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What is new in the psychology of chronic itch?

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Abstract

Itch is often regarded as unpleasant or bothersome and is accompanied by symptoms of distress and impairments in daily life. The biopsychosocial model of chronic itch describes how psychological factors can contribute to the improvement or exacerbation of chronic itch and related scratching behaviour. Recent research underlines the important role of cognitive-affective information processing, such as attention, affect and expectancies. This may not only play a role for acute itch states, but may particularly apply to the process of itch chronification, for example, due to the vicious cycle in which these factors shape the experience of itch. The present paper focuses on new insights into the relation between itch and the cognitive-affective factors of attention, affect and expectancies. These factors are thought to play a possible aggravating role in itch in the long term and have received increasing attention in the recent empirical literature on maintaining and exacerbating factors for chronic physical symptoms. Possible psychophysiological and neurobiological pathways regarding these factors are discussed, as well as possible intervention methods.

KEYWORDS

affect, attention, expectancy, placebo effect, pruritus

1 | INTRODUCTION

Itch is often regarded as unpleasant and disturbing and is frequently accompanied by symptoms of distress and impairments in daily functioning (eg,^[1,2]) In addition, the related scratching behaviour has many negative consequences for the patient's emotional well-being in the long run (eg, depressed mood), which in turn might result in increased scratching behaviour and worsening of the skin condition (ie, itch-scratch cycle).^[1-4] Accordingly, in many studies, stress, anxiety and depression have been linked to chronic itch in patients with skin diseases (eg,^[2,27]) Psychological factors, as described in biopsychosocial models, can contribute to the worsening or improvement of chronic itch. For example, relatively stable personality characteristics of neuroticism, or illness cognitions like helplessness and perceived stigmatization, can contribute to excessive scratching and non-adherence to treatment prescriptions.^[4-7] However,

less attention has been paid to cognitive-affective information-processing factors that reflect aspects that are more dynamic over time, such as the perception and interpretation of itch during or after an itch stimulus. Recent models of chronic physical symptoms particularly emphasize the possible role that more dynamic, cognitive-affective factors such as attention, affect and expectancies may play in the experience and chronification of symptoms.^[8,9] These cognitive-affective factors are theorized to play an important role in the processing of itch, due to the vicious cycles in which they shape the experience of itch by altered perceptions and interpretations. In this paper, we focus on new insights into the relation between itch and psychological factors, particularly those information-processing factors that are thought to aggravate itch in the long term and that have received increasing attention in the recent empirical literature on maintaining and exacerbating factors of chronic physical symptoms, specifically attention, affect and expectancies.

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2 | ATTENTION AND ITCH

Itch is a bodily signal that draws attention as an integral characteristic of its function. Itch signals the presence of potentially harmful agents in the environment, for example, an insect that may be infectious.^[10,11] Once we are aware of potential harm, we can take action to prevent hazardous situations, for example, by removing the insect.^[11] However, this entails an interruption in our attention for the task we are performing.^[12] When itch is chronic—for example, as a consequence of a dermatological condition—patients will be recurrently disturbed by the itch, scratching behaviour, and potentially also by social reactions of others (eg, stigmatization), which can have a great impact on their quality of life.^[4,13–15]

Although research into attentional processing of itch is relatively young, attention theories for pain have evolved over the years,^[12,16,17] and these may also apply to itch. Pain is also a somatosensory sensation whose primary function is to alarm us to potential harm to bodily integrity. For pain, it has been shown that whether attention is immediately shifted to what is perceived depends on the characteristics of the incoming stimuli. When stimuli are more intense, new and threatening, they are likely to capture attention.^[17] On the one hand, stimuli are also more likely to capture attention when they are considered relevant to the current task (attentional set hypothesis).^[17] On the other hand, attention is less likely to be interrupted by task-irrelevant input when one is highly engaged in current task performance (ie, all attentional resources have been recruited; attentional load hypothesis) and one is highly dedicated to accomplishing set goals.^[12,16,17] In line, itch, particularly when novel and intense, may initiate an involuntary shift in attention from the current focus towards the itch location. More intense itch has been shown to interfere in daily life and affect quality of life to a larger extent.^[14] Experimental studies in healthy individuals also indicate that itch can impair task performance,^[18] although evidence is inconclusive.^[19] Additionally, attention is not consistently drawn to the location where itch is perceived.^[18,19] The spatial attention allocation of itch may be different when an individual suffers from clinical itch, but this has not been investigated to our knowledge.

