

The Effect of Visual Stimuli on Itch Perception and in the Induction of "Contagious"
Scratching in Atopic Dermatitis

NEA Final Report

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Introduction

It is well-known that itch can be contagious by sight: watching other people scratch can induce a sensation of itch and a subsequent desire to scratch, although the exact mechanism for this type of "itch transmission" is poorly understood. Insights into the central mechanisms occurring in the brain to explain these behavioral responses are generally lacking and they could help our understanding of itch neurophysiology and pathophysiology (e.g. chronic itch of atopic eczema).

In this study, we aimed to investigate the effect of visual stimuli - contained in video clips depicting people scratching - on the perception of itch induced experimentally and on the spontaneous scratching they induce in atopic eczema patients and healthy controls.

Methodology • Highlights

- Subjects. Fifteen healthy subjects and atopic eczema patients participated in the study.
- Exposure to visual stimuli: participants were asked to watch short video clips of 5 minutes, depicting people scratching (or neutral content video clips as a control);
- Itch induction: A histamine solution 1% (or a mock itch stimulus, a saline aqueous solution used as control) was delivered by iontophoresis on the forearm to induce a local sensation of itch immediately prior to presentation of video clips.
- Visual (stimuli) control, participants watched also a neutral video content, depicting the same persons shown in the scratching videos, but sitting idle, in a relaxed state.
- Sequence, blinding and randomization: the order of administration of the actual itch stimulus (histamine) or control (saline) was randomized and the participants were not informed about the nature of the solution administered at any given time.
- Rating of itch: participants self-rated continuously the intensity of itch sensation by computer-assisted visual analog scale (COVAS), for the full time they watched the video clips (5 minutes). At the end of each session, average itch was also rated using a Visual Analog Scale (VAS) graded from 0 to 10.
- Scratching: participants were instructed to freely scratch their itch.
- Video-capture of scratching behavior: while the subjects watched the video clips, they were also videotaped unobtrusively, with a digital camcorder placed at about 3-4 meters laterally, at an angle that captured images of both their hands and entire body.
- Video recordings were examined for frequency, duration, localization of scratching episodes, the extension of scratched areas and the intensity of scratching motions.
- The experiment comprised of six sessions: four sessions of actual itch induced with histamine, repeated once with for each type of video clip; a mock itch stimulus control (saline) was administered once for each type of video clip.

The Making of the Video Clips Showing People Scratching. Video recordings were made with the help of Creative Solutions department at Wake Forest University Health Sciences, featuring various subjects itching & scratching. A panel of unbiased raters selected the most convincing itch & scratch recordings; subsequently, a final montage 5 minutes in length was cut. A neutral content video as a visual stimuli control displayed the same persons appearing in the "scratching video", but sitting relaxed.

Results

A. Atopic Dermatitis Patients Reported Increased Itch Ratings with Mock Stimuli while Watching Itch Videos

The rating of itch increased significantly when atopic dermatitis patients watched an itch video versus a neutral video ($p = 0.009$) (Fig. 1), while in healthy controls it slightly increased but not significantly ($p = 0.13$).

