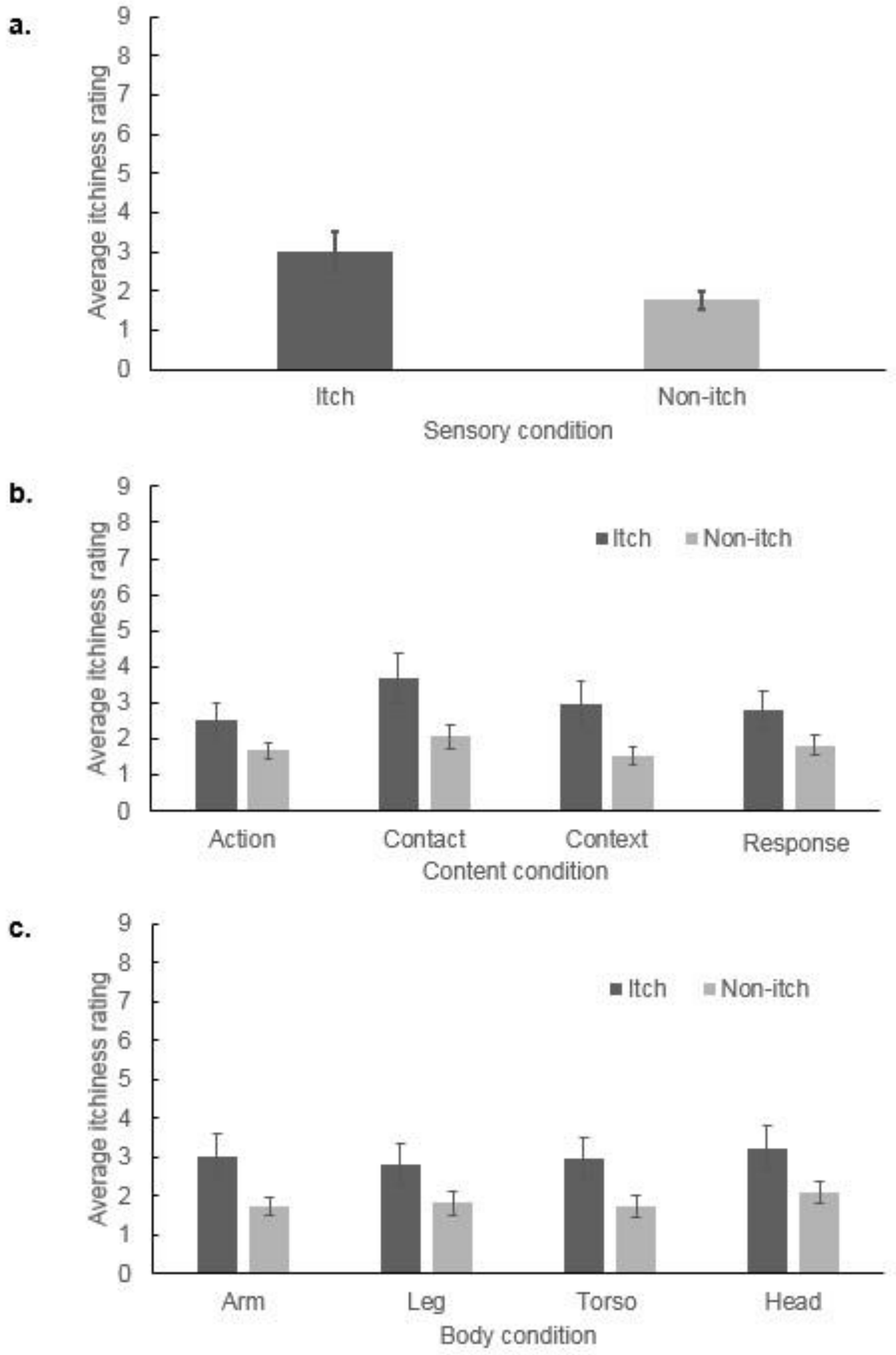


Figure 3.3 Comparison of mean itchiness ratings for a. the sensory condition, b. the content condition and c. the body condition. Error bars represent 95% confidence intervals.

3.3.1 Image content

Based on the findings of Lloyd et al. (2013), we hypothesised that irritant contact images would be rated itchiest. There was a significant main effect of Image Content [$F_{(3,90)}$=13.01, p<.001] and an interaction with Sensory Condition [$F_{(3,90)}$=4.91, p<.01]. Pairwise comparisons revealed that irritant contact images (e.g., insects crawling on the skin) were rated significantly itchier than all other image contents (p<.001).

One explanation for this result is that irritant contact images may have evoked the most empathy (Schut et al., 2015). Contact images depict a potentially shared experience (e.g., environments with a high concentration of insects), making it easier to empathise in those situations. Lloyd et al. (2013) found a high correlation between self and other itch ratings for contact and response trials, supporting this explanation. These findings might also support a threat detection based explanation of VEI (Dey et al., 2005; Stante, Hanna, & Lotti, 2005) as images featuring contact with a potentially dangerous insect most directly depicts an itch-threat scenario.

3.3.2 Body locations

In terms of body locations, Holle et al. (2012) found that people rated images of the left upper arm as itchiest (from a selection of upper/lower arms, and chest). However, a later analysis of this data by Ward et al., (2013) found people preferentially scratched their heads regardless of the body part viewed. Our study used images with a broader range of body parts including the head and, as predicted, there was a significant main effect of Body Part [$F_{(3,90)}$=8.47, p<.001] with images of the head rated significantly itchier (p<.05) than the arms, legs and torso. However, there was no interaction between Body Part and Sensory Condition [$F_{(3,90)}$=1.06, n.s.] These findings indicate that the preference for head scratching found by Ward et al., (2013) may be part of a more general susceptibility to itch in that body part. As VEI is strongest for images that correspond with that preferred scratch location, it implies a connection between the image content and scratch behaviour.

3.3.3 Hysteresis

Hysteresis is the effect of previous experiences within an experiment affecting subsequent outcomes. This analysis was applied to investigate whether the itchiness reported in these ratings directly related to the image in each trial, or whether they were influenced by the content of preceding trials. The trials were grouped into blocks of 4 consecutive itch or non-itch trials so if a hysteresis effect was present it would be apparent in a change in ratings across and between blocks. As table 3.1 shows, there was no significant differences between the first and last trials in each block for either itch or non-itch. There also was no difference between the average ratings of the first trial in blocks that were either the same or different to the previous block. This therefore indicates that itchiness ratings are a trial specific measure driven by individual stimulus content, rather than a result of built-up exposure to these images.

It is interesting to note that this lack of trial overlap was only the case for the itchiness ratings, while other measures showed distinguishable patterns across consecutive trials. The ratings measure may reflect an immediate cognitive appraisal of itchiness in relation to the stimulus image, as opposed to the slower accumulating physiological responses reported as located itches and observed scratches.

Table 3.1 a. Average itchiness ratings for the first and last trial in each block of 4. b. Average itchiness ratings for the first trial of each block after either a matching or different block.

a.

	Itch		Non-itch	
	First	Last	First	Last
Average rating	3.11	2.94	1.66	1.78
Standard deviation	1.52	1.49	0.62	0.73

b.

	Non-itch -> non-itch	Itch -> non-itch	Non-itch -> itch	Itch -> itch
Average rating	1.68	1.53	3.23	2.96
Standard deviation	065	0.66	1.74	1.56

3.4 Itch and scratch

3.4.1 Itch

Itch location has not previously been used as a measure in VEI experiments and as such, this study provides highly novel evidence on the somatotopic mapping between itch location and scratch response. In order to examine the itch locations in relation to the other measures, the data was recoded into four body categories (arms, legs, torso and head). Each participant reported on average 59 itches (SD=37) during the experiment, with the most frequent location being the head (37%). A Chi Square test revealed a significant relationship between the stimulus body location and the itch location, $X^2(12)=632.05$, $p<.001$. For each condition, the congruent body location yielded a significantly higher frequency of itches than the incongruent locations.

3.4.2 Scratch

Each participant scratched on average 27 times (SD=26) during the experiment and the most frequent target was the head (41%). However, a Chi square analysis indicated no significant relationship between the body part in the image and the location of scratches, $X^2(12)=7.92$, $p=.791$, n.s.

Itches were significantly more common in congruent (with the body part depicted in the image) body locations, whereas scratches were not, even though both itches and scratches were most frequently directed to the head overall. Unlike the findings of Ward et al., (2013) we show a clear relationship between body part viewed and the location of, not just the scratch response but importantly, the sensation of itch. This highlights the importance of distinguishing between the different measures of itch and scratch and the inferences made from these measures.

3.4.3 Comparison of locations

The heat maps of itches and scratches shows the density of reported itches and observed scratches across all 30 participants involved in the study (Figure 3.4). These appear to be distributed across the entire body (with the exception of the genitalia), although some distinct clusters are apparent. The highest concentration of both itches and scratches was on the head and face, despite the four body part conditions being represented equally in the stimuli.

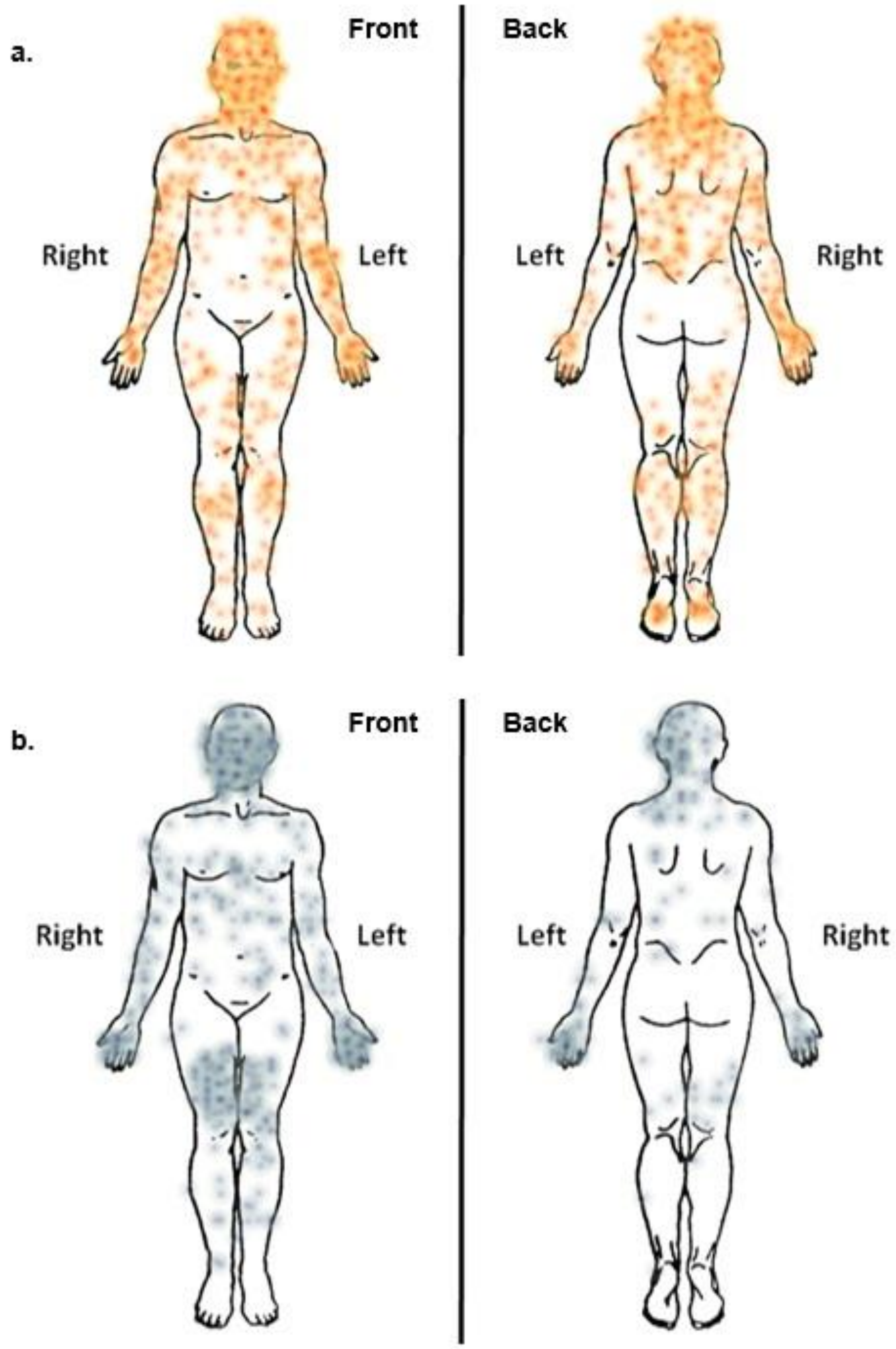


Figure 3.4 Heat map of a. itch locations and b. scratch locations in total by all participants.
Each point denotes a single reported itch or observed scratch.

There also appear to be areas with a high density of itches but relatively few scratches such as the back of the torso and legs, and the soles of the feet. Conversely there are areas with relatively few itches compared to the number of scratches such as the front of the thighs and to a lesser extent the hands. It is evident that itches are not all equally likely to be responded to. Some are scratched rarely and others often, suggesting that scratch is gate-kept by other considerations. For example it may be the case that inaccessible areas such as the soles of the feet while wearing shoes, experience itches that are not sufficiently salient to be worth the additional effort required to attend to them. Conversely, commonly touched locations such as the thighs when participants hands rested in their laps, may be scratched out of habit or fidgeting without the motivation of an itch. In either case it is clear that itch and scratch measures do not reflect identical experiences, although it remains to be seen how VEI specifically influences itches left unscratched and the scratching of non-itches.

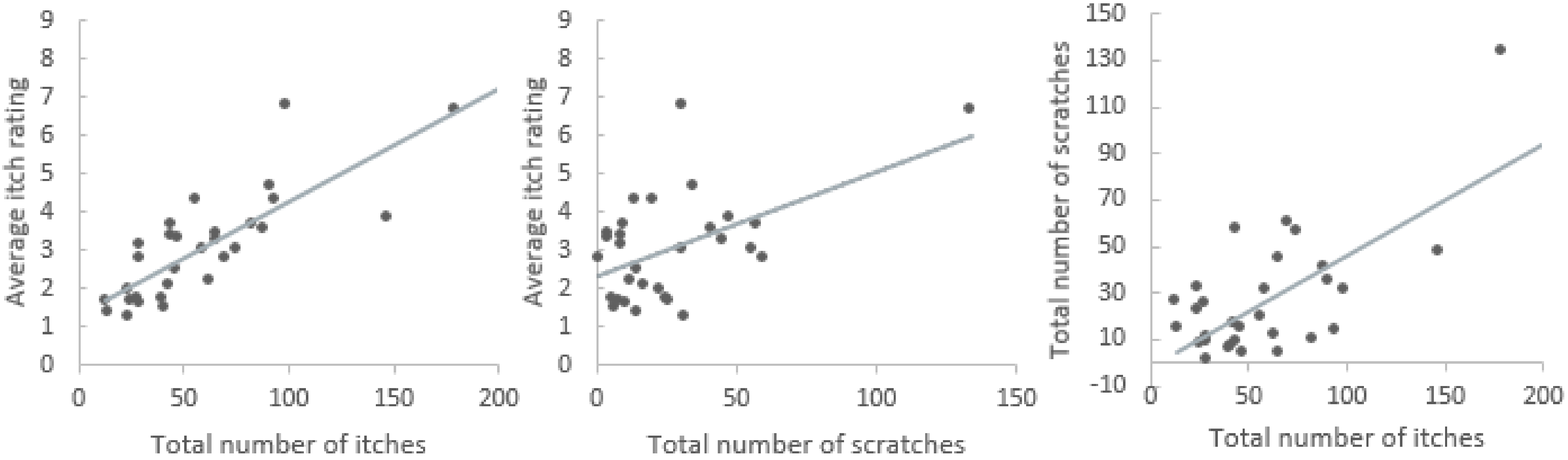


Figure 3.5 Scatterplots showing the correlation between the three variables

3.5 Relationships between measures

3.5.1 Correlations

As with previous investigations (Lloyd et al., 2013), we found no direct link between itchiness ratings and scratch frequency with a weak correlation between average itchiness rating (itch trials only) and total scratches of rho=.29, (p=.113, n.s). There was, however, a strong positive correlation between average itchiness rating and total number of itches reported on the 2D model, rho=.81, $p<.001$, and a moderate positive correlation between total itches reported and total scratches, rho=.40, $p<0.05$. These correlations are shown in Figure 3.5.

3.5.2 Measures across time

To test whether the effects of VEI built up over the duration of the experiment, the average itchiness ratings (figure 3.6a), average number of itches (figure 3.6b) and average number of scratches (figure 3.6c) for each trial position regardless of content were calculated. Trend lines fitted to these data show that the level of itchiness (gradient ~0) overall remained consistent throughout the experiment, as did the quantity of itches (gradient 0.03), so it can be assumed that participants were experiencing a similar saliency of physiological response to the stimuli throughout. The quantity of scratches however did increase slightly across time (gradient 0.11), further adding to the idea that scratching operates via different or additional mechanisms to the pure itch experience. It may be that the desire to scratch built up over time, or that factors which inhibit scratching behaviour were diminished over time. Either way it is apparent that additional factors are modulating the behavioural outcome, while the urge remains consistent.

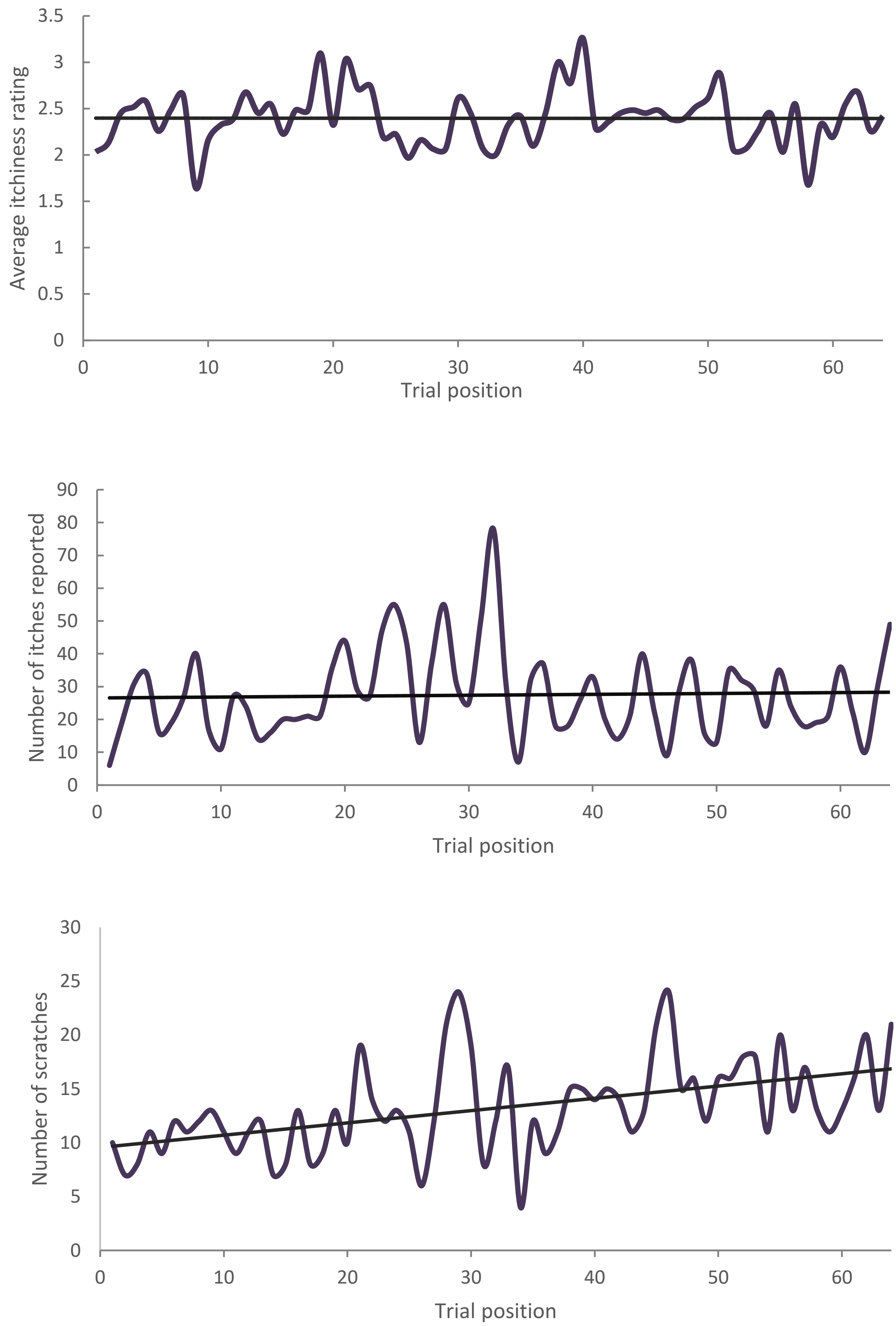


Figure 3.6 a. Average itchiness rating in each trial position across time. b. average number of itches reported in each trial position across time. c. average number of scratches recorded in each trial position across time.

3.6 Patterns

Recording the locations of individual itches allows for those itches to be directly compared with co-located scratches. We modelled the pattern of responses produced by VEI across the duration of the experiment by means of probabilistic suffix trees. The method is based on identifying significant patterns in a set of sequences. We created 120 sequences (30 participants x 4 body part conditions), one for each participant's body part, in which each trial was coded as either '0' (no itch), 'itch' (reported itch) or 'scratch' (observed scratch). For trials in which both itching was reported and scratching observed, we coded this as two separate trials with an itch preceding the scratch. The possible sequences are outlined in the flowchart in Figure 3.7.

It is worth noting that the more itches and scratches a participant reports or exhibits, the more data they contribute to these sequences. As there is considerable variability between participants, a highly susceptible subset of the participant group are represented more in this analysis. Therefore the patterns of itches and scratches across trials are a reflection of the sensations and actions resulting from VEI in people who experience VEI strongly, with the assumption that these patterns are generalisable to people who experience fewer sensations overall.

3.6.1 Sequences of itches

Following a sequence of itch events, the probability of the next trial containing either an itch or a scratch was calculated and is shown in Table 3.3. The longer the sequence (of up to three consecutive itches) the more likely it was to be followed by an itch or a scratch, but the rarer it was for this pattern to occur. This indicates that the longer a sequence of itches lasts, the more likely it is to indicate a build-up of a persistent itch that becomes more likely to require a scratch.

A possible explanation for this is that the potency of an individual itch accumulates across multiple trials (even though overall itchiness ratings remain level) and becomes established as a persistent experience, rather than a transient one that may spontaneously diminish. Indeed, Table 3.2 shows that the probability of a neutral trial (no itches or scratches) decreases as sequence length increases. Thus, the motivation to scratch reaches a sufficient level for a scratch to become necessary.

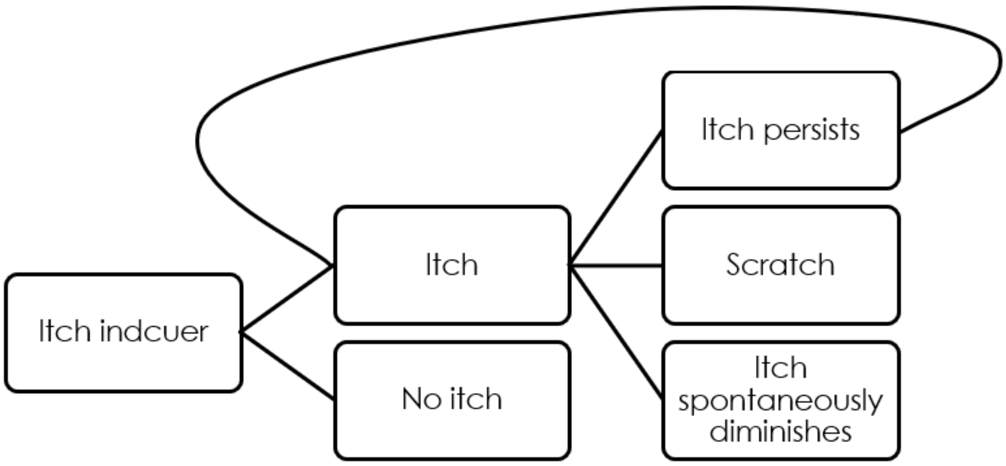


Figure 3.7 A flowchart depicting the possible sequences of events

3.6.2 Sequences leading to scratches

Not all itch sequences end in a scratch. There may be other factors influencing behaviour against scratching such as inaccessibility (e.g., soles of the feet), social inappropriateness (greater motivation to resist), or lack of salience (weak itches not worth scratching). Research that only considers the scratch response as a proxy for itching may miss these lower level perceptions.

We calculated which sequences of four events are most likely to predict a scratch. Two or three itches in a row were good predictors of scratch, which suggests that in many cases specific itch sensations build up over multiple trials and then culminate in a scratch. Interestingly, two of the sequences include scratches themselves, suggesting that a recent scratch event may prime for another. It is possible that once the cognitive and motor mechanisms to carry out a scratch action have been initiated, the next itch does not need to be as salient or as persistent to reinitiate the action.

Table 3.2 Probability of itches and scratches following sequences of events.

Sequence	0	Itch	Scratch	N of occurrences
Sequences of consecutive itches				
0-itch	0.59	0.19	0.22	811
0-itch-itch	0.54	0.22	0.23	156
0-itch-itch-itch	0.44	0.26	0.29	34
0-itch-itch-itch-itch	0.33	0.44	0.22	9
Sequences preceding a scratch				
Itch-scratch-itch	0.29	0.18	0.52	
Scratch-0-itch	0.38	0.21	0.42	
Itch-itch-itch	0.35	0.32	0.32	
0-itch-itch	0.54	0.22	0.23	

The distinction between transient single trial itches and persistent itches which may culminate in a scratch illuminates a potential issue with how itch is conceptualised by measures of VEI. It is possible that an individual trial based approach to reporting VEI may over-represent less intense or more ambiguous tactile sensations, or simply minor itches that are only noticed while they are attended to. Whereas the itches that, once established, persist and/or culminate in a scratch may be more representative of what is commonly described as itch in the context of chronic itch. The pattern analysis confirms that these itches are also triggered by VEI and show a traceable pattern of reports/behaviour.

3.7 Conclusions

This study concurs with previous findings that the content of images used to elicit VEI affects the strength of the effect. Depictions of insects in contact with the skin are the most potent inducers of VEI, which may be due to the evolutionary salience of this situation: contact with a potential irritant can be seen as a threat, for which scratch is the mechanism for removing the irritant (Dey et al., 2005). Images of heads were rated itchier than other body parts, which may be related to the greater tendency to scratch this area and so reflect a general pruritic focus.

Our novel design and analysis, uniquely compares these two phenomena, which has revealed differences between the experience of an itch and the behavioural outcome of a scratch in terms of frequency and distribution. Participants reported more than twice as many itches as scratches, which makes it clear that itching does not always lead to scratching directly, but requires an accumulation of itchiness for scratching to occur, validating our approach.

Itch location adds another important dimension to how VEI relates to image content. Scratches themselves do not relate to the body part featured, but itches do. Analysis of patterns of itches and scratches further revealed that repeated itches are often followed by scratches, which implies that somatotopically-mapped transmission of itch is a possibility in VEI and builds up over a longer duration than individual trials are able to capture. Furthermore, sequences containing scratches also predict further scratches, indicating that VEI does not occur in isolation for each image but instead influences our ongoing propensity to experience itch and act upon it. This has implications for understanding how the itch-scratch cycle of pruritus occurs and propagates.

It is clear that the information contained in the itch location measure bridges the gap between existing measures, and elucidates relationships between components of VEI which seem intuitively connected. Further work should focus on investigating these relationships to establish what factors are involved in the transfer of visual itchiness to quantifiable itches and which itches then result in scratches and why. It seems that the path from itch inducer to itch sensation to scratch is not linear, direct or immediate. It is crucial to examine the pattern of experiences across trials and across measures to gain a more connected and coherent explanation of VEI and enhance the wider understanding of itch and scratch.

3.7.1 Limitations

There is a possible limitation to the scratch observation measure, in that participants' awareness of being filmed may have had an additional influence on their experiences during the experiment. Durlik, Cardini and Tsakiris (2014) found that the presence of a video camera altered their participants' tactile sensitivity. If a similar effect occurred in the present study, it may have contributed to participants propensity to itch. However, Durlik, Cardini and Tsakiris (2014) used an overt camera placement designed to draw participants attention to the fact they were being filmed. Our camera was placed out of eyeshot and participants often did not appear to acknowledge its presence (even though they knew they were being filmed), so were unlikely to have experienced the heightened self-awareness and resultant sensitivity changes associated with feeling 'watched' to the same extent. Nonetheless, this potential influenced was not controlled for.

Another limitation was the reliance on a single experimenter to transcribe the behavioural observations from the video recordings. It would have been advantageous to have an additional person perform this task in order to verify the inter-rater reliability of these results. Six of the videos were transcribed a second time on a different day in order to ensure intra-rater reliability and to resolve ambiguity in the observations. The consistency between transcriptions for these videos indicated high intra-rater reliability.

3.7.2 Key contributions made by this study

This study builds upon current knowledge of what elements evoke VEI most effectively using more controlled stimuli (in terms of image matching and extraneous cues) than previous studies. It is also the first study to directly measure and locate participants' distinct itches rather than infer this information from their scratches. This adds a valuable new dimension to the study of subjective itch experiences and allows for more precise interpretations of the processes involved in VEI. It also enables a comparison of itch and scratch locations which revealed a link between these outcomes and the content of the images that created them, where previous studies were unable to find a connection.

Using these measures in combination highlights the importance of the pattern of responses across trials as well as within trials, and thus clarifies that the immediate response to an itch inducer is distinct from the initiation of an itch, and distinct further still from the decision to scratch. The three outcome measures used do appear to be linked and interrelated, but they also operate differently and thus can inform on different aspects of VEI. Underlining these differences and the importance of measuring each distinct component is an important step towards gaining a more complete understanding of the processes behind VEI and how the itch-scratch cycle of pruritus occurs and propagates.

Chapter 4 : To what extent is visually-evoked itch a visual effect?

4.1 Introduction

Visually-evoked itch has been studied in various forms of audio-visual itch transmission. Although the effect was initially elicited using lectures (Niemeier et al., 2000), this has progressively narrowed down to videos (Schut, Radel, Frey, Gieler, & Kupfer, 2016), to videos without sound (Ogden & Zoukas, 2009), and to static images (Lloyd et al., 2013). Recently, Swithenbank, Cowdell and Holle (2016) isolated the itch-inducing effects of scratching sounds without accompanying visual information. These studies have focused on the modality of the stimulus, but there is still the possibility that other forms of priming or influence to itch are present in the VEI paradigm.

To get a genuine sense of how visual transmission of itch occurs, it is important to isolate the visual perception element. Identifying and separating visual and non-visual influences from the composite effect makes it possible to determine how much these components are contributing to the creation of itches. For VEI to be considered truly visually-evoked as opposed to merely visually-influenced, we need to ascertain that the visual component is indeed driving the effect. Elsewise, it may become necessary to reconsider how VEI is defined as a perceptual effect, within the wider framework of psychological itch transmission.

4.1.1 Suggestion and nocebo effects

A clear example of non-visual itch priming is seen in how verbal suggestions induce and intensify itch via the nocebo effect (van Laarhoven et al. 2010; Napadow et al., 2015; Stumpf et al., 2016). Telling participants how unpleasant or intense an itch will be influences their expectations of what they will experience during the experiment, which then goes on to affect their subjective itch experiences. Schut et al. (2016) deliberately manipulated expectations about VEI in their experiment and found that participants primed to catastrophise (by being told the video would produce an intense and unpleasant itch) experienced a stronger VEI effect resulting in more scratching than participants who were given neutral information. However, this was only the case for participants with atopic dermatitis; there were no significant differences for participants with healthy skin.

The influence of manipulating expectations through verbal suggestion appears to be particularly effective when the verbal cues are combined with conditioning to visual itch cues (Bartels et al., 2014). This fits with the idea of contagious itch as a multisensory effect, which can be induced in different modalities. Therefore, it is possible that other elements of the VEI procedure are contributing to the suggestion and expectation of feeling itch, producing a similar cumulative effect to that found by Bartels et al. (2014).

There are several ways an experimental procedure can unintentionally influence the results of a study, for example demand characteristics (Rosenthal & Rosnow, 2009), experimenter bias (Rosenthal & Fode, 1963) and observer effects (Rosenthal & Rubin, 1978). This is especially relevant for studies pertaining to the perception of one’s own body state; focusing on potential symptoms can trick a person into thinking they are experiencing them (Mechanic, 1962). Indeed, Ogden (2003) highlighted this as an issue with the frequent use of questionnaires in clinical studies, in that they prime participants to experience the symptoms the questions are attempting to measure.

4.1.2 Questions and expectation cues in previous studies

Ogden and Zoukas (2009) acknowledged the possible influence of questioning participants’ experiences in their study of VEI; they chose not to use a neutral control condition in their experiment due to the possibility that completing a symptom checklist could generate symptoms in and of itself. Instead they only questioned participants after having them view itch videos and used other participant groups viewing pain- or cold-related videos as control data. The issue of inducing symptoms by asking about them remains the case though, they merely removed the possibility of this happening prior to viewing the stimuli.

Niemeier, Kupfer and Gieler (2000) took the opposite approach by measuring participants itchiness at the very beginning of the experiment prior to the stimulus presentation. Interestingly, they found that these ratings were higher than at the end of the experiment, after the control condition. This suggests that whatever influenced participants at that point, be it expectations of the experiment or an initial response to answering itch questions that they had not previously considered, it had a greater effect than any carry over from the itch-inducing component of the experiment. This highlights the influence of non-visual psychological suggestion in VEI experiments and strongly suggests that these aspects of contagious itch require disentangling.

This may also have been an issue for Lloyd et al. (2013), who explicitly instructed their participants to imagine themselves as the person in the picture, potentially increasing the empathetic response. This was a deliberate choice to assist participants in considering how itchy they themselves and the person in the picture felt, but may also have amplified the participants itch experiences compared to if they had been viewing the images without this assimilation in mind. It is also possible that this influenced the finding that participants scratched more when viewing scratch images, as the encouraged affinity could have amplified their unconscious mirroring of scratch behaviour.

4.1.3 Scratching as a VEI outcome measure

Scratch has been used as a measure of itch in most investigations of VEI. Such studies have found that, in addition to visual itch stimuli being rated as itchier than non-itch stimuli, participants exhibited more scratching behaviour in response to these images (Lloyd, Hall, Hall, & McGlone, 2013; Niemeier, Kupfer, & Gieler, 2000; Ogden & Zoukas, 2009; Papoiu et al., 2011; Ward, Burckhardt, & Holle, 2013). Common to all the aforementioned studies is the use of scratch observations in conjunction with itch measures, which require the participant to answer questions and report their experiences. Therefore, it is not currently possible to determine whether these means of measurement interact with one another. The question and report methods used to extract itch information may affect the overall intensity of VEI in a similar way to that highlighted above from previous studies. This raises the question of to what extent itch images alone, without any questions implying a possible itch experience, would be able to provoke a scratch response based purely on the visual transmission of itch.

It is important to note that while scratch is not an adequate proxy for itch and thus the itch status of a participant cannot be directly inferred from their scratch behaviour, scratch frequency does consistently increase in response to itch images (Lloyd et al. 2013; Niemeier et al., 2000). Furthermore, Niemeier, Kupfer and Gieler (2000) found a strong correlation between itch and scratch ratings (although they did not comment on the relationship to scratch behaviour). While no firm conclusions about itch can be drawn from it, it is still possible to use scratch as a consistent and reliable outcome of VEI.

4.1.4 Aims and hypotheses

To isolate the effect of VEI driven by the itch content of the images, it is crucial to disentangle it from the potential effects of induction or amplification of itch from the suggestion inherent in the questions asked about it. This study aimed to use a purely observational approach to investigate the effects of viewing itch images and to examine the extent to which VEI is a visual effect. To do this, it used the same basic procedure as the initial VEI study described in Chapter 3, but using neutral irrelevant questions instead of asking participants about their itch status. The scratch observation results were then compared to those of the original sample from Chapter 3.

If both methods produce similar scratch results, it would indicate that the images are driving the effect and the questions do not have a suggestive influence. If VEI is absent for participants who are asked neutral questions, it would indicate that the effect is driven by suggestion and expectation of the experiment more than the images themselves. If the results show that, without the questions, VEI is amplified, diminished or found to interact differently with image content then it may be necessary to reconsider how VEI is characterised as a psychological itch-inducer. As the choice of questions have likely influenced previous studies of VEI it is hypothesised that the latter will be the case and VEI will be diminished in the absence of itch-related questions.

4.2 Methods

4.2.1 Participants

Thirty new participants without pruritic skin conditions were recruited from the University of Leeds and gave their informed consent to take part. These participants formed the neutral question group and comprised 29 females and 1 male. They had an average age of 20 years (SD 2.4). Data collected from the 30 participants recruited to the VEI study in Chapter 3 was also used in this study with no further participation involved. These participants formed the itch question group and comprised 25 females, 4 males, and 2 non-binary. They had an average age of 23 years (SD 5.56). All participants had normal or corrected to normal vision with no known neurological, visual or motor deficits. Ethical approval for this study was given by the School of Psychology at the University of Leeds, reference number:15-0029 (5/2/2015).

4.2.2 Materials

The experiment was conducted using PsychoPy version 1.82.01 (Peirce, 2007) and displayed on a 21 inch, 1366x768 resolution computer screen. The stimuli were the pairs of itch and non-itch images as described fully in chapter 2. Data was analysed using IBM SPSS Statistics 21 (SPSS Inc., Chicago, IL). Scratch location was recorded via a webcam following the procedures outlined in Chapter 2. The webcam was unobtrusively positioned above head height facing the participant, angled to capture their entire seated body in the shot. This position was similar to the recordings taken in the VEI study, with the same proportion of the body visible, but the recordings were made in a different room.