Experimental itch research on attention has mainly used (audio-)visual stimuli, such as crawling insects, scratch sounds and other people scratching. Patients have been shown to respond with higher levels of perceived itch and scratching when compared to healthy controls upon observing itchy audiovisual material.^[20–22] This phenomenon is called *contagious itch*.^[3] Neurobiological findings of itch contagion demonstrate involvement of regions that are involved in motivation, craving, motor functions, decision-making, memory retrieval, empathy and attentional processes (probably facilitating the observation of itch cues from the environment).^[20,21] Furthermore, heightened attention, that is, attentional bias, towards disease-related words has been found in patients with psoriasis compared to healthy controls.^[23] A small study in patients with postburn itch showed that the patients displayed an attentional bias for itch-related as opposed to neutral words, but this

was not significantly different from healthy controls.^[24] Another study demonstrated that healthy individuals also display an attentional bias towards itch-related information.^[19] To a certain extent, it seems evolutionarily advantageous for everybody to be biased towards itch-related information as this may signal danger. A possibly higher attentional bias in patients with chronic itch could be the result of a state in which management of itch symptoms becomes a goal in itself. As a result, patients may prioritize signals congruent to the condition, such as itch. Whilst more attention may increase itch,^[25] symptom experience may lead to more attention and related scratching behaviour, initiating a vicious cycle with devastating effects on patients' daily life.

3 | AFFECT AND ITCH

Itch is a somatosensory sensation that has a large affective component.^[26] The experience of chronic itch is generally also accompanied by negative affectivity, including psychological stress, anxiety and depressive symptoms (for a thorough review see^[27]). These affective symptoms may not only be a consequence of itch, but can also exacerbate the itch and scratching behaviour in chronic itch within a vicious cycle of increased negative affect and itch.^[4,27,28]

Most studies that have been conducted with regard to negative affect in patients with chronic itch are cross-sectional studies showing an association between higher levels of itch and negative affect.^[24,27] For instance, in patients with chronic itch due to psoriasis or chronic urticaria, clinical levels of itch were found to be associated with psychological stress,^[29] anxiety^[30–32] and depression.^[31,33] A possibly causal role of negative affect for itch is suggested by studies in patients with chronic itch of dermatological and systemic origin who report stress to be an itch-aggravating factor (see review^[27]). Moreover, retrospective studies in patients with atopic dermatitis, psoriasis and chronic urticaria have shown that stressful life-events preceded (exacerbation of) dermatological symptoms, including itch (eg,^[13,29,34,35]). Itch levels were also associated with the degree of stress the patients with psoriasis and atopic dermatitis had previously experienced.^[27] In addition, a large study assessing the effects of stress due to the Great Hanshin Earthquake demonstrated that atopic dermatitis symptoms, including itch, were highest in the areas with the largest damage, with stress being the most prominent predictor.^[36] Meanwhile, a prospective study in patients with psoriasis has demonstrated a relation between stressors and future worsening of itch and disease severity over a 6-month period,^[37] and a study in patients with postburn itch demonstrates that individuals with post-traumatic stress have a higher risk of developing chronic postburn itch.^[38]

In addition to the role of stress in chronic itch, there is also convincing evidence for the relation between stress exposure and acute itch in non-clinical or clinical samples. Heightened stress levels, for example due to examinations, have been found to be related to itch and other skin problems in non-clinical samples, as demonstrated in cross-sectional studies in undergraduates.^[39]

Experimental research has further demonstrated that acute stress can aggravate itch perception.^[40] Acute induction of negative mood, by watching a negatively valenced video, is associated with more intense histamine-evoked itch in healthy volunteers.^[41] By contrast, when patients with chronic itch due to atopic dermatitis were exposed to acute social stress, they perceived less intense experimentally evoked itch, but displayed increased off-site scratching behavior⁽⁴²⁾.