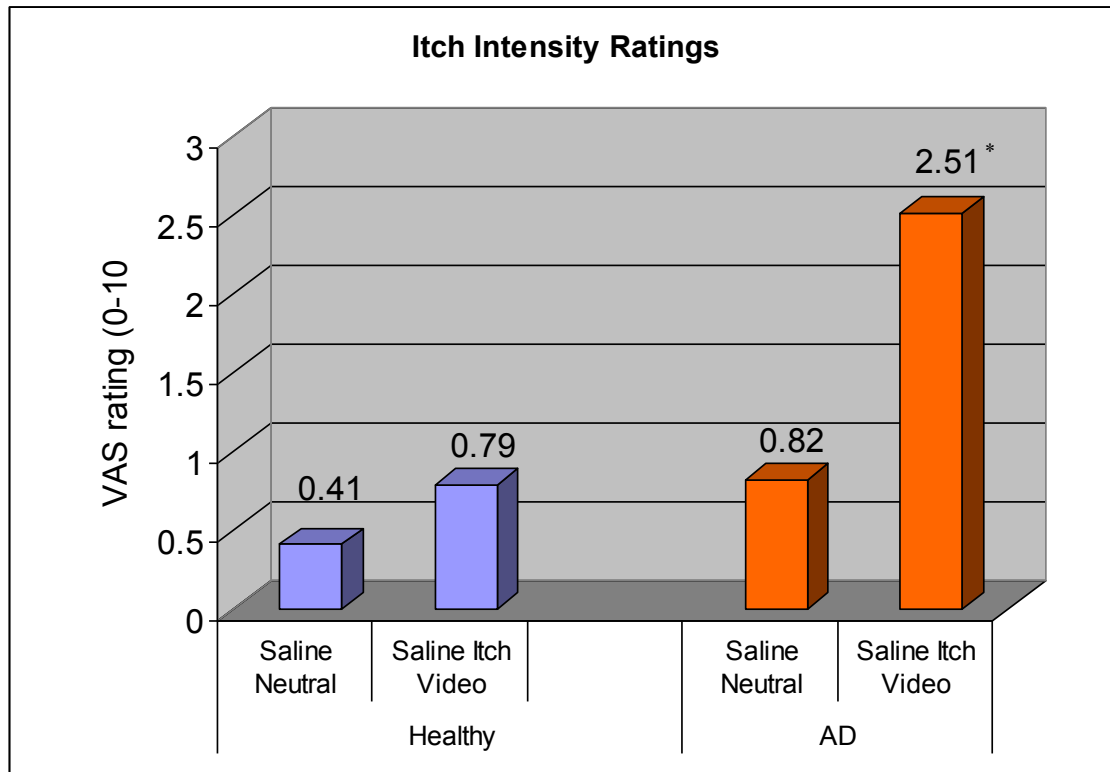


Figure 1. Ratings of itch following mock itch stimulus (aq. isotonic saline) increase significantly in atopic subjects watching scratching videos ($p=0.009$), but not in healthy subjects ($p=0.136$). (*indicates statistical significance of the contrast AD vs. Healthy, $p < 0.05$).

B. The perception of histamine-induced itch changes significantly in atopic dermatitis patients only at the second exposure to itch stimuli

- In healthy subjects and atopic dermatitis subjects the perception of histamine-induced itch did increase slightly but not in significant fashion while watching video clips for the first time, in comparison with watching a neutral video ($p = 0.8, p = 0.7$) respectively in healthy and AD, Fig. 2).
- Atopic dermatitis patients responded more strongly to visual cues of itch by increasing their perception of the histamine-induced itch when they watched video clips of itch *for the second time*, in comparison with watching a neutral video ($p = 0.04$) for the second time, respectively. This response had a much higher amplitude compared to the slight increase observed in healthy volunteers ($p = 0.04$) (Fig. 2).

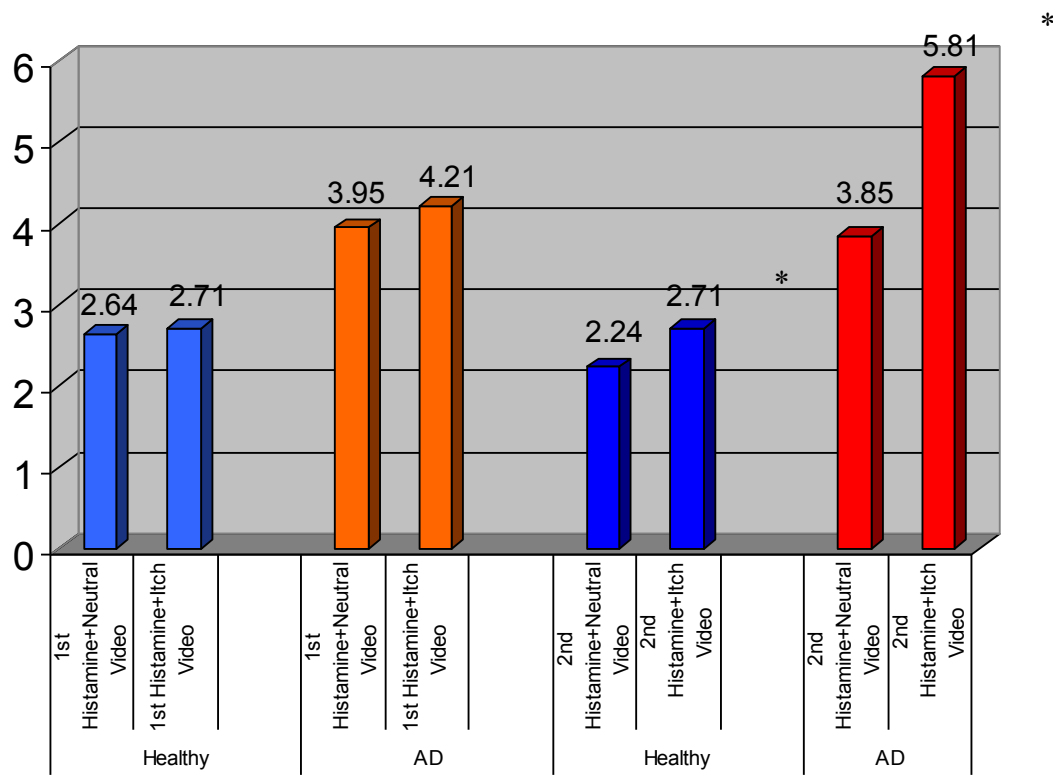


Figure 2. Itch intensity of histamine induced itch during exposure to video clips of scratching in atopic subjects and healthy participants (* indicates statistical significance of the contrast AD vs. Healthy, $p < 0.05$).