4.2.3 Design

A 2x2x4 factorial between-groups design was used. The independent variables were: Question Group (itch question or neutral question), Sensory Condition (itch or non-itch), and Image Content (action, contact, context, or response). The dependent variable was Scratch Frequency, observed by the experimenter via video recordings.

The itch question group had been asked to rate their itchiness and report the locations of any itches experienced in each trial. The neutral question group were asked to rate the interestingness of the images and to report the locations of the body part seen in the stimulus, with no mention of itch. Other than this, the design and procedure of the experiment was identical to that of Chapter 3.

There were 64 trials in total, with no repetition of images. Stimuli were grouped into blocks of 4 trials that were either all itch or all non-itch, with image content and body part conditions equally represented. The blocks were presented in a random order between participants, and trials within each block were also randomised. This reduced order effects whilst still allowing time for itch sensations to build across 4 consecutive trials.

4.2.4 Procedure

Participants were seated 70cm from the screen with unrestricted arm and leg movements. There were three non-itch practice trials to familiarise participants with the task, followed by 64 experimental trials.

Figure 4.1 illustrates the procedure of a trial. In each trial the image was shown for 8 seconds. Participants were then presented with a scale from 1 (not interesting at all) to 9 (very interesting) and asked to rate how interesting they found the image. The next screen displayed two body outlines (front and back) in which participants clicked locations on the body map to indicate any body parts that had been visible in the images. These were marked with a red circle upon each click. Participants were knowingly yet unobtrusively filmed throughout the experiment. Observed scratches were marked on a body map and recorded with the trial they occurred in. The criteria outlined in Chapter 2 for determining what constitutes an individual scratch were used to classify the actions observed.

Participants were not informed as to the purpose of the experiment until they had completed their participation. Itch was not mentioned on the participant information leaflet (given prior to participation), other than being referenced in the project title. An explanation of the experiment was included in the debrief.

Figure 4.1 The procedure used in each trial
Stimulus presentation, followed by a rating of how interesting they found the image, and then a location measure asking what body part was featured in the image.

4.3 Results and Discussion

4.3.1 Ratings correlation

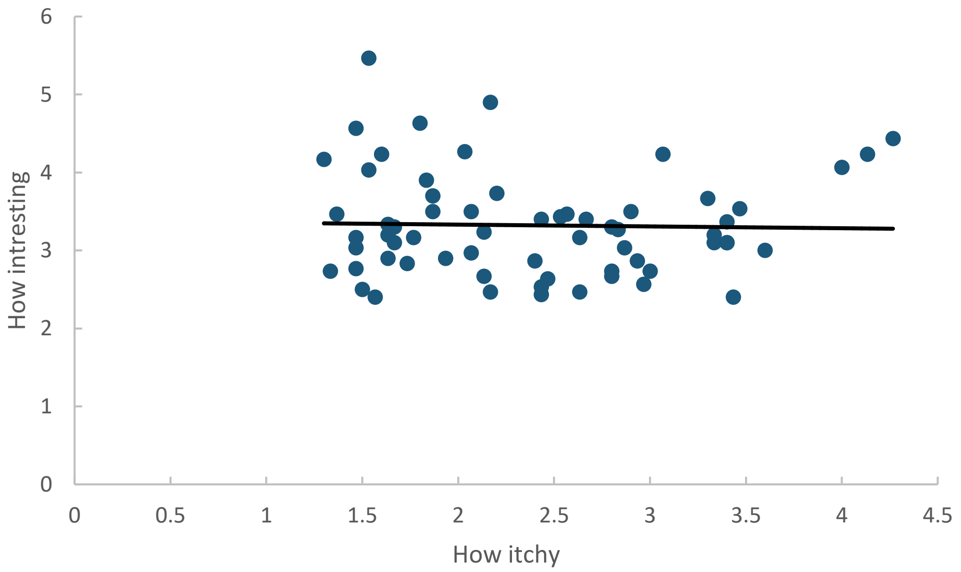


Figure 4.2 Correlation between ratings of itchiness and interestingness for each image

The stimuli were matched for level of stimulation and visual-interest as verified by the stimulus development survey (see Chapter 2). To ensure that this matching allowed for level of interest and itchiness to be identified as distinct variables, a correlation analysis was performed between ratings of interestingness and ratings of itchiness. This revealed no correlation between these ratings (Pearson's r of 0.027, n.s.) as can be seen in Figure 4.2. Thus, it can be inferred that the interestingness of the images is a distinct property from the itchiness of the images.

4.3.2 Results across time

The ratings of interestingness shown in Figure 4.3a for the neutral question group follow the same flat trend as the ratings of itchiness for the itch question group (both with gradients >0.01); the images are, on average, deemed consistently interesting throughout the experiment. Therefore, this measure can be seen as a suitable substitute for the itchiness ratings.

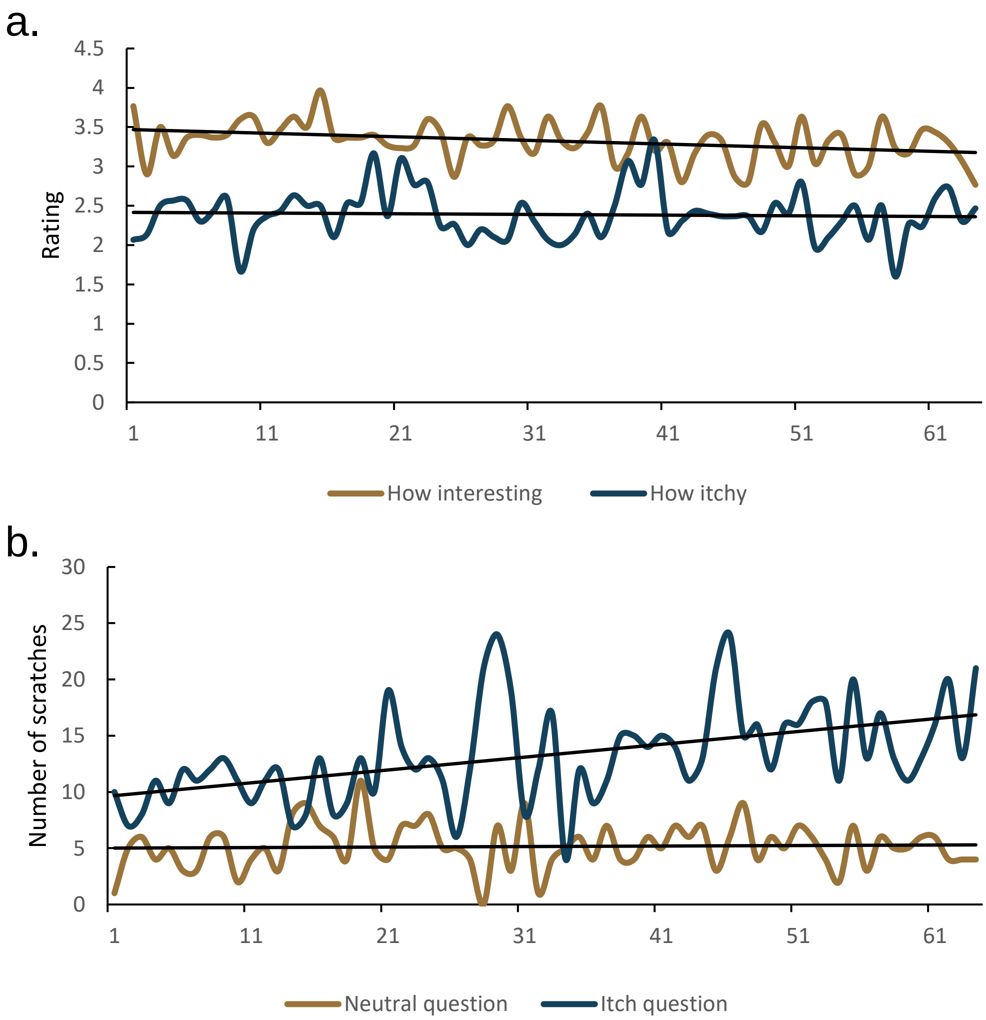


Figure 4.3 a. Participants' interest ratings at each trial position across time, b. Number of scratches at each trial position across time.

The frequency of scratching however does appear to differ between groups. For the itch question group there is an increase across time (gradient 0.11) visible in Figure 4.3b, indicating that the inclination to scratch builds up with the cumulative exposure to the task. For the neutral question group the frequency of scratches is fairly stable across time (gradient >0.01).

4.3.3 Scratch frequency by group

The Box and whisker plot shown in Figure 4.4 indicates a difference between the frequency of scratches between the two groups; participants who were not questioned about their itching exhibited fewer scratches (with a mean of 10.9) than participants who were directly questioned about itch (with a mean of 28.33). There were also visible differences in the distribution of scores. The neutral question group also had a much smaller standard deviation (7.05) compared to the itch question group (26.85). This suggests that individual differences in susceptibility to VEI are amplified by itch specific questioning, whereas the effect created by the images alone is more consistent.

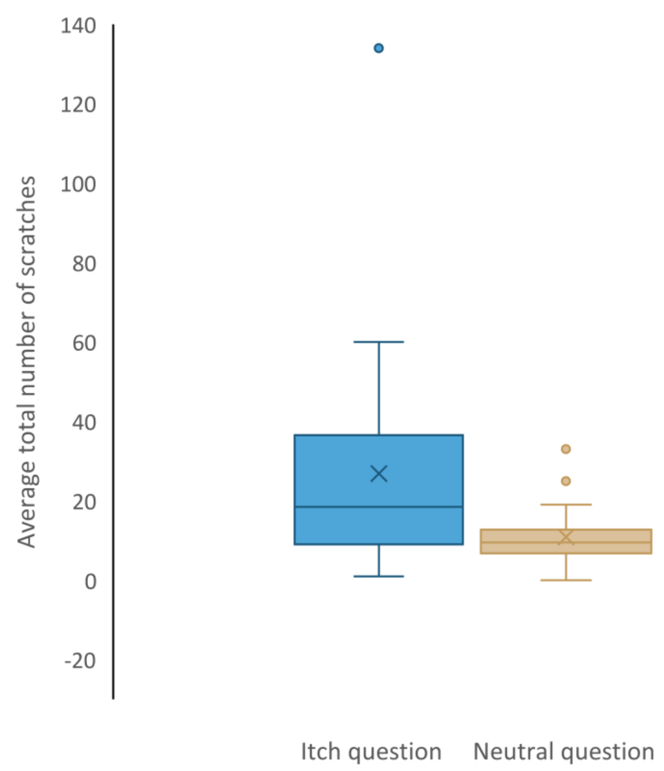


Figure 4.4 Box and whisker plot of the average total scratches for participants in the itch question and neutral question groups.

4.3.4 Itch vs. Non-itch

As there is a well-established difference between the frequency of scratches while viewing itch or non-itch images (Lloyd et al., 2013; Niemeier et al., 2000), a mixed design 2 x 2 ANOVA was used to investigate whether such a difference occurred in this experiment and whether it interacted with the difference between groups. The results of this comparison are shown in Figure 4.5. A log transformation was applied to the ratings to normalise the positively skewed distributions prior to conducting this parametric analysis.

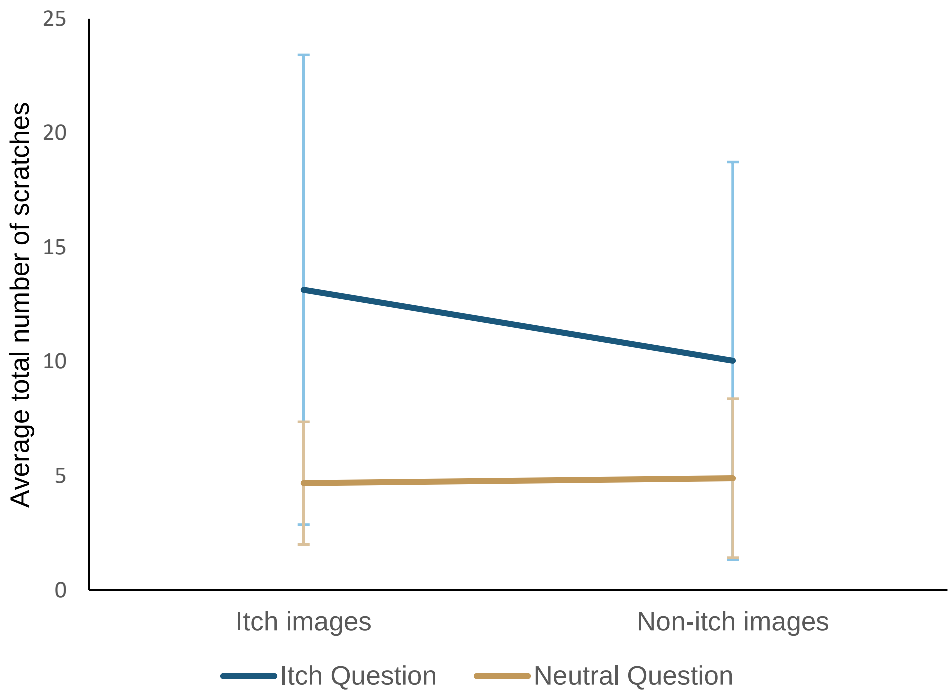


Figure 4.5 The average total scratches recorded during itch image trials and non-itch image trials, by question group.
Error bars represent standard deviations.

The ANOVA revealed no main effect of the sensory condition (itch vs. non-itch), $F(1,54)= 3.58$, $p=.064$, n.s. There was a significant main effect of group, $F(1,54)=12.61$, $p=.001$, with the itch question group scratching more frequently than the neutral question group. There was also an interaction between the sensory condition and the groups, $F(1,54)=5.52$, $p=.023$, with the itch question group scratching more frequently in response to itch images (average of 15.2 scratches, with a standard deviation of 15.6) than non-itch images (average of 11.67 scratches, with a standard deviation of 12.36), and the neutral question group showing little difference in the number of scratches to each image type (average of 5.2 scratches for itch and 5.7 scratches for non-itch, with standard deviations of 3.36 and 4.56 respectively).

It is possible that the itch questions prompted more immediate scratch responses. In considering and identifying where they might be itching it would be logical to then immediately extinguish those itches if it is convenient to do so. By comparison, the more subtle suggestion of itch from simply looking at itchy images might induce a slower, more cumulative effect before an itch is persistent or salient enough to require an action to extinguish it. In which case, such an itch would not be scratched within a single trial and thus a link to the stimulus it originated from would not be evident. It was shown in Chapter 3 that itches often persisted across multiple trials before concluding in spontaneous extinction or a scratch. It is possible that the greater number of scratches exhibited by the itch question group comprised of both this cumulative effect and of scratches occurring within a trial at the point of questioning, whereas the neutral question group's scratches may be mainly the former. It is also possible that the smaller number of scratches produced by the neutral question group may simply have diminished the effect such that it is no longer apparent.

4.3.5 Image content

Chapter 3 demonstrated no link between the body locations featured in the images and the locations of participants' scratches for the itch question group. A chi^2 analysis showed that this lack of a connection was also the case for the neutral question group $X^2(12)=10.02$, $p=.615$, n.s., with a similar overall trend to scratching the head most frequently (which accounted for 74.45% of all scratches) regardless of the body part in the stimulus. No other image content effects were found for the neutral question group which is likely due to the more subtle differences between conditions being rendered inaccessible when the overall effect of VEI is reduced.

Analysis of the neutral question group also indicated that scratching was not significantly more frequent in response to scratch images. This concurs with the findings in the itch question group as described in Chapter 3, and further indicates that Lloyd et al.'s (2013) finding of a significant increase is not replicable with this experimental design.

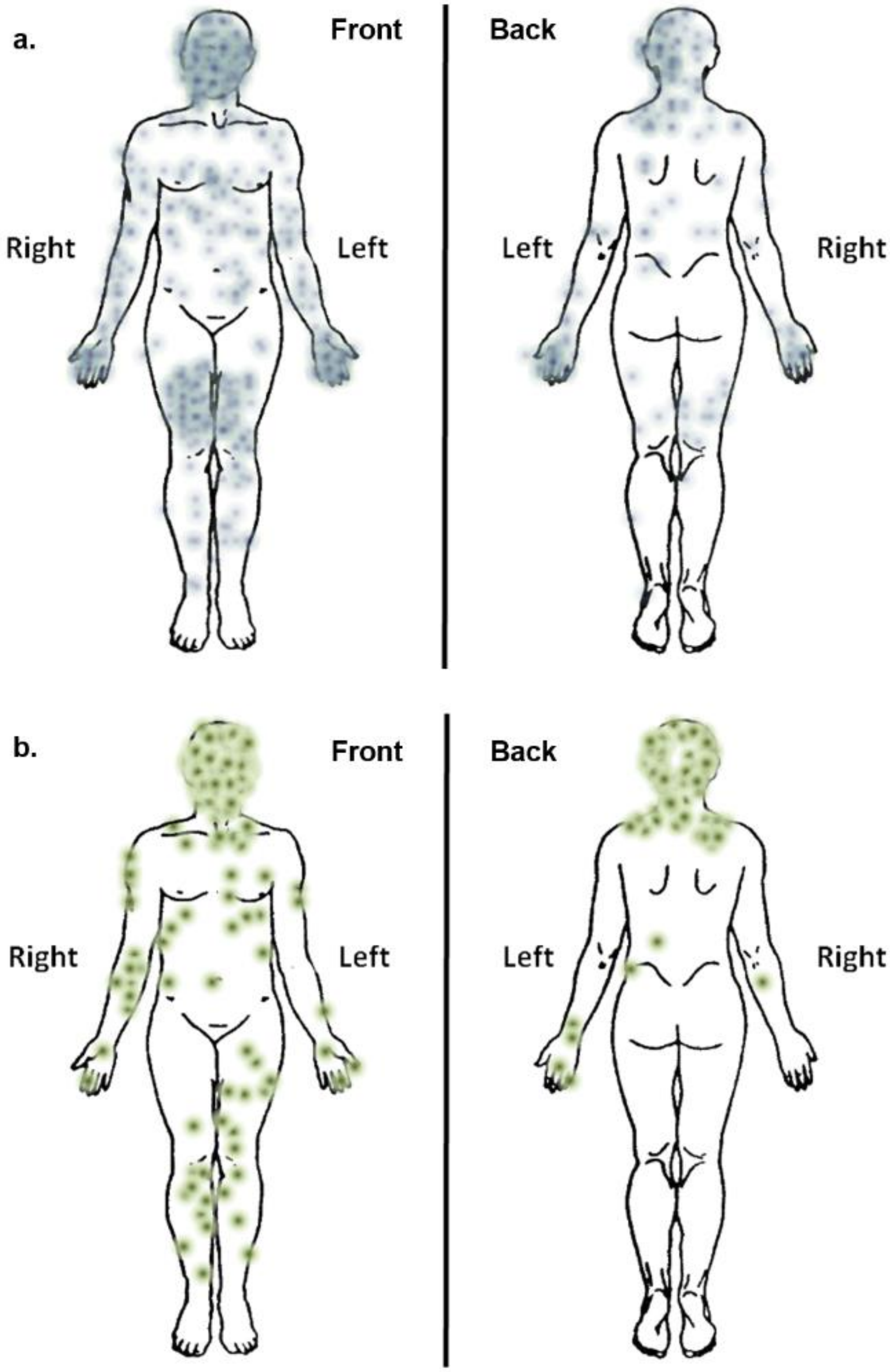


Figure 4.6 The distribution of scratches by all participants in a. the question group and b. the neutral group.

4.3.6 Locations of scratches

Although there were fewer scratches overall for the neutral question group, the distribution across the body appears to be similar to that of the itch question group, as shown in Figure 4.6. The head and face are by far the most prominent scratch targets for both groups. The clusters of scratches on the hands and upper thighs in the itch question group are less evident in the neutral question group. This may simply be a result of fewer scratches overall diminishing the less populated patterns. However, it might also reflect a difference in the bodily focus evoked by the questions. Asking which body part was featured in the image prompts a wide focus as the stimuli represented an even range of body locations. Asking where a person is itching, by comparison, may direct focus to towards the hands and the areas easiest to reach for a scratch, resulting in a bias towards those more accessible areas.

4.4 General Discussion

The results indicate that participants who viewed itch and non-itch images but were asked neutral questions (not relating to itch) scratched less frequently than participants who viewed the images and were asked to rate their itchiness and identify itches on their body. This suggests that the effect of VEI can be produced purely by viewing itch images, but is amplified when this is combined with questions requiring participants to consider their current itch state.

4.4.1 Interoceptive body scan

A potential mechanism for how itch questions can produce or amplify itch sensations is interoceptive body scanning. The experience of questioning whether one is itching, how much, or where, inherently prompts a review of the person’s current sensory state. This review is likely to take the form of mentally scanning the body for itch sensations. Under normal circumstances, spontaneous itches are detected when they reach a level of salience or persistence to be noticed from the person’s continuous unconscious monitoring of their body. Itches or similar sensations which do not meet that criterion do not garner enough attention to require a response. However, when a person is prompted by itch questions to conduct an interoceptive body scan they essentially go looking for these sensations and thus become aware of them more easily.

It is likely that interoceptive body scanning reflects a more general bodily defence mechanism, which can be triggered by any suggestion that an aversive stimulus might be present. Kupfer and Fessler's (2018) view of itch generation and scratch response as a defence against ectoparasites is consistent with this and refers to ‘increasing bodily vigilance’ as a likely part of the process. While directly asking whether a person is experiencing itch is an overt way to increase this vigilance and trigger an interoceptive body scan, it may be that the suggestion of insects in the environment acts as a covert trigger. “is this happening to me too?” is a sensible enquiry when watching someone else experience itching. Searching for a sensation that might need to be addressed as a problem is a useful adaptation regardless of what prompted the search.

It is not yet certain whether interoceptively scanning the body for itches allows more itches to be discovered or whether it creates more itches as a product of expecting to find them. In previous studies, Mirams et al. (2013) found that participants tactile sensitivity increased after using a body-scan based mindfulness meditation technique, and Van Hulle et al. (2013) found that directing endogenous attention in a similar way to specific body parts improved tactile sensitivity in those areas. These findings suggest that a body scan prompted by VEI might likewise increase sensitivity for detecting itch. However, Mirams et al.’s (2010) study suggested that scanning the body for somatic disturbances can result in the over-perception of subtle bodily sensations which can become confused with genuine tactile signals. It is equally true that this may be the case in VEI, with innocuous signals being over-interpreted as itchy when the participant is encouraged to examine them. Indeed, Schut et al. (2016) found that when they manipulated participants’ expectations about VEI, participants who were primed to catastrophise scratched more than controls did. It is possible that itch questions inherently prime participants to catastrophise and thus expect itches to be present when scanning for them. This may be reinforced when potential sensations are identified, confirming the catastrophised expectations.

A possible source of sensations that could be available for an interoceptive body scan to detect are the spontaneous sensations described by (Michael et al., 2012). They found that when participants focused on their hand with no sensory input they reported perceiving up to 14 different sensations, which included tickling, tingling and itching. This indicates that there are indeed tactile sensations which can be perceived if allotted sufficient bodily attention but otherwise go unnoticed. However, this process alone cannot account for the itching induced by VEI, as Michael et al.'s (2012) participants only reported itch as 1.8% of the total sensations making it one of the least common in the study. It appears that interoceptive body scanning for sensations is not sufficient; it requires the itch-threat context of VEI for these sensations to be interpreted as itch.

4.4.2 Experimental bias or effect?

Altering the results of a study by changing the wording of the questions is reminiscent of investigator biases. This has long been regarded as an issue with psychological research, particularly when it is attempting to measure subjective experience (Rosenthal & Rosnow, 2009; Rosenthal & Fode, 1963; Rosenthal & Rubin, 1978). In this particular case though the issue is more complex, as an unintended effect that influences what participants genuinely experience is still a desirable outcome in this context.

Investigator effects primarily bias the responses participants give, rather than changing the underlying experiences they have. For VEI, it cannot be assumed that different results reflect an altered report of an identical sensation rather than a change in the sensation itself. Itch nocebo effects show that participants experiences of a stimulus can be influenced by the experimenter's language and suggestions in a similar way (Napadow et al., 2015; A. I M van Laarhoven, Kraaimaat, Wilder-Smith, van de Kerkhof, & Evers, 2010). Additional evidence from Stumpf et al. (2016) showed an increase in subjective report of itch intensity corresponded with a heightened cutaneous reaction during nocebo induction, indicating a physical change is possible. Futhermore, if the itch questions were artificially increasing VEI measures, this would mainly result in a bias in self-report measures. The current study did not use self-report measures, and as participants were not aware of being filmed, they are unlikely to be consciously altering their scratch behaviour. Scratch can thus be considered a less subjective measure and so less likely to be susceptible to investigator effects. Experimental biases influencing participants behaviour in this kind of study is certainly possible; however, it does not appear to be the case when changing the questions asked during VEI.

4.4.3 Visually-evoked and question-evoked itch

The question influencing the effect is not necessarily a problem for VEI as it does not diminish the effect itself. Ultimately it is still a form of nocebo; questioning a participant about their itch state does not irritate the skin nor touch the person in any way. It is a purely psychological trigger that increases itching, verified by the resultant increase in scratching. The effect still stands but must be reframed in the wider sense of psychologically-induced contagious nocebo itching rather than the more narrowly defined VEI.

That is not to say that the itching experienced in this study was not still visually-evoked. The influence of the questions does not remove the image content from the equation it just demotes it from the main driver to a contributing factor in psychologically-induced itch. It might be better considered visually-modulated itch, which is diminished but not erased by altering the question. The images are still actively involved in creating the effect and evidenced by the different visual inputs inducing itch to different extents. When the type of question is kept constant, the itch images definitely induce more VEI than the non-itch images (Niemeier, Kupfer, & Gieler, 2000; Schut, Radel, Frey, Gieler, & Kupfer, 2016; Ogden & Zoukas, 2009; Lloyd, Hall, Hall, & McGlone, 2013a). Chapter 3 has firmly established a replicable (with Lloyd et al. 2013) effect of image content. Finding another strong influence on the creation of itch does not undermine these established findings, although it could provide a change in context and consequently alter the interpretation. VEI in the form that it has been studied may actually be a composite effect of visually-evoked and question-evoked itch. Therefore, any explanation posited for this phenomenon needs to incorporate both aspects.

4.4.4 Methodological issues

The one major drawback in this design is that there was no true scratch baseline, therefore it was not possible to compare the frequency of scratching for the images alone to how often people scratch generally in a task that is not itch focused. This is true, however, for all experiments of this kind. No previous studies of VEI have directly measured this baseline either, nor has the general itch literature reported baseline statistics for the healthy population. It is assumed to be so low as to be negligible, or that a non-itch control condition sufficiently represents this baseline level. Using that standard, this study has as close to a baseline as any other study achieves, but it is still not a true baseline for spontaneous scratching. In addition to this, as with Chapter 3, there is the possibility that the presence of a video camera may have affected participants' tactile sensitivity (Durlik et al., 2014) and thus altered their underlying propensity to itch in these circumstances.

The neutral questions provided no genuine data but were used to match the procedure as closely as possible to the itch questions in terms of how the participants experienced the trials: Engaging with the images, considering a rating, thinking about body locations, all without providing the explicit context of itch. These questions did produce consistent ratings across time in a similar way to the itchy questions, so can be considered sufficiently neutral to act as a control for asking about itch. The preliminary development work in Chapter 2 indicated that the itch and non-itch images were well matched in terms of how stimulating participants found them, but this stimulating/interesting rating does not appear to correlate with how itchy the images seemed. Thus we can be confident that the interestingness of the images is independent from the itchiness of the images.

The neutral tasks were also designed to match the experience of providing responses as closely as possible: participants passively viewed the images for the same length of time, then moved the mouse to click on the rating scale, then clicked to mark locations on the body map. As such, the task required the same physical movements at the same intervals. As participants appear to use these intervals and pre-initiated movements as opportunities to scratch, the design neither encouraged or discouraged any additional behaviour. Despite this, there was a substantial difference in variance between the two groups. A within-subjects design may have allowed for a neater comparison, but would have been far harder to implement and less efficient as the itch question group's data already existed.

4.4.5 Clinical implications

These findings should serve as a caution to clinical practice. Repeatedly asking a person how much and where they are itching amplifies the itch they experience. Unfortunately, asking these questions is an integral aspect of monitoring a patient's symptom status so is difficult to prevent this effect from exacerbating issues in a clinical setting. In particular, chronic itch interventions based on habit reversal techniques rely heavily on recording scratch frequency (Grillo, Long & Long, 2007; Nilsson, Levinsson & Schouenborg, 1997). It is possible that the question-induced amplification of itch is hampering the therapeutic value of this approach. It would be impractical to suggest avoiding these kinds of questions, but minimising the extent that patients log their itch may be advisable. More importantly though, the suggested body scan mechanism behind the effect may warrant a targeted intervention to reduce the tendency to examine the body for itch sensations.

4.5 Conclusions

VEI is evoked when participants view itchy images, resulting in scratching. This is increased when participants are questioned explicitly about their current itch state. Asking neutral non-itch related questions allowed for the pure effect of the images to be revealed; participants still scratched but less so than those who had been asked about itch. These findings essentially mean that the results of VEI in previous studied cannot be considered a purely visually-driven effect. The visual stimulus contributes to the creation of itch and scratch, but the questions used also contribute their own suggestive nocebo.

These findings suggest a general mechanism in psychologically-induced itching that involves prompting the participant to conduct an interoceptive body scan to monitor for sensations which could be indicative of itch threats. The itch questions in the experiment explicitly trigger this search by requesting a report of itch sensations, but the VEI images alone may provide a more subtle prompt to engage in searching for sensations by creating the suggestion that a search may be beneficial. This implies a distinction between the itch outcomes of VEI in a laboratory setting which may be heavily influenced by the former and itch outcomes of VEI in the real world which may come about purely by the latter.

Chapter 5 : Does visually-evoked itch alter tactile sensitivity?

5.1 Introduction

Itch has been linked to a variety of changes in skin sensitivity. For example, histamine-induced itch and subsequent skin sensitisation has been shown to result in alloknesis – the phenomenon of innocuous mechanical stimulation being perceived as itch (Simone, Alreja, & Lamotte, 1991). In terms of chronic itch, Ikoma et al. (2004) found that participants with atopic dermatitis showed central sensitisation to itch stimuli, which resulted in nociceptive stimuli becoming perceived as an itch sensation. Furthermore, Ikoma et al. (2003) concluded that sensitization is not simply the result of skin inflammation, but is more likely to be due to central sensitization of itch processing neurons in patients with atopic dermatitis. While these studies have provided insights into naturally occurring and physically-induced itching, no previous studies have examined whether psychologically-induced itch involves changes in tactile sensitivity in a comparable way. The following chapter aims to address this question.

5.1.1 Signal in noise

Common to all modes of sensory perception is the issue of detecting signal in noise, to filter targeted percepts from the melee of inputs picked up by the sensory organs. While VEI is fundamentally a psychological effect, in order to investigate what mechanisms underpin it, it is useful to consider how top-down cognitive processes interface with sensory inputs. It is often implied that VEI directly creates physical itches, but it is alternatively possible that VEI is a product of manipulating the brains' interpretation of bodily experience, as suggested by the findings presented in Chapters 3 and 4. It is possible that this interpretation is based, at least partially, on the ability to distinguish true itch signals from somatosensory noise. VEI may reduce this ability such that other somatosensory events become over interpreted. Conversely, it is possible that, as sensitivity increases, additional sensations are perceived. Therefore, this study used psychophysics to investigate what changes in perception and cognition occur when people experience VEI.

5.1.2 Itch vs. touch

The main drawback of examining itch in terms of tactile sensitivity is that these sensations are not identical or interchangeable. It is assumed that they are interlinked such that itch relies on somatosensory signals to some extent, but this cannot provide a full account of how itch perception works. Thus, the findings of this study are limited in that they are only an inference from one modality to the other.

Ideally, it would be useful to conduct a signal detection experiment with direct induction of itch stimulation; however, the currently available methods lack the precision to examine fine-tuned differences in stimulus intensity to satisfy a psychophysics approach. Chemical induction of itch by cowhage or histamine are difficult to dose accurately and cannot be altered once administered, and while electrical induction of itch has been demonstrated in previous studies (for example, Ikoma, Handwerker, Miyachi, and Schmelz, 2005), it is difficult to achieve and reliably replicate similar sensations across participants (Tuckett, 1982). Investigating sensory changes in the tactile domain after VEI is the best available method, and so making inferences across modalities is an informative approach for this initial investigation.

5.1.3 The Somatic Signal Detection Task

The Somatic Signal Detection Task (SSDT) was created by Lloyd, Mason, Brown, and Poliakoff (2008). It provides a well-established method for measuring tactile signal detection in terms of changes in tactile sensitivity and response bias. The SSDT paradigm involves participants judging whether or not they detected a weak tactile pulse delivered to their left index finger. On some trials this was accompanied by a non-informative visual cue in the form of a light, which creates uncertainty and thus produces a range of hits, misses, false alarms and correct rejections. According to Lloyd et al. (2008) when the light is present it increases the number of false alarms and the number of hits. This results in a change in response criterion but not in sensitivity to the stimulus: participants do not get better at detecting the vibration, but they do become more likely to report a sensation whether there was one or not.

McKenzie et al. (2012) investigated these effects further and found that false alarms were more common when the light was present even without any priming to expect a connection between light and touch. While training an association between the two could manipulate the number of false alarms, it was not required to produce them. McKenzie et al. (2012) concluded that in the absence of tactile stimulation, the light may have been used to resolve the tactile ambiguity and allow for the perception of touch. This can be considered analogous to the perception of itch created by VEI in the absence of a physical itch inducer at the skin site. It is possible that the visual suggestion produced by itch images may affect how the ambiguous tactile stimulation is processed and interpreted. McKenzie et al. (2012) also commented that this effect may that due to a tendency to use visual information when the tactile information is degraded or uncertain (based on the findings of Johnson, Burton and Ro, 2006). This makes the tactile uncertainty produced by the SSDT well suited to measuring differences produced by the visually-dominant effect of VEI, thus underlining the compatibility of these methods and effects.

5.1.4 Factors affecting SSDT performance

Cognitive, attentional and perceptual factors can affect the outcomes of the SSDT in a variety of ways. How the brain interprets the state of the body can alter both sensitivity and criterion. Perera, Newport and McKenzie (2015) found that creating the illusion of stretching or shrinking the stimulated finger, enhanced tactile signal detection. Even just heightened self-awareness of the body can enhance tactile sensitivity, as found by Durlik, Cardini and Tsakiris (2014) using the presence of a video camera overtly recording their participants. Conversely, increased body awareness has also been shown have a detrimental effect on tactile detection. Mirams et al. (2010) found that viewing the body increased somatic interference leading to more false alarms, possibly due to increased attention to internal bodily sensations.

Attention to the body appears to be an important factor in SSDT performance. Mirams et al. (2012) found that interoceptive and exteroceptive attention had opposite effects on somatosensory perception, with the interoceptive task leading to an increase in the number of vibrations reported, and the exteroceptive task leading to a decrease. The different attentional focuses appeared to shift the response criterion in different directions, indicating that the propensity to report a stimulus can be modulated by where attention is directed. Conversely, Mirams et al. (2013) found that body-scan based mindfulness meditation (which encourages interoceptive attentional focus) resulted in an increase in sensitivity but not a change in response criterion, suggesting instead that a focus on the body improves the ability to accurate perceive a stimulus. Interoceptive body-scanning was highlighted in the previous chapter as a potential mechanism in VEI creation, so it is highly plausible that bodily attention may interact with tactile perception in this study.

5.1.5 Aims and hypotheses

This study aimed to investigate whether viewing itch images can affect tactile perception. Firstly, whether experiencing VEI changed participants' sensitivity in terms of their ability to detect tactile stimuli presented at near threshold level. Secondly, whether experiencing VEI altered their response criterion in terms of whether their propensity to report a sensation increased or decreased. Finally, we aimed to establish if their overall perceptual threshold was affected, indicated by a higher or lower stimulus intensity to reliably detect a signal.

To investigate these aims we combined the SSDT paradigm and the VEI procedure used in previous chapters such that participants would be experiencing VEI effects whilst performing the SSDT. It was expected that the basic SSDT results of the light shifting the response criterion would be replicated. It was then hypothesised that participants would either show greater sensitivity when experiencing VEI, indicating an increased ability to detect sensations accurately, or a lowering of the response criterion indicating a shift towards over-interpreting ambiguous signals. The former would indicate that itch had altered somatosensory perception in a similar way to Mirams et al. (2013), suggesting that body-scanning for itch may improve the ability to detect sensations. The latter would indicate that itch had altered it in a similar way to Mirams et al. (2012), suggesting that VEI may modulate the attentional focus linked to criterion shifts. It was not hypothesised whether or not overall thresholds would change after experiencing VEI.

5.2 Methods

5.2.1 Participants

Forty-one participants with self-reported healthy skin and no pruritic skin conditions were recruited from the University of Leeds and gave their informed consent to take part. One was excluded due to poor performance resulting in a threshold value that was unlikely to be genuine. Of the remaining 40 participants, 31 were female and 9 were male, with an average age of 20 years (SD 2.97). All participants were right-handed and had normal or corrected to normal vision with no known neurological, visual, motor or sensory deficits. Ethical approval was given for this study by the School of Psychology at the University of Leeds, reference number:16-0201 (21/7/2016).

5.2.2 Materials

The experiment was conducted using PsychoPy version 1.82.01 (Peirce, 2007) and displayed on a 15 inch, 1024×768 resolution laptop computer screen. The VEI stimulus set outlined in Chapter 2 was used with no modifications made. White noise was provided using ‘Relaxio’ white noise generator app (Relaxio, n.d.) and data was analysed using IBM SPSS Statistics 21 (IBM Corp, 2012).

The tactile stimulation was administered using a piezoelectric tactile stimulator with a vibrating surface 1.6cm wide and 2.4cm long (Dancer Design, St. Helens, UK). Vibrations were produced using amplified sound waves delivered from the experimental PC through a tactile amplifier (TactAmp 4.2, Dancer Design). An adhesive pad was attached to the surface to hold the participant’s finger in place. The tactile stimulator was mounted on a polystyrene block along with a 10mm red light-emitting diode (LED). This set up is depicted in Figure 5.1.