In a recent thorough review paper, Sanders and Akiyama (2018) outline how affective processes may play a role in chronic itch.^[27] They hypothesize that particularly anxiety plays a crucial role in the vicious cycle of negative affect and increased itch. The experience of itch can lead to anxiety, which may be triggered by the perception of stress (both related and unrelated to the itch condition). Both the autonomic nervous system, including dysfunctional sympathetic and parasympathetic responses, and the hypothalamic-pituitary-adrenal (HPA) axis are hypothesized to play an important role here.^[27,44] Possibly due to the negative feedback regulation of the HPA-axis, stress may also be related to improvements in symptoms such as itch or pain and a decrease in inflammatory responses.^[27,43,44] Clinical studies show somewhat inconsistent findings regarding (para) sympathetic activity, with some studies reporting findings such as an increased baseline sympathetic activity in patients with atopic dermatitis^[45] or decreased heart rate variability in patients with chronic uraemic itch,^[46] whereas other studies do not find altered autonomic nervous system functioning in patients with chronic itch compared to healthy controls.^[27] Also, following psychological stress induction, findings are not entirely consistent as to whether patients respond differently from healthy controls with regard to endocrine functioning.^[27,44] For example, cortisol levels of patients with chronic itch due to skin diseases were found to be normal at rest, but reduced for patients with high stress,^[47] and mixed findings were reported regarding reduced, increased or unchanged cortisol reactivity in response to stress,^[48] see.^[27] More research is required to demonstrate the role of the specific mechanisms of stress, anxiety and depressive symptoms in the vicious cycle of itch and scratching behaviour.

4 | EXPECTANCY AND ITCH

Expectancies can shape the experience of itch. Expectancies of sensations like itch tend to act as self-fulfilling prophecies: if itch is expected to reduce or intensify, the itch perception tends to assimilate to the expectation.^[8,49,50] For example, expecting itch relief from a topical lotion can reduce itch.^[51] Patients' expectations about itch can be shaped by multiple factors, including doctor-patient communication, medication information leaflets and a patient's own previous experiences.^[52] As such, patients' expectancies play an important role in the treatment of itch. Research into the influence of expectancies on itch is still in its infancy, leaning heavily on the vast body of research into expectancy effects on pain, and with relevant research having been conducted almost exclusively in the last decade.

The influence of expectancies on itch has been demonstrated in research on placebo and nocebo effects. Placebo and nocebo effects refer to beneficial and negative treatment outcomes, respectively, that cannot be ascribed to pharmacological or physical treatment components but are due to other mechanisms, such as expectancies. For example, in the placebo arm of randomized clinical trials, patients often report symptom improvements, as has also been demonstrated in connection with itch.^[53] In line with research into placebo effects on pain,^[54-56] experimental research has shown that the mere suggestion that an inert ointment is an active antipruritic drug can cause it to relieve itch.^[51] This effect does not appear robust however, as similar suggestions have not been observed to affect itch in other studies.^[57-61] Nocebo suggestions appear to have a more consistent effect on itch. For example, a suggestion that a sham electrode will aggravate itch can increase itch.^[57] Similarly, suggestions of experiencing itch from diverse stimuli can intensify experienced itch.^[61-64] Placebo and nocebo effects on itch, as on pain, appear stronger when suggestions are reinforced using a classical conditioning paradigm, as demonstrated in a laboratory study in which the suggested effect of the sham activation of an electrode on itch was reinforced by repeatedly modulating the intensity of electrical itch-stimulation,^[57] see also.^[65]

In recent years, several studies have provided further insight into the neurobiological mechanisms involved in placebo and nocebo effects. Recent studies have indicated that suggestions can sometimes elicit placebo effects on wheal or flare responses to histamine or control applications,^[62] and that these effects may be moderated by the degree to which the provider of the suggestion exhibits warmth and competence.^[66] Research in patients with atopic dermatitis further indicated that nocebo-induced itch from saline believed to be an allergen was associated with increased activity in brain areas thought to be important for attention, cognitive and motivational processing.^[67] More recently, conditioned nocebo effects on histamine-evoked itch in healthy volunteers were found to be associated with brain activations hypothesized to reflect the integration of expectations with somatosensory information and top-down modulation of itch.^[68]

Most placebo research demonstrating how itch is shaped by expectancies is laboratory-based research in which itch is experimentally evoked in healthy volunteers by using pruritogens like histamine or by applying electrical stimulation.^[69] Virtually no research has been done on the role of expectancies in the maintenance and exacerbation of chronic itch. Research in clinical samples is limited to the observation of nocebo effects in the response to clinically relevant but brief stimuli (ie, supposed allergens) in atopic dermatitis patients^[64] and a pilot study indicating that open-label placebos may improve allergic rhinitis symptoms.^[70] Research into pain suggests that modulating expectancies with suggestions regarding the beneficial effects of (sham) treatment may be insufficient to elicit substantial effects on chronic symptoms.^[56] By contrast however, as mentioned above, patients with chronic itch appear to be more sensitive than healthy controls to the phenomenon of

contagious itch,^[3,21,51] which may affect susceptibility to nocebo effects. Further research is required to establish the possible differential effects of positive and negative expectations on itch in patients with chronic itch. Moreover, research is needed into the possible role that expectancies might play in the chronification of itch,^[8] for example, due to the vicious cycle in which expectations of itch shape the experience of itch, and in which experiences of itch shape expectations of itch.