C. Differences in scratching response between healthy volunteers and atopic eczema patients exposed to visual stimuli of itch.

Significant differences between healthy controls and AD subjects were noted in the "scratching behavior". They are summarized in the following figures and tables. (Fig. 3, table 1).

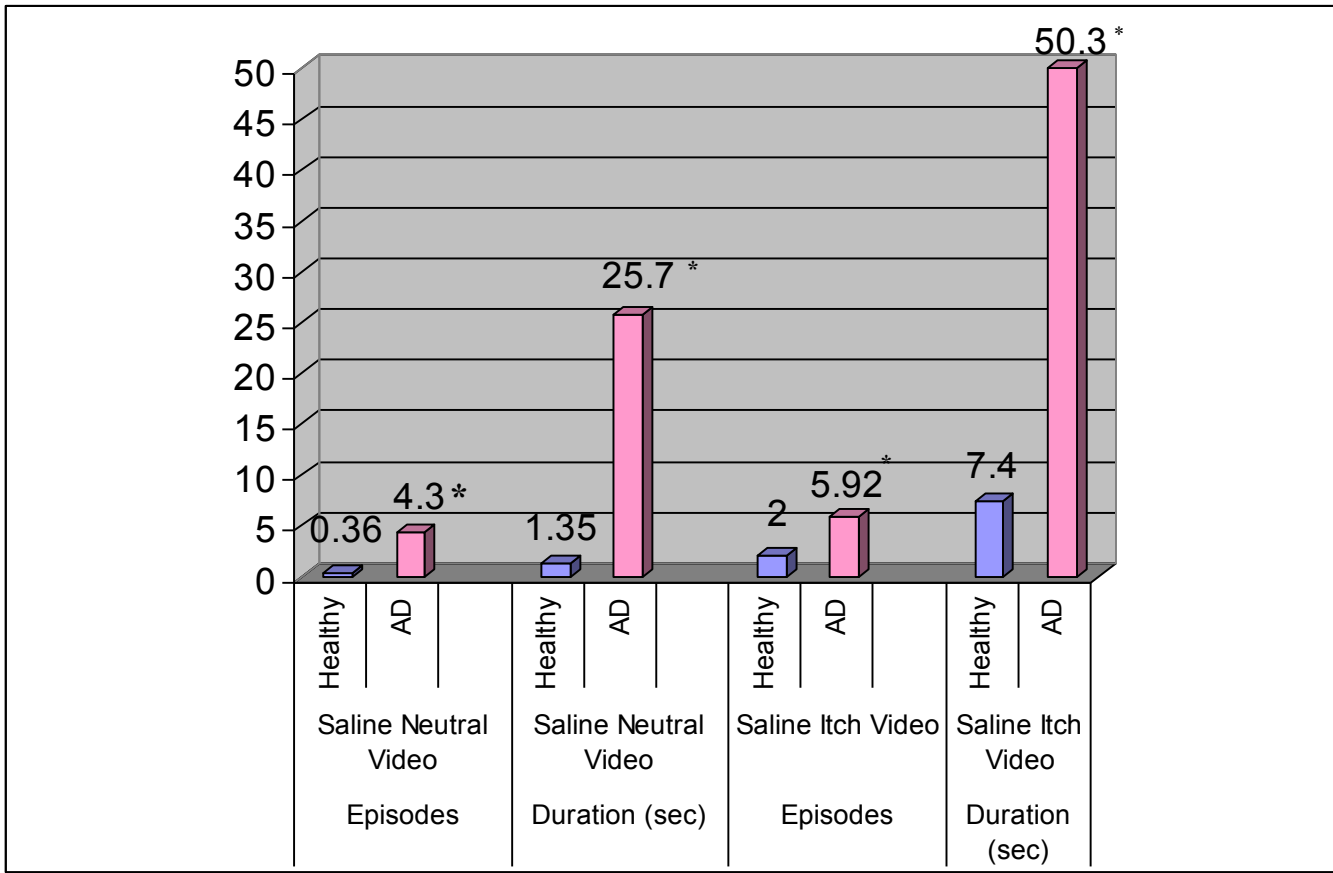


Figure 3. The average number of scratching episodes and duration performed by healthy volunteers and AD patients exposed to a mock itch stimulus (aq. saline) in the presence or absence of visual stimuli of scratching. (* indicates statistical significance of the contrast AD vs. Healthy, $p < 0.05$).