Participants’ responses in the threshold and SSDT tasks were given via a button box with 4 labelled buttons. Buttons 1 and 2 were used in the threshold task to indicate whether touch was present in the first or second presentation. All four buttons were used in the SSDT task to indicate whether the participant believed the stimulus to have been present. These were coded as 1 - definitely yes; 2 -maybe yes; 3 - maybe no; 4 - definitely no. For the VEI task, trials followed the basic VEI paradigm outlined in Chapter 2 with participants' responses given via a mouse click on the scale presented, to indicate how itchy they felt from 1 (not itchy at all) to 9 (very itchy).

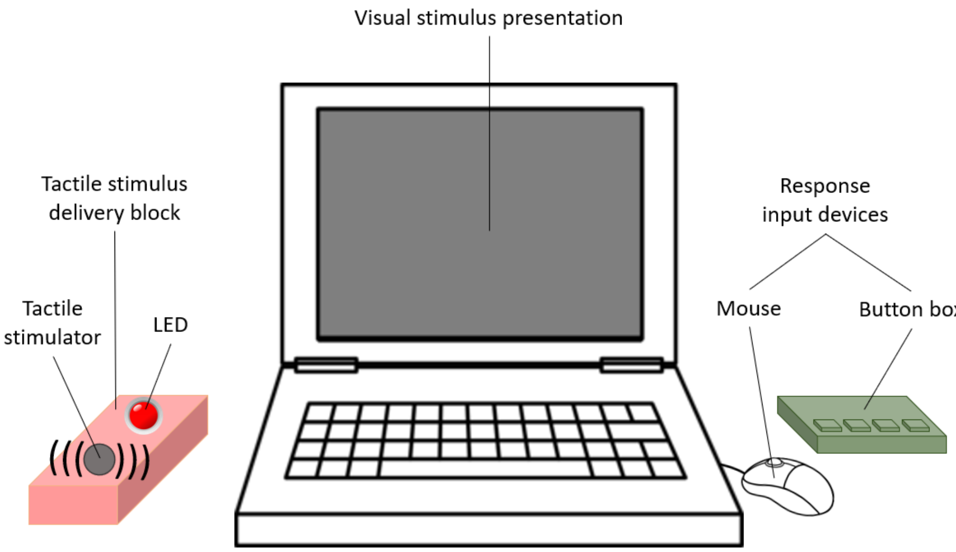


Figure 5.1 The experimental set-up used in the experiment.
It shows the laptop centred in front of the participant, the tactile stimulus delivery block with tactile stimulator and LED on the left and the response inputs, mouse and button box on the right.

5.2.3 Design

For the SSDT measure, a 2x2x2 factorial within-groups design was used. The independent variables were: light condition (light present or absent), tactile condition (vibration present or absent), and image condition (itch or non-itch). The dependent variable was the proportion of trials where the participant reported feeling the tactile stimulus. For the threshold measure, a 2x3 factorial mixed design was used, with the between-subjects variable of task order group (itch first or non-itch first) and the within-subjects variable of time (timepoints T1, T2, or T3). The dependent variable was the stimulus intensity value. VEI itchiness ratings and scratch frequency were used as a manipulation check to ensure the effect was occurring as and when expected in this experiment.

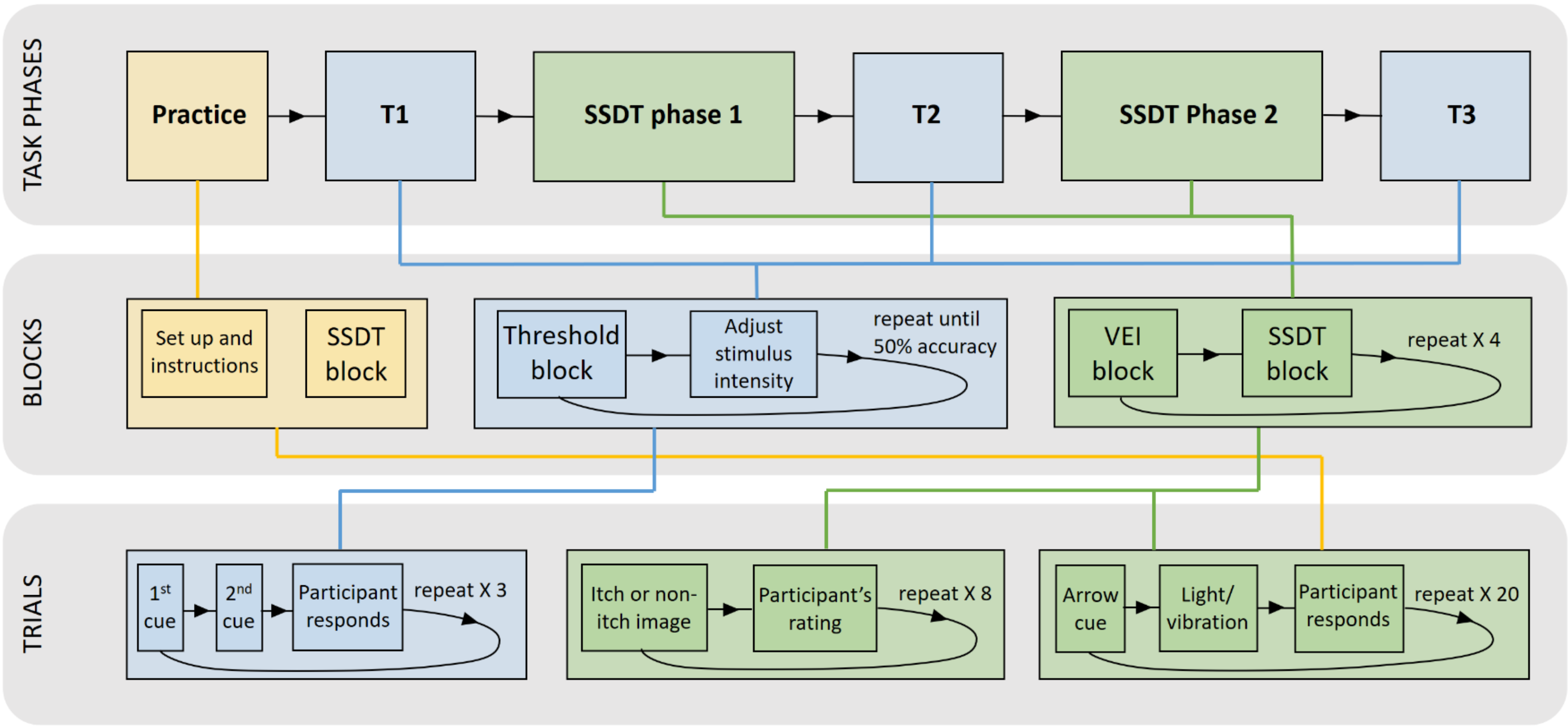


Figure 5.2 : The overall structure of the experiment, outlined at the task phase, block, and trial levels. The task phase section (top) depicts the timeline for the experiment. The block (middle) section breaks down the sequence of events within each type of task phases and the trial (bottom) section breaks down the sequence of events within each block.

The experiment was structured such that there was a repetition of the thresholding task at 3 time points, before and after each SSDT phase (see Figure 5.2). One SSDT phase used only itch images, and the other used only non-itch images. The order of these SSDT phases was counterbalanced across participants, and this grouping was subsequently used as the task order group variable in the analysis.

The threshold task was initially intended to be used to ensure participants were performing consistently throughout the experiment and to test for any order effects or fatigue. It was subsequently used as a major outcome measure when it became evident that it revealed a clear difference in the results and was informative of a larger effect.

5.2.4 Procedure

Participants were seated at a desk approximately 60cm from the laptop screen. The lights in the testing room were dimmed to enable participants to see the LED clearly and white noise was played at an audible but unobtrusive level throughout the experiment to prevent any risk of them hearing the vibrations. Participants were asked to place their left index finger on the vibration pad with a light touch, not pressing down and not moving their finger. They were told not to remove their hand during the tasks or in the breaks between tasks. Their right hand was directed towards the button box and mouse.

Participants were given 20 practice trials of the SSDT to familiarise themselves with the task. The threshold task did not require practice trials as the early trials constituted practice in and of themselves and practice was deemed unnecessary for the VEI task given the simplicity of just providing ratings.

The thresholding tasks at T1 and T2 were used to set the stimulus intensity for the first and second SSDT phases respectively. The thresholding task at T3 was used purely as a comparison. Each SSDT phase consisted of alternating blocks of VEI and SSDT trials, beginning with a VEI block so that participants always experienced VEI directly before completing the SSDT. There were 4 VEI blocks and 4 SSDT blocks, presented in a random order between participants. Each VEI block comprised 8 randomised trials, totalling 32 trials, which used either the full itch or non-itch set with no repetition. Each SSDT block contained 20 randomised trials with each trial type (neither light nor vibration, light only, vibration only, and both light and vibration) equally represented. Participants' scratching behaviour was observed and recorded by experimenter observation noting down scratches throughout the SSDT phases. Scratch frequency was recorded for each SSDT phase according to the procedure outlined in Chapter 2.

The experiment lasted 1 hour in total. Experimental set up and practice tasks took 10 minutes; the SSDT phases took 15 minutes each (x2 SSDT phases totalling 30 minutes); the thresholding task took approximately 5 minutes, depending on participants' performance (x3 task repetitions totalling 15 minutes); and the remaining 5-10 minutes were taken up by short breaks between tasks.

Threshold task:

The threshold task was used to determine the lowest level of signal participants could reliably detect. To do this, it used a two-alternative forced choice, Parameter Estimation by Sequential Testing (PEST; Taylor & Creelman, 1967) staircase procedure. As shown in Figure 5.3, participants were presented with two consecutive visual cues in the form of arrows labelled "1" and "2" which appeared for 250ms. After each cue, there was a period of 1020ms which operated as a stimulus window. In one of these windows, a 100Hz tactile pulse was delivered for 20ms after a 500ms delay, and not in the other. Participants were then prompted to report which one it was, by pressing button 1 for delivery of the tactile stimulus after the 1st cue or 2 for delivery after the 2nd cue (see figure 3). The participants were told that it would become harder to feel the difference as the task progressed and were encouraged to guess on trials where they could not feel it.

Stimulus intensity was measured in arbitrary units. Changes in intensity were determined using a Wald sequential probability ratio test (SPRT) by calculating the W statistic after each trial using equation 5.1, where N(c)=number of correct responses since last step change, Pt=desired probability threshold, and N(t)=number of trials completed since last step change.

$$W = (N(c) - Pt.) \times N(t) \quad (5.1)$$

If participants were correct on significantly more than 75% of trials in a block, the Wald SRPT would be greater than W=1, so the signal intensity was decreased. If they were correct on significantly less than 75% of trials, the Wald SRPT would be less than W=-1, so the signal intensity was increased. The initial step size was 800, the minimum was 50 and the maximum 3200.

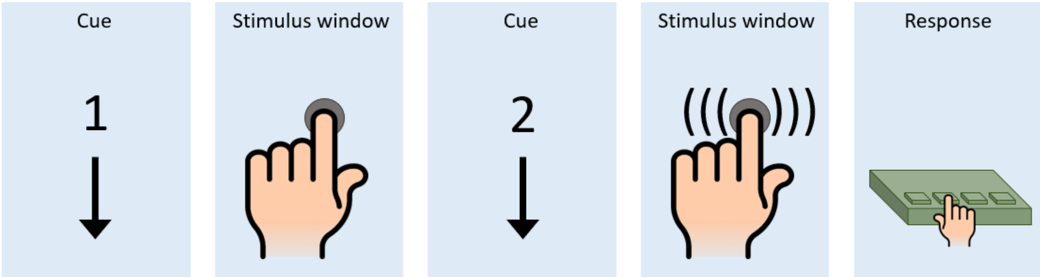


Figure 5.3 The procedure of a trial in the threshold task.
Participants were presented with a tactile stimulus after either one of two arrow cues, they then respond with a button press to indicate which cue it followed.

SSDT task:

The SSDT task consisted of 20 randomised trials, comprising 5 of each trial type: vibration only, light only, both, and neither, as depicted in Figure 5.4. Participants were informed that the vibration would be present on some trials and not on others and they were asked to report whether or not they felt it. They were told to look at their left hand during this task but were not informed of the purpose of the light.

The start of each trial was cued with an arrow, presented for 250ms. This was followed by a period of 1020ms, in which there was either a 20ms 100Hz vibration set at the intensity established in the most recent thresholding task (‘vibration only’ trials); a light emitted from the LED for 20ms (‘light only’ trials); both a vibration and light presented simultaneously (‘both’ trials); or no stimuli presented (‘neither’ trials). After the stimulus presentation window, participants were prompted to respond with 4 options as to whether they felt the vibration “1: definitely yes”, “2: maybe yes”, “3: maybe no”, or “4: definitely no”.

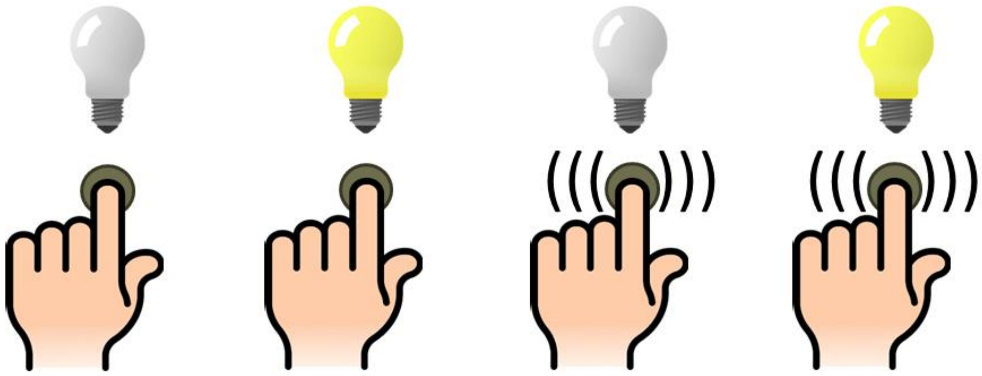


Figure 5.4 Trial types from left to right:
Neither (light absent and touch absent), light only (light present and touch absent), vibration only (light absent and touch present), and both (light present and touch present).

VEI task:

The VEI task used the basic procedure outlined in Chapter 2: In each trial an image from the stimulus set was presented for 8 seconds. Participants were then given a scale from 1 (not itchy at all) to 9 (very itchy) and asked to rate how itchy they felt at that moment, using a mouse click. There were 8 trials in each block.

5.2.5 Data analysis

One participant was removed due to scoring >0.7 on the second threshold task, compared to all other scores in the sample ranging between 0.2 – 0.5. The itch first and non-itch first groups were compared on all measures to check for order effects. As there were several differences between the two task order groups, this grouping was used as a between-subjects variable in all analyses. This resulted in there being 20 participants in each group and thus did not drastically diminish statistical power.

For the SSDT task, the participants responses of ‘definitely yes’ and ‘maybe yes’ were collapsed into a single category of ‘yes’ responses and ‘definitely no’ and ‘maybe no’ were collapsed into a single category of ‘no’ responses.

When the tactile stimulus was present, trials where the participant correctly identified it (‘yes’ responses) were recorded as hits and trials where they did not identify it (‘no’ responses) were recorded as misses. When the tactile stimulus was absent, trials where the participant incorrectly reported it as present (‘yes’ responses) were recorded as false alarms, and trials where they did not identify it (‘no’ responses) were recorded as correct rejections. Floor (0%, 0.0) and ceiling (100%, 1.0) effects were adjusted using a log-linear correction. The hit and false alarm rates were used to calculate the d’ statistic, which indicates perceptual sensitivity, and the c statistic, which indicates the criterion for reporting the stimulus as present, respectively. These statistics were calculated using the formulas shown in equations 5.2 and 5.3, where H=hits F=false alarms and z represents the z-score of these.

$$C = - [z(H) + z(F)]/2 \tag{5.2}$$

$$d' = z(H) - z(F) \tag{5.3}$$

Repeated-measures ANOVAs were used to compare the effects of the light condition (present or absent) and the image condition (itch or non-itch) for the hit rates, false alarm rates, d’ statistics and c statistics.

5.3 Results and Discussion

5.3.1 VEI measures

The VEI measures were primarily used to establish whether participants were experiencing VEI during the study. As depicted in Figure 5.5, participants itchiness ratings were significantly higher for the itch images than the non-itch images overall, $F(1,38)=262.168$, $p<.001$. There was a small, but significant group difference between the task-order groups, $F(1,38)=4.248$, $p=.046$, and an interaction between group and image condition, $F(1,38)=4.290$, $p=.045$, with the itch first group having a lower average itchiness rating than the non-itch first group for the itch SSDT phase. Participants also scratched more frequently during the itch SSDT phase than the non-itch SSDT phase overall, $F(1,38)=85.660$, $p<.001$, but this did not differ by task order group, $F(1,38)=0.883$, $p=.353$ (n.s.). and there was no significant interaction between scratch frequency and group F(1,38)=012, p=.914 (n.s.).

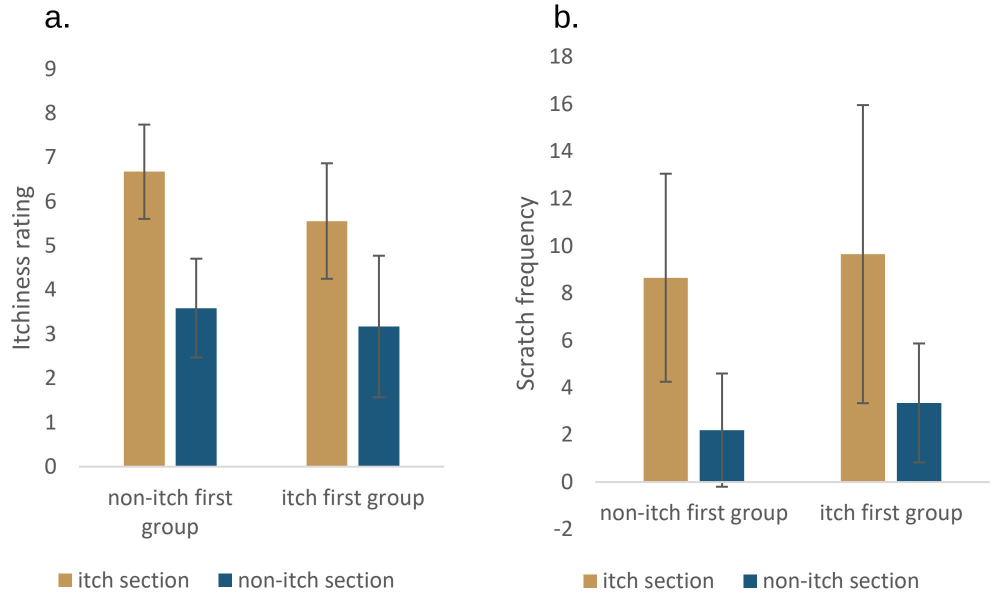


Figure 5.5 VEI measures for all participants divided by SSDT phase. a. average itchiness ratings and b. average scratch frequency. Error bars represent standard deviation.

These results indicate participants did experience VEI during the experiment as expected, so it can be inferred from this that differences found between the two SSDT phases are related to the differences between the VEI effects produced by itch and non-itch images. The strength of this effect also differed between the task order groups, but it is unclear whether this difference influenced the other results.

5.3.2 SSDT: Hit rate and false alarm rate

The number of hits and false alarms indicates how often participants claimed to have experienced the stimulus. The hit rates and false alarm rates were a little higher for the itch phase than the non-itch phase (as shown in Figure 5.6); however, these results were not statistically significant (F(1,32)=0.795k p=.379 (n.s.) for hits and F(1,32)=0.004, p=.948 (n.s.) for false alarms). There was a significant main effect of task order group on the hit rate, F(1,32)=8.069, p<.01, but not on the false alarm rate F(1,32)=1.364, p=.251 (n.s.), which seems to be driven by the non-itch first group getting fewer hits on the non-itch block, as depicted in Figure 5.6. It appears that the induction of VEI during the itch SSDT phase corresponds with a greater ability to detect signals that are present during and after that experience. The presence of the light did not significantly affect either the hit rate $F(1,32)= 2.051$, $p=.162$ (n.s.) or false alarm rate $F(1,32)=0.487$, $p=.490$ (n.s.) and there were no significant interactions between variables.

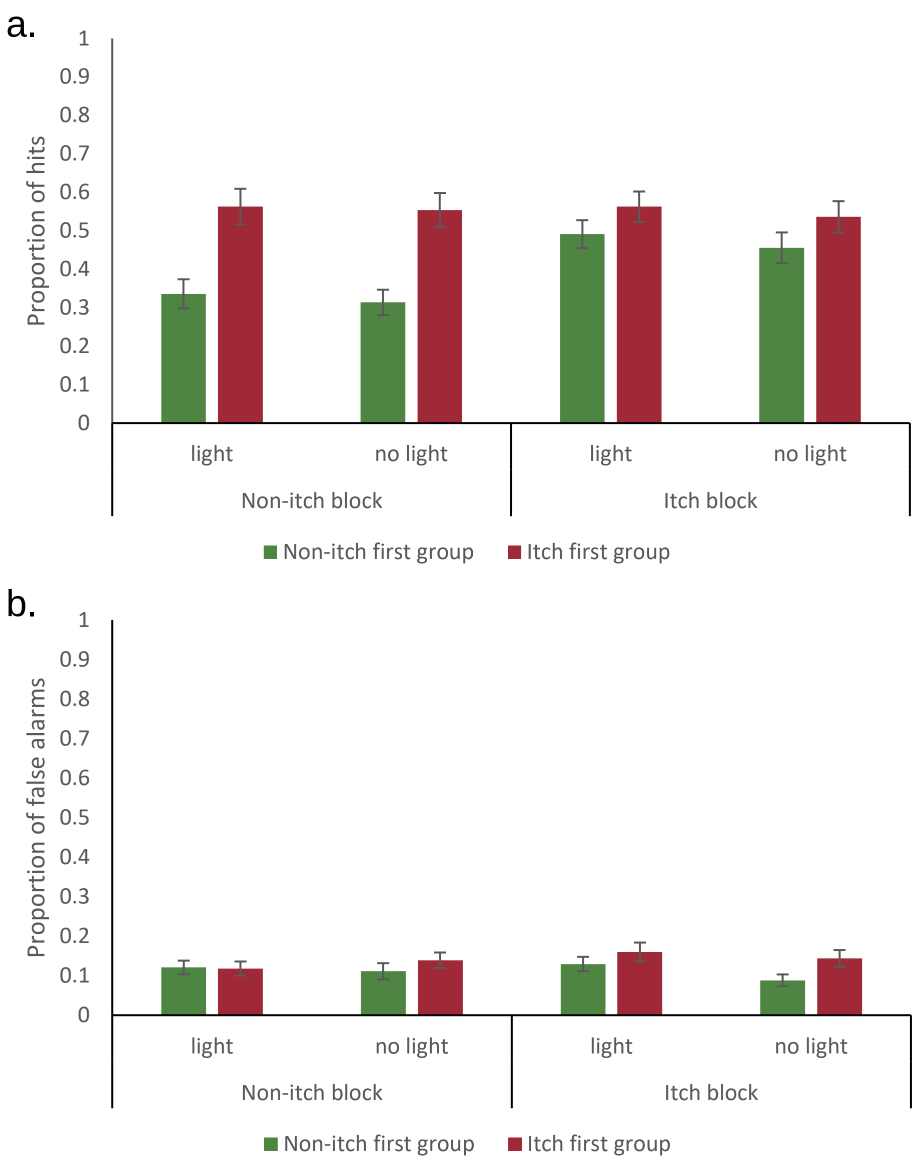


Figure 5.6 Average a. Hit rate and b. false alarm rate for trials where the light was present or absent in both the itch and non-itch blocks. Rates are presented as proportions of responses and error bars represent standard error.

Table 5.1 Mean sensitivity (d') values and response criterion (c) values for each condition.
Presented by task order group and overall mean, with standard deviations in brackets.

		Sensitivity d'			Response criterion c		
		Itch first	Non-itch first	Overall	Itch first	Non-itch first	Overall
Itch	Light	1.480 (0.94)	1.318 (0.94)	1.404 (0.93)	0.463 (0.60)	0.700 (0.39)	0.575 (0.51)
	no light	1.359 (1.07)	1.37 (0.93)	1.365 (0.99)	0.550 (0.53)	0.902 (0.42)	0.716 (0.50)
Non-itch	Light	1.582 (1.07)	0.895 (0.91)	1.259 (1.04)	0.589 (0.62)	0.897 (0.49)	0.734 (0.58)
	no light	1.415 (0.90)	0.923 (0.72)	1.184 (0.84)	0.569 (0.67)	0.957 (0.50)	0.752 (0.62)

5.3.3 SSDT: Sensitivity and criterion

Perceptual sensitivity described by the d’ statistic and the criterion for reporting the stimulus as present described by the c statistic are outlined in Table 5.1. There appears to be a trend towards the non-itch first group having lower sensitivity on the non-itch SSDT phase, most likely as a result of their significantly lower hit rate. However, the main effects of sensitivity $F(1,32)=0.574$, $p=.454$ (n.s.) and of trial order group $F(1,32)=2.723$, $p=.109$ (n.s.) were not significantly different. Indeed, neither the effect of the light $F(1,32)=0.484$, $p=.492$ (n.s.) nor any of the interactions were significant. While it appears that there are subtle differences in sensitivity, these were not picked up strongly by the SSDT itself.

The response criterion does, however, appear to shift (albeit not statistically significantly, $F(1,32)=0.819$, $p=.372$, (n.s.)) overall between the itch and non-itch blocks, particularly when the light is present. There was still no effect of light $F(1,32)=2.606$, $p=.116$ (n.s.), but there was a significant main effect of task order group, $F(1,32)=5.674$, $p=.023$, in that the itch-first group had a lower response criterion than the non-itch group. These shifts towards a lower criterion indicate that participants are responding ‘yes’ more often overall, without a change in their accuracy. It is possible that this represents an inclination to interpret ambiguous sensations as signal rather than noise while experiencing VEI.

5.3.4 Threshold Differences

The threshold task results consisted of 3 data points for each participant, indicating their overall somatosensory threshold value at the beginning of the experiment before the first SSDT phase (T1), between the first and second SSDT phases (T2) and after the second SSDT phase (T3). The averages of these values are displayed in Figure 7.

There was a highly significant main effect of time, $F(2,76)=12.145$, $p<.001$, with overall average thresholds increasing across each timepoint (T1, T2 and T3). There was also a group by time interaction, $F(2,76)= 3.391$ $p<.039$, as this increase was not uniform across both task order groups, as Figure 6 shows, but no overall main effect of group, $F(2,38)=0.239$, $p=.614$, (n.s.). At T1, the average thresholds were similar for both groups, as expected for the beginning of the experiment. At T2, the itch first group's average threshold had risen, while the non-itch first group's average threshold showed little difference. At T3, the itch-first group's average threshold remained fairly similar to that found at T2, and the non-itch first group's average threshold increased to above that of the itch first group. In other words, after each SSDT phase the thresholds of participants who had completed the itch SSDT phase increased, whereas there was little change in those who completed a non-itch SSDT phase.

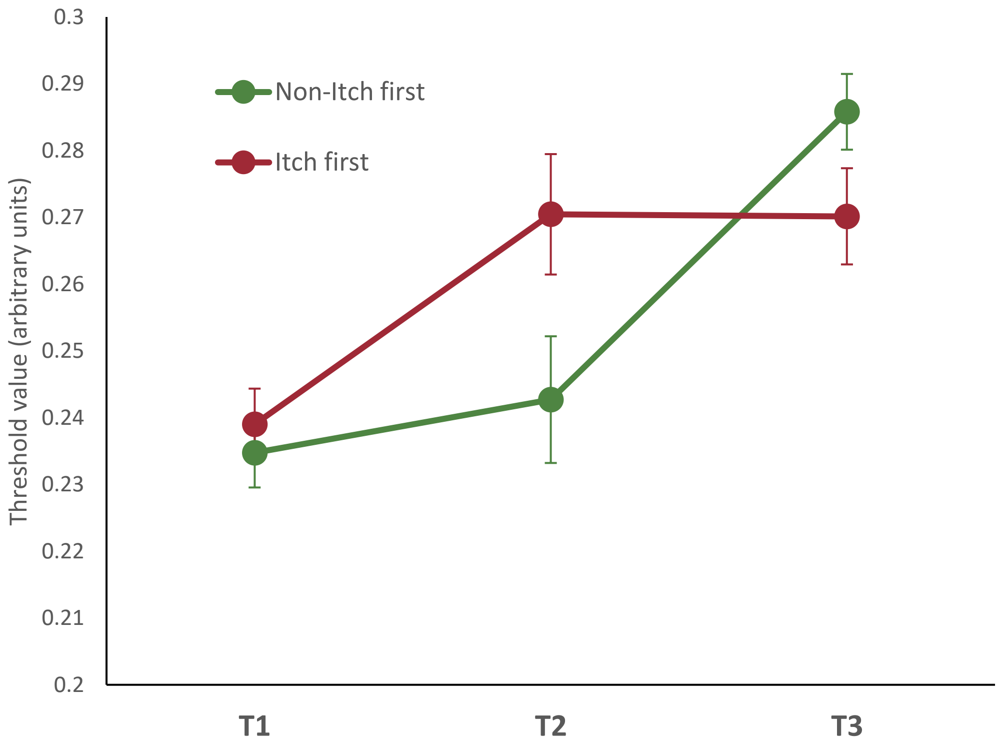


Figure 5.7 Average somatosensory threshold values at 3 timepoints across the experiment, for the itch first and non-itch first groups. Error bars represent standard error.

Experiencing VEI appears to correspond with decreased overall tactile sensitivity. If VEI were a matter of becoming more perceptive of itches, we would expect an increase in sensitivity rather than a decrease. It appears that rather than a mechanism for directly identifying these sensations more, VEI paradoxically reduces sensitivity to skin stimulation while increasing the amount of sensations that are perceived. This may be a product of the way this effect was measured. VEI may not reduce sensitivity overall, but simply divert it away from the focus on the fingertip and direct it across the wider body, resulting in a decrease in localised sensitivity at the fingertip.

5.4 General Discussion

The threshold value changes across the experiment and lack of SSDT sensitivity difference within SSDT phases indicates that the change in tactile perception is more of an overt enduring change than a fine-tuned improvement or reduction. Participants' ability to distinguish tactile signal from noise at threshold level is not compromised or amplified while viewing itch-inducing images, but the stimulus intensity required to achieve that threshold itself does increase. Their bias towards reporting a sensation more often, however, suggests participants may be more attuned to potential sensations and show greater vigilance, even if this does not increase their performance. This may reflect a slight criterion shift in what sensations are deemed to be an itch, with potentially more ambiguous sensations passing this perceptual boundary after VEI is induced, while no change in sensitivity indicates that this does not correspond with them getting better at detecting spontaneously occurring itches. This fits with what we know of VEI as an increase of itch sensations would be easier to create by over-interpreting and 'mistaking' more sensations as itch than by becoming more accurate.

5.4.1 Visually-evoked itch and body interpretation

The results suggest that the mechanism behind VEI involves manipulating the ability to separate signal from noise by offering contextual information regarding the possible state of the body. This additional context may increase the propensity to classify ambiguous sensations as the presence of itch: VEI might not directly increase the number of itches present on the skin, but instead increase the number of itches identified from the available skin sensations by means of a possible criterion shift towards positive identification. It may be that noise in the form of transient minor sensations become interpreted as signals of itch during VEI, and thus get processed as the presence of itch threat at the skin site. This in turn would mean that participants' ability to distinguish genuine itch threats from somatosensory noise is compromised during VEI. Drawing cues to increase somatosensory vigilance from observing other people's itch experiences may reflect a social element to tactile processing that VEI plays on (Durlik, Cardini & Tsakiris 2014).

In support of this interpretation, Mirams et al.'s (2010) study concluded that directing attention towards the body leads to the over-perception of bodily sensations by increasing awareness of subtle, otherwise unperceived sensations, which become confused with the induced tactile stimulation. They inferred from this that constant scanning of the body for somatic disturbances can result in the over-perception of bodily sensations. Katzer et al. (2011) have shown that people with medically unexplained symptoms (MUS) have a greater propensity to misinterpret sensations in this way, which may be contributing to their experiences of illness (Mirams et al., 2010). This raises the question of whether people with MUS are particularly susceptible to VEI as a result of this, as it is likely that a similar scanning process is occurring in the creation of VEI. Participants scanning and monitoring the state of their body for possible itches may be resulting in over-perception of otherwise unnoticed sensations.

5.4.2 The role of bodily attention

The attentional component of interpreting bodily experiences appears critical to the perceptual changes that occur when experiencing VEI. According to Mirams et al. (2012), internal and external bodily attentional focuses shift the response criterion in different directions: interoceptive attention lowers the criterion and exteroceptive raises it. In line with this, we found that viewing itch images also led to a slightly more liberal response criterion with interoceptive attentional focus, rather than an exteroceptive focus on the images themselves.

A further distinction can be made within interoceptive bodily attention in terms of how narrow or wide across the body this attentional focus is. Mirams et al. (2013) concluded that the differences they found between their mindfulness and non-mindful interoceptive attention tasks might have been a matter of how wide an attentional focus the tasks encouraged. The former directed attention to various parts of the body via a body-scan meditation procedure, whereas the latter required participants to focus attention solely on their fingertip. It seems plausible that a similar distinction can be made in our results between the wider distributed bodily attention required monitoring itches that could be occurring anywhere on the body, and the narrower bodily attention required to perform the SSDT accurately. The VEI effect is likely to be diverting attentional focus from the targeted loci to the more distributed locus, inducing an overall body sensitivity rather than sensitivity at the single point on the fingertip captured by the SSDT. Indeed, a future direction could be to manipulate this attentional locus and measure sensitivity across multiple body locations rather than requiring attention to be focused in one place.

A possible reason for attention to be directed in this way would be to maintain a heightened level of vigilance for itch-threats. In a high itch-risk environment, attending to the whole of the body and scanning for sensations would enable threats to be detected and thus dealt with sooner, minimising the harm they cause prior to detection. The images used to invoke VEI create the suggestion of such an environment. Van Hulle et al. (2013) found that focusing attention on specific parts of the body improves tactile change detection at those locations. They suggested that participants adopted purpose-based “attentional control settings” (p.300) for directing attention to the presence of relevant features of the environment. In the context of viewing itch images, potential itch sensations may become priority features to direct attention to. The overt increase in threshold values while experiencing VEI suggests that participants are casting a wider attentional net for potential sensations and the small criterion change suggests this might be accompanied by a shift towards allowing more sensations to be captured by that net. As a result, when a harmful itch seems more likely, the perceptual systems adjust attentional priorities to interpret the body accordingly.

5.4.3 Attention or distraction?

The threshold effect was interpreted as indicating that bodily attention was shifted from a focal point at the fingertip to a distributed focus across the body to enable vigilance for itch sensations. However, this result could be explained more simply as a result of induced itches distracting participants from the task. The creation of VEI creates additional attention drawing sensations, which can require a response and so provide competition for cognitive resources. While this interpretation is reasonable, it does not account for the threshold changes enduring after VEI diminishes. While it is certainly possible that the distraction of additional itches could account for the higher thresholds after the itch block, it would then be expected that these would decrease again, at least partially, after completing the non-itch block for the itch-first group. The final threshold measure for this group was taken at least 20 minutes after the itch block, so it is assumed that there would be no carry-over effects, although there is no clear evidence to determine how long VEI effects persist after exposure to itch images. The VEI ratings and scratch frequency measures support the assumption though, as they indicate that participants were not experiencing VEI during the non-itch block, so there were no added itches to distract them. The elevated thresholds at this point must be related to a longer lasting attentional shift in response to viewing itch images, rather than a direct distraction of competing sensations.

Furthermore, the increases in thresholds with no subsequent decreases could be deemed to be partially a fatigue or boredom effect, leading to a decrease in performance across time. However, Mirams et al. (2013) also collected threshold measures at multiple timepoints and found no differences between them. Therefore, it is fair to conclude that the threshold changes we found were a response to the experimental manipulation and not an artefact of the paradigm.

5.4.4 Limitations of comparing across phases

The decision to measure the threshold and thus adjust the stimulus intensity separately before each condition phase may reduce the ability to directly compare the measures of sensitivity and criterion between these conditions. However, if the alternative option had been taken and a single threshold value used for both, the differences in participants performance on their second block (evidenced by the changes found in the threshold results) may have been subject to floor or ceiling effects due to the stimulus intensity no longer being at threshold level for them.

5.4.5 Replication of the SSDT

It was unpredicted that the primary SSDT effect of the presence of the light could not be replicated in this study. Although we cannot be certain why this is, it is not unprecedented. Durlik, Cardini and Tsakiris (2014) also failed to replicate an improvement in performance with the light present in their study and concluded that this was likely to be because the influence of their experimental manipulation was powerful enough to override the influence of the light. They concluded this more subtle effect was diminished by the self-directed attention from being watched. Similarly, Mirams et al. (2010) found that when participants were not able see the hand that was being stimulated, the presence of the light did not increase false alarm rates and inferred that this was because attention was not so closely focused on the stimulation site. Attention directed towards the body does appear to be highly influential generally, and it seems that distributed bodily attention reduces the power of SSDT effects. In the case of our experiment specifically, it is likely there were too many attention-diverting effects in play to be able to see any effect from the presence of the light.

5.4.6 Replication of VEI

The results do contribute a slightly different replication of the VEI effect itself. The findings of Chapters 3 and 4 were replicated with itch and non-itch images presented in separate SSDT phases as opposed to intermixed, which they have been in all previous studies with this stimulus set. This confirmed that participants do scratch more frequently while viewing the itch images, which was harder to establish as clearly from mixed designs.

Furthermore, the difference in itchiness ratings for the itch phase between the itch first and non-itch first groups indicates that separating out the VEI conditions in this design did alter how participants experienced VEI to some extent. This could possibly be explained by the findings of Chapter 4 in that VEI is not purely a visual effect and the influence of asking participants about their itch state contributes to it. Thus, it is possible that asking about participants’ itchiness in the absence of itchy image content (in the non-itch block) affected participants differently depending on whether they had already experienced VEI (in the itch block) during the experiment. This questioning in the non-itch SSDT phase may have primed the non-itch first participants to rate VEI higher when they actually did experience it in the itch SSDT phase. As this difference only existed in the ratings and did not extend to the scratch frequency, this is likely to be a matter of subjective reporting bias.