5 | DISCUSSION

As a sensation that signals potential harm, itch by definition draws attention, induces negative affect, and triggers itch-related outcome expectancies. Attention, affect and expectancies are also an inherent part of being human and have a strong impact on our daily functioning. For example, attention entails various processes that together regulate the selection and prioritization of incoming information.^[16] Psychological factors such as attentional focus, affect and expectancies are also shaped by our previous learning history, including past experiences of itch and scratching, which in turn can trigger future experiences, such as a worsening of itch.^[71] Based on these theoretical grounds, research has increasingly focused on the extent to which attention, affect and expectancies play a role in itch, both in healthy subjects and in patients. Results demonstrate that these cognitive-affective factors could play a crucial role in the maintenance and exacerbation of itch.

The close interplay between itch and psychological factors such as attention, affect and expectancies is also plausible from a physiological point of view. Under stress, certain neuropeptides are released which cause neurogenic inflammation and a worsening of skin symptoms.^[72] Moreover, it is known that mechanical stimulation of the skin during scratching leads to a release of proinflammatory cytokines^[73] which in turn worsen itch. Moreover, placebo research on expectancies has shown that immune and endocrine reactions can be learned by conditioning and evoked without pharmacologically active substances.^[74,75] Attention, negative affect and expectancies also influence the behavioural component of itch, such as scratching behaviour and limited medication adherence in chronic skin disease, which may additionally result in poorer skin condition and more itch.^[2,76,77]

Attention, affect, and expectancy components are commonly interwoven in multidimensional psychological treatments for itch and scratching (eg, stress management mindfulness meditation, distraction, relaxation training, or habit-reversal strategies to focus on another habit when the urge to scratch emerges).^[28,76,78-80] Interventions primarily focusing on only one of these aspects are scarce. Multimodal interventions are usually offered because the factors interact. For example, there is some evidence that more complex and engaging attentional distraction tasks can effectively reduce patients' itch and scratching,^[81] whereas a simple distraction task seems ineffective.^[82] Also, a proof-of-principle attention

bias modification training, as commonly used in different research areas with incongruent results,^[83-86] has not been shown to effectively retrain healthy individuals' attention.^[87] Such attention training has not been studied in clinical itch samples. Interventions directed at reducing negative affect too are usually multimodal, often combining various techniques from cognitive behavioural therapy. Such interventions have been shown to be effective in chronic skin diseases, also when administered in a digital setting (eg,^[28,76,79,80]) Finally, multimodal expectancy-based treatments have also been developed, with promising effects, as a preparation for medical procedures, for example, heart surgery.^[88] A possible additional strategy for attenuating negative expectancies in itch is counterconditioning. In a recent experimental study in healthy volunteers, conditioned nocebo effects on itch could be reversed with a counterconditioning paradigm, in which the negative expectations were reversed into placebo effects of itch reduction.^[71] Another possible avenue for clinically applying placebo effects is by openly giving patients placebos, without deception. A pilot study has indicated that open-label placebos may improve the allergic symptoms of patients with allergic rhinitis, although no effects on itch were observed.^[70] In recent laboratory research, open-label suggestions (without administration of a placebo) were effective in altering itch expectancies,^[89] and under specific circumstances also itch.^[89,90] This calls for more research into this innovative strategy.

Further research is required into these and other strategies for modulating and optimizing patients' attentional focus, negative affect, and expectancies. The field would benefit from sophisticated theoretical developments on the role of attention, affect, and expectancies in itch. This will enhance our understanding of the mechanisms involved. In turn, this can contribute to further optimizing existing interventions and developing new ones to improve clinical care for itch.

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CONFLICT OF INTEREST

The authors have declared no conflicting interest.

AUTHOR CONTRIBUTIONS

All authors have (a) made substantial contributions to conception and design; (b) been involved in drafting the manuscript or revising it critically for important intellectual content; (c) given final approval of the version to be published; and (d) agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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