D. Atopic dermatitis patients scratched bilaterally and more extensively than healthy controls beyond the local area of histamine induced itch, in response to visual itch stimuli,

AD patients scratched more extensively in areas distributed bilaterally (on both arms) and on their face, cheek, forehead, nose, upper lip, neck, back and legs when they watched itch videos, irrespective of the nature of stimulus applied. When AD patients watched itch videos and were administered a mock stimulus, they scratched Areas Extended Bilaterally (AEB) with an average of 4.3 episodes for 23.5 seconds, while healthy controls scratched an average of 0.85 episodes for 2.2 seconds in the same setting, differences being meaningful with p values of 0.03 / 0.0046 respectively (Fig. 4, Table 1). When exposed to histamine while watching itch videos, AD subjects scratched an average of 5.0 episodes in AEB for an average duration of 32.4 seconds, versus 1.0 episode of 4.6 seconds duration in healthy volunteers, and these differences are significant with p values of 0.023 / 0.018 respectively (see Fig. 5).

The distribution of scratching episodes depending on the site and spatial extension of the area scratched (classified as 1- localized, 2- limited to the forearm, 3- extended unilaterally or 4- extended bilaterally) is presented in the following Figures 4-6.

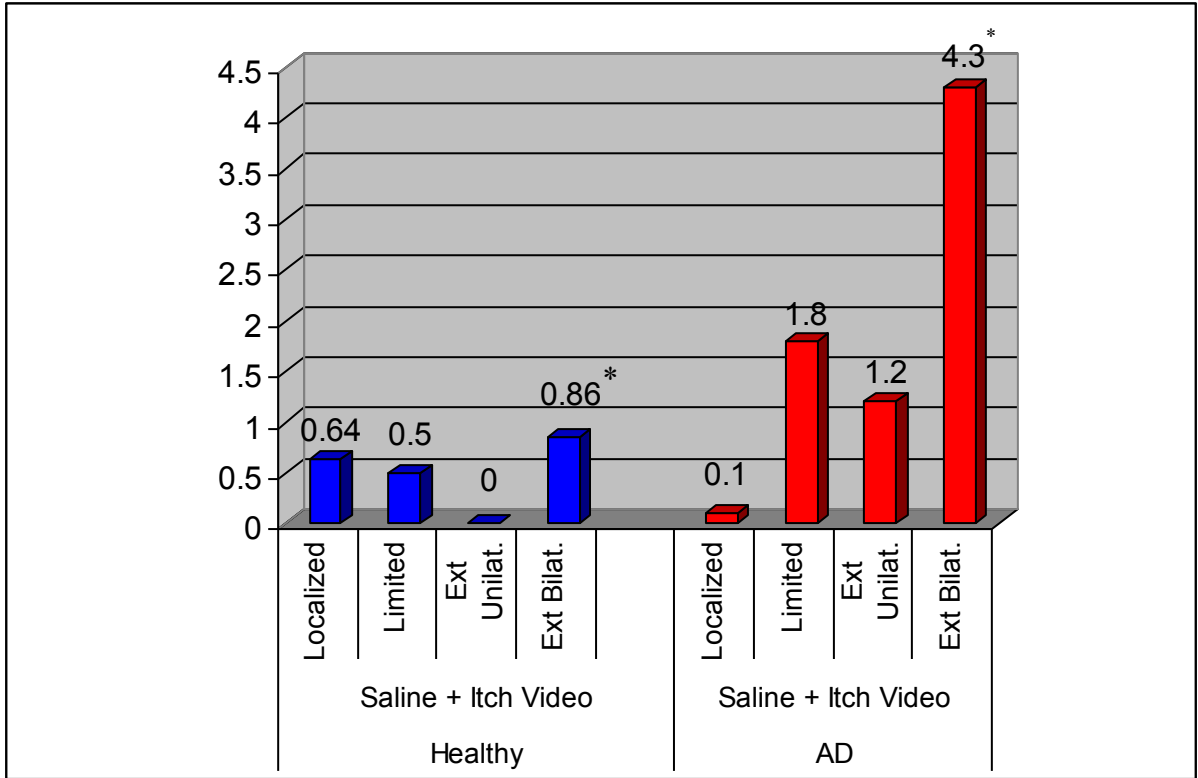


Figure 4. The distribution of the average number of scratching episodes in four extension "zones" in AD and healthy subjects receiving a mock itch stimulus (aq. saline) and watching itch videos. (* indicates statistical significance of the AD vs. Healthy contrast, $p < 0.05$).