5.4.7 Applications to chronic itch

The SSDT has been applied to the study of clinical conditions such as somatoform disorders and medically unexplained symptoms (MUS) (Brown, Brunt, Poliakoff, & Lloyd, 2010; Katzer et al., 2011). There are mixed findings from the MUS literature regarding whether attention towards or away from the body increases MUS, as Brown (2010) found both body vigilance and body avoidance to be involved. For this reason, it would be valuable specifically manipulate attentional focus in VEI whilst using SSDT to establish whether similar effects may be found for itch, rather than rely on the inferences about attention from the findings presented in this chapter.

For a clinical population specifically, Katzer et al. (2011) found that changes in response criterion were linked to both medically unexplained symptoms and to general health anxiety, suggesting that clinical participants' appraisal of, and emotional response to, their clinical condition may influence how they experience these effects. It is possible that a similar link may be found for people with chronic itch conditions, which hints that the SSDT could potentially function as a screening method to identify people whose criterion shifts easily through wariness and hypervigilance and may make them more susceptible to itch triggers. It would be interesting to examine a clinical sample for both the option of targeting stimulation on or near participants' skin lesion sites as an itch focal point, and for covarying the results with psychodermatology scales.

5.5 Conclusions

Visually-evoked itch does correspond with a change in overall perceptual thresholds and slight lowering of the response criterion to the detection of non-itch touch. Viewing itch images seems to direct attention more generally to the body and prompt hypervigilance to somatosensory signals. This in turn makes it harder to hone in on a single tactile stimulus at the fingertip, reducing sensitivity in terms of d', but also encouraging over-interpretation of ambiguous somatosensory signals and thus reporting more sensations overall.

This suggests a mechanism for VEI based on using widely distributed bodily attention to scan for sensations and thus enabling people to notice more sensations and over-interpret these as more potential itches. The creation of VEI is essentially prompting participants to cast a wide net for potential sensations and interpret their bodily experience accordingly.

Chapter 6 : What role does visual attention play in susceptibility to VEI?

6.1 Introduction

Attentional bias is the tendency to attend to one particular type of stimulus over another. It is found when a participant is quicker to respond to a probe that is presented in a congruent location with the bias-relevant stimulus, compared to a non-biased stimulus. It can also manifest as a preference for making saccadic eye-movements towards that stimulus, or sustaining gaze upon it. Such stimuli often depict some form of threat and "[reflect the] person's current concerns" (Mark, Williams, Mathews, & Macleod, 1996, p.14) and previous experiences.

Attentional biases can be divided into implicit and explicit (Mogg, Bradley, Field, & De Houwer, 2003). Implicit biases represent what people are initially drawn to and are not part of a cognitive decision making process. Implicit bias can be captured by using short stimulus presentations (around 100ms), which are too quick for participants to process the visual content or make eye-movements towards or away from it. Explicit biases represent where attention ends up through conscious cognitive processing. They are captured by longer stimulus presentations (multiple seconds), where participants have time to look at and visually explore the stimulus.

6.1.1 Attentional bias towards threat

The threat of harm is a key feature in many studies of attentional bias. Van Damme et al. (2009) found that tactile attention was biased towards the location of images featuring physical threat and Poliakoff et al. (2007) found greater tactile attentional facilitation for images of snakes than non-threatening images. Öhman, Flykt and Esteves (2001) found a similar bias towards specifically feared targets, for example spiders but not snakes or vice versa, depending on the participants' individual phobias.

It is clear that danger is attention grabbing, but in addition to generic depictions of harm, individually relevant distress or discomfort can also divert visual attention. People who suffer from anxiety show attentional biases towards angry or threatening faces (Bantin, Stevens, Gerlach, & Hermann, 2016; Mogg, Millar, & Bradley, 2000; Waters, Bradley, & Mogg, 2014) or threatening words (Rinck & Becker, 2005). This is particularly the case for people with physical or mental health conditions: People with eating disorders, for example, show an attentional bias towards images of thin bodies (Glauert, Rhodes, Fink, & Grammer, 2009). While such attentional biases tend to focus on clinically-relevant content, this does not always manifest as a bias towards the more pertinent stimuli. Duque and Vázquez (2015) found a negative attentional bias for sad faces in participants with major depressive disorder, which was also correlated with the severity of their symptoms. In terms of threat, Pine et al. (2005) found that the severity of physical abuse, and resulting post-traumatic stress disorder experienced by participants, predicted attentional avoidance of threatening faces.

6.1.2 Attentional bias towards pain

Pain serves as a particularly visceral form of threat, but despite being widely researched, attentional bias for pain is not a straightforward picture. In their meta-analysis, Crombez et al. (2013) conclude that attentional bias is not a robust phenomenon, making it difficult to identify, generate, and replicate. Dear et al. (2011) also commented on the literature having ‘considerable inconsistency’, and Van Damme et al. (2004) listed several conflicting results.

Nevertheless, the literature does reveal attentional biases towards pain in a variety of clinical conditions, including chronic headache (Liossi, Schoth, Bradley, & Mogg, 2009), fibromyalgia (Vago & Nakamura, 2011), and vulvar vestibulitis syndrome (Payne, Binik, Amsel, & Khalifé, 2005). For the former, a bias was found even when there was no clear threat implied by the stimuli, which were headache-related images (Schoth & Liossi, 2010), indicating that threat is not necessarily the driving force in all cases.

Threat and individual responses to threat are still a prevalent interpretation of attentional biases to pain. Khatibi et al. (2009) found that attentional bias towards painful faces was attenuated in individuals that have greater fear of pain and injury. In addition, Keogh et al. (2001) found that participants with a greater fear of pain showed an attentional bias towards pain information. Interestingly, Asmundson, Kuperos and Norton (1997) found that clinical and healthy participants did not differ in their responses to pain or injury-based stimuli; they concluded that attentional processing may be more dependent on the individual's predisposition to the fear of pain.

Dey, Landrum and Oaklander (2005) claimed that pain and itch are complementary responses in that pain provokes withdrawal of the body from a threat, and itch provokes the removal of a threat from the body. Given the evolutionary parallels drawn between pain and itch (Stante, Hanna & Lotti, 2005), it is likely that an evolved threat detection mechanism would result in a similar attentional bias in both modalities (Yiend & Mathews, 2001). It is unfortunate that the contradictions in the pain literature make it difficult to predict the features of an attentional bias for itch.

6.1.3 Attention bias towards itch

Only one study has so far specifically investigated attentional bias in a clinical itch population. Fortune et al. (2003) used a modified Stroop task in which participants with psoriasis and matched healthy controls were asked to name the colour of words while ignoring the semantic content. The word list featured psoriasis-specific words (eg. 'scaling', 'bleed'), emotionally-charged words relating to the self (eg. 'stupid', 'outcast') and others (eg. 'disgust', 'whisper'), or neutral words (eg. 'rectangle', 'seating'). They found that interference was significantly stronger in psoriasis participants for disease-specific stimuli, and that these participants were able to recall more of the psoriasis-specific words than the healthy controls, which suggests that this condition garnered greater cognitive processing. They concluded that the attentional bias to disease-relevant stimuli was accounted for by the presence or absence of psoriasis, and not influenced by psychological distress (on measures of anxiety/depression). However, disease-relevant stimuli in this case does not equate to itch-focused, as only two words within the psoriasis-specific list directly referred to itching ('itching' and 'scratch') plus a few tangentially-related words (e.g. 'flaking'). So while this suggests that some form of attentional bias exists in relation to itchy skin conditions, it remains to be seen whether this will translate to a bias towards visual depictions of itch.

Attentional bias to itch images has also been found in participants with healthy skin by Van Laarhoven et al. (2017). They used three measures of attentional bias: (i) A modified Stroop task for itch-related words, similar to that used by Fortune et al. (2003). (ii) A dot-probe task for itch images whereby participants responded to the location of a probe, which either corresponded with the prior presentation of an itch or non-itch image. (iii) A somatosensory attention task whereby participants received electric itch stimulation on either their left or right hand, then responded to the location of a light appearing to the left or right of a fixation light, which was either congruent or incongruent with the stimulated hand. They found an attentional bias towards the itch stimuli for the modified Stroop and dot-probe tasks, but no significant results for the somatosensory attention task. From this they inferred that these tasks may reflect different aspects of attentional processing and concluded that overall the results show that attentional processing is relevant for itch and an attentional bias is present in the non-clinical population. However, there were clear limitations in the stimuli used in this study. The dot probe task only contained 40 trials using 10 image pairs, which were controlled for complexity and colour but not for content (the modified Stroop task used unrelated words, so it is possible the images were also unrelated). The larger and more meticulously matched stimulus set of 32 image pairs created in this thesis, allows for a more extensive and controlled investigation of attentional bias.

6.1.4 Using VEI to measure attentional bias

Visually-Evoked Itch (VEI) is a well-documented phenomenon in both healthy and clinical itch populations (Niemeier, Kupfer & Gieler, 2000; Ogden & Zoukas, 2009; Papoiu et al., 2011; Lloyd et al., 2013), whereby participants report more itches and scratch more frequently in response to itch-related images compared to non-itch images. As it is clear that these images are able to produce a sensation of itch, which can be considered a threat to the body, they are ideal for testing whether itch garners an attentional bias. Therefore, the current study utilised the VEI stimulus set outlined in Chapter 2 to investigate whether participants show an attentional bias towards the VEI-inducing itch images.

In the current study we used a reaction time based visual probe paradigm (MacLeod, Mathews, & Tata, 1986), with an arrow probe (as opposed to the dot probe used by Van Laarhoven et al., 2017), as this has the advantage of forcing participants to consider the probe directional information, rather than just note its presence (Mogg & Bradley, 1999). We also chose to combine this with eye-tracking to gain insight into covert visual attention during the task, using additional measures of the number and duration of saccadic eye-movements made to each image, and the duration and direction of the first saccade. Furthermore, we compared participants with (i) healthy skin, to (ii) chronic itch, in order to determine whether there is a link between itchy skin conditions and attentional bias towards itch images.

Using these measures, we aimed to investigate the role of visual attention in susceptibility to VEI by measuring whether itch content biases participants attention towards VEI stimuli. We did this by examining implicit and explicit attentional biases for itch and non-itch images. We predicted a bias towards itch images for clinical participants but not healthy participants, resulting in faster reaction times for probes presented congruently with the itch images and a greater number and duration of saccadic eye-movements towards itch images. The study of VEI described in Chapter 3 found that images featuring insects in contact with human skin induced the strongest itch response in healthy participants, so it was hypothesised that the same condition would draw a stronger attentional bias than images of people scratching, rashes on skin or just insects.

6.2 Methods

6.2.1 Participants

Sixty-two participants were recruited for this study and gave their informed consent to take part. Thirty-one of these were participants with healthy skin, who were recruited from the undergraduate student population at the University of Leeds. Twenty-six of these participants were female and 5 were male; they had an average age of 19 years (SD 3.5). A further thirty-two participants had self-reported mild pruritic skin conditions (see below for details) and were recruited via opportunity sampling from the general Leeds population. One clinical participant was excluded from the sample for having consistently slow reaction times (longer than 2500ms), leaving 31 participants in the final sample for this group. Twenty-five of these participants were female and 6 were male; they had an average age of 27 years (SD 10.17). All participants were right handed and had normal or corrected to normal vision with no known neurological, visual or motor deficits. Ethical approval for this study was given by the School of Psychology at the University of Leeds, reference number:15-0343 (1/12/2015).

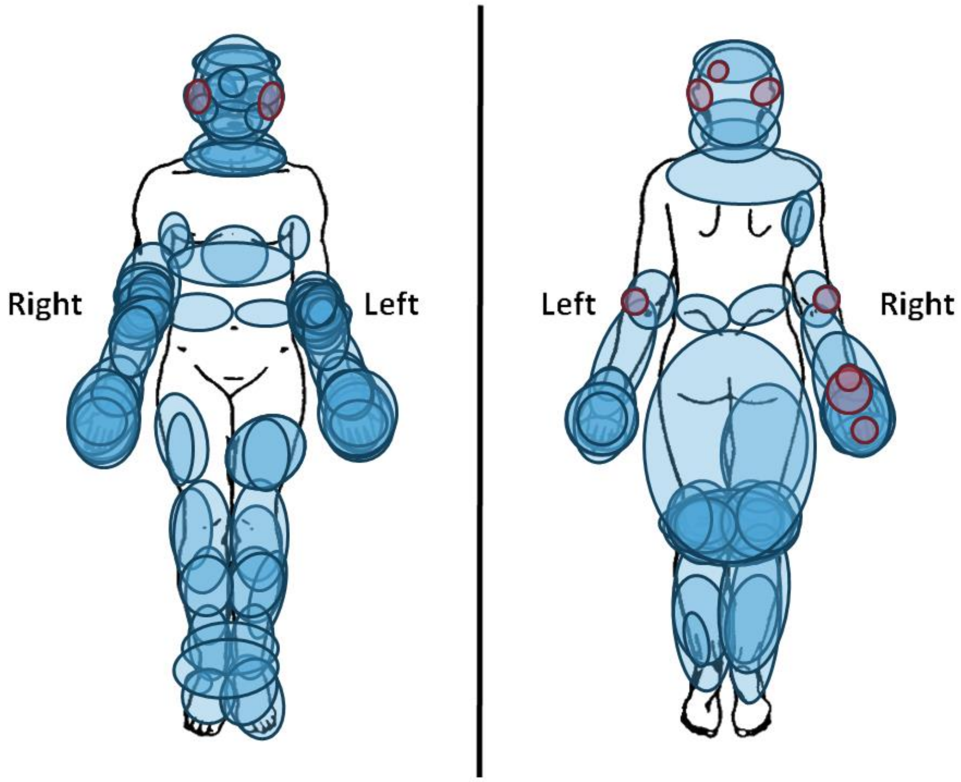


Figure 6.1 Clinical participants' affected areas.
Reported at the time of testing by drawing on a printed copy of a body outline (adapted from Melzack, 1975). Blue circles indicate participants with eczema and red circles indicate participants with all other skin conditions.

6.2.2 Clinical characteristics

The clinical group were selected on the basis of self-reported itchy skin conditions. Twenty-four had eczema, 3 had psoriasis, 1 had allergic contact dermatitis, 1 had urticaria, and 2 had unspecified forms of dermatitis. One participant was recruited as part of the healthy sample but disclosed a skin condition during testing. For this participant, their experimental data was transferred to the clinical group, but details of their condition were not collected in the same way and so are not included in the following numbers.

Fourteen participants reported having had their conditions since birth, and a further 6 since early childhood. The remaining 10 developed skin conditions in their teens or later, with 6 reporting symptoms beginning within the last 5 years and 4 having had their condition for 10-20 or years. Participants also reported on the severity of their condition in general and at the time of testing, on a scale of 1-10, with 10 being the most severe. On average, participants' ratings of their condition at the time of testing were similar to their ratings of their condition generally (4.67 (SD1.86) and 4.33 (SD 1.45) respectively). Fourteen participants reported their symptoms as more severe than usual (with a maximum of 4 points difference), 11 reported their symptoms as less severe than usual (with a maximum of 3 points difference) and 5 reported no difference in severity. Participants identified the locations of any symptoms they were currently experiencing at the time of testing, the full range of these are displayed in Figure 6.1.

6.2.3 Materials

Figure 6.2 An example of an Eyelink eye-tracker set-up as described in the materials.

Stimuli were presented using Experiment Builder (SR Research Ltd, Osgoode, Canada) on a 21″ CRT monitor in a dark room. Stimulus images and targets were 240 (height) x 320 (width) pixels, 10 degrees of visual angle from central fixation, and presented on a black background. Participants were seated 57 cm from the monitor with their heads on a forehead and chin rest to reduce head movements during the task. Eye-movements were recorded using an EyeLink 1,000Hz eye-tracker tower mount set-up, as depicted in Figure 6.2 (SR Research Ltd, Osgoode, Canada) and participants' eye-movement data were obtained using Data Viewer software (SR research, Canada). Key press to measure reaction time and accuracy responses were collected using a button box (Cedrus, Ltd.) placed in front of the participant.

6.2.4 Stimuli

Thirty-two pairs of itch and non-itch images were matched on visual characteristics including colour-range, size and arrangement (see Figure 6.3). All models were light skinned. Their positions, the angle of view and the body parts featured were matched as closely as possible. Any additional itch-relevant details were removed, facial expressions were pixelated, and a white background was added to remove context. The matched pairs were divided into four image content conditions: action (scratching/touching), response (rashes/bruises), irritant contact (insects on skin/objects on skin), and context (insects alone/visually similar objects). There were 4 additional pairs of images used for practice trials, which were not edited to the same standards.

Figure 6.3 Examples of images in each stimulus condition, presented in their matched pairs.

6.2.5 Design

A 2 x 2 x 2 x 4 within-subjects design was used. The independent variables were: Congruence of itch image and probe (congruent or incongruent), Duration of stimulus presentation (100ms or 2000ms), Sensory Condition (itch or non-itch), and Image Content (action, contact, context, or response). The Dependent variables were the behavioural reaction times (time taken ms to make a key-press response to probe onset), direction of the first saccade (towards the itch or non-itch image), speed of the first saccade (ms), number of saccades made (count), and duration of gaze within specified image regions of interest (as a percentage of trial overall trial duration).

There were 256 trials in total, split into 4 blocks of 64. Trials were presented in a random order within blocks, but each block featured the full set of 32 image pairs twice. The stimulus set comprised 8 images pairs for each of the 4 image content conditions. Thus there were 8 repetitions of each image pair in the total 256 trials. An equal proportion of shorter 100ms trials and longer 2000ms trials were randomised within each block and the location of the itch image and of the probe was counterbalanced.

Reaction time measures used both the 100ms and 2000ms trials. The eye-tracking analysis used only the 2000ms trials, as 100ms was too short for a saccadic eye movement to be made to the visual images (targets) (Fischer & Weber, 1993).

6.2.6 Procedure

At the beginning of the experiment a 9-point calibration was performed in which participants focused their gaze sequentially on a grid of 9 dots, followed by a validation of the eye position to within 0.5° of the targets. A drift correction was performed at the beginning of each block. The experiment was split into 4 experimental blocks, each lasting approximately 7 minutes, during which participants were requested to not remove their heads from the chin and forehead rest of the eye-tracker. There was also a practice block of 4 non-itch trials at the beginning of the experiment to familiarise participants with the task.

In each trial, participants began by looking at a central fixation cross, which was presented until fixation was sustained for 500ms. This was then replaced by two images which appeared either side of the cross' previous location; one itch image and one matched non-itch image. After either 100ms or 2000ms, the images were replaced by a target probe located either in place of the itch image (congruent trials) or the non-itch image (incongruent trials), which remained until a response was given by the participant. The probe image was an arrow, which pointed either up or down. Participants indicated the direction by pressing the corresponding up or down arrow on the button box. Reaction time was defined as the time between the onset of the probe and the downward press of the button, and participants were instructed to respond as quickly and accurately as possible.

Between each block, participants were given a short break with the lights turned on, and resumed the task when they felt inclined to do so. During this break (and also at the end of testing), they were asked to rate how itchy they felt on a scale of 1-10. The experimenter also recorded the number of times they scratched during the break.

6.2.7 Data analysis

Behavioural reaction times and eye-tracking data were derived automatically using DataViewer (SR research Ltd, Osgoode, Canada) and analysed using IBM SPSS Statistics 21 (SPSS Inc., Chicago, IL). Multivariate main effects and interactions among variables were evaluated with Bonferroni corrected post-hoc tests. A significance level of $p<.05$ was established for all statistical analyses.

Measures of VEI were used as a manipulation check to ensure that participants were experiencing VEI, in terms of whether scratches were observed and participants considered themselves to be feeling itchy during the experiment. These data were not sufficiently detailed for a full analysis so are presented as descriptive statistics.

Behavioural button box reaction times shorter than 250ms or longer than 1000ms were removed, as these times represent predictive/anticipatory press responses or failures to provide a reactive response respectively. The remaining reaction times were transformed into z-scores for each participant, in order to reduce the effects of differences in the overall mean reaction time between our participants and focus on the observed shift between conditions and participant groups.

The eye-movement parameters of interest included: (a) region of interest (ROI) analysis (gaze duration): how long participants spent looking at the itch or non-itch image during the trial as a percentage of overall trial length (excluding delay time), to provide an estimate of encoding time on targets, b) number of saccades into ROI, c) reaction time of the first saccade to either image d) direction of the first saccade e.g. to the itch or non-itch image.

The regions of interest (ROIs) were defined as the area within the edge boundaries of the stimulus image, with two ROIs (one for the itch image, one for the non-itch image) in each trial presentations. Single repeated-measures analysis of variance was used for all the eye-movement parameters, and the results were separated into the following factors: Sensory Condition (itch or non-itch), and Image Content (action, contact, context, or response).

Reaction times for saccades were calculated from image onset (itch and non-itch pairs) to saccade onset. Saccade onset was taken as eye velocity and acceleration exceeding 30°/s and 8000° / s-2 respectively. We then selected saccades relevant to our ROI. Saccades shorter than 100ms were excluded as these were too fast to be considered a reaction to the stimulus and may simply be anticipatory eye-movements (Fischer & Weber, 1993). As such, the first saccade was considered to be the shortest eye reaction time greater than 100ms but less than 2000ms (which would be outside of the stimulus presentation window and unlikely to reflect a true reaction to the probe). The number of fixations made on an image was measured as the number of times a saccade entered an image region and was momentarily still, within the 2000ms trials. Eye-movements within a region were not recorded separately. Gaze duration was calculated as the percentage of the overall trial duration spent looking within the boundary of each image area during the 2000ms trials.

6.3 Results and Discussion

6.3.1 Visually evoked itch

The itchiness ratings and number of scratches recorded after each block were used to establish whether participants experienced VEI effects during the study. Participants' ratings of itchiness tended to increase across the experiment for both groups, with clinical participants consistently rating their itchiness higher than healthy participants (Figure 6.4a). Scratching was observed in both groups, with the frequency increasing after blocks 2 and 3 for the clinical participants, while remaining fairly stable for the healthy participants (Figure 6.4b). These ratings and observations indicate that both groups of participants did appear to experience VEI in a way that is consistent with previous studies of the effect. Thus the results of this study can be inferred to relate to the itch inducing properties of the images used.

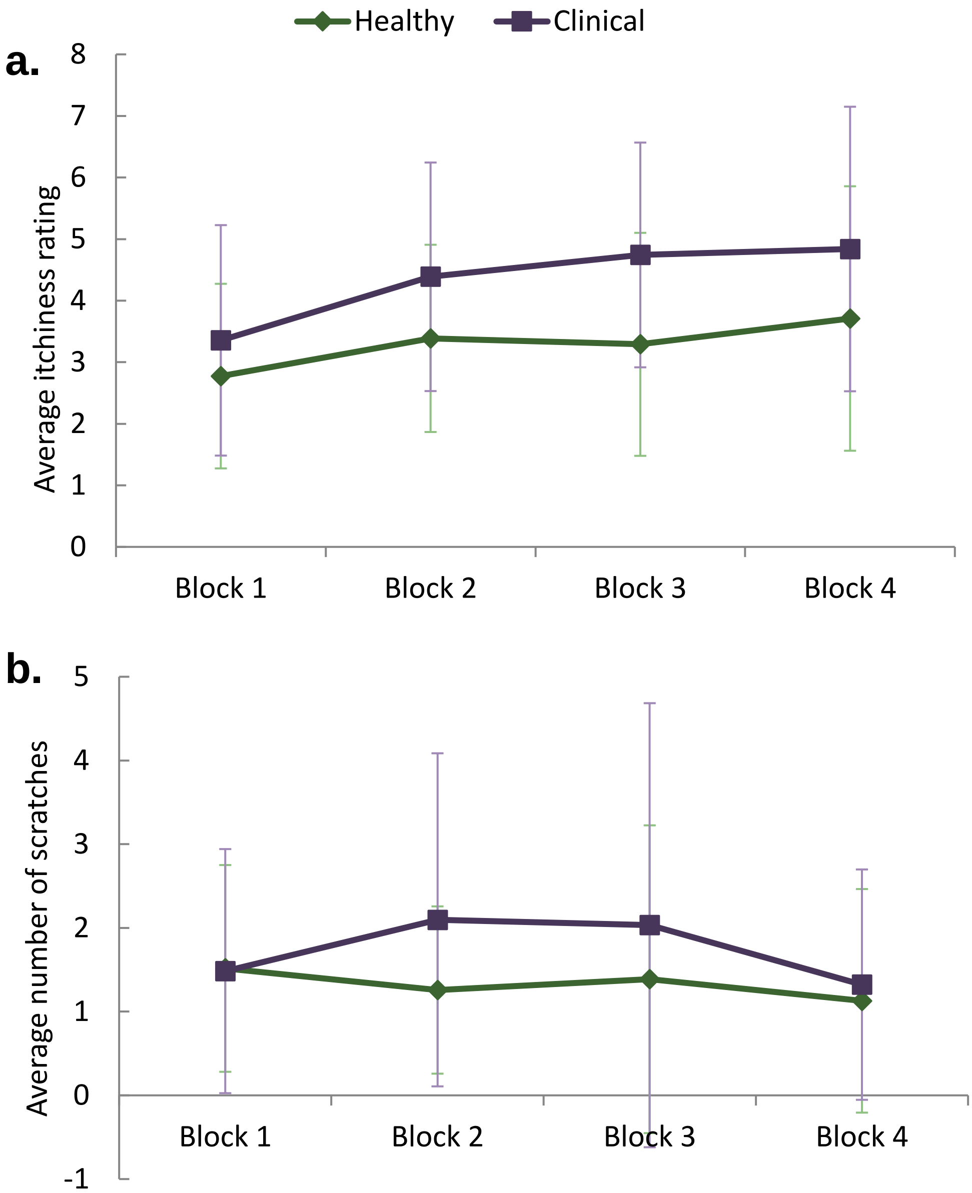


Figure 6.4 a. The average itchiness ratings for clinical and healthy participants after each block of testing. b. The average number of scratches observed in healthy and clinical participants after each block of testing.
Error bars represent standard deviation.

6.3.2 Behavioural reaction times overall

The button box reaction times for participants responding correctly to a probe in the congruent position to the itch stimulus were compared to reaction times for correct responses to a probe in the incongruent position. As expected, there was a highly significant main effect of duration, $F(1,60)= 74.828$, $p<.001$, with the 100ms trials yielding faster reaction times than the 2000ms trials, indicating a difference in timing and anticipation between the two trial types. There was no significant main effect of group $F(1,60)=0.676$, $p=.414$, which suggests that the z-score transformation successfully removed the variance due to age from between the groups. The raw scores for these analyses are shown in Table 6.1.

Table 6.1 Average raw scores with standard deviations for the implicit and explicit conditions, divided by congruence and group.

	100ms		2000ms	
	Congruent	Incongruent	Congruent	Incongruent
Clinical group				
Average	514.96	519.98	541.95	551.30
Standard deviation	72.1	71.38	69.67	73.38
Healthy group				
Average	481.66	484.10	487.98	480.98
Standard deviation	68.94	67.33	51.4	60.93

There was a significant main effect of congruence $F(1,60)= 4.181$, $p=.045$, evident at both durations, and congruence also significantly interacted with group, $F(1,60)= 8.553$, $p=.005$. Overall the clinical group had faster reaction times for the congruent trials and slower reaction times for the incongruent trials, compared to the healthy group, indicating a greater attentional bias towards the itch images. This was the case for both the 100ms trials and the 2000ms trials, showing that this bias was present at both the implicit and explicit levels. Participants were initially drawn to the itch images and, when given the chance to visually explore, their attention remained drawn to these stimuli. The healthy group show a more complex pattern of responses though. On the 100ms trials they have faster reaction times for the incongruent condition; their attention is drawn more to the non-itch images suggesting an aversive reaction to the itch content. However, on the 2000ms trials, they do not appear to show a bias in either direction; there is little difference in their reaction times for the congruent and incongruent conditions (see Figure 6.5).

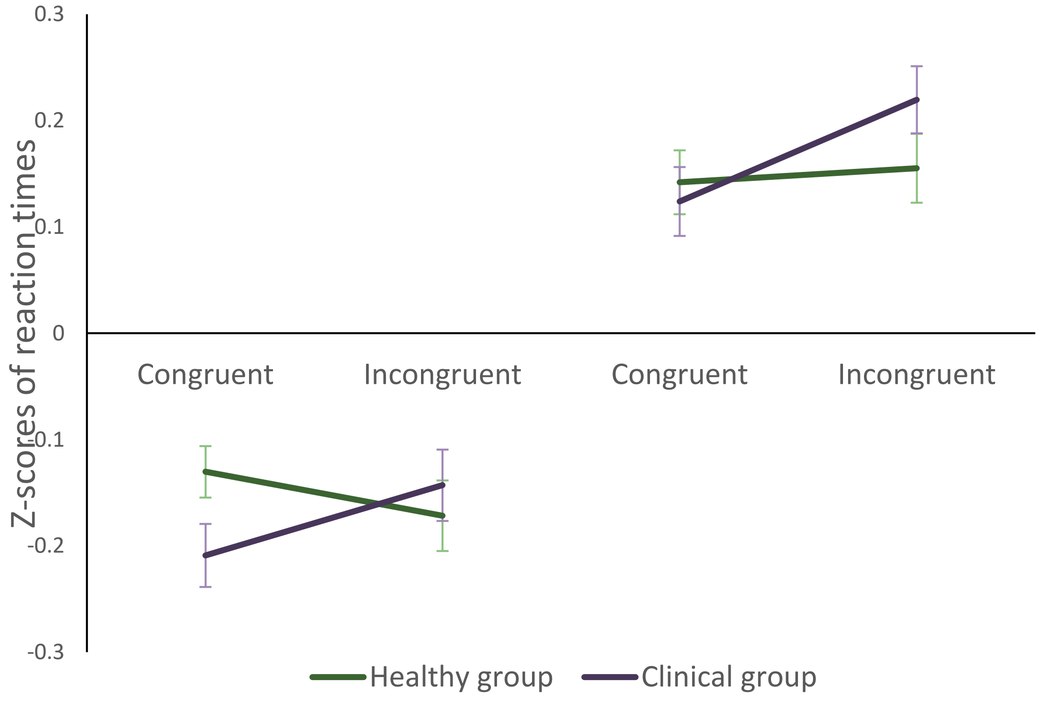


Figure 6.5 Z-scores of mean behavioural reaction times comparing the interaction of congruent and incongruent trials for the healthy and clinical groups.
The comparison for 100ms trials is presented on the left and 2000ms trials on the right. Error bars represent standard error.

It appears that participants with healthy skin and those with an itchy skin condition show opposite implicit biases, with the former group initially orienting away from the itch image content, and the latter orienting towards it. This difference in attentional bias endures at the explicit level, as while the healthy group's initial aversion diminishes to indifference, the clinical group's initial attentional focus on itch is sustained. This shows a clear distinction in the perceptual and cognitive processing of itch image content for people with and without itchy skin conditions.

Table 6.2 Average raw scores for the image content conditions, divided by congruence and group, with standard deviations in brackets.

		Contact	Context	Action	Response
Clinical group	Congruent	549.02 (75.66)	546.64 (69.91)	537.17 (75.97)	534.74 (65.72)
	Incongruent	558.18 (71.06)	553.50 (72.15)	544.02 (75.68)	549.62 (83.01)
Healthy group	Congruent	493.06 (69.97)	499.80 (66.65)	498.39 (70.42)	485.43 (68.43)
	Incongruent	495.36 (67.5)	498.95 (69.76)	499.68 (69.73)	486.86 (66.42)

6.3.3 Behavioural reaction times by content

The behavioural reaction time results were subdivided into image content conditions to examine whether different kinds of itch image attract visual attention differently. Figure 6.6 shows the z-scores of the reaction times for each of the content conditions: contact (insects on skin), context (insects), action (scratching), and response (rashes), comparing congruence and group for each. The raw scores for these analyses are shown in Table 6.2.

The results show a highly significant main effect of content, $F(3,180)=9.675$, $p<.001$, indicating that the type of itch scenario depicted in the images affects attentional bias. Pairwise comparisons revealed that this effect is driven by the response condition differing significantly from all others ($p<.001$ for contact and action, and $p<.01$ for context). This overall difference may be a result of both healthy and clinical groups performing faster on these trials, rather than differing as they do on others. Response is the only condition which depicts direct damage to the skin in both the itch and non-itch conditions, in the form of rashes/skin irritation and bruises. It may be the case that this aspect of threat is attention grabbing in all cases. However, itch is still a relevant aspect, as the healthy group show little difference between congruent and incongruent trials, indicating that they are equally drawn to these depictions of harm, regardless of what form it takes. Clinical participants on the other hand still show a bias towards the itch-based harm over the pain-based harm (bruises), implying that the clinically relevant form of harm is more attention grabbing for them in particular.

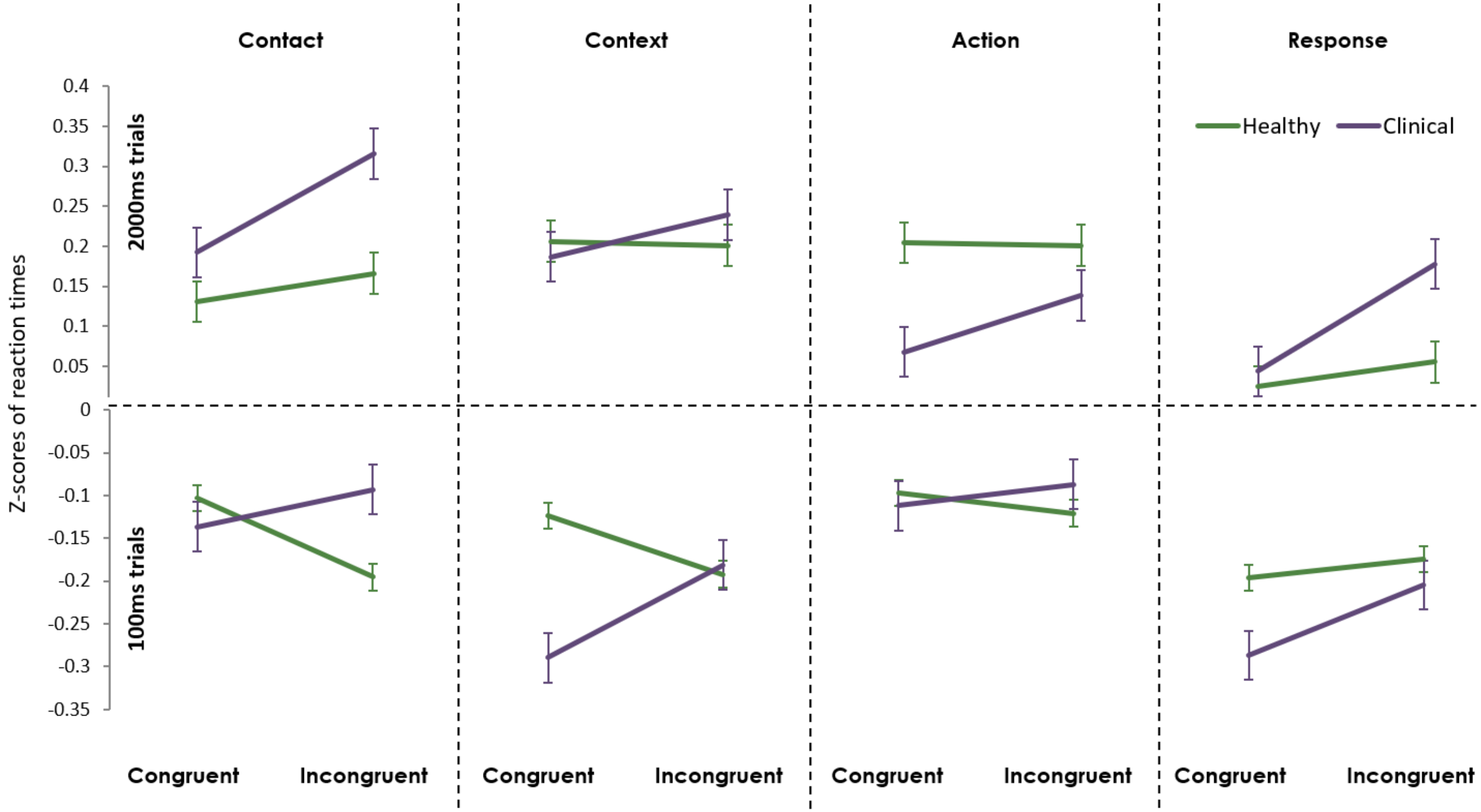
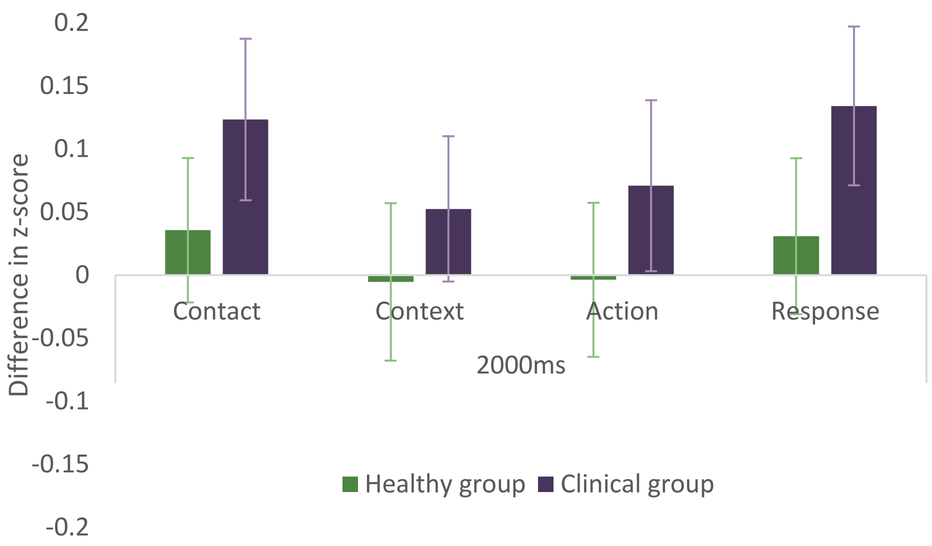


Figure 6.6 Z-scores of mean behavioural reaction times comparing the interaction of congruent and incongruent trials, for the healthy and clinical groups.

Comparisons are displayed for each of the four image content conditions: contact, context, action, and response. The results for 2000ms trials are displayed above the x-axis and the results for 100ms trials are displayed below the x-axis. Error bars represent standard error.

a.



b.

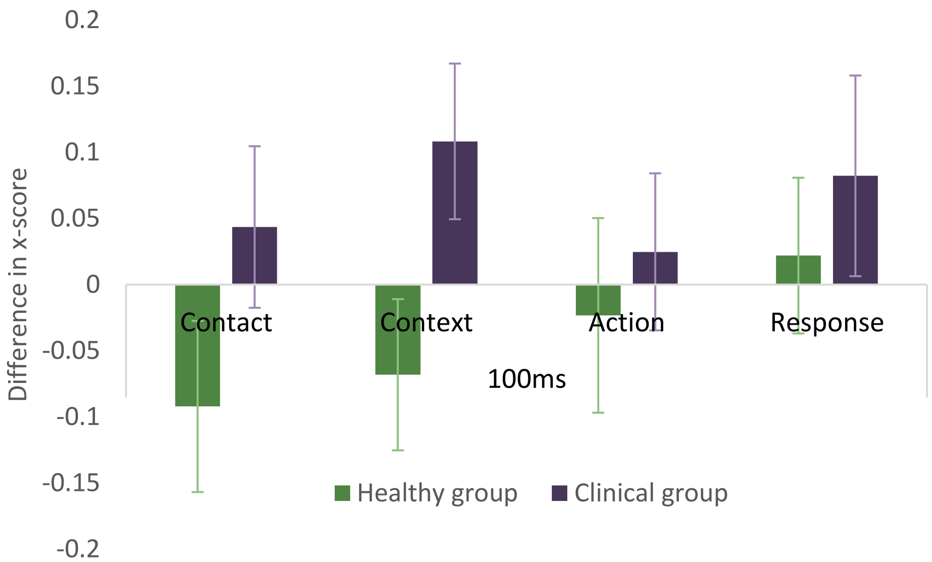


Figure 6.7 The difference in Z-scores of mean behavioural reaction times, comparing the congruency effects between image content conditions, (incongruent - congruent). Results are presented separately for a. 2000ms trials and b. 100ms trials.
Positive values represent an attentional bias towards itch images and negative values represent an attentional bias towards non-itch images. Error bars represent standard error.

Image content also interacted with other conditions. There was a significant interaction with trial duration, $F(3,180)= 3.618$, $p=.014$, which reveals that the image content has differing effects on implicit and explicit attention. For action and contact (scratching and insects on skin, respectively) the ability to process the images in the 2000ms trials lead to a stronger bias than on the 100ms trials for the clinical group, whereas for context (insects) this additional processing diminished the bias. There was also a significant interaction with group, F(3,180)=2.913, p.036. These interaction results reflect different influences on healthy and clinical participants' patterns of initial and subsequent allocation of attention. Response (rashes), for example, appears to be attention grabbing in an immediate instinctive way, whereas action (scratching) and contact (insects on skin) require some cognitive processing of cause and effect to perceive the threatening aspect in an itch context, so they attract attention differently at the implicit and explicit levels for the different groups. Congruence and content did not significantly interact, F(3,180)= 0.609, p=.61 (n.s.), as can be seen more clearly in figure 6.7. This appears to be due to the presence or absence of attentional biases being fairly consistent within groups and trial durations. This suggests that although the results differed between image content conditions this was a product of how the groups responded differently at different time points rather than an overall difference in the congruency effect between conditions.

6.3.4 Initial saccadic eye movement

The direction of the first saccade provides evidence of where participants' attention is initially drawn; either the itch or the non-itch image. There appear to be only small differences for which stimuli were oriented to first, as displayed in Figure 6.7. For action and response, there was a slight preference for the itch image in both groups. The healthy group also showed a slight preference for non-itch in the context condition and the clinical group showed a slight preference for non-itch in the contact condition. These findings are unexpected, given that clinical participants showed a clear implicit bias in behavioural reaction times towards the itch stimuli for contact and context. It seems that at 100ms their attention is drawn towards the itch images, but after that their first eye movement is often drawn to the non-itch image. Table 6.3 shows the number of first saccades in each direction along with the average reaction time of the eye movements: There were no significant differences between the clinical and healthy groups, F(1,60)=0.02, p=.887 (n.s.).

Table 6.3 The average eye reaction time (ms) for the first saccades in each trial to either the itch or non-itch image.

	Healthy group		Clinical group	
	Itch image	Non-itch image	Itch image	Non-itch image
Contact	349.27 (153.62)	347.9 (154.12)	339.94 (163.35)	332.23 (151.55)
Context	360.37 (159.92)	353.33 (137.79)	378.49 (228.9)	345.81 (184.61)
Action	332.92 (145.23)	343.72 (123.22)	327.32 (142.64)	333.84 (154.18)
Response	360.79 (158.46)	360.14 (143.37)	346.82 (187.62)	361.85 (169.69)

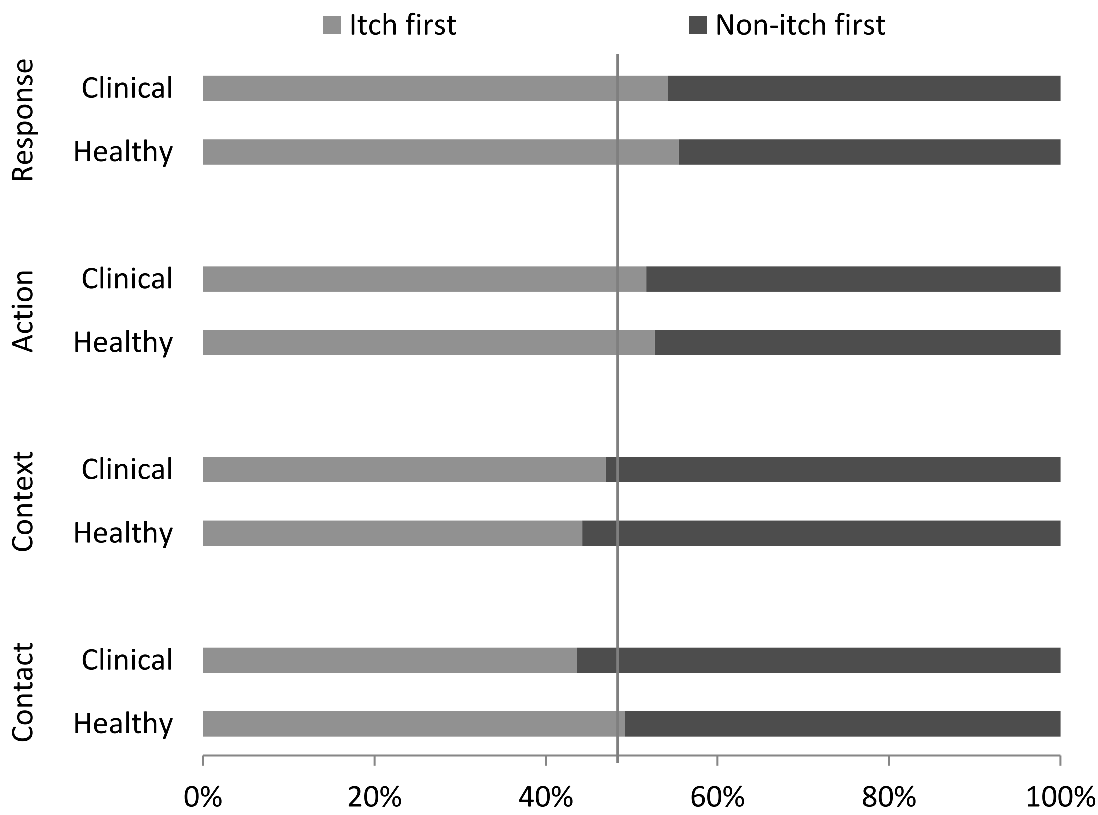


Figure 6.8 The percentage of trials in which the first saccades were made to the itch and non-itch images, displayed by content condition and comparing healthy and clinical participants.

6.3.5 Number of fixations

The number of fixations on each image serves as a measure of where participants' visual attention was drawn to most frequently. The number of fixations is depicted in Figure 6.8 as the difference between the average number of itch and non-itch fixations.

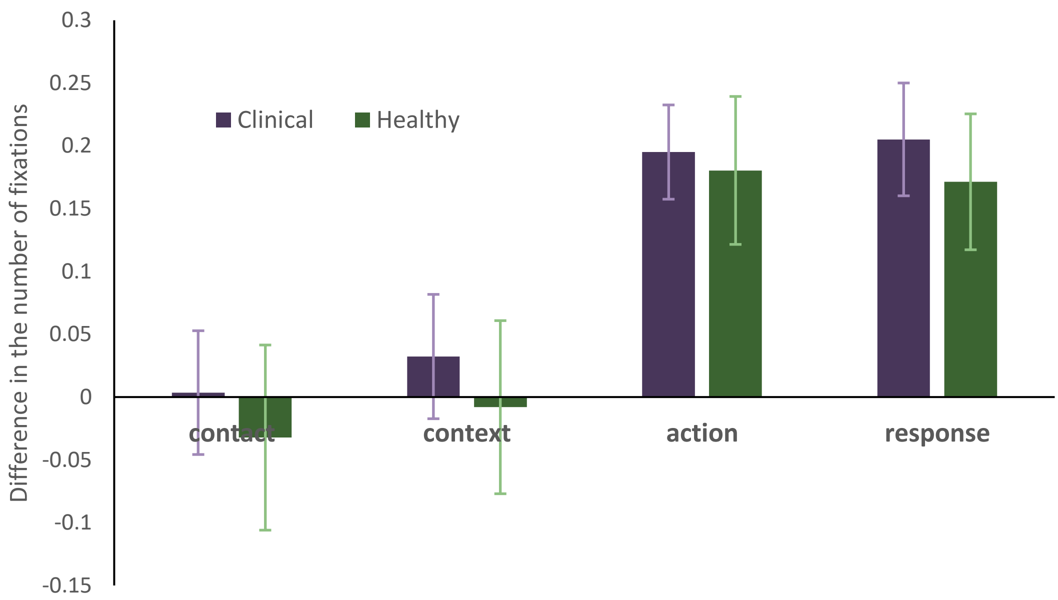


Figure 6.9 The difference between the number of fixations (during the image presentations) to itch and non-itch images made by each group, comparing image content conditions.
Positive values indicate more fixations on the itch stimuli and negative values indicate more fixations on the non-itch stimuli. Error bars represent standard error.

There was a highly significant main effect of group, $F(1,60)=22.308$, $p<.001$, with clinical participants making more fixations on the itch images than healthy participants, as expected. This reflects the attentional biases found in the behavioural reaction time results. There was also a significant main effect of sensory condition, $F(1,60)=4.788$, $p=.033$, with more fixations on the itch images overall. This suggests that even though healthy participants did not show an overt attentional bias, they were still drawn to itch content to some degree. The differences between the types of itch stimuli had a strong influence on image content, $F(3,180)= 4.880$, $p=.003$, and a highly significant interaction between the sensory and content conditions was found, $F(3,180)= 7.019$, $p<0.001$. It is clear that the action (scratching) and response (rashes) conditions drew more of a bias for fixating on the itch images than the non-itch images for both groups. These conditions both depict damage to the body more clearly than the others, which correspond with the focus on the response condition found in the behavioural reaction times.

6.3.6 Duration of gaze

Complementary to the fixation count, the gaze duration measure indicates which images held participants attention for longest. This is depicted in Figure 6.9 as the difference between the average gaze durations for itch and non-itch images.

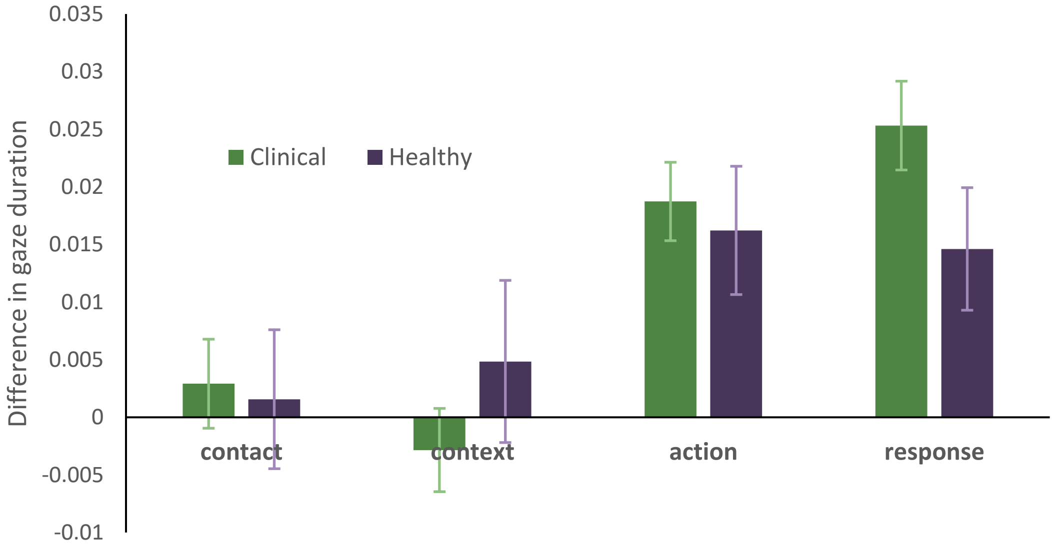


Figure 6.10 The difference between the average gaze duration (as a percentage of overall image presentation duration) to itch and non-itch images for each group.
Data is split into image content conditions for comparisons. Positive values indicate longer gaze duration on the itch images and negative values indicate longer gaze duration on the non-itch images. Error bars represent standard error.

There was also a significant main effect of group, $F(1,60)=11.913$, $p<.001$, with the clinical group spending more time looking at itch images than the healthy group, which reflects their attentional bias in reaction times. There was also a significant main effect of sensory condition, $F(1,60)=6.674$, $p=.012$, and a highly significant interaction between sensory condition and content condition, $F(3,180)=7.840$, $p<.001$. This indicates that the itch images were looked at for longer overall and particularly in the action and response conditions, although the main effect of content itself was not significant, $F(3,180)=1.953$, $p=.123$ (n.s.). Again, the conditions that feature skin damage by scratching or rashes seem to attract more attention for the clinical participants.

The results show a similar pattern to those found in the number of fixations, with some interesting differences that indicate that longer gaze duration for itch images is not simply a product of making more saccades to those images. Gaze duration produced a larger difference between the healthy and clinical participants than the fixation count did for the action and response conditions (scratching and rashes). This indicates that the individual fixations made on the itch images lasted longer than those made on the non-itch images, suggesting greater processing of itch images. Additionally, a different pattern of trends emerged for the contact (insects on skin) and context (insects) conditions. Healthy participants spent longer looking at the itch images, but made more saccades towards the non-itch images in the contact condition. Conversely, the clinical participants spent longer looking at the non-itch images, but made more saccades towards the itch images in the context condition.

6.4 General Discussion

Attentional bias for itch images is evident in both behavioural and eye-tracking measures. The behavioural results reveal that clinical and healthy participants had opposite implicit reactions: clinical participants oriented towards itch images, and healthy participants oriented away. Their explicit reactions also differed as clinical participants' attention remained with the itch images, whereas healthy participants showed no explicit bias. These differences clearly indicate that having an itchy skin condition alters how visual attention is allocated to itch and non-itch images.

These biases were affected by the image contents, most notably in terms of the response condition. For the response images, healthy participants were equally drawn to the bodily harm depicted by rashes (itch) and bruises (non-itch), whereas clinical participants were specifically biased towards the itch-relevant form of harm. The eye-tracking results supported the notion of action and response images drawing the strongest attentional bias as these conditions produced a greater number of fixations and a larger percentage of time spent looking at the itch image. It is likely that the damage to the body depicted in these images of scratching and rashes is driving the effect.

6.4.1 Visually-evoked itch and the itch-scratch cycle

The images used in this study have been previously shown to induce VEI, although interestingly, their saliency as VEI inducers did not turn out to be the most attention-grabbing aspect. Regardless, the results can still illuminate components of the mechanism behind VEI. In this study, contact images featuring insects on skin have been shown to produce the strongest VEI effects. Clinical participants' explicit bias towards itch in this condition is notably greater than their implicit bias. This may be because VEI requires cognitive processing to take effect; thus, while contact is not particularly attention grabbing at the implicit level, once processed it garners a stronger attentional bias, possibly due to its potency as an itch inducer.

It has been suggested throughout this thesis that VEI may act as a pathway into the itch-scratch cycle, but this process is likely to be modulated by the individual response to the itch inducer in question. While sustained attention to an itch inducer can produce an itch effect via VEI, there seems to be no instinctive drive within healthy participants to provide the necessary attention unless prompted. At the implicit level they even show an aversive reaction (or inhibitory drive) to divert attention away from these images. It is possible that this acts as a gating system, inhibiting their susceptibility to VEI in their everyday lives, and thus protecting against accessing the itch-scratch cycle in this way. Clinical participants, however, appear to be drawn to itch inducers at both the implicit and explicit levels, which means they are liable to experience greater exposure to itch triggers, therefore increasing the likelihood of entry to the itch-scratch cycle via VEI effects. Attentional biases may be a crucial factor in whether a person is drawn into the itch-scratch cycle by the presence of an itch inducer.

6.4.2 Comparison of findings with previous studies

Although there are few studies directly investigating visual attention to itch, our findings are in keeping with those from other fields. Healthy participants rarely show a reliable attentional bias on the dot-probe tasks in other modalities according to Schmukle (2005), so a lack of bias in the healthy population is consistent with the wider literature in this sense. In addition, the interpretation of the differences between healthy and clinical participants' reaction times mirrors the inferences made by Yiend and Mathews (2001) on the subject of attentional bias to threatening words. They suggested that people prone to anxiety may become more vigilant, adopting a "checking mode" (p.680) which results in a bias. Whereas for people who do not have anxiety, the same event is likely to provoke either indifference or active avoidance. This similarity implies that the pattern of clinical participants displaying an attentional bias towards clinically-relevant stimuli while healthy controls have either an aversive or neutral response is not specific to itch, but may reflect a more general pattern in clinical-based attentional biases.

The results also correspond with those of Fortune et al. (2003), as it is disease-relevant stimuli that produce the attentional bias in the clinical group, thus providing evidence that this effect is robust across different methodologies. Fortune et al.'s interpretation of their results suggested that attentional bias is cognitively driven as a product of personal knowledge and experience of psoriasis and that this then leads to maintenance of a distress response. Our findings regarding faster reaction times for the response condition in both groups implies that vigilance towards threat was relevant for both, rather than just being a product of disease anxiety. Following this, it seems likely that this is actually a general mechanism that is individually calibrated based upon a personal interpretation of harm and threat. Fortune et al. (2003) also speculated that automatic processing may play a greater role than intentional allocation of attention in psoriasis: in other words, that the implicit bias may be more influential than the explicit bias. This seems unlikely in light of our findings, as the implicit and explicit biases show a similar trend. They may both play a symbiotic role in orienting and sustaining focus on itch content.

6.4.3 Comparison with the findings of Van Laarhoven et al. (2017)

Van Laarhoven et al.'s (2017) used the most directly comparable methodology to the current study, yet they came to very different conclusions. They found an attentional bias towards itch images in healthy participants using a similar visual-probe method, as well an attentional bias on a modified Stroop task, but not on a somatosensory attention task. This directly contradicts with what we found in our healthy participants, although there are a few differences in the methods that may potentially account for this discrepancy. Firstly, they used a trial duration of 500ms, which is slightly too long to measure an implicit bias, but also rather short to capture an explicit bias as it does not allow time for much exploration of the images. This makes it hard to directly compare to either the 100ms trials or the 2000ms trials used in this study, so they could arguably be describing a different stage in the allocation of attention. There may also have been a greater difference in the visual saliency of their itch and non-itch images (which were not matched as closely as those used in this study) that could have influenced the results.

The second noteworthy difference is the method used to analyse the reaction time data. Instead of comparing congruent and incongruent conditions directly, they used a 2x2 ANOVA with itch image position and probe position as independent variables. They found an attentional bias by way of a significant interaction between these. Given the counterbalancing between image and probe positions, it would be entirely possible to collapse those four averages into congruent and incongruent overall. Doing this would appear to result in smaller differences between those averages (around 10ms) and thus less of an attentional bias. To verify this assumption we generated a hypothetical model of their dataset with the same number of participants, averages and standard deviations, but analysed in congruent vs. incongruent format (see appendix B). This modelled data resulted in no significant differences ($p=.253$). While it is not possible to comment on their actual data, this strongly suggests that the findings might not be so different if the analyses were conducted in the same way as reported here.

The third possibility is that the non-random task order allowed for interference from previous tasks. The dot-probe and modified Stroop tasks were always administered after the somatosensory attention task. This task, unlike the other two, involved the direct physical induction of itch sensations. Experiencing this just prior to performing the dot-probe task may have primed the participants to become attuned to itch and vigilant to potential sources of itch. In short, they may have become temporarily predisposed to respond in a similar way to people who have chronic itch conditions. Interestingly, the somatosensory attention task itself revealed no overall attentional bias, and the only significant trend was slower reaction times for congruent stimuli in half of the data. So it appears that on the first task Van Laarhoven et al.'s (2017) participants undertook, the outcomes were quite similar to the lack of attentional bias/aversion found for healthy participants in our study. It was only after exposure to itch sensations that the attentional bias towards itch emerged. It is unfortunate that they were not able to fully counterbalance the task order to control for this, but it also opens a gap in the literature for direct investigation of whether healthy participants can be deliberately primed to display a visual attentional bias towards itch by manipulating their sensory experiences of itch. Most chronic itch conditions come in transient outbreaks of fluctuating severity (Schmied & Saurat, 1991), so this may in fact provide a model for how chronic itch affects perception and cognition, as it is possible that attentional bias is modulated as a function of recent itch experiences.

6.4.4 Limitations

The parallels between itch and pain are clear; however, itch images do not provide a direct itch equivalent to pain-related stimuli, as images depicting pain and painful experiences do not create the experience of pain in the same way that VEI creates itches (Vandenbroucke et al., 2013). This renders comparisons with the outcomes of pain studies, even those that use visual images in a similar way, difficult to determine. Due to this unique property of itch images, itch requires further specific study to verify the effects found in this experiment.

It should also be noted that the interpretation of threat detection driving attentional biases is not unanimously agreed upon. Koster et al. (2004) have argued that instead of vigilance towards threat, responses in visual-probe tasks may actually reflect difficulty to disengage from threat. They do concede, however, that a bias found on short stimulus presentations (less than 500ms, thus as found our implicit 100ms trials) may reflect a facilitated response to threat an early stage of information processing.

A further potential issue was that the clinical group was somewhat more socially diverse than the healthy group, as they were recruited from the general university population, whereas the healthy group were mostly psychology undergraduates. This most notably affected the age ranges of the groups, which was a potential issue as reaction times generally decline with age (although this effect is most pronounced after age 45) (Houx & Jolles, 1993). The raw reaction time data did indeed show that the clinical group were slower overall. However, to mitigate this we employed z-scores instead of raw reaction times. Thus, the potential confounds resulting from age differences have been adequately controlled for in our study.

6.4.5 Implications for clinical itch

Yiend and Mathews (2001) have argued that while attentional bias to threat is an adaptive mechanism for detecting and avoiding danger, it becomes maladaptive when attuned to suggestions of threat from words or images (which do not contain actual danger). This misapplied threat detection needlessly diverts attentional resources and interrupts other tasks and processes. In this sense, any attentional bias in clinical populations is wasting resources and interfering with other processing unnecessarily, even if only to a minor extent. It could thus be considered a cognitive symptom of having a chronic itch condition, which would justify a desire to modify it.

Healthy participants' initial aversive reaction to itch stimuli diminishes upon consideration of the threat, whereas clinical participants' initial attraction endures. This suggests that there may be an attentional filtering (inhibitory) mechanism, which allows healthy participants to disregard the stimuli as not a salient or realistic threat, and is suppressed or faulty in participants with chronic itch. While it is difficult to infer a causal relationship, it is plausible that this lack of a filter could be exacerbating clinical participants' conditions by compelling them to focus excessively on itch and thus on their symptoms. If this is the case, then interventions which focus on redirecting attention and thus encouraging patients to disregard itch threats, may be a useful approach for clinicians to adopt.

There is evidence that attentional biases can be manipulated or reduced by interventions. Browning et al. (2012) managed to reduce the chances of depression recurring using attentional bias modification to counteract a bias towards negative facial expressions. In terms of threat detection, Dandeneau et al. (2007) showed that stress responses could be reduced after altering participants' attentional focus by changing their vigilance and response to threat. Unfortunately, Mogoase and Koste (2014) concluded from their meta-analysis that the therapeutic benefits of attentional bias modification are limited, and that further development of the method is needed before it can become a useful clinical tool. However, See, MacLeod and Bridle (2009) and others have had success in reducing anxiety by means of an attentional probe training procedure, which participants completed at home via the internet. This indicates that a practical method for applying a behavioural modification regime may become an accessible option for dermatologists if one were to be developed and fully validated.

6.5 Conclusions

This study has demonstrated that an attentional bias for itch images does exist in participants with pruritic skin conditions, but not in participants with healthy skin. Clinical participants displayed both implicit and explicit attentional biases towards itch images, indicating that they are initially drawn to itch content prior to cognitive processing and that they sustain this focus on itch when given time to explore and process the image. Healthy participants, on the other hand, displayed an aversive implicit bias as they initially orient away from itch content. This aversion faded to a neutral indifference when the image was cognitively processed, resulting in no explicit attentional bias.

These effects appear to be heavily influenced by the presence or suggestion of skin damage in the images, as participants responded more quickly to images of rashes than other image contents. Eye-tracking results support this idea of skin damage as a driving factor, as participants in both groups tended to look at the itch stimulus first, look at it more often, and look at it for longer, when these images featured people scratching or rashes on skin. This focus on harm to the body is not a tangentially related general bias; it manifests in a specific itch-harm bias in clinical participants. The clinical group show a strong attentional bias for pictures of rashes over pictures of bruises, whereas healthy participants are drawn to the two forms of skin damage to an equal extent.

It appears to be a chicken and egg scenario as to whether having an inclination to orient towards possible itch-triggers predisposes people to chronic itch, or whether the experience of living with a skin condition primes them to focus on itch threat. The attentional biases found in our results are clearly linked to clinical experiences. However, if these individuals are attending more to things in their environment that can trigger itch through VEI, then this may be exacerbating their symptoms through a feedback loop leading them back into the itch-scratch cycle. Attentional bias modification techniques have not yet been applied to chronic itch, so there is potential for the development of a clinical intervention to combat these issues in the future.

Chapter 7 : Discussion

7.1 Key findings from experimental chapters

The experiments described in the previous chapters used VEI to elucidate how viewing itch images can alter the sensory experience of itch, but more specifically, to examine the mechanisms underlying this effect. They were intended to develop an account of the processes that lead from inducer to itch to scratch based on a synthesis with the existing literature and current theories. The methodology and four main studies have contributed the following new knowledge about these processes.

7.1.1 Development of stimuli and methods

Chapter 2 laid the foundations for the experimental chapters. It presented a newly designed stimulus set, which was controlled in greater detail and balanced across more conditions than those used in previous studies. A survey confirmed that the itch and non-itch image pairs were well-matched in terms of being visually stimulating. This development process may be used to inform the creation of stimuli in future studies of contagious itch by focusing on the level of detail in matching the images and covering the variety of content.

The thematic analysis of the most evocative image content further shows which elements in this content have the greatest influence. It also demonstrates the replicability of the basic effect of VEI across different populations of the general public outside of the more commonly studied university environment.

This chapter also outlined the version of the VEI paradigm used in the subsequent four experimental chapters. This paradigm has proved replicable across different experimental set-ups, indicating that the set of timings and parameters selected are able to consistently produce a VEI effect. Therefore, this method may be useful for other researchers to use as a reference point when designing studies which involve VEI in a similar way.

7.1.2 The relationship between itch and scratch

Chapter 3 provided the groundwork for the thesis overall, beginning with a direct investigation of the basic VEI effect. This served as a means to test both the new stimulus set and the implementation of the paradigm, to ensure replicability of the effect as described in previous work (Lloyd et al., 2013; Niemeier et al., 2000; Ogden & Zoukas, 2009; Schut et al., 2015). Instead of a straightforward replication, this study also extended the method by adding a new measure of participants’ reported itches and their locations.

The results showed that the effect does indeed replicate, with depictions of insects in contact with the skin inducing VEI the strongest. Furthermore, this experiment was able to uncover the links between the three measures used. Scratch locations do not relate to the stimulus content, but itch locations do. However, participants reported far more itches than there were scratches observed so not all of these itches lead to a scratch, which is a crucial component in understanding VEI that had not previously been evident. An analysis of the patterns of itches and scratches across multiple trials revealed that VEI is not a direct response to an individual itch image but is instead an ongoing process of manipulating the propensity to itch and scratch.

Previous studies had been unable to identify how itch and scratch are connected in terms of VEI outcomes, as this connection was not apparent in the measures used. Adding an itch location measure and performing a pattern analysis on itch and scratch locations bridges these gaps and adds a new dimension to the understanding of the relationship between itch inducers, itches and scratches, and elucidates how an itch develops across time. It highlights the importance of measuring each distinct component of VEI to garner a complete understanding of the effect.

7.1.3 The visual element of VEI

Chapter 4 focused on distinguishing the visual components of VEI from other contagious itch cues. It did this by paring down the itch inducing aspects of the experiment to solely the image contents, without any priming from the wording and questions used, which has been present in all other studies of VEI. Thus, it is the first study to measure itch that is purely visually-evoked.

The results showed that participants who were asked about their itch experience scratched more, but those who were asked neutral, non-itch-related questions still scratched, indicating that the questions used to measure the effect also influence the effect. The influence of the itch questions is a form of nocebo itch induction, supplementary to the visual element of VEI. This suggests that the process of questioning one's itch state encourages discovery of the sensation in question, a process that can be characterised as an interoceptive body scan, which is a new mechanism to add to theories of how VEI occurs.

It is valuable to know that VEI is able to function purely as a visual effect and does not require reinforcement from other modalities. This also points to a possible disparity between VEI in an experimental setting and how it is experienced in a real-world setting, as the more natural experience of viewing itch without being questioned has not previously been considered. Furthermore, it highlights the importance of considering the wording and methodology in VEI experiments as the effects found are likely to be a combination of visual stimuli and other forms of priming.

7.1.4 Changes in tactile sensitivity during VEI

Chapter 5 made the first attempt to investigate VEI in terms of psychophysics by combing the basic VEI paradigm with the SSDT. This allowed us to investigate changes in perceptual sensitivity with precise external measurements rather than the more common subjective self-report measures.

The key findings were that VEI corresponds with a slight lowering of the response criterion and a change in overall perceptual thresholds. This new evidence points towards bodily attention being involved in the creation of VEI. Itch images seem to shift attention from being focused on the tactile stimulus to being distributed across the body to allow for hypervigilance to somatosensory signals. This in turn supports the notion that VEI prompts people to do a body scan for potential itch sensations. The slight change in criterion suggests participants might be overinterpreting the ambiguous somatosensory signals that they then find, implying that itches could be overinterpreted in a similar manner.

These findings contradict behaviourally-based explanations, as it is now clear that participants are not just scratching more during VEI, but that actual changes occur in their perception of sensations on the skin. Instead, they point towards a different view of VEI, with a scan for potential sensations and a change in how sensations are interpreted to create the perception of itch.

7.1.5 Attentional bias in chronic itch and healthy participants

Chapter 6 addressed the role of visual attention in moderating exposure to itch cues. It is one of only a few studies to investigate attentional bias in itch and the first to combine behavioural reaction times with eye tracking measures. It is also the only study which separated out implicit and explicit as distinct attentional biases with different effects.

It provides a direct comparison of how participants with chronic itch and healthy skin process itch images and presents evidence that contradicts previous findings (Van Laarhoven et al., 2017). Clinical participants show both implicit and explicit attentional biases towards itch images, but healthy participants showed an aversive implicit attentional bias and no explicit attentional bias. This study was also the first to link attentional bias to specific itch content and found that participants show a greater attentional bias towards images depicting damage to the skin.

These findings suggest that clinical participants may also be attending to more itch-inducing images in the real world, thus giving them more exposure to VEI. This new explanation of how chronic itch can be exacerbated by itch images would account for the psychological aspects of remaining trapped in the itch-scratch cycle. It also hints towards the possibility of attentional bias modification being developed into a novel intervention in chronic itch.

7.2 The Threshold Model of VEI

By synthesizing the new information from the experimental chapters into the existing literature outlined in Chapter 1, a model for the processes that enable visual perception of an itch trigger to construct an itch sensation has been developed. The 'Threshold Model' proposes that entering into the itch-scratch cycle via VEI consists of perceptual thresholds using input from attentional and interoceptive processes and modulated by threat detection systems. These mechanisms are discussed in greater detail in sections 7.3 to 7.6. The basis of this model is that itch is an interpreted experience; VEI provides the context which informs and manipulates the interpretation. Figure 7.1 outlines the model in full, with the components described below.

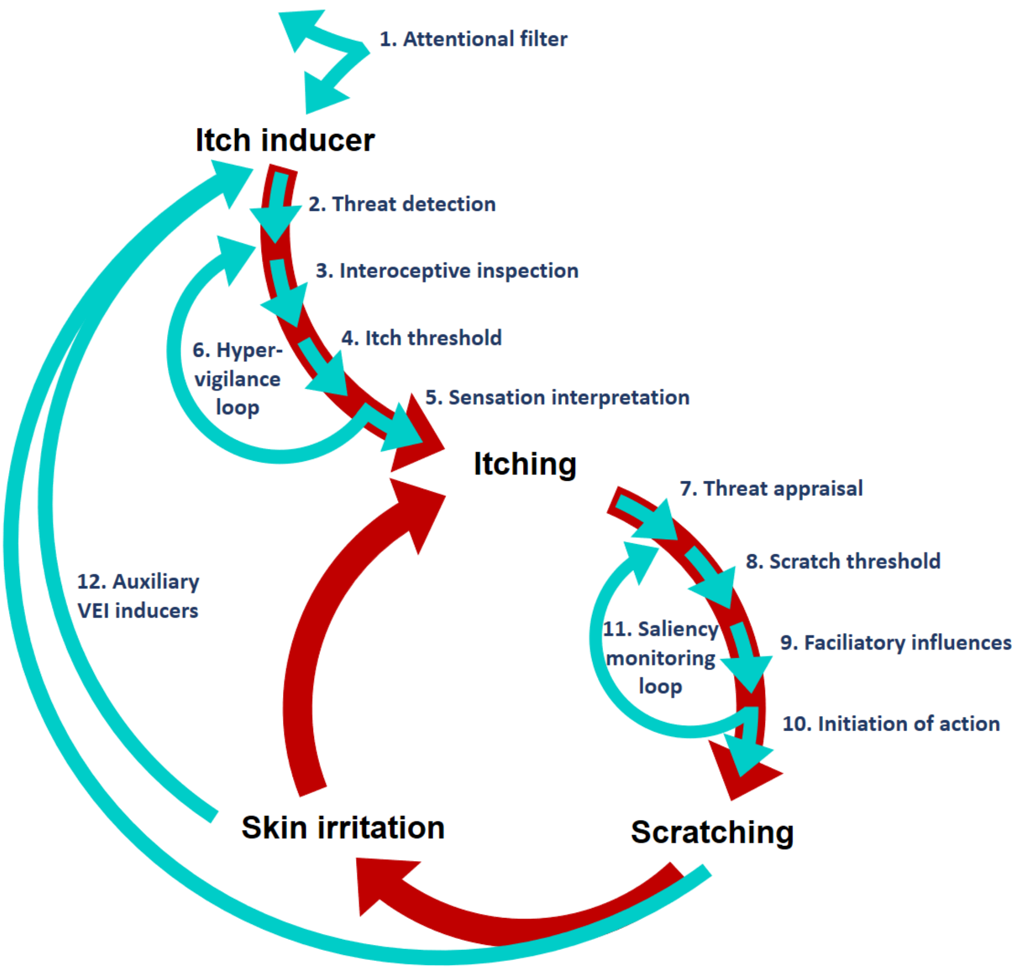


Figure 7.1 The Threshold Model of psychologically-induced itch in terms of the itch-scratch cycle.
Red arrows depict the original view of the cycle, amalgamated from previous literature, with the psychological inducer leading into the cycle and physical causes perpetuating it. Teal arrows depict the newly proposed psychological cycle of the model.

1. Attentional filter

The first element of the model is an attentional filter that activates upon exposure to a psychological itch inducer. When an inducer is perceived, the initial response is to either allot visual attention to it or ignore it; therefore, it follows that there must be an attentional filtering system leading either towards the itch inducer or away from it, that determines this initial reaction.

2. Threat detection

Threat detection is proposed as the next stage in the process. Once an inducer is attended to, its saliency is assessed in terms of how threatening it may be to the body. Itch is an inherently threatening experience as it evolved to remove harmful irritants from the skin (Dey et al., 2005; Olek-Hrab et al., 2016; Stante et al., 2005). With this evolutionary drive in play, a stimulus that carries the suggestion (in any modality) of an itch-threat being present initiates procedures for assessing the threat level.

3. Interoceptive inspection

Once threat detection is engaged, the next logical step is to interpret whether the inducer is a potential threat or an active one: It is necessary to determine what sensations are present on the skin. An interoceptive body-scan inspection is carried out to search for evidence of whether the threat is currently present. Bodily attention is directed to the skin across the body to conduct an audit of somatosensory inputs and potential itches.

4. Itch threshold

The key element of this model is the process of adjusting the thresholds in response to the context provided by the itch inducer. When potential sensations are detected by the body scan, the itch threshold determines whether they are experienced as itch or touch sensations. If the threshold is lowered, sensations are more readily accepted as itches.

5. Sensations interpreted

After the threshold has altered, the next step is for sensations to be categorised as itch or touch in accordance with this boundary. Once a sensation reaches the itch threshold it becomes interpreted as an itch. Skin sensations which would previously be sub-threshold (and thus go unnoticed) are recoded in the context of itch being more likely due to the heightened threat level. This is a distinct change in the interpretation of the sensation as VEI neither uncovers unnoticed itches nor does it create new ones. The Threshold Model proposes that VEI causes existing unnoticed sensations to be reinterpreted as itches and thus brings them into conscious awareness as possibly requiring a scratch response.

6. Hypervigilance loop

While the threatening itch inducer is present, the threat level remains high and the person remains in a hypervigilant state. On the model, this functions as a hypervigilance loop that allows the aforementioned processes to continue from the interoceptive inspection stage: The body is scanned and monitored for the presence of itches and thresholds remain set at an appropriate level to detect them. The loop is only broken when the threat level is lowered an undetermined amount of time after the threat is removed, meaning that sensations no longer require additional monitoring.

7. Threat appraisal

A threat appraisal process is suggested as the first element on the pathway between itching and scratching. In the same way that threat detection is used to appraise the level of threat posed by an external inducer, once an itch is established a further appraisal is required to determine whether it represents a sufficient threat to the body to require removal. The purpose of threat detection is ultimately to trigger an appropriate response to defend the body. Scratching causes harm to the body and so can only be considered defensive if it removes a greater threat. Therefore, itches are brought into continuous conscious awareness in order to monitor the threat level they pose so an appropriate response can be initiated.

8. Scratch threshold

The second threshold in the model is decision based, although the decision is primarily an unconscious one. Once an itch is considered sufficiently representative of a threat, a threshold for deciding whether to respond with a scratch or not is established. This acts as a gating system preventing scratching occurring immediately for every itch, which would result in many false alarms where there was no physical threat present. The consequences for acting overzealously range from unnecessarily irritated skin to interruption of other actions or tasks, so this process may be important for balancing the costs and benefits of scratching.

9. Faciliatory influences

While the appraisal of threat is maintaining a set threshold for when a scratch is required, other influences may facilitate the initiation of a scratch. It seems likely the appraisal mechanism would factor in both the saliency of the itch and the ease of scratching it.

10. Initiation of scratch action

If all these processes are completed and a scratch is deemed necessary, possible, and worthwhile, this action is then initiated and the scratch ensues. The regular itch-scratch cycle of skin irritation and further itching proceeds from this point of physical skin damage onwards.

11. Saliency monitoring loop

If a scratch is not initiated, the perception of an itch persists and so cycles back around in a monitoring loop, returning to assess the itch from the threat appraisal stage. While the itch is present, its threat level and saliency continues to be assessed until it either reaches the scratch threshold or is extinguished.

12. Auxiliary VEI inducers

Once a scratch has occurred, the basic physical itch-scratch cycle of itch, scratch, and skin irritation is well underway. The latter two occurrences are physical reactions but also have a visual component. These visual aspects of scratching and skin irritation from within the cycle then act as additional VEI cues, psychologically reinforcing the induced itch.

7.3 Threat detection

Threat detection and hypervigilance to threats has been speculated to be involved in the creation of VEI in previous studies (Kupfer & Fessler, 2018); this idea is well supported by the findings in this thesis. For this reason, the Threshold Model conceptualises the activation of threat detection as the main mechanism for instigating VEI. This mechanism is a driving force in the threat detection and threat appraisal stages, but is also influential in the attentional filter and hypervigilance loop, as shown in Figure 7.2.

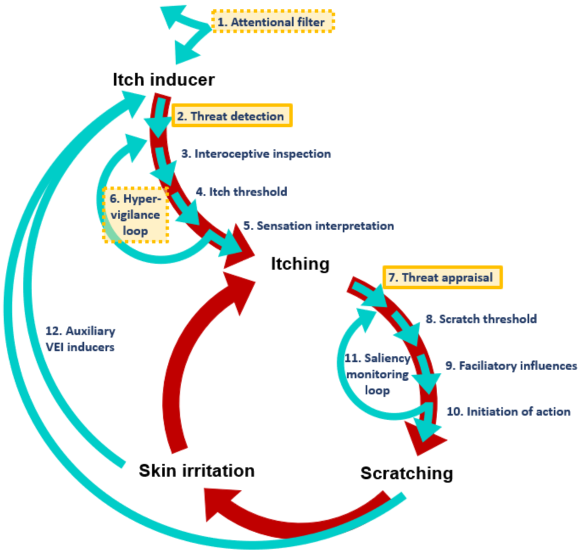


Figure 7.2 Parts of the Threshold Model which involve the threat detection mechanism

7.3.1 Evidence from Chapter 3

The main argument supporting threat detection is that the content of stimuli influences how itchy participants feel. This was established in Chapter 3, which showed that irritants in contact with the skin were the most potent itch inducers. These images provide the most direct depiction of an environmental threat to the skin, indicating that VEI is greater in response to more salient threats. Schut (2015) argues that negative affect resulting from viewing itch experiences is more important than what is seen, with regard to how influential a stimulus is. This indirectly supports the idea of threat detection, as the negative affect is tied into the level of threat implied by the images.

Chapter 3 also described how patterns of itches and scratches correspond with one another. Itches recorded in specific locations often persisted over multiple trials rather than being scratched immediately, which indicates that, while they were consciously perceived as itch, they had been appraised as not threatening or salient enough to require removal right away and were instead being monitored. This supports the idea that the severity of threat posed by an itch determines how great an influence on behaviour it has. This severity could be due to the strength of evidence that an irritant is touching the skin or simply that the intensity of the itch is so distracting or unpleasant as to impede the person's ability to function normally. For a scratch to take place, the threat posed must be greater than the threat of harm by scratching, which Chapter 3 suggests is the case for some but not all recorded itches.

7.3.2 Threat detection vs. other explanations

If threat detection was not the driving force in psychologically-induced itch, then the socially contagious aspects would likely have greater influence over the results. We would expect images featuring another person scratching to be a stronger itch inducer, or more directly, a better scratch inducer if the behaviour is mirrored. Images featuring scratching have previously been found to produce more scratching behaviour (Lloyd et al., 2013) but this effect was not replicated in the experimental chapters. This indicates that while scratching may produce a subtle influence towards mirroring that behaviour, threat detection accounts for the dominance of irritant contact images in creating VEI, justifying the Threshold Model's focus on this mechanism.

7.3.3 Loops

Loops are an important mechanism for controlling the sequence of events in the Threshold Model. It is clear from the pattern analysis results in Chapter 3 that itch induction is not a straightforward or direct route; some itches appear instantly, some take longer to develop, some are scratched immediately, some persist to be scratched at a later point, and some spontaneously diminish after any duration of being present. For this reason loops are necessary to break up the linear process through the cycle and to account for the varying time offsets between measurable itch and scratch events.

The loops proposed in the Threshold Model can be considered a form of constant threat assessment. The hypervigilance loop maintains a response to the heightened threat level and allows for rapid identification if and when itches arise from the suggested threat. Likewise, the saliency monitoring loop maintains alertness to the threat posed by an itch and enables the most appropriate response to the threat to be continuously re-evaluated. In both cases, an ongoing process of monitoring threat level primes the system to detect and monitor further sensations while the threat of itch implied by the inducer is likely to be present. Ultimately, perceiving and responding to the threat of an itch inducer requires dynamic interpretation rather a single judgement, which loops enable the model to account for.

7.3.4 Evolutionary purpose

It has previously been suggested that itch evolved to remove irritants from the body (Stante, Hanna & Lotti, 2005), with scratch as a defensive reflex (Olek-Hrab et al., 2016). Threat detection is the mechanism most consistent with this evolutionary purpose for irritant-based itching, so it is likely that the heightened threat level from psychologically-induced itch is dealt with in the same way. It is an overapplication of an evolved defence to situations that no longer contain the threat itself.

It has been suggested that itch is complementary to pain as means of avoiding physical threats (Dey, Landrum and Oaklander, 2005). Kupfer and Fessler (2018) have extended this idea to suggest that itch works in tandem with disgust to remove potential irritants (specifically in their view, ectoparasites). Overall it is likely that a network of threat detection and avoidance systems have evolved to deal with a range of potential threats to the body. The Threshold Model accounts only for itch but would be compatible with this wider network.

7.3.5 An involuntary reflex?

In support of the idea of threat detection mechanisms as an evolutionarily beneficial defence, it can be argued that this defence is part of an instinctive primitive drive to protect oneself. Threat detection is not necessarily consciously appraised. It is an instinctive alertness to threat rather than a choice to treat a stimulus as threatening. This may go some way to explain why the system is activated when faced with a still image of an irritant. Rationally it would be discounted as not threatening, but the brain responds as if it were. The inability to prevent VEI from occurring, even when it defies rational analysis of the present threats, suggests that it is an involuntary response. Yiend and Mathews (2001) described attentional biases to threats as maladaptive for this reason, as they do not distinguish between real danger and the suggestion of danger from words or images, which then diverts attentional resources unnecessarily.

7.4 Attention

Attentional processes appear to be an important mechanism throughout the model. Attentional bias has specifically been demonstrated in both the previous literature (Fortune et al., 2003; Van Laarhoven et al., 2017) and in Chapter 6; therefore, the model contains an attentional filter at the beginning of the cycle to determine whether a stimulus is attended to or ignored. This element is also involved in determining how the auxiliary inducers perpetuate the cycle after a scratch. Bodily attention plays a further role in the model as the interoceptive inspection relies on attention to the body to scan for potential itches, as shown in Figure 7.3.

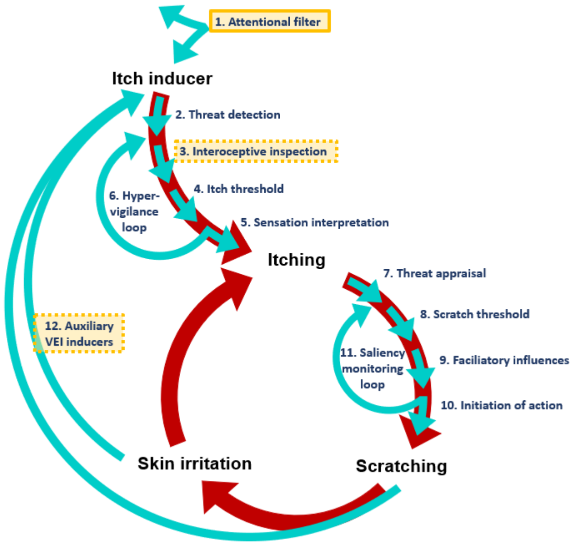


Figure 7.3 Parts of the Threshold Model which involve the attention mechanism.

7.4.1 Attentional bias as a filter

The attentional filter leading either towards the itch inducer or away from it is a direct representation of the differential visual attentional biases found in Chapter 6. Healthy participants displayed an aversive initial attentional bias, which would strongly suggest they are following the path of the filter leading away from entering the cycle via the itch inducer. Their subsequent indifference to the itch image would also make them more likely to filter away from the inducer in a content rich environment. Clinical itch participants displayed both an initial instinctive and a conscious attentional bias towards itch content, which would lead them into the cycle by focusing on the itch inducer over other things in their environment.

It is also likely that having an ongoing bias towards itch inducers makes it harder to disengage from them once visual attention has been allotted. This is reflected in the eye-tracking results, as clinical participants made more saccades to the itch images rather than just spending longer looking at them overall, which suggests they were repeatedly drawn back towards the itch content.

7.4.2 Filtering or creating itch inducers?

The differences between healthy and clinical participants is assumed to reflect differences in susceptibility to itch and to support established differences in how the two groups experience VEI. Instead of simply representing how attentional bias differs by response to an itch inducer, it is instead possible that the attentional filter provides a means for attentional bias to control whether an image becomes an itch inducer.

The attentional filter may form a first line of defence in the healthy population's ability to avoid the itch-scratch cycle. If people with pre-existing itch conditions attend more readily to itch images, this would then provide greater exposure to those as inducers, making the subsequent VEI effects more likely to take hold. Conversely, people without skin problems may only experience substantial exposure to the itch images when their visual attention is deliberately and explicitly directed towards them. Incidental exposure to itch cues may often be filtered out without obtaining the necessary cognitive processing to become an itch inducer. Thus, from this perspective, an itch image is not inherently a VEI inducer, but 'thinking makes it so' when the image is allotted sufficient attentional processing to initiate threat detection mechanisms.

7.4.3 Attention to threat

Attention is a complementary mechanism to threat detection, as it can expand upon a threat-based account of psychologically-induced itch by suggesting a means for identifying threats. The itch stimuli that clinical participants showed a bias towards carry the implication of threatening itch situations. This is particularly true for clinically relevant threats, as images depicting rashes or scratching garnered the strongest attentional bias and is also reflected in the disease-specific attentional biases found by Fortune et al. (2003).

Furthermore, a probable reason that healthy participants filter out more itch inducers is that they are a less salient threat for this group. They are less accustomed to experiencing itch and do not have a health concern that hinges on how often they experience it. This seems to suggest that threat detection is only influential at the perceptual level of processing for those who are particularly vulnerable to itch, whereas otherwise it is only activated when an inducer has been fully processed.

Previous studies have hinted at a link between susceptibility to VEI and both anxiety and neuroticism (Holle, Warne, Seth, Critchley, & Ward, 2012b; Ogden & Zoukas, 2009a) which suggests that having highly attuned threat detection may activate these processes more easily, which may also be the case for people with chronic itch. These predispositions may feed back into the attentional filter, making threat more easily detected.

7.4.4 Bodily attention

In addition to the visual attentional biases at the beginning of the model, attention is involved as a more general mechanism throughout the body scanning and threshold setting stages. Bodily attention is an inherent part of the interoceptive body scan, as the question of where on the body a sensation is felt can only be answered by attending to internal sensations. This appears to be guided by interoceptive attention rather than visual attention, as vision of the body does not appear to be necessary to prompt a scan. Swithenbank, Cowdell and Holle (2016) produced contagious itch with auditory stimuli, which implies that the scan is directing attention to search within the body, rather than visually guiding attention to correspond with itch inducers on another person’s body. Thus, although VEI is visually-evoked, visual identification of a body-based inducer is not required for a domain general attentional scan of the body to take place.

This concurs with the evidence from Chapter 5, which implicated bodily attention in performance on the SSDT: when viewing itch images, participants’ perceptual thresholds at the fingertip increased, indicating that attention was drawn away from that specific body part to attend generally to the whole body. This suggests that they switch form monitoring the sensation relevant for the experiment, to monitoring their body for itch, employing a continuous hypervigilance in case a sensation appears. This redirection of attention enables the interoceptive body scanning to continue and the threat appraisal for scratching to be applied throughout the duration of VEI.

Attending to the body has been linked to a range of perceptual effects that may contribute to or interact with VEI. For example, inducing sensations in a body part by focusing attention on it (Tihanyi & Köteles, 2017), improving tactile change detection (Van Hulle et al., 2013), or increasing somatic interference to create false impressions of touch (Mirams, et al., 2010). One particularly relevant attentional effect found by Durlik, Cardini and Tsakiris (2014) is that awareness of being filmed can alter tactile perception. They speculated that this was due to a shift in bodily attention prompted by the feeling of having their body observed. This presents a potential problem for the methods used in Chapters 3 and 4, as both relied on filming participants for observation. As Chapter 5 shows that VEI also involves changes in tactile perception, it is possible that the filming could have contaminated the results in some way.

7.5 Interoceptive body scan

The interoceptive body scan is suggested to be the active component in identifying itches during VEI. Body scan meditation and interoceptive endogenous attention have been previously described in the wider perception literature but have not previously been implicated in psychologically-induced itch. This mechanism is directly activated during the interoceptive inspection stage of the model to examine whether potential itch sensations are present. It is further utilised in the saliency monitoring loop to maintain awareness and appraisal of an identified itch sensation, as shown in Figure 7.4.

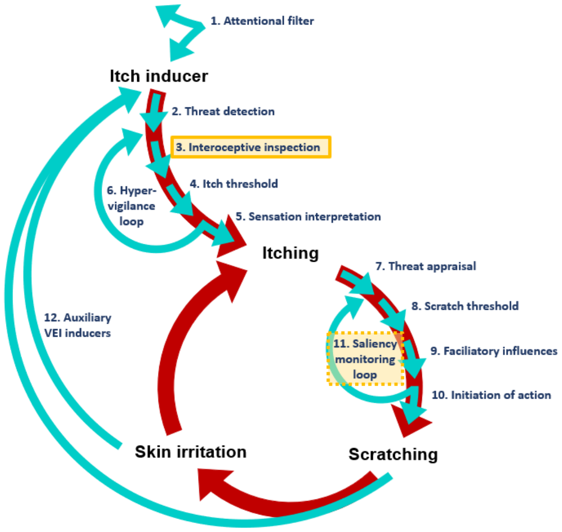


Figure 7.4 Parts of the Threshold Model which involve the interoceptive body scan mechanism.

7.5.1 Evidence from Chapter 4 and Chapter 3

The idea of a mechanism that scans the body for sensations stems from the apparent influence of the itch-related questions in Chapter 4. Participants scratched more frequently when asked if, where, and how much they itched, which implies that these questions were explicitly triggering an interoceptive body scan to search for itches and examine them. Furthermore, scratching increased across time for the itch question group but not the neutral question group, which suggests that the body scan was repeated in response to the itch questions, but with the neutral questions the scan may have been less thorough or less frequent as the images alone carry only a subtle prompt to complete a scan.

Support for this mechanism is also provided by the itch and scratch distributions in Chapter 3. Itch is generally conceived of in terms of a sensation that provokes a scratch; however, there were considerably more reported itches than observed scratches. Many of these itches may perhaps have been less intense than those that eventually did culminate in a scratch. It is possible that the explicit questioning of where itches occurred may have overrepresented these minor itches or more ambiguous itchy sensations by directly requesting a report of what the body scan found. The wide distribution of these itches across the body further supports the idea that the interoceptive body scan examines the body in its entirety rather than honing in on targeted areas.

7.5.2 Scanning for threats

The purpose of the interoceptive body scan is to check whether an abstract threat is present in current sensations. Threat detection places the person on high alert for potential itches and so it is reasonable that they would then search for sensations that confirm this suspicion, in similar terms to the experimental questions: How itchy and where? The context provided by viewing itch inducers affects how motivated and thorough that search is, by manipulating the perceived likelihood of the threat. It may be that the greater the implied threat, the more diligent the interoceptive body scan.

This also links to empathy. Seeing another person in an itch state implicitly raises the questions of “if something is making them itch, is it also happening to me?”, which forms a sensible enquiry if there is the possibility of a threat that has not yet been detected. An empathic response is derived from the potential of it being a shared experience. Schut et al. (2015) have suggested a link between empathy and susceptibility to VEI so it seems likely that empathy could play a role in the model by encouraging the interoceptive body scan, as discussed in section 7.7.1.

7.5.3 Top-down or bottom-up?

The inherent assumption of VEI is that the induction of itches must be a top-down process. Perceiving the itch inducer leads to the creation of more itches rather than more itches spontaneously appearing at the skin level. The interoceptive body scan is not incompatible with the latter idea though: The crucial distinction is whether the scan uncovers existing itches or creates new ones from potential sensations.

In the bottom-up scenario, there would be itches present on the skin that are not consciously perceived. The interoceptive body scan would bring these unnoticed itches into conscious awareness by directing attention towards them. From a threat detection perspective this is a sensible mechanism for controlling the body’s defences: Scanning for itches expediates discovery of irritants instead of waiting for skin irritation to become severe enough to be unavoidably attention grabbing. The sensations themselves are processed bottom-up, but the interoceptive body scan looks for itches to process and so more easily identifies them.

In the top-down scenario there are no additional itches going undetected on the skin. The interoceptive body scan instead creates new itches by generating sensations to match the expectation of finding them, as simply focusing attention on the body can create and intensify physical sensations (Tihanyi and Köteles, 2017). While this appears superficially less adaptive than uncovering pre-existing itches, creating sensations can be just as productive in threat detection. The goal of scratching is to remove irritants from the skin, so causing the brain to initiate more scratches serves to defend against a psychologically perceived threat without requiring a signal from the skin to inform of that threat. The interoceptive body scan mechanism is equally compatible with the top-down and bottom-up accounts, but the operation of the threshold mechanism is key to determining which is more functional in VEI.

7.5.4 Spontaneous vs visually-evoked itches

The process of identifying itches via interoceptive inspection is supported by Michael et al.‘s (2012) study of spontaneous sensations, which indicates that there are low level sensations that can be brought into conscious awareness by scanning for them. Itch, however, was one of the least frequently reported sensations in their study, representing only 1.8% of the total reports. This strongly suggests that interoceptive body scanning as a mechanism on its own is not sufficient to create the quantity of itches induced by VEI, but instead requires the presence of a stimulus that alters the itch-threat context to prompt the shift towards an itch-based interpretation. Furthermore, Beaudoin and Michael (2014) demonstrated that movement inhibits the perception of spontaneous tactile sensations. This does not appear to be the case for the itch sensations induced by VEI, as the basic paradigm requires frequent hand movements. Conversely, it was observed in Chapters 3 and 4 that the movements made by participants to provide mouse and keypress responses were often continued to perform a scratch before coming to rest again. It seems clear that VEI is not merely a gained awareness of background spontaneous sensations, but a change in perception.

7.6 Setting thresholds

Setting and adjusting thresholds to respond to the current itch situation is the crucial mechanism in the Threshold Model's account of VEI, as shown in Figure 7.5. Despite the threshold being presented as one overall mechanism, there is a functional distinction between the perceptual threshold in the itch threshold component of the model, which is used to determine whether a sensation is perceived as an itch, and the decision threshold in the scratch threshold component, which is used to determine whether that itch requires a scratch. The former serves to interpret the body's current state and the latter to select an appropriate response to that state.

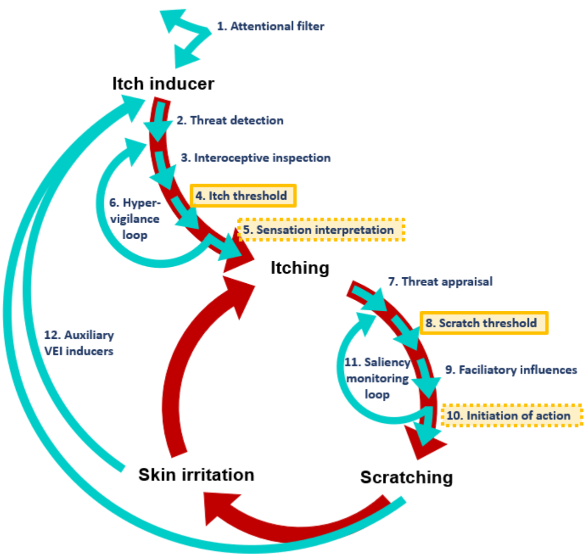


Figure 7.5 Parts of the Threshold Model which involve the threshold setting mechanism.

7.6.1 Evidence from Chapter 5

Evidence for the involvement of thresholds comes from the slight criterion shift found in Chapter 5. Viewing itch images corresponded with a tendency towards reporting a tactile stimulus as present more frequently, without a commensurate increase in sensitivity. This indicates a change in what potential sensations are accepted as signal instead of noise. In terms of itch, somatosensory noise in the form of low level tactile sensations (where clothes touch the skin, the movement of hair follicles, etc.) exist on the body constantly, but are filtered out as irrelevant inputs and so unattended to and unnoticed. If the thresholds for experiencing an itch are lowered, they will no longer be deemed irrelevant and so will enter awareness.

7.6.2 Perceptual threshold

The itch threshold is a perceptual threshold, with the purpose of distinguishing signal from noise and inferring sensation accordingly. The interoceptive body scan mechanism does not distinguish between sensations, so while it is able to detect unnoticed itches for the most part it identifies potential sensations that have not been categorised or processed yet. If the threshold is met, the sensation is deemed to be signal and is consequently experienced as an itch. If it is not met, the sensation is considered to be noise and so not imbued with the qualities of an itch as no further action is needed. This recoding of sensation is not simply a change in how the sensation is viewed, but is a physical change of felt experience, as confirmed by the physiological evidence from Napadow et al. (2015) and Stumpf et al. (2016).

By contrast, it is possible to bring minor unnoticed pain sensations into conscious awareness by conducting an interoceptive body scan, yet there is no pain equivalent for VEI (Vandenbroucke et al., 2013). Pain appears to be limited to sensations which are already present, either noticed or ignored but not altered. New itches are continually reported during VEI (as shown in Chapter 3), which is unlikely to represent the piecemeal uncovering of minor itches in a comparable way. Instead it is more plausible that potential sensations are being identified and reinterpreted throughout to create the perception of successively materialising itches.

7.6.3 Evidence from Chapter 3

Chapter 3 found that participants’ itches that persist across multiple trials either culminated in a scratch or were spontaneously extinguished. The Threshold Model proposes that a threshold is set for the point at which taking action for the former is more advantageous than waiting for the latter. In addition to this, Chapter 3 also found that scratch frequency increased across the duration of the experiment, whereas the number of itches did not. This suggests that the scratch threshold is not solely the product of itch saliency, other factors influence when and how much an itch is scratched.

7.6.4 Decision threshold

The scratch threshold is a decision threshold to determine whether an itch should be scratched or tolerated. Given the influence of threat detection throughout the model, this decision is likely to be based on a cost-benefit analysis of whether the minor skin irritation harm of a scratch is worth accepting in order to extinguish the itch. If the itch does not reach this threshold it may be easily ignored or likely to spontaneously diminish without requiring a scratch.

The costs and benefits of scratching are a dynamic response to the itch situation, rather than a simple evaluation of the potential harm and reward. For example, once a scratch has been initiated, the harm cost is paid. If this does not result in a subsequent relief benefit, it may become easier to initiate another scratch to obtain that benefit. The urge provided by the persisting itch may be at a constant level, but the threshold for further scratches would be lowered as a result of the sunk cost. This may also explain one element of why scratching is more easily initiated for people with chronic itch (Schut et al., 2017). For these individuals, the rewarding aspects of scratching are well established through repeated experiences, and the resulting skin irritation has already developed into rashes and lesions. In the immediate term, another scratch offers great rewards for only a small contribution to the damage, despite the long-term harm.

7.6.5 Itch as an interpreted experience

The culmination of the Threshold Model is that itch is an interpreted experience, for which the thresholds themselves define the interpretation that is consciously experienced. VEI and other psychological itch triggers form the context that informs the interpretation and thus enables the increased itching. Threat detection is used to interpret the context, attention is used to interpret the threat, the interoceptive body scan is used to interpret the state of the body, and the thresholds are used to interpret how the sensation should be experienced.

In a naturally occurring or histaminergic itch situation, the signal from the body is clear and often so is the context provided by an obvious cause. However, it has been shown that itch and pain imagery activate the same brain regions (Mochizuki et al., 2013) and use overlapping nerve pathways (Handwerker, Forster, & Kirchhoff, 1991). Interpretation is needed, even in a clear cut itch scenario, to differentiate the nociceptive sensations and translate them into the experience. In VEI however, the signal is ambiguous, and so the contextual information provided from other modalities is more heavily relied upon to interpret it. Therefore, the thresholds are more easily manipulated in this uncertainty, which results in the additional 'visually-evoked' itches.

7.7 Facilitatory influences

Other explanations for VEI have previously been posited as outlined in Chapter 1, the main ideas focusing on motor and perceptual mirror neurons, classical conditioning, and individual differences. These do not feature heavily in the Threshold Model as, although they are supported to various extents in the previous literature, they lack explanatory power in light of the evidence presented here in the experimental chapters. They are not necessarily in conflict with the Threshold Model though, as they form parts of VEI but not the whole so are likely to be contributing faciliatory influences and amplifying the influence of auxiliary inducers, as shown in Figure 7.6.

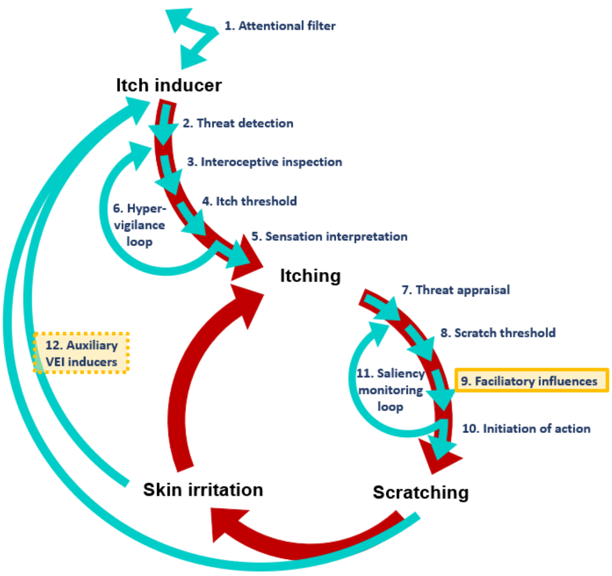


Figure 7.6 Parts of the Threshold Model which involve faciliatory mechanisms.

7.7.1 Personality traits

As outlined in Chapter 1, there is little agreement within the contagious itch literature as to what personality traits influence VEI and how. The studies outlined in the experimental chapters did not wade into this debate so no personality measures were used. For this reason, the Threshold Model does not factor any personality traits into the processes and instead gives a general account of how VEI occurs. This does not, however, exclude the possibility that individual differences influence how a person responds to VEI within these processes. Indeed, the variability between participants in Chapter 1 affirms that individual differences are evident in the results.

Empathy in particular has previously been highlighted as an influence on VEI susceptibility (Lloyd et al., 2013; Schut et al., 2015). This may encourage the interoceptive body scan mechanism by reinforcing the sense of collective social threat: The itch experience may be threatening 'us' rather than just the viewed person. Therefore, attention should be oriented from the viewed person's bodily state to the participants' own. The threat detection mechanism may also interact with neuroticism (as suggested by Holle et al. (2012)) and anxiety (as suggested by Ogden and Zoukas (2009)) by predisposing people to be more vigilant to threat, thus enhancing threat detection and setting lower thresholds for interpreting a sensation as itch.

7.7.2 Mirror neurons

Previous work has claimed the motor mirror neuron system is likely to be involved in VEI (Holle et al., 2012), although this is probably limited to instances where the inducer is another person scratching. While this gives it limited explanatory power for psychologically-induced itching as a whole and multifaceted phenomena, it may function within the Threshold Model to facilitate the initiation of scratching. If a subconscious impulse to mirror behaviour is present while experiencing VEI, it could augment the compulsion to scratch, thus lowering the scratch threshold beyond what an appraisal of the itch would set it at.

7.7.3 Scratch access

Another influence that can facilitate or inhibit the initiation of scratching is the location of the itch in question and how easily accessible that location is. The itch and scratch location maps from both Chapter 3 and Chapter 4 show that participants frequently scratch their hands and head. These are areas where the skin is most accessible, particularly as the hands only require a small movement to scratch. Conversely, there were clusters of itches on the soles of the feet with no corresponding scratches; these were highly inaccessible without removing shoes, which no participant attempted to do. It is apparent that the easier an itch is to reach, the more likely it is to be scratched; a higher scratch threshold must be met when scratching is inconvenient. Furthermore, participants tended to make their scratch actions while moving to use the mouse or keyboard. It was less common for a scratch to be completed in a separate movement. It seems that the threshold for scratching is lowered when movement has already been initiated by another action.

7.7.4 Classical conditioning

Classical conditioning between viewing itchy situations and experiencing itch has been suggested as a mechanism for the creation of VEI (Schut et al., 2015). This seems insufficient as an explanation for VEI as a whole, but may well be involved in establishing and altering the mechanism within the model. The itch threshold itself may become habitually altered in response to experiencing itch situations, forming a connection between the visual cue of the itch images and the physical response of the changed criterion.

Schut et al. (2015) also suggested that classical conditioning pairs scratching and skin irritation images with itch sensations in regular life. People with chronic itch have an abundance of experiences to reinforce this connection, which may be why their responses in Chapter 6 differed from heathy participants. However, this may explain better why the cycle propagates rather than how VEI itself is created. Chapter 3 demonstrated that irritant contact images were the strongest inducers of VEI, but this reflects the least common itch situations so would have the least opportunity to establish a conditioned connection. Therefore, it is unlikely to be such a connection driving the effect overall.

7.7.5 Auxiliary VEI inducers

Conditioning to itch inducers may go on to explain why the cycle propagates for people with chronic itch, as they are constantly producing their own VEI cues. The Threshold Model proposes that rather than producing itch as an outright conditioned response, the pairing of these events forms an expectancy link. Conditioning the visuals of seeing oneself scratching an irritated area of skin with the resultant itch perception creates an expectancy of itch upon further exposure to the sight of scratching actions or irritated skin. Van Laarhoven et al. (2010) showed that expectations of greater itching results in higher levels of itch. This solidifies the role of scratches and skin irritation as within-cycle events as additional psychological itch inducers.

Chronic itch patients experience frequent visual exposure to the physical outcomes of their skin conditions; therefore, they are continually vulnerable to the VEI triggering aspects of these. Classical conditioning strengthens this association and increases their potency as personally relevant itch threats. The previously described cognitive and perceptual processes and mechanisms involved in VEI, in conjunction with their cutaneous symptoms, exacerbate the amount of itching they experience. These top-down effects contribute to entry into the cycle but also perpetuate it, rendering it drastically harder to break.

7.8 Questions that remain

The Threshold Model is still in the early stages of development, so while the explanation it provides is internally consistent, it is not fully empirically supported yet. There are many elements that remain untested or unexplored. A selection of the most prominent matters to address are outlined in this section.

7.8.1 What are the neural correlates of these mechanisms?

The Threshold Model takes a cognitive approach to understanding contagious itch, but it remains to be seen how the neural processes responsible for the effect align with the cognitive and perceptual mechanisms proposed by the model.

A selection of neural mechanisms have been identified as involved in the experience of itching generally and characterised as an 'itch matrix' (Greaves & Khalifa, 2004). These comprise the anterior insula, cingulate cortex, primary somatosensory cortex, premotor cortex, prefrontal cortex, thalamus, and cerebellum, shown in Figure 7.7. Holle et al. (2012) have speculated that the itch matrix may contribute to the creation of psychogenic itch disorders if frequently activated, as they found activation in this network of brain activity when participants viewed another person scratching. Specifically, they identified the anterior insula, primary somatosensory, prefrontal and premotor cortices. Another study Schut et al. (2017) identified supplementary motor area, left ventral striatum and right orbitofrontal cortex as being the key areas active when participants with atopic dermatitis experience contagious itch.

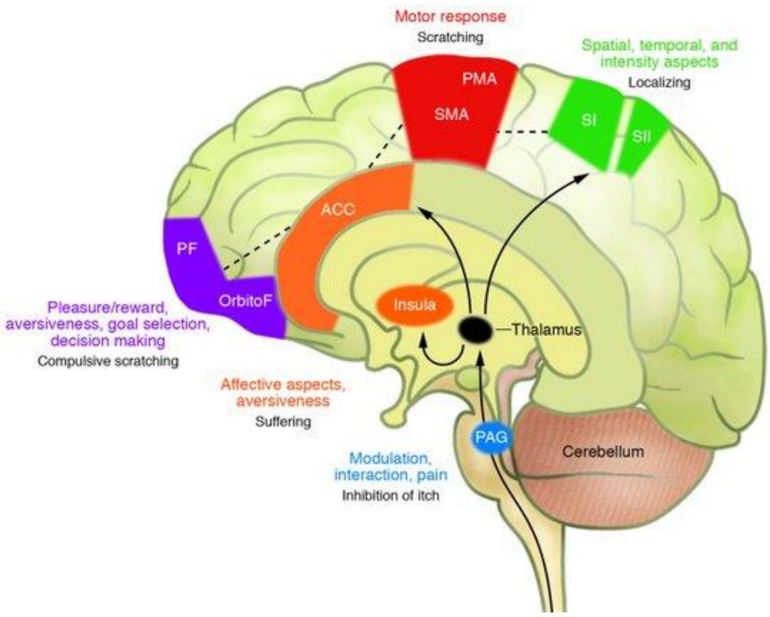


Figure 7.7 Central processing of pruritus (in general, not just as a product of VEI), highlighting the main brain areas identified in the 'itch matrix'.
Image adapted and reprinted from "Frontiers in pruritus research: scratching the brain for more effective itch therapy" by R. Paus, M. Schmelz, T. Biro, and M. Steinhoff, 2006, The journal of clinical investigation, 116 (5), 1178. Copyright 2018 by the American Society for Clinical Investigation.

None of these findings directly conflict with the cognitive and perceptual mechanisms proposed in the Threshold Model, but if the model is correct then they are unlikely to be the full picture. One notable absence is the Extrastriate Body Area (EBA), which no studies thus far have targeted as an area of interest. This is a key area that would be expected to play a role given that it has previously been implicated in body awareness and schema (Cazzato, Mian, Serino, Mele, & Urgesi, 2014; Limanowski, Lutti, & Blankenburg, 2014), and is activated when looking at body parts, which is an integral part of most VEI situations. Indeed, Holle et al. (2012) suggested that top-down predictions of interoceptive signals may be the process behind the activation of the anterior insula activity they found. If this is the case, it would be reasonable to expect some EBA activity to coincide with that of interoceptive representation.

In addition, the Threshold Model's account of contagious itch would involve other brain processes tangentially related to the itch experience. The neural underpinnings of visual attention as a general cognitive mechanism have been studied extensively, but thus far attention in terms of itch has only been examined using psychological methods (Van Laarhoven et al., 2010; Van Laarhoven et al., 2017). There is scope for investigation of how the established attentional processes are involved in VEI. Combining eye tracking with EEG would be an ideal way to approach this question. Similarly, the focus on threat detection as a driving force in creating VEI implies that a neural response to threat should be present in some form. Given that itches pose a low level threat that would produce more suspicion than outright fear, this may not come in the obvious form of amygdala or other limbic activation. Instead, perhaps some more subtle activity for threat processing may be missed if not targeted as regions of interest.

Further investigation of the neural underpinnings of the Threshold Model should also focus on how well the processes align with the more well-established brain activity in itch. For example, can the threshold for initiating a scratch be identified temporally by comparing activity levels between the somatosensory and motor cortices over time? Or even more specifically by distinguishing a change in the level of itch matrix activity at which the motor cortex increases activity to initiate a scratch? Chapter 5 established that changes in tactile perceptual threshold and, to a lesser extent, criterion occur when experiencing VEI, which raises the question of whether this change corresponds with a measurable change in brain activity in the somatosensory cortex. If so, could using TMS over this area be used to manipulate a person’s perceptual thresholds and would this then affect how strongly they experience VEI? If this proves possible it would have great implications for developing chronic itch interventions.

7.8.2 Why does VEI occur?

The Threshold Model attempts to provide an account of how VEI occurs, but it does not broach the subject of why. Although it may be consistent with how sensory information is processed, the fact still remains that VEI is maladaptive. Creating itch sensations when there is no irritant to remove and thus causing the minor harm of a scratch is a cost to the body with no corresponding benefit.

It can be conceptualised as a cautious system that favours false alarms over misses; however, it is clear that scratching and the resultant skin irritation are a prevalent issue in the population (Matterne et al., 2013), so it can easily be argued that the balance struck is not appropriate. This raises the question of why it evolved to be this way and whether the evolutionary pressures that created it have altered in the modern world, or whether this overcautious approach has always been the lesser of two evils. Furthermore, has this approach evolved to differential levels in populations who have been exposed to greater or less itch threat in their environment?

To fully understand why VEI occurs, it is crucial to examine how the Threshold Model fits within the wider network of threat detection and removal systems. Kupfer and Fessler (2018) suggested this network of complementary systems, with itch removing hazards which are attached to the skin, pain removing the body from contact with hazards, and disgust preventing hazards from being ingested. Conceptually this is a sensible and coherent view of how the body defends itself, but empirically there is a lack of information on how this operates and interacts as a multimodal network. This is particularly an issue for ambiguous or overlapping sensation; if the Threshold Model is correct in itch sensations being the product of thresholds for interpreting them as such, then does it follow that the same mechanism is responsible for interpreting as other types of threat? There are many other sensory inputs that the body may need to defend against, for example cold or brightness. Do these reactions all call upon separate segments of the threat defence network, or does the withdrawal from aversive stimuli use one overarching mechanism to select the appropriate defence. If it is the former, it would be interesting to know whether other defence systems operate in a similar way to the Threshold Model, or if it is the latter then whether the Threshold Model applies more widely that it has been conceptualised for.

7.8.3 What modulates scratching?

Scratching is pleasurable (Mochizuki et al., 2014), so it is important to be able to factor this rewarding aspect into the Threshold Model. At present there is insufficient evidence to draw firm inferences, but it can be speculated that if classical conditioning is involved in perpetuating the cycle, there may also be some operant conditioning in effect. This could be pairing the itch inducers with pleasurable reward of scratching, thus providing a motivation to lower the scratch threshold. For this reason, the pleasure and reward of scratching needs to be balanced against an inhibitory influence to prevent unrestrained scratching damaging the skin. Inhibition by gating systems in the form of a scratch threshold that needs to be reached are accounted for by the model, but we can only speculate as to what circumstances affect the threshold level and the weighting afforded to each. Likely candidates include the saliency of the itch sensation, the severity of harm the perceived irritant could cause, and the probability of being correct that the suggested irritant is present. If these factors could be manipulated, future research may be able to elucidate how the brain balances the costs and benefits of acting on a perceived itch.

The Threshold Model focuses primarily on the processes that precede a scratch, but scratching is an ongoing process rather than an individual response to each itch. Therefore, another interesting area to investigate would be whether it is possible to activate the itch-scratch cycle from the point of scratching prior to itching. If the model is correct it should be possible for scratching to lead to itching around the psychological loop. It is possible that artificially beginning the process of scratching could trigger a snowball effect of itching by manipulating the scratch threshold. If scratching a specific non-itching location were to induce the widely distributed itches across the body typically created by VEI, it would constitute evidence of this. It would be very interesting to see whether this is indeed possible, as studies that have used scratching a non-itching skin site (as a control for comparing the relief of scratching an itch), such as Papiou et al. (2013), have not included any measures of whether itching was subsequently increased.

7.8.4 What else can induce itch?

Audiovisual and static visual images have been the focus of most studies of VEI. As such, the results from these modalities have formed the Threshold Model, and so the model carries with it the assumptions underlying our understanding of those modalities. Itch is a multisensory experience though, which requires breaking down into all component parts as it is possible that other stimuli are able to induce itch, or to affect outcomes of VEI in different ways.

The overlapping literature of nocebo verbal and semantic priming indicates that these effects can produce a psychologically-induced itch effect, which is supported by the findings from Chapter 4. As we have shown that visual stimuli without asking participants about their experiences can produce itch, it prompts the question of whether the reverse is also true. It is possible, but not yet studied, that repeatedly asking a participant if they feel itchy without using visual itch stimuli could produce itching alone. Bartels et al. (2017) and Van Laarhoven et al. (2011) have shown that verbal suggestion can be a powerful influence and so is ripe for further study.

The auditory domain is understudied in contagious itch. Swithenbank et al. (2016) have attempted to use just auditory stimuli, with no visuals and were able to exacerbate histaminergic itch, but they did not create a purely psychological induction. It remains to be seen whether an auditory-evoked itch paradigm would work in the same way as visually-evoked itch. Scratching sounds or the buzz of insects may alert threat detection systems in a similar way to visual images of scratching and of the insects in question, if the mechanisms are indeed domain general as they are assumed to be.

7.8.5 How should we approach future investigations of VEI?

In addition to the need for further study of VEI itself, it is also important to consider methodological questions that arise from our present understanding of the effect. Threshold Model characterises VEI as a dynamic process which utilises feedback loops and thresholds as gating systems to regulate the progression of itch induction. These elements render it difficult to design experiments that account for these processes in the way they capture information. As Chapter 3 demonstrated, trial-by-trial designs only allow for a snapshot of VEI in response to each stimulus. A multi-trial pattern analysis over the course of the experiment was required to measure the full effects of itch induction, itching and scratching that follow exposure to itch inducers. It appears likely that the most common way the VEI paradigm is implemented misses the connections between these outcomes, so it may be beneficial for future research to opt more for blocked designs (as was used in Chapter 5) to engage these effects over a longer duration.

Regardless of the method chosen, there are further limitations to how feedback loops in the model can be investigated, as it is difficult to trace the origins of effects that have been influenced by feedback from within the system. For example, it is not possible to directly measure whether a sensation is in the saliency monitoring loop until the threshold for a scratch is reached and the behavioural outcome can be observed. Nor is it possible to quantify precisely how long a heightened threat level is maintained by the hypervigilance loop. It would be beneficial for future investigations to aim to capture information in a way that allows for inferences to be made about these mechanisms from indirect measures.

7.8.6 How do clinical samples differ?

VEI is experienced by most people, but does not become a recurrent cyclical issue for people with healthy skin, or indeed it can be conversely viewed as people maintain the health of their skin by not having it become cyclical. People with itchy skin experience constant reinforcement of VEI in the outcomes of itch, in addition to physical exacerbation, so it remains to be seen how this influences their susceptibility to VEI as compared to the healthy participants we tested.

Only Papoiu et al. (2011) and Schut et al. (2017) have directly looked at VEI with clinical groups, but their versions of VEI induction methods are quite different and so cannot stand in for a comparable study using the stimulus set and itch location measures of Chapter 3. Unfortunately, limited availability means there were not enough clinical participants available for more than one study; it was more informative to test an entirely new area of attentional bias instead for this thesis. Using a clinical group in Chapter 6 has made a distinct contribution to the scant information available on attentional bias to itch images, but the findings of this study do contradict the existing literature. Van Laarhoven et al. (2017) found the opposite pattern of responses for their healthy participants, so further research on this effect is necessary to determine which set of findings replicate. In either case, it is also necessary to compare this within participants to the basic VEI measures to examine how an attentional bias to itch images correlates with susceptibility to VEI, and whether manipulating visual attention modulates VEI.

From the theoretical point of view, the key piece of information that is lacking is how itch and scratch thresholds differ in the clinical population. Van Laarhoven et al. (2007; 2013) have previously shown that people with chronic itch do have lower sensory thresholds for perceiving physical itch stimuli, so it is likely that a similar difference is present for psychologically-induced itch thresholds. It may be that their thresholds are set lower in general, either as a result of, or a predisposition to, their conditions. Alternatively, they may have more responsive thresholds that shift more easily when provoked. Further investigation of the SSDT may illuminate this issue by comparing the criterion shift of healthy and chronic itch participants. Furthermore, it is important to differentiate between whether people with chronic itch experience more itching during VEI, indicating a generally lower itch perception threshold, or whether they are less able to prevent scratching as a habitual response, indicating a generally lower scratch threshold.

7.9 Practical applications of the model

Although there is still much to be refined and developed in the Threshold Model, in its current form it has much to offer academic and clinical fields. The knowledge gained from studies of contagious itch and the theoretical framework provided by the Threshold Model contribute to clinical approaches to treating chronic itch and may be useful in developing future interventions. In may also be useful for framing the interpretation of clinical or academic studies of itch.

7.9.1 Interpreting itch research

The model can be used as a framework for interpreting clinical research on itch, offering a new perspective to approach and explain the findings of VEI studies. Indeed, it is possible that existing research could be interpreted differently if considered in light of this model.

An example of such a study is Schineller's (2018) recent work which found that, although autistic people had previously been found to display less spontaneous mirroring of contagious yawning compared to neurotypical people, with contagious itch they showed a heightened response compared to neurotypicals. The authors inferred from this that behavioural mirroring was not was impaired as previously assumed. This is a fair conclusion to draw from much of the previous literature on VEI; however, an alternative interpretation in light of the Threshold Model would be that while yawning may be heavily reliant on mirroring, in VEI it plays only a faciliatory role.

The Threshold Model and the studies from which it was constructed lean towards a view of VEI as primarily a sensory effect. A wealth of evidence from autism research reports enhanced tactile sensitivity and susceptibility to overstimulation as characteristic of autism (Green, Hernandez, Bookheimer, & Dapretto, 2016; Hazen, Stornelli, O'Rourke, Koesterer, & McDougle, 2014; Robertson & Baron-Cohen, 2017) and so it is particularly consistent that an effect such as VEI that plays on overinterpretation of sensory signals would be enhanced in this population. In this particular example, examining the findings using the Threshold Model would allow for a more parsimonious interpretation of why these results occurred.

7.9.2 Current Itch reduction methods

Treating itch as a symptom of skin disease primarily relies on medicated steroid topical creams, which accelerate healing and reduce skin inflammation. But while such creams are effective in achieving those particular outcomes (Reitamo et al., 2002; Wahn et al., 2002) they cannot substantially reduce the urge to scratch, nor can they tackle habitual or cognitively driven scratching behaviour. Thus, it is vital that medical treatments are combined with itch-focused cognitive or behavioural therapies to fully eliminate the symptoms of skin disease and optimise treatment outcomes (Elmariah, 2017; Pavlis & Yosipovitch, 2017).

At present, a small number of non-pharmacological approaches to treating itch have been proposed with various degrees of success. Habit reversal is the most commonly used tactic (Grillo, Long & Long, 2007; Nilsson, Levinsson & Schouenborg, 1997), with patients encouraged to avoid scratching or replace it with other non-damaging behaviours. A study by Stewart and Thomas (2006) augmented this approach with hypnosis to alter scratching behaviour and found an improvement in their participants condition. It is unclear whether this approach had a genuine influence on how participants experienced their symptoms or whether it simply heightened compliance with the scratching avoidance regime. Either way, this approach relies on consciously adjusting behaviour when in an itch state so while in the long term it can avoid physical perpetuation through skin damage, in the immediate situation it does nothing to reduce the itch and instead encourages an attentional focus on it. This focus allows the irritated skin to operate as a psychological itch inducer, reinforcing the cycle and prolonging the urge to scratch which must be resisted.

A small number of physical interventions have been used to attempt to alter the psychological perception of itch. Cutaneous field electrical stimulation was proposed as a treatment option in 1997 (Nilsson et al., 1997), but does not seem to have gained much traction in the 20 years hence; the absence of any studies replicating or successfully implementing it implies that none have been able to. Recently, Mochizuki, Schut, Nattkemper, and Yosipovitch (2017) have had more success using Transcranial Direct Current Stimulation (tDCS) to attenuate itch processing in the brain. For these kinds of interventions to be effective, it is necessary to target not only the immediate itch sensations, but the propensity to itch. As we do not yet fully understand the brain processes behind the itch-scratch cycle, there is a lot of scope for interventions using tDCS, or rTMS to be refined and improved upon. Targeting the mechanisms suggested by the Threshold Model would be a productive way to expand this area.

7.9.3 Recommendations for clinical practice

While the aforementioned avenues exist for treating itch symptoms, this does not necessarily mean that they are utilised in the majority of cases. In the UK, patients seeking treatment for chronic skin conditions are treated according to the NHS clinical pathways, which are set out in the National Institute for health and Care Excellence (NICE) guidelines. With regard to itch symptoms, the NICE guidelines for the most common skin complaints are as outlined in Figure 7.8.

Self-care advice

- Offer the person self-care advice:
    - When bathing:
        - Reduce the amount of time spent in the bath to less than 20 minutes.
        - Bathe less frequently, if possible. Wash the axillae, genital area, and under the breasts daily, but other skin areas can be washed 2–3 times weekly.
        - Use cool or lukewarm water (hot water can be drying).
        - Avoid bubble baths, soaps, and perfumed products. Use mild, alcohol-free cleansers, or use an emollient as a soap substitute.
        - If bath oils are used, use a non-slip bath mat to avoid injury.
        - Avoid vigorously drying the skin. Pat it dry instead.
    - A cool shower may offer immediate short-term relief from itch, but avoid excessive showering as this may dry the skin.
    - Keep nails short to minimize skin damage. Try to rub or pat rather than scratch skin if the urge to relieve the itch is unavoidable.
    - Keep the indoor environment cool (particularly the bedroom) and consider humidifying the air, particularly during the cold winter months.
    - Wear clothing that does not irritate the skin (for example cotton or silk). Avoid wool or synthetic fabrics.
    - Avoid spicy foods, alcohol, and caffeine as they may cause vasodilation.
- Offer written advice, for example patient information from the British Association of Dermatologists, available on their website www.bad.org.uk

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Figure 7.8 Self-advice recommended for clinicians to give to their patients, as outlined in the NICE guidelines. ("Itch - widespread - NICE CKS," n.d.)

The omissions of any guidance on psychological management of itch means that patients may not be receiving optimum therapeutic treatment under our current understanding of chronic itch, which may be why the symptoms often persists despite overall improvement in the skin's condition (Arthur & Shelley, 1958; Rystedt, 1985). Incorporating the knowledge gained from the Threshold Model and from the contagious itch literature may help to improve upon and refine the clinical approach to treating this aspect of skin disease.

The main recommendation derived from the Threshold Model would be to emphasise the importance of minimising itch triggers and cues. The most obvious advice that follows from this is to block the audio-visual evidence of itching to prevent it from becoming a psychological itch inducer: covering the rash whenever possible, not looking when scratching, not talking about it more than is necessary, etc. Therefore, it is important to identify where these itch triggers may be occurring in both the clinical environment as part of the diagnosis and treatment procedures, and also in the patient's regular life and how they approach management of their condition.

In the clinical environment, there are several opportunities for clinicians to contribute to this, for example by discouraging patients from monitoring or recording their symptoms unless needed for diagnosis. Evers et al. (2009) has already warned that clinicians should be aware of nocebo and environmental influences that can exacerbate itch; however, they focused on drug nocebo side-effects. Psychological itch inducers should be treated in a similar manner and avoided whenever possible. Outside of the clinic, support and communities are available online for people to help one another manage their symptoms. However, it is likely that discussing these symptoms or sharing photos may also be providing additional exposure to VEI. Bartholomew, Wessely and Rubin (2012) have argued that the plethora of uncontrolled information available online about medical conditions and their treatments have contributed a phenomenon of "mass psychogenic illness" (p.509) whereby people exacerbate their problems by becoming preoccupied with information seeking. The itch-scratch cycle would be a prime candidate for this problem as allotting additional visual attention allows for this information to act as itch inducers.

7.9.4 Screening for VEI susceptibility

Clinical screening can be an effective tool for identifying individuals who are at a higher risk of developing a particular medical issue and thus allowing for early intervention before they develop severe enough symptoms to seek treatment. At present, there is no coherent set of personality characteristics or behaviours that consistently predict chronic itch in such a way that could be used to produce a screening tool, despite many traits being suggested (Bartels et al., 2014; Ogden & Zoukas, 2009b; Christina Schut, Bosbach, Gieler, & Kupfer, 2014). Susceptibility to VEI, however, could potentially work as a predictor of chronic itch development, in which case the VEI paradigm would provide a method of screening for this susceptibility.

The obvious downside to this approach is the unnecessary itches the process would induce in the potentially clinically vulnerable person. Therefore, instead of using VEI directly, it would be more sensible to utilise the findings of Chapter 6 regarding the different patterns of attentional bias shown by clinical and healthy participants. This difference could be used to identify people whose attentional filter operates in a way that is similar to the clinical group before they develop symptoms. As an additional benefit, it would be simple to implement this along with existing screens for personality traits to see whether they covary with attentional bias.

7.9.5 Modifying VEI susceptibility

The next logical approach once a chronic-itch profile for attentional bias has been established is to attempt to modify this bias. Currently there are no attentional bias modification programmes for itch, but attentional bias modification has been successful in combatting other clinical conditions, such as depression (Browning et al., 2012) by altering bias to negative facial expressions; stress response (Dandeneau et al., 2007) by altering vigilance and threat responses; and anxiety (See et al., 2009) by attentional probe training. These studies offer a promising avenue for the development of a similar regime for itch, as they demonstrate that attentional biases can be manipulated or reduced. However, a meta-analysis by Mogoaşe, David and Koster (2014) found little therapeutic benefit from attentional bias methods in their current incarnation, and so it appears any itch tool using these methods would require a great deal of development before it becomes useful in clinical practice.

7.10 Conclusions

Breaking the itch-scratch is possible only when we know how the cycle is entered into and propagated from both a physical and psychological perspective, as both contain mechanisms to exacerbate the problem. Current knowledge of visually-evoked itch and psychologically-induced itching in general can be synthesised into a theoretical framework based on varying thresholds for detection and action. This traces the underlying processes from the psychological trigger to the itch sensation then to the scratch response and thus illuminates the relationship between them.

The Threshold Model offers a cohesive explanation for all facets of VEI and includes the contributions of previously suggested mechanisms. Fundamentally, it considers VEI to be a matter of itch being an interpreted experience that occurs as a result of psychological inputs garnering enough visual *attention* to change the *threat detection* context, triggering an *interoceptive inspection* for bodily sensations that reach a sufficient *threshold* to be interpreted as itches. Thus, an itch is felt. An induced itch then goes on to be appraised within the current *threat context*, monitored using bodily *attention* and *interoceptive inspection* to establish whether it meets the *threshold* to be interpreted as requiring a scratch to remove. Thus, a scratch is initiated.

This model requires a great deal of development and refining, but in its current state is able to provide a range of suggestions for clinical practice and possible interventions. With further research it may be possible to interrupt the psychological induction and perpetuation of itches and thus to break the itch-scratch cycle.

References

Arthur, R. P., & Shelley, W. B. (1958). The nature of itching in dermatitic skin. *Annals of Internal Medicine*, *49*(4), 900. https://doi.org/10.7326/0003-4819-49-4-900

Asmundson, G. J. G., Kuperos, J. L., & Norton, G. R. (1997). Do patients with chronic pain selectively attend to pain-related information?: Preliminary evidence for the mediating role of fear. *Pain*, *72*(1–2), 27–32. https://doi.org/10.1016/S0304-3959(97)00010-9

Atopic eczema - NHS. (2016). Retrieved September 26, 2018, from https://www.nhs.uk/conditions/atopic-eczema/

Augustin, M., & Radtke, M. A. (2014). Quality of life in psoriasis patients. *Expert Review of Pharmacoeconomics & Outcomes Research*, *14*(4), 559–568. https://doi.org/10.1586/14737167.2014.914437

Azevedo, R. T., Macaluso, E., Avenanti, A., Santangelo, V., Cazzato, V., & Aglioti, S. M. (2013). Their pain is not our pain: Brain and autonomic correlates of empathic resonance with the pain of same and different race individuals. *Human Brain Mapping*, *34*(12), 3168–3181. https://doi.org/10.1002/hbm.22133

Bantin, T., Stevens, S., Gerlach, A. L., & Hermann, C. (2016). What does the facial dot-probe task tell us about attentional processes in social anxiety? A systematic review. *Journal of Behavior Therapy and Experimental Psychiatry*, *50*, 40–51. https://doi.org/10.1016/J.JBTEP.2015.04.009

Bartels, D. J. P., van Laarhoven, A. I. M., Haverkamp, E. A., Wilder-Smith, O. H., Donders, A. R. T., van Middendorp, H., … Evers, A. W. M. (2014). Role of Conditioning and Verbal Suggestion in Placebo and Nocebo Effects on Itch. *PLoS ONE*, *9*(3), e91727. https://doi.org/10.1371/journal.pone.0091727

Bartels, D. J. P., van Laarhoven, A. I. M., Stroo, M., Hijne, K., Peerdeman, K. J., Donders, A. R. T., … Evers, A. W. M. (2017). Minimizing nocebo effects by conditioning with verbal suggestion: A randomized clinical trial in healthy humans. *PLOS ONE*, *12*(9), e0182959. https://doi.org/10.1371/journal.pone.0182959

Bartholomew, R. E., Wessely, S., & Rubin, G. J. (2012). Mass psychogenic illness and the social network: is it changing the pattern of outbreaks? *Journal of the Royal Society of Medicine*, *105*(12), 509–512. https://doi.org/10.1258/jrsm.2012.120053

Bautista, D. M., Wilson, S. R., & Hoon, M. A. (2014). Why we scratch an itch: the molecules, cells and circuits of itch. *Nature Neuroscience*, *17*(2), 175–182. https://doi.org/10.1038/nn.3619

Beaudoin, R., & Michael, G. A. (2014). Gating of spontaneous somatic sensations by movement. *Somatosensory & Motor Research*, *31*(3), 111–121. https://doi.org/10.3109/08990220.2014.888992

Bernhard, J. D. (2005). Itch and pruritus: What are they, and how should itches be classified? *Dermatologic Therapy*, *18*(4), 288–291. https://doi.org/10.1111/j.1529-8019.2005.00040.x

Blome, C., Radtke, M. A., Eissing, L., & Augustin, M. (2016). Quality of Life in Patients with Atopic Dermatitis: Disease Burden, Measurement, and Treatment Benefit. *American Journal of Clinical Dermatology*, *17*(2), 163–169. https://doi.org/10.1007/s40257-015-0171-3

Bradley, M. M., & Lang, P. J. (1994). Measuring emotion: The self-assessment manikin and the semantic differential. *Journal of Behavior Therapy and Experimental Psychiatry*, *25*(1), 49–59. https://doi.org/10.1016/0005-7916(94)90063-9

Brown, R. J., Brunt, N., Poliakoff, E., & Lloyd, D. M. (2010). Illusory touch and tactile perception in somatoform dissociators. *Journal of Psychosomatic Research*, *69*(3), 241–248. https://doi.org/10.1016/j.jpsychores.2009.11.010

Brown, R. J., Danquah, A. N., Miles, E., Holmes, E., & Poliakoff, E. (2010). Attention to the body in nonclinical somatoform dissociation depends on emotional state. *Journal of Psychosomatic Research*, *69*(3), 249–257. https://doi.org/10.1016/J.JPSYCHORES.2010.04.010

Browning, M., Holmes, E. A., Charles, M., Cowen, P. J., & Harmer, C. J. (2012). Using Attentional Bias Modification as a Cognitive Vaccine Against Depression. *Biological Psychiatry*, *72*(7), 572–579. https://doi.org/10.1016/J.BIOPSYCH.2012.04.014

Cazzato, V., Mian, E., Serino, A., Mele, S., & Urgesi, C. (2014). Distinct contributions of extrastriate body area and temporoparietal junction in perceiving one’s own and others’ body. *Cognitive, Affective and Behavioral Neuroscience*. https://doi.org/10.3758/s13415-014-0312-9

Contact dermatitis - NHS. (2018). Retrieved September 26, 2018, from https://www.nhs.uk/conditions/contact-dermatitis/

Corp, I. (2012). IBM SPSS Statistics for Windows. Armonk, NY: IBM Corp.

Crombez, G., Van Ryckeghem, D. M. L., Eccleston, C., & Van Damme, S. (2013). Attentional bias to pain-related information: A meta-analysis. *Pain*, *154*(4), 497–510. https://doi.org/10.1016/j.pain.2012.11.013

Curatolo, M., Arendt-Nielsen, L., & Petersen-Felix, S. (2006). Central Hypersensitivity in Chronic Pain: Mechanisms and Clinical Implications. *Phys Med Rehabil Clin N Am*, *17*, 287–302. https://doi.org/10.1016/j.pmr.2005.12.010

Dandeneau, S. D., Baldwin, M. W., Baccus, J. R., Sakellaropoulo, M., & Pruessner, J. C. (2007). Cutting stress off at the pass: reducing vigilance and responsiveness to social threat by manipulating attention. *Journal of Personality and Social Psychology*, *93*(4), 651–666. https://doi.org/10.1037/0022-3514.93.4.651

Dawn, A., Papoiu, A. D. P., Chan, Y. H., Rapp, S. R., Rassette, N., & Yosipovitch, G. (2009). Itch characteristics in atopic dermatitis: results of a web-based questionnaire. *British Journal of Dermatology*, *160*(3), 642–644. https://doi.org/10.1111/j.1365-2133.2008.08941.x

Dear, B. F., Sharpe, L., Nicholas, M. K., & Refshauge, K. (2011). Pain-Related Attentional Biases: The Importance of the Personal Relevance and Ecological Validity of Stimuli. *The Journal of Pain*, *12*(6), 625–632. https://doi.org/10.1016/J.JPAIN.2010.11.010

Dey, D. D., Landrum, O., & Oaklander, A. L. (2005). Central neuropathic itch from spinal-cord cavernous hemangioma: a human case, a possible animal model, and hypotheses about pathogenesis. *Pain*, *113*(1–2), 233–237. https://doi.org/10.1016/J.PAIN.2004.09.032

Discoid eczema - NHS. (n.d.). Retrieved September 26, 2018, from https://www.nhs.uk/conditions/discoid-eczema/

Duque, A., & Vázquez, C. (2015). Double attention bias for positive and negative emotional faces in clinical depression: Evidence from an eye-tracking study. *Journal of Behavior Therapy and Experimental Psychiatry*, *46*, 107–114. https://doi.org/10.1016/J.JBTEP.2014.09.005

Durlik, C., Cardini, F., & Tsakiris, M. (2014). Being watched: The effect of social self-focus on interoceptive and exteroceptive somatosensory perception. *Consciousness and Cognition*, *25*(1), 42–50. https://doi.org/10.1016/j.concog.2014.01.010

Eberth, J., & Sedlmeier, P. (2012). The Effects of Mindfulness Meditation: A Meta-Analysis. *Mindfulness*, *3*(3), 174–189. https://doi.org/10.1007/s12671-012-0101-x

Elmariah, S. B. (2017). Adjunctive Management of Itch in Atopic Dermatitis. *Dermatologic Clinics*, *35*(3), 373–394. https://doi.org/10.1016/J.DET.2017.02.011

Eucerin. (2015). Eczema flare-up | Atopic Skin | Eucerin. Retrieved December 19, 2018, from https://www.eucerin.co.uk/skin-concerns/atopic-dermatitis/atopic-eczema-flare-up

Evers, A. W. M., Duller, P., De Jong, E. M. G. J., Otero, M. E., Verhaak, C. M., Van Der Valk, P. G. M., … Kraaimaat, F. W. (2009). Effectiveness of a multidisciplinary itch-coping training programme in adults with atopic dermatitis. *Acta Dermato-Venereologica*, *89*(1), 57–63. https://doi.org/10.2340/00015555-0556

Feneran, A. N., O’Donnell, R., Press, A., Yosipovitch, G., Cline, M., Dugan, G., … Shively, C. A. (2013). Monkey see, monkey do: Contagious itch in nonhuman primates. *Acta Dermato-Venereologica*, *93*(1), 27–29. https://doi.org/10.2340/00015555-1406

Finlay, A. Y., & Khan, G. K. (1994). Dermatology Life Quality Index (DLQI)-a simple practical measure for routine clinical use. *Clinical and Experimental Dermatology*, *19*(3), 210–216. https://doi.org/10.1111/j.1365-2230.1994.tb01167.x

Fischer, B., & Weber, H. (1993). Express saccades and visual attention. *Behavioral and Brain Sciences*, *16*(3), 553. https://doi.org/10.1017/S0140525X00031575

Fortune, D. ´ O. G., Richards, H. L., Corrin, A., Taylor, R. J., Griffiths, C. E. M., & Main, C. J. (2003). *Attentional Bias for Psoriasis-Specific and Psychosocial Threat in Patients With Psoriasis*. *Journal of Behavioral*

Medicine (Vol. 17). Retrieved from https://link.springer.com/content/pdf/10.1023%2FA%3A1023408503807.pdf

Glauert, R., Rhodes, G., Fink, B., & Grammer, K. (2009). Body dissatisfaction and attentional bias to thin bodies. *International Journal of Eating Disorders*, *43*(1), NA-NA. https://doi.org/10.1002/eat.20663

Greaves, M. W., & Khalifa, N. (2004). Itch: more than skin deep. *International Archives of Allergy and Immunology*, *135*(2), 166–172. https://doi.org/10.1159/000080898

Green, S. A., Hernandez, L., Bookheimer, S. Y., & Dapretto, M. (2016). Salience Network Connectivity in Autism Is Related to Brain and Behavioral Markers of Sensory Overresponsivity. *Journal of the American Academy of Child and Adolescent Psychiatry*, *55*(7), 618–626.e1. https://doi.org/10.1016/j.jaac.2016.04.013

Grillo, M. P., Long, R. a, & Long, D. (2007). Habit Reversal Training for the Itch-Scratch Cycle Associated with Pruritic Skin Conditions. *Dermatology Nursing*, *19*(3), 243–248.

Handwerker, H. O., Forster, C., & Kirchhoff, C. (1991). Discharge patterns of human C-fibers induced by itching and burning stimuli. *Journal of Neurophysiology*, *66*(1), 307–315. https://doi.org/10.1152/jn.1991.66.1.307

Hazen, E. P., Stornelli, J. L., O'Rourke, J. A., Koesterer, K., & McDougle, C. J. (2014). Sensory Symptoms in Autism Spectrum Disorders. *Harvard Review of Psychiatry*, *22*(2), 112–124. https://doi.org/10.1097/01.HRP.0000445143.08773.58

Hilton, L., Hempel, S., Ewing, B. A., Apaydin, E., Xenakis, L., Newberry, S., … Maglione, M. A. (2017). Mindfulness Meditation for Chronic Pain: Systematic Review and Meta-analysis. *Annals of Behavioral Medicine*, *51*(2), 199–213. https://doi.org/10.1007/s12160-016-9844-2

Hives - NHS. (2018). Retrieved September 26, 2018, from https://www.nhs.uk/conditions/hives/

Holle, H., Warne, K., Seth, A. K., Critchley, H. D., & Ward, J. (2012a). Neural basis of contagious itch and why some people are more prone to it. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(48), 19816–19821. https://doi.org/10.1073/pnas.1216160109

Horne, J. (2015). Psychosocial factors in dermatology. Retrieved December 19, 2018, from https://www.dermnetnz.org/topics/psychosocial-factors-in-dermatology/

Houx, P. J., & Jolles, J. (1993). Age-Related Decline of Psychomotor Speed: Effects of Age, Brain Health, Sex, and Education. *Perceptual and Motor Skills*, *76*(1), 195–211. https://doi.org/10.2466/pms.1993.76.1.195

Ikoma, A., Fartasch, M., Heyer, G., Miyachi, Y., Handwerker, H., & Schmelz, M. (2004). Painful stimuli evoke itch in patients with chronic pruritus: central sensitization for itch. *Neurology*, *62*(2), 212–217. https://doi.org/10.1212/WNL.62.2.212

Ikoma, A., Handwerker, H., Miyachi, Y., & Schmelz, M. (2005). Electrically evoked itch in humans. *Pain*, *113*(1), 148–154. https://doi.org/10.1016/j.pain.2004.10.003

Ikoma, A., Rukwied, R., Ständer, S., Steinhoff, M., Miyachi, Y., & Schmelz, M. (2003a). Neuronal Sensitization for Histamine-Induced Itch in Lesional Skin of Patients With Atopic Dermatitis. *Archives of Dermatology*, *139*(11), 1455–1458. https://doi.org/10.1001/archderm.139.11.1455

Ikoma, A., Rukwied, R., Ständer, S., Steinhoff, M., Miyachi, Y., & Schmelz, M. (2003b). Neurophysiology of Pruritus. *Archives of Dermatology*, *139*(11), 221–226. https://doi.org/10.1001/archderm.139.11.1475

Ikoma, A., Steinhoff, M., Ständer, S., Yosipovitch, G., & Schmelz, M. (2006). The neurobiology of itch. *Nature Reviews Neuroscience*, *7*(7), 535–547. https://doi.org/10.1038/nrn1950

Ikoma, A., Steinhoff, M., Ständer, S., Yosipovitch, G., Schmelz, M., Fartasch, M., … Lotti, T. (2005). Itch, pain, and metaesthetic sensation. *Dermatologic Therapy*, *18*(4), 308–313. https://doi.org/10.1111/j.1529-8019.2005.00037.x

Johnson, R. M., Burton, P. C., & Ro, T. (2006). Visually induced feelings of touch. https://doi.org/10.1016/j.brainr

Jordan, J. M., & Whitlock, F. A. (1974). Anxiety Atopic Dermatitis and Conditioned Scratch. *Journal of Psychosomatic Research*, *18*(5), 297–299.

Kabat-Zinn, J., Wheeler, E., Light, T., Skillings, A., Scharf, M. J., Cropley, T. G., & Bernhard, J. D. (1998). *Influence of a Mindfulness Meditation-Based Stress Reduction Intervention on Rates of Skin Clearing in Patients With Moderate to Severe Psoriasis Undergoing Phototherapy (UVB) and Photochemotherapy (PUVA)*. Retrieved from http://sophro-axe.fr/fs/articles_scientifiques_mindfulness/6lwqn-kabat_zinn_et_al_1998_mbsr_and_psoriasis_pm.pdf

Kaneko, S. (2018). Approach for Aggravating Factors in Atopic Dermatitis. In *Evolution of Atopic Dermatitis in the 21st Century* (pp. 311–319). Singapore: Springer Singapore. https://doi.org/10.1007/978-981-10-5541-6_24

Katzer, A., Oberfeld, D., Hiller, W., & Witthöft, M. (2011). Tactile perceptual processes and their relationship to medically unexplained symptoms and health anxiety. *Journal of Psychosomatic Research*, *71*(5), 335–341. https://doi.org/10.1016/j.jpsychores.2011.03.009

Keogh, E., Dillon, C., Georgiou, G., & Hunt, C. (2001). Selective attentional biases for physical threat in physical anxiety sensitivity. *Journal of Anxiety Disorders*, *15*(4), 299–315. https://doi.org/10.1016/S0887-6185(01)00065-2

Khatibi, A., Dehghani, M., Sharpe, L., Asmundson, G. J. G., & Pouretemad, H. (2009). Selective attention towards painful faces among chronic pain patients: Evidence from a modified version of the dot-probe. *Pain*, *142*(1–2), 42–47. https://doi.org/10.1016/j.pain.2008.11.020

Kini, S. P., DeLong, L. K., Veledar, E., McKenzie-Brown, A. M., Schaufele, M., & Chen, S. C. (2011). The Impact of Pruritus on Quality of Life. *Archives of Dermatology*, *147*(10), 1153. https://doi.org/10.1001/archdermatol.2011.178

Komori, M., & Keene, C. (n.d.). Thematic Analysis | Design Research Techniques. Retrieved December 19, 2018, from http://designresearchtechniques.com/casestudies/thematic-analysis/

Koo, J., & Lebwohl, A. (2001). Psycho dermatology: the mind and skin connection. *American Family Physician*, *64*(11), 1873–1878. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11764865

Koster, E. H. W., Crombez, G., Verschuere, B., & De Houwer, J. (2004). Selective attention to threat in the dot probe paradigm: differentiating vigilance and difficulty to disengage. *Behaviour Research and Therapy*, *42*(10), 1183–1192. https://doi.org/10.1016/J.BRAT.2003.08.001

Kupfer, T., & Fessler, D. (2018). Ectoparasite defence in humans: Relationships to pathogen avoidance, and clinical implications. *Danielmtfessler.com*. Retrieved from http://www.danielmtfessler.com/wp-content/uploads/2018/01/Kupfer-Fessler-in-press-human-ectoparasite-defense.pdf

Lichen Simplex Patient Information. (n.d.). Retrieved September 26, 2018, from http://www.wwl.nhs.uk/library/all_new_pi_docs/audio_leaflets/prosser_white/lichen_simplex/ft_lichen_simplex_hc.html

Lifschitz, C. (2015). The impact of atopic dermatitis on quality of life. *Annals of Nutrition & Metabolism*, *66 Suppl 1*(Suppl. 1), 34–40. https://doi.org/10.1159/000370226

Limanowski, J., Lutti, A., & Blankenburg, F. (2014). The extrastriate body area is involved in illusory limb ownership. *NeuroImage*, *86*, 514–524. https://doi.org/10.1016/J.NEUROIMAGE.2013.10.035

Liossi, C., Schoth, D. E., Bradley, B. P., & Mogg, K. (2009). Time-course of attentional bias for pain-related cues in chronic daily headache sufferers. *European Journal of Pain*, *13*(9), 963–969. https://doi.org/10.1016/j.ejpain.2008.11.007

Liu, T., & Ji, R.-R. (2013). New insights into the mechanisms of itch: are pain and itch controlled by distinct mechanisms? *Pflugers Archiv : European Journal of Physiology*, *465*(12), 1671–1685. https://doi.org/10.1007/s00424-013-1284-2

Lloyd, D. M., Dodd, R., Higgins, C., Burke, M. R., & McGlone, F. (2017). Are sex and history of pruritic skin conditions factors which affect the phenomenon of visually evoked itch? An exploratory study. *Itch*, 1. https://doi.org/10.1097/itx.0000000000000010

Lloyd, D. M., Hall, E., Hall, S., & McGlone, F. P. (2013). Can itch-related visual stimuli alone provoke a scratch response in healthy individuals? *The British Journal of Dermatology*, *168*(1), 106–111. https://doi.org/10.1111/bjd.12132

LLloyd, D. M., Mason, L., Brown, R. J., & Poliakoff, E. (2008). Development of a paradigm for measuring somatic disturbance in clinical populations with medically unexplained symptoms. *Journal of Psychosomatic Research*, *64*(1), 21–24. https://doi.org/10.1016/j.jpsychores.2007.06.004

MacLeod, C., Mathews, A., & Tata, P. (1986). Attentional bias in emotional disorders. *Journal of Abnormal Psychology*, *95*(1), 15–20. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/3700842

Mark, J., Williams, G., Mathews, A., & Macleod, C. (1996). *The Emotional Stroop Task and Psychopathology*. *Psychological Bulletin* (Vol. 120). Retrieved from http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.924.5225&rep=rep1&type=pdf

Matterne, U., Apfelbacher, C., Vogelgsang, L., Loerbroks, A., & Weisshaar, E. (2013). Incidence and Determinants of Chronic Pruritus: A Population-based Cohort Study. *Acta Dermato Venereologica*, *93*(5), 532–537. https://doi.org/10.2340/00015555-1572

Mazzoni, G., Foan, L., Hyland, M. E., & Kirsch, I. (2010). The Effects of Observation and Gender on Psychogenic Symptoms. *Health Psychology*, *29*(2), 181–185. Retrieved from https://insights.ovid.com/health-psychology/hepsy/2010/03/000/effects-observation-gender-psychogenic-symptoms/12/00003615

McKenzie, K. J., Lloyd, D. M., Brown, R. J., Plummer, F., & Poliakoff, E. (2012). Investigating the mechanisms of visually-evoked tactile sensations. *Acta Psychologica*, *139*(1), 46–53. https://doi.org/10.1016/j.actpsy.2011.09.012

Mechanic, D. (1962). The concept of illness behavior. *Journal of Chronic Diseases*, *15*(2), 189–194. https://doi.org/10.1016/0021-9681(62)90068-1

Melzack, R. (1975). The McGill Pain Questionnaire: Major properties and scoring methods. *PAIN*, *1*(3), 277–299. https://doi.org/10.1016/0304-3959(75)90044-5

Mercan, S., & Kivanç Altunay, İ. (2006). *Psychodermatology: A Collaborative Subject of Psychiatry and Dermatology*. *Turkish Journal of Psychiatry* (Vol. 17). Retrieved from http://www.turkpsikiyatri.com/C17S4/en/17-4-8.pdf

Michael, G. A., Dupuy, M. A., Deleuze, A., Humblot, M., Simon, B., & Naveteur, J. (2012). Interacting effects of vision and attention in perceiving spontaneous sensations arising on the hands. *Experimental Brain Research*, *216*(1), 21–34. https://doi.org/10.1007/s00221-011-2901-y

Mirams, L., Poliakoff, E., Brown, R. J., & Lloyd, D. M. (2010). Vision of the body increases interference on the somatic signal detection task. *Experimental Brain Research*, *202*(4), 787–794. https://doi.org/10.1007/s00221-010-2185-7

Mirams, L., Poliakoff, E., Brown, R. J., & Lloyd, D. M. (2012). Interoceptive and exteroceptive attention have opposite effects on subsequent somatosensory perceptual decision making. *Quarterly Journal of Experimental Psychology (2006)*, *65*(5), 926–938. https://doi.org/10.1080/17470218.2011.636823

Mirams, L., Poliakoff, E., Brown, R. J., & Lloyd, D. M. (2013). Brief body-scan meditation practice improves somatosensory perceptual decision making. *Consciousness and Cognition*, *22*(1), 348–359. https://doi.org/10.1016/j.concog.2012.07.009

Mitchell, C. W. (1995). Effects of Subliminally Presented Auditory Suggestions of Itching on Scratching Behavior. *Perceptual and Motor Skills*, *80*(1), 87–96. https://doi.org/10.2466/pms.1995.80.1.87

Mochizuki, H., Baumgärtner, U., Kamping, S., Ruttorf, M., Schad, L. R., Flor, H., … Treede, R.-D. (2013). Cortico-subcortical activation patterns for itch and pain imagery. *PAIN®*, *154*(10), 1989–1998. https://doi.org/10.1016/j.pain.2013.06.007

Mochizuki, H., Papoiu, A. D. P., Nattkemper, L. A., Lin, A. C., Kraft, R. A., Coghill, R. C., & Yosipovitch, G. (2015). Scratching Induces Overactivity in Motor-Related Regions and Reward System in Chronic Itch Patients. *Journal of Investigative Dermatology*, *135*(10), 2814–2823. https://doi.org/10.1038/jid.2015.223

Mochizuki, H., Schut, C., Nattkemper, L. A., & Yosipovitch, G. (2017). Brain mechanism of itch in atopic dermatitis and its possible alteration through non-invasive treatments. *Allergology International*, *66*(1), 14–21. https://doi.org/10.1016/j.alit.2016.08.013

Mochizuki, H., Tanaka, S., Morita, T., Wasaka, T., Sadato, N., & Kakigi, R. (2014). The cerebral representation of scratching-induced pleasantness. *Journal of Neurophysiology*. https://doi.org/10.1152/jn.00374.2013

Mogg, K., & Bradley, B. P. (1999). Some methodological issues in assessing attentional biases for threatening faces in anxiety: a replication study using a modified version of the probe detection task. *Behaviour Research and Therapy*, *37*(6), 595–604. https://doi.org/10.1016/S0005-7967(98)00158-2

Mogg, K., Bradley, B. P., Field, M., & De Houwer, J. (2003). Eye movements to smoking-related pictures in smokers: relationship between attentional biases and implicit and explicit measures of stimulus valence. *Addiction*, *98*(6), 825–836. https://doi.org/10.1046/j.1360-0443.2003.00392.x

Mogg, K., McNamara, J., Powys, M., Rawlinson, H., Seiffer, A., & Bradley, B. P. (2000). Selective attention to threat: A test of two cognitive models of anxiety. *Cognition & Emotion*, *14*(3), 375–399. https://doi.org/10.1080/026999300378888

Mogg, K., Millar, N., & Bradley, B. P. (2000). Biases in eye movements to threatening facial expressions in generalized anxiety disorder and depressive disorder. *Journal of Abnormal Psychology*, *109*(4), 695–704. https://doi.org/10.1037//0021-843X.109.4.695

Mogoaşe, C., David, D., & Koster, E. H. W. (2014). Clinical Efficacy of Attentional Bias Modification Procedures: An Updated Meta-Analysis. *Journal of Clinical Psychology*, *70*(12), 1133–1157.

https://doi.org/10.1002/jclp.22081

Mueller, S. M., Hogg, S., Mueller, J. M., McKie, S., Itin, P., Reinhardt, J., … Kleyn, C. E. (2017). Functional magnetic resonance imaging in dermatology: The skin, the brain and the invisible. *Experimental Dermatology*, *26*(10), 845–853. https://doi.org/10.1111/exd.13305

Napadow, V., Li, A., Loggia, M. L., Kim, J., Mawla, I., Desbordes, G., … Pfab, F. (2015). The imagined itch: Brain circuitry supporting nocebo-induced itch in atopic dermatitis patients. *Allergy: European Journal of Allergy and Clinical Immunology*, *70*(11). https://doi.org/10.1111/all.12727

National Eczema Association. (2013). Eczema Symptoms & Causes | National Eczema Association. Retrieved December 19, 2018, from https://nationaleczema.org/eczema/

Niemeier, V., Kupfer, J., & Gieler, U. (2000). Observations during an Itch-Inducing Lecture. *Dermatology Psychosomatics*, *1*, 15–18. https://doi.org/10.1159/000057993

Nilsson, H.-J., Levinsson, A., & Schouenborg, J. (1997). Cutaneous field stimulation (CFS): a new powerful method to combat itch. *Pain*, *71*(1), 49–55. https://doi.org/10.1016/S0304-3959(97)03339-3

Obradors, M., Blanch, C., Comellas, M., Figueras, M., & Lizan, L. (2016). Health-related quality of life in patients with psoriasis: a systematic review of the European literature. *Quality of Life Research*, *25*(11), 2739–2754. https://doi.org/10.1007/s11136-016-1321-7

Ogden, J. (2003). Some problems with social cognition models: A pragmatic and conceptual analysis. *Health Psychology*, *22*(4), 424–428. https://doi.org/10.1037/0278-6133.22.4.424

Ogden, J., & Zoukas, S. (2009). Generating physical symptoms from visual cues: an experimental study. *Psychology, Health and Medicine*, *14*, 695–704.

Ohman, A., Flykt, A., & Esteves, F. (2001). Emotion drives attention: detecting the snake in the grass. *Journal of Experimental Psychology. General*, *130*(3), 466–478. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11561921

Olek-Hrab, K., Hrab, M., Szyfter-Harris, J., & Adamski, Z. (2016). Pruritus in selected dermatoses. *European Review for Medical and Pharmacological Sciences*, *20*(17), 3628–3641. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/27649664

Papoiu, A. D. P., Nattkemper, L. A., Sanders, K. M., Kraft, R. A., Chan, Y.-H., Coghill, R. C., & Yosipovitch, G. (2013). Brain's reward circuits mediate itch relief. a functional MRI study of active scratching. *PloS One*, *8*(12), e82389. https://doi.org/10.1371/journal.pone.0082389

Papoiu, A. D. P., Wang, H., Coghill, R. C., Chan, Y. H., & Yosipovitch, G. (2011). Contagious itch in humans: A study of visual "transmission" of itch in atopic dermatitis and healthy subjects. *British Journal of Dermatology*. https://doi.org/10.1111/j.1365-2133.2011.10318.x

Pavlis, J., & Yosipovitch, G. (2017). Management of Itch in Atopic Dermatitis. *American Journal of Clinical Dermatology*, 1–14. https://doi.org/10.1007/s40257-017-0335-4

Payne, K. A., Binik, Y. M., Amsel, R., & Khalifé, S. (2005). When sex hurts, anxiety and fear orient attention towards pain. *European Journal of Pain*, *9*(4), 427–427. https://doi.org/10.1016/j.ejpain.2004.10.003

Peirce, J. W. (2007). PsychoPy—Psychophysics software in Python. *Journal of Neuroscience Methods*, *162*(1–2), 8–13. https://doi.org/10.1016/J.JNEUMETH.2006.11.017

Pine, D. S., Mogg, K., Bradley, B. P., Montgomery, L., Monk, C. S., McClure, E., … Kaufman, J. (2005). Attention Bias to Threat in Maltreated Children: Implications for Vulnerability to Stress-Related Psychopathology. *American Journal of Psychiatry*, *162*(2), 291–296. https://doi.org/10.1176/appi.ajp.162.2.291

Poliakoff, E., Miles, E., Li, X., & Blanchette, I. (2007). The effect of visual threat on spatial attention to touch. *Cognition*, *102*(3), 405–414. https://doi.org/10.1016/j.cognition.2006.01.006

Psoriasis - NHS. (2018). Retrieved September 26, 2018, from https://www.nhs.uk/conditions/psoriasis/

Rechenberger, I. (1981). [Pruritus as a psychic phenomenon (author's transl)]. *MMW, Munchener Medizinische Wochenschrift*, *123*(24), 1005–1006. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/6789162

Reich, A., Hrehorow, E., & Szepietowski, J. (2010). Pruritus is an Important Factor Negatively Influencing the Well-being of Psoriatic Patients. *Acta Dermato Venereologica*, *90*(3), 257–263. https://doi.org/10.2340/00015555-0851

Reitamo, S., Rustin, M., Ruzicka, T., Cambazard, F., Kalimo, K., Friedmann, P. S., … European Tacrolimus Ointment Study Group. (2002). Efficacy and safety of tacrolimus ointment compared with that of hydrocortisone butyrate ointment in adult patients with atopic dermatitis. *The Journal of Allergy and Clinical Immunology*, *109*(3), 547–555. https://doi.org/10.1067/MAI.2002.121832

Relaxio. (n.d.). White Noise Generator – Apps on Google Play. Retrieved December 19, 2018, from https://play.google.com/store/apps/details?id=net.relaxio.relaxio&hl=en_GB

Rinck, M., & Becker, E. S. (2005). A Comparison of Attentional Biases and Memory Biases in Women With Social Phobia and Major Depression. *Journal of Abnormal Psychology*, *114*(1), 62–74. https://doi.org/10.1037/0021-843X.114.1.62

Robertson, C. E., & Baron-Cohen, S. (2017). Sensory perception in autism. *Nature Publishing Group*, *18*. https://doi.org/10.1038/nrn.2017.112

Rosenthal, R., & Fode, K. L. (1963). Psychology of the Scientist: V. Three Experiments in Experimenter Bias. *Psychological Reports*, *12*(2), 491–511. https://doi.org/10.2466/pr0.1963.12.2.491

Rosenthal, R., & Rosnow, R. L. (2009). *Artifacts in behavioral research : Robert Rosenthal and Ralph L. Rosnow's classic books : a re-issue of Artifact in behavioral research, Experimenter effects in behavioral research and the volunteer subject*. Oxford University Press. Retrieved from https://books.google.co.uk/books?id=zAMeF0JOtY0C&printsec=frontcover&dq=Artifacts+in+Behavioral+Research:+Robert+Rosenthal+and+Ralph+L.+Rosnow%27s+Classic+Books&hl=en&sa=X&ved=0ahUKEwi174iX1NvZAhXBK8AKHQP0BOwQ6AEIKzAA#v=onepage&q=Artifacts in Behavioral Research%3A Robert Rosenthal and Ralph L. Rosnow's Classic Books&f=false

Rosenthal, R., & Rubin, D. B. (1978). Interpersonal expectancy effects: the first 345 studies. *Behavioral and Brain Sciences*, *1*(3), 377. https://doi.org/10.1017/S0140525X00075506

Russell, M., Dark, K. A., Cummins, R. W., Ellman, G., Callaway, E., & Peeke, H. V. (1984). Learned histamine release. *Science (New York, N.Y.)*, *225*(4663), 733–734. https://doi.org/10.1126/SCIENCE.6205449

Rystedt, I. (1985). Prognostic factors in atopic dermatitis. *Acta Dermato-Venereologica*, *65*(3), 206–213. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/2411075

Sanders, K. M., & Akiyama, T. (2018). The vicious cycle of itch and anxiety. *Neuroscience & Biobehavioral Reviews*, *87*, 17–26. https://doi.org/10.1016/J.NEUBIOREV.2018.01.009

Schineller, M. (2018). *Increased Contagious Itch in Children with Autism Spectrum Disorder (ASD)*. Retrieved from https://digitalrepository.trincoll.edu/theses/705

Schmied, C., & Saurat, J.-H. (1991). Epidemiology of Atopic Eczema. In *Handbook of Atopic Eczema* (pp. 9–14). Berlin, Heidelberg: Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-662-02671-7_2

Schmukle, S. C. (2005). Unreliability of the Dot Probe Task. *European Journal of Personality Eur. J. Pers*, *19*, 595–605. https://doi.org/10.1002/per.554

Schoth, D. E., & Liossi, C. (2010). Attentional Bias Toward Pictorial Representations of Pain in Individuals With Chronic Headache. *The Clinical Journal of Pain*, *26*(3), 244–250. https://doi.org/10.1097/AJP.0b013e3181bed0f9

Schut, C., Bosbach, S., Gieler, U., & Kupfer, J. (2014). Personality traits, depression and itch in patients with atopic dermatitis in an experimental setting: a regression analysis. *Acta Dermato-Venereologica*, *94*, 20–25. https://doi.org/10.2340/00015555-1634

Schut, C., Grossman, S., Gieler, U., Kupfer, J., & Yosipovitch, G. (2015). Contagious itch: what we know and what we would like to know. *Frontiers in Human Neuroscience*. https://doi.org/10.3389/fnhum.2015.00057

Schut, C., Mochizuki, H., Grossman, S. K., Lin, A. C., Conklin, C. J., Mohamed, F. B., … Yosipovitch, G. (2017). Brain Processing of

Contagious Itch in Patients with Atopic Dermatitis. *Frontiers in Psychology*, *8*, 1267. https://doi.org/10.3389/fpsyg.2017.01267

Schut, C., Radel, A., Frey, L., Gieler, U., & Kupfer, J. (2016). Role of personality and expectations for itch and scratching induced by audiovisual itch stimuli. *European Journal of Pain (United Kingdom)*, *20*(1), 14–18. https://doi.org/10.1002/ejp.751

See, J., MacLeod, C., & Bridle, R. (2009). The reduction of anxiety vulnerability through the modification of attentional bias: a real-world study using a home-based cognitive bias modification procedure. *Journal of Abnormal Psychology*, *118*(1), 65–75. https://doi.org/10.1037/a0014377

Simone, D. A., Alreja, M., & Lamotte, R. H. (1991). Psychophysical Studies of the Itch Sensation and Itchy Skin (“Alloknesis”) Produced by Intracutaneous Injection of Histamine. *Somatosensory & Motor Research*, *8*(3), 271–279. https://doi.org/10.3109/08990229109144750

Skelton, J., & Pennebaker, J. (1982). Social Psychology of Health and Illness. In G. S. Sanders & J. M. Suls (Eds.) (pp. 226–248). L. Erlbaum Associates. https://doi.org/10.1017/CBO9780511801921.010

Smith, B. W., Tooley, E. M., Montague, E. Q., Robinson, A. E., Cosper, C. J., & Mullins, P. G. (2008). Habituation and sensitization to heat and cold pain in women with fibromyalgia and healthy controls. *PAIN*, *140*(3), 420–428. https://doi.org/10.1016/J.PAIN.2008.09.018

Ständer, S., & Schmelz, M. (2006). Chronic itch and pain-Similarities and differences. *European Journal of Pain*, *10*(5), 473–473. https://doi.org/10.1016/j.ejpain.2006.03.005

Stante, M., Hanna, D., & Lotti, T. (2005). Itch, pain, and metaesthetic sensation. *Dermatologic Therapy*, *18*(4), 308–313. https://doi.org/10.1111/j.1529-8019.2005.00037.x

Stewart, A. C., & Thomas, S. E. (2006). Hypnotherapy as a treatment for atopic dermatitis in adults and children. *British Journal of Dermatology*, *132*(5), 778–783. https://doi.org/10.1111/j.1365-2133.1995.tb00726.x

Stumpf, A., Zerey, V., Heuft, G., Ständer, S., Pfleiderer, B., & Schneider, G. (2016). Itch perception and skin reactions as modulated by verbal suggestions: Role of participant’s and investigator’s sex. *Acta Dermato-Venereologica*, *96*(5), 619–623. https://doi.org/10.2340/00015555-2336

Swithenbank, S., Cowdell, F., & Holle, H. (2016). The role of auditory itch contagion in psoriasis. *Acta Dermato-Venereologica*, *96*(6), 728–731. https://doi.org/10.2340/00015555-2320

Szepietowski, J. C., & Reszke, R. (2017). Itch and Stress. In *Stress and Skin Disorders* (pp. 55–74). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-46352-0_6

Taylor, M. M., & Creelman, C. D. (2005). PEST: Efficient Estimates on Probability Functions. *The Journal of the Acoustical Society of America*, *41*(4A), 782–787. https://doi.org/10.1121/1.1910407

Tihanyi, B., & Köteles, F. (2017). Physiological and psychological correlates of attention-related body sensations (tingling and warmth). *Physiology International*, *104*(3), 235–246. https://doi.org/10.1556/2060.104.2017.3.4

Treshi-marie Perera, A., Newport, R., & McKenzie, K. J. (2015). Multisensory distortions of the hand have differential effects on tactile perception. *Experimental Brain Research*, *233*(11), 3153–3161. https://doi.org/10.1007/s00221-015-4384-8

Tuckett, R. P. (1982). *Itch Evoked by Electrical Stimulation of the Skin* (Vol. 79). https://doi.org/10.1111/1523-1747.ep12529734

Vago, D. R., & Nakamura, Y. (2011). Selective Attentional Bias Towards Pain-Related Threat in Fibromyalgia: Preliminary Evidence for Effects of Mindfulness Meditation Training. *Cognitive Therapy and Research*, *35*(6), 581–594. https://doi.org/10.1007/s10608-011-9391-x

van Damme, S., Crombez, G., Eccleston, C., & Roelofs, J. (2004). The role of hypervigilance in the experience of pain. *Understanding and Treating Fear of Pain*, (January), 71–90.

Van Damme, S., Gallace, A., Spence, C., Crombez, G., & Moseley, G. L. (2009). Does the sight of physical threat induce a tactile processing bias?. Modality-specific attentional facilitation induced by viewing threatening pictures. *Brain Research*, *1253*, 100–106. https://doi.org/10.1016/j.brainres.2008.11.072

Van Hulle, L., Van Damme, S., Spence, C., Crombez, G., & Gallace, A. (2013). Spatial attention modulates tactile change detection. *Experimental Brain Research*, *224*(2), 295–302. https://doi.org/10.1007/s00221-012-3311-5

Van Laarhoven, A. I. M., Kraaimaat, F. W., Wilder-Smith, O. H., & Evers, A. W. M. (2010). Role of attentional focus on bodily sensations in sensitivity to itch and pain. *Acta Dermato-Venereologica*, *90*(1), 46–51. https://doi.org/10.2340/00015555-0743

van Laarhoven, A. I. M., Kraaimaat, F. W., Wilder-Smith, O. H., van de Kerkhof, P. C. M., & Evers, A. W. M. (2010). Heterotopic pruritic conditioning and itch - Analogous to DNIC in pain? *Pain*, *149*(2), 332–337. https://doi.org/10.1016/j.pain.2010.02.026

van Laarhoven, A. I. M., van Damme, S., Lavrijsen, A. P. M., van Ryckeghem, D. M., Crombez, G., & Evers, A. W. M. (2018). Attentional processing of itch. *Psychological Research*, *82*(5), 876–888. https://doi.org/10.1007/s00426-017-0878-2

Van Laarhoven, A. I. M., Vogelaar, M. L., Wilder-Smith, O. H., Van Riel, P. L. C. M., Van De Kerkhof, P. C. M., Kraaimaat, F. W., & Evers, A. W. M. (2011). Induction of nocebo and placebo effects on itch and pain by verbal suggestions. *Pain*, *152*(7), 1486–1494. https://doi.org/10.1016/j.pain.2011.01.043

Vandenbroucke, S., Crombez, G., Van Ryckeghem, D. M. L., Brass, M., Van Damme, S., & Goubert, L. (2013). Vicarious pain while observing another in pain: an experimental approach. *Frontiers in Human Neuroscience*, *7*(May 2014). https://doi.org/10.3389/fnhum.2013.00265

Varicose eczema - NHS. (2016). Retrieved September 26, 2018, from https://www.nhs.uk/conditions/varicose-eczema/

Verhoeven, E. W. M., de Klerk, S., Kraaimaat, F. W., van de Kerkhof, P. C. M., de Jong, E. M. G. J., & Evers, A. W. M. (2008). Biopsychosocial mechanisms of chronic itch in patients with skin diseases: a review. *Acta Dermato-Venereologica*, *88*(3), 211–218. https://doi.org/10.2340/00015555-0452

Wahn, U., Bos, J. D., Goodfield, M., Caputo, R., Papp, K., Manjra, A., … de Prost, Y. (2002). Efficacy and Safety of Pimecrolimus Cream in the Long-Term Management of Atopic Dermatitis in Children. *PEDIATRICS*. https://doi.org/10.1542/peds.110.1.e2

Walter, G. (2011). ITCH SCRATCH CYCLE | Don't just treat it - Eliminate it! Retrieved December 19, 2018, from http://www.apsolvo.com/itch-scratch-cycle

Ward, J., Burckhardt, V., & Holle, H. (2013). Contagious scratching: shared feelings but not shared body locations. *Frontiers in Human Neuroscience*, *7*(May), 122. https://doi.org/10.3389/fnhum.2013.00122

Waters, A. M., Bradley, B. P., & Mogg, K. (2014). Biased attention to threat in paediatric anxiety disorders (generalized anxiety disorder, social phobia, specific phobia, separation anxiety disorder) as a function of "distress" versus "fear" diagnostic categorization. *Psychological Medicine*, *44*(3), 607–616. https://doi.org/10.1017/S0033291713000779

Weisshaar, E., & Dalgard, F. (2009). Epidemiology of itch: Adding to the burden of skin morbidity. *Acta Dermato-Venereologica*, *89*(4), 339–350. https://doi.org/10.2340/00015555-0662

Woods, S. M., Natterson, J., & Silverman, J. (1966). Medical students' disease: hypochondriasis in medical education. *Journal of Medical Education*, *41*(8), 785–790. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/4380602

Yiend, J., & Mathews, A. (2001). Anxiety and Attention to Threatening Pictures. *The Quarterly Journal of Experimental Psychology Section A*, *54*(3), 665–681. https://doi.org/10.1080/713755991

Yosipovitch, G., Ansari, N., Goon, A., Chan, Y. H., & Goh, C. L. (2002). Clinical characteristics of pruritus in chronic idiopathic urticaria. *British Journal of Dermatology*, *147*(1), 32–36. https://doi.org/10.1046/j.1365-2133.2002.04758.x

Yosipovitch, G., Carstens, E., & McGlone, F. (2007). Chronic itch and chronic pain: Analogous mechanisms. *Pain*, *131*(1–2), 4–7. https://doi.org/10.1016/j.pain.2007.04.017

Yosipovitch, G., & Papoiu, A. D. P. (2008). What causes itch in atopic dermatitis? *Current Allergy and Asthma Reports*. https://doi.org/10.1007/s11882-008-0049-z

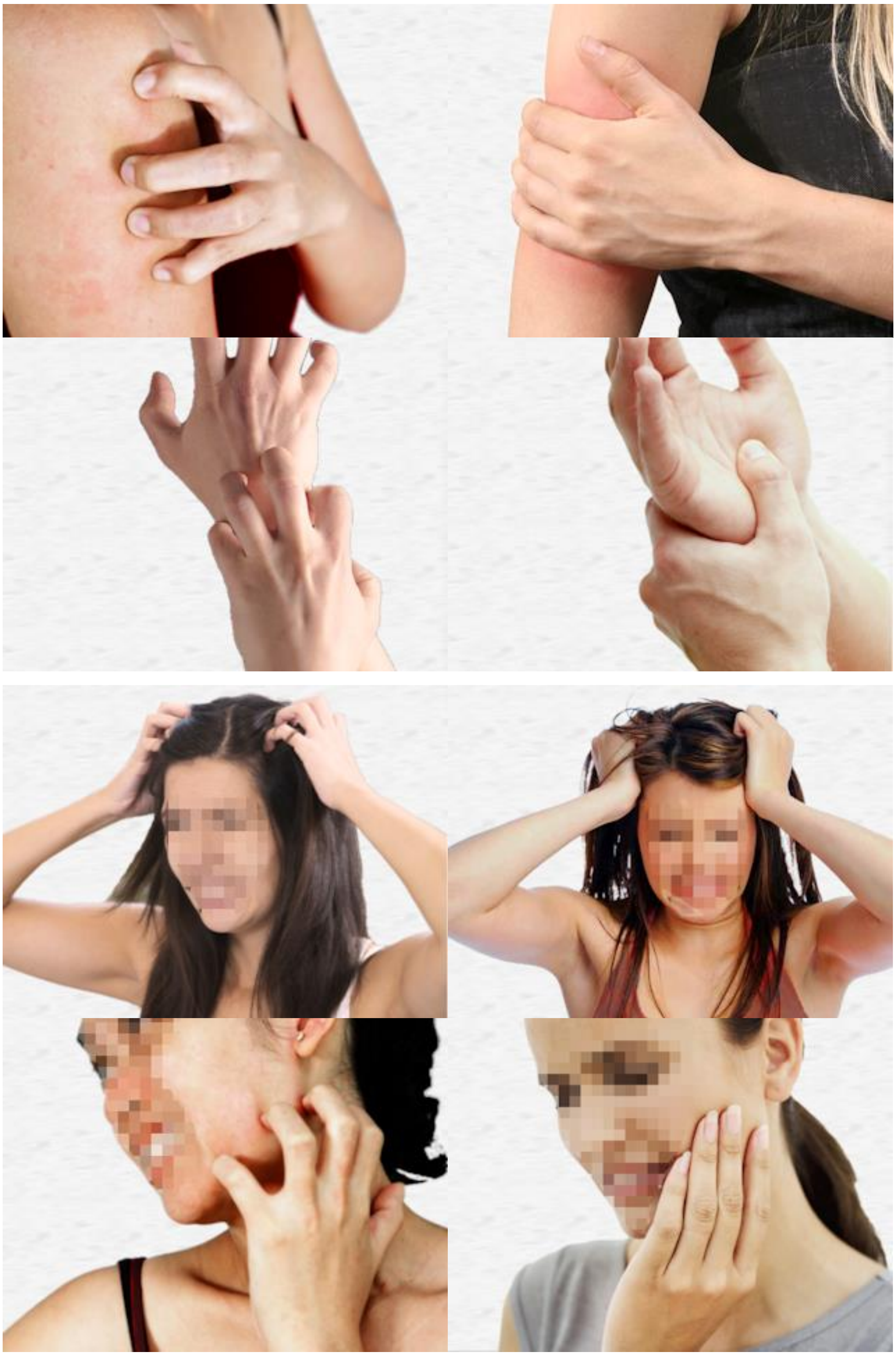
Yu, Y.-Q., Barry, D. M., Hao, Y., Liu, X.-T., & Chen, Z.-F. (2017). Molecular and neural basis of contagious itch behavior in mice. *Science (New York, N.Y.)*, *355*(6329), 1072–1076. https://doi.org/10.1126/science.aak9748

Zhao, Z.-Q., Liu, X.-Y., Jeffry, J., Karunarathne, W. K. A., Li, J.-L., Munanairi, A., … Chen, Z.-F. (2014). Descending Control of Itch Transmission by the Serotonergic System via 5-HT1A-Facilitated GRP-GRPR Signaling. *Neuron*, *84*(4), 821–834. https://doi.org/10.1016/J.NEURON.2014.10.003

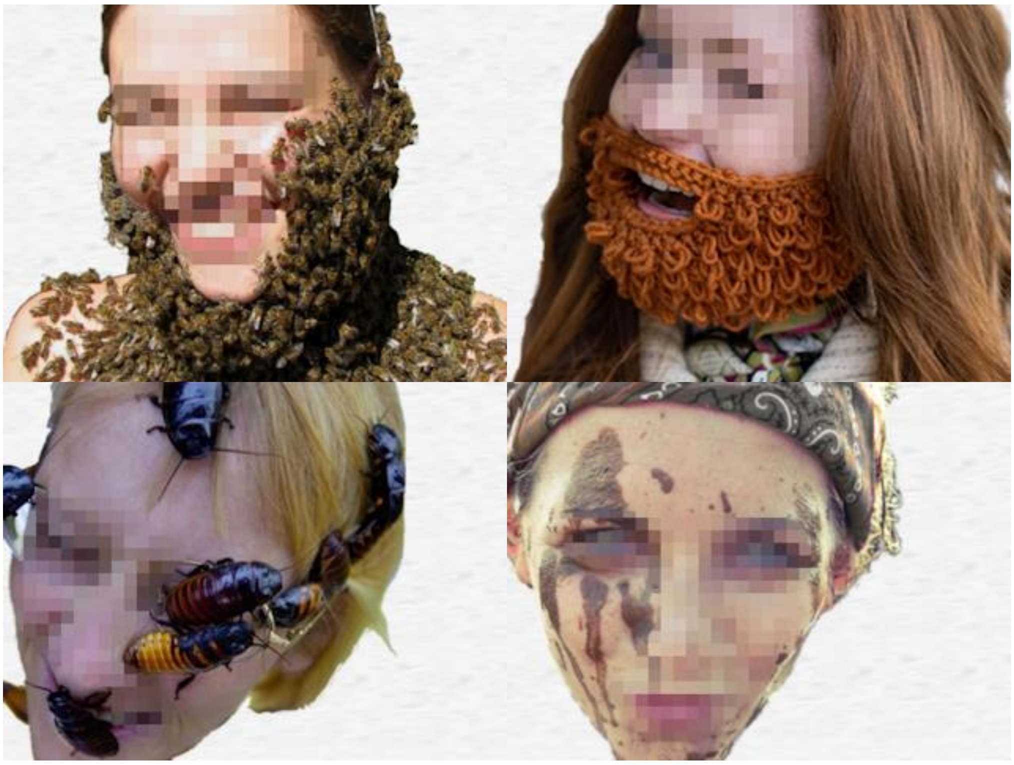
Appendix A

Large copies of the stimulus set

Action

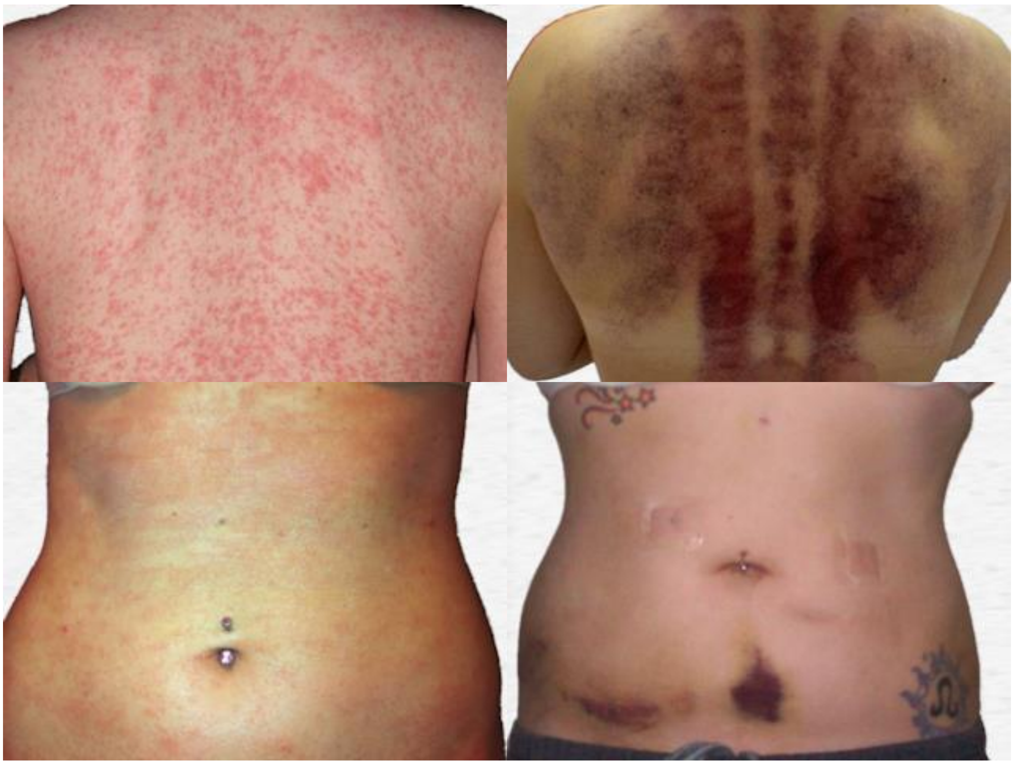


Irritant contact



Irritant context

Skin response



Appendix B

Hypothetical data generated to model the dataset of Van Laarhoven et al. (2017), with the same number of participants, averages and standard deviations.

Congruent	Incongruent
251.7185369	354.813633
270.5354921	346.842872
312.7033429	338.943409
322.9448208	312.749208
263.3783795	331.157915
344.8427052	252.572401
264.9363494	322.731558
348.3180695	339.165736
286.0436052	277.233853
317.9770986	366.955517
309.8444669	353.583439
286.6262841	353.248852
277.8567311	312.941363
234.8393673	285.68718
367.2084366	287.765436
404.0172366	336.215676
354.6649142	322.0293
375.5113992	233.552702
250.117334	333.833725
379.3200112	319.982209
255.714341	285.950076
339.3994439	355.13953
351.5236763	292.759202
339.8039033	395.250302

340.9437407	349.827877
246.4788064	330.29304
257.232811	388.775457
230.1553921	355.700915
294.3459142	352.844895
333.3672984	280.372112
291.86402	285.964345
280.6668316	317.059252
253.2464128	323.230427
312.8207053	307.309855
327.7637594	317.256219
234.5655408	301.594357
386.0121938	334.195487
289.9249909	368.625862
307.699718	275.550331
344.2500673	259.859737
362.2158517	354.734738
380.9026833	345.13009
361.7534276	277.103445
334.3047103	373.454811
333.754135	324.941475
331.3730015	295.41709
282.4660947	266.707734
358.2343006	316.824738
265.4139208	326.314752
258.9632946	306.291722
366.1077347	286.508621
290.9774241	357.477997
346.5179785	307.268789
307.8958565	305.507349
367.3675988	379.484672
220.9934687	231.345418

371.6911213	311.325732
246.0329458	347.17541
345.9184941	321.863597
287.2378139	356.644733
354.6470856	245.009457
297.3010978	372.732252
263.4217162	330.032027
282.7920822	211.122298
328.0653869	288.93067
270.5899476	351.583313
211.5178158	431.354017
289.582983	367.883858
253.5033272	268.969752
304.7544734	388.580674
345.9114522	315.903411
354.4318287	240.138568
280.3721627	342.000731
333.3174527	254.691476
334.0308279	354.695858
428.7186228	304.455871
276.0685902	306.678776
294.479799	292.671551
290.4238157	236.185015
351.6207272	390.421198
372.1362257	291.38699
245.1065747	288.684063