Legend (for Figures 4 and 5). The scratching episodes were classified by site and extension area as follows: 1 - localized to the area on the forearm where the wheal and flare are induced by the itch stimulus (or where control mock stimulus) was applied within a radius of 5 cm; equivalent to an area 10 cm in maximum length. 2 - limited to the same-side forearm: on an area larger than 10 cm but not extending beyond the same forearm where stimulus was applied. 3- extended unilaterally: if the subject scratched on the same arm beyond the forearm on the same side where the stimulus was applied, but not extending to any other areas of the body; 4 - extended contralaterally and/or bilaterally: where the subject scratched another site on the body, beyond the arm where the itch stimulus was applied; e.g.: scratching on both arms, forehead, ear, cheek, nose, back of the neck, neck, chest, back, leg etc. All scratching episodes including the bilaterally extended episodes were counted only if they lasted longer than 2 seconds, to eliminate any incidental, habitual, short-lived scratching bouts that may be unrelated to the study's paradigm.

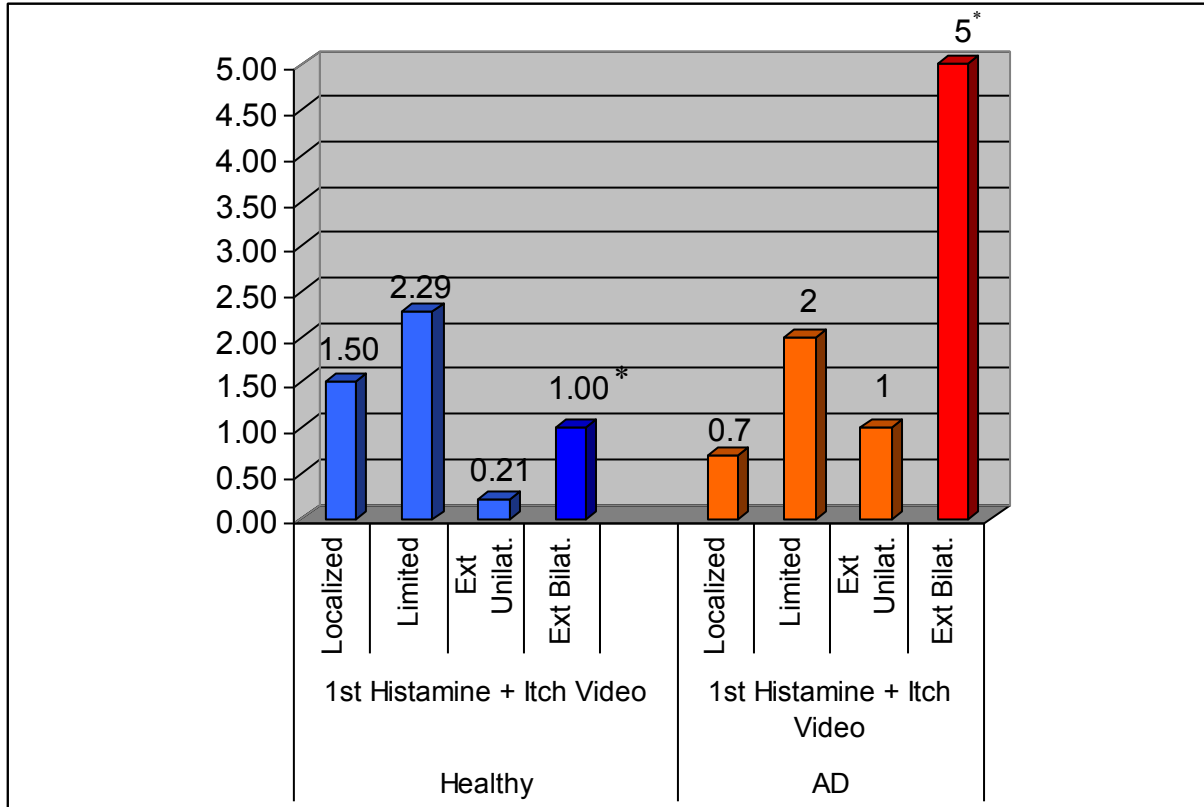


Figure 5. The distribution of scratching episodes (average number) in four extension "zones" in AD and healthy subjects receiving a histamine and watching itch videos for the first time. (see legend above; * indicates statistical significance of the AD vs. Healthy contrast, $p < 0.05$).

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Conclusions

- Atopic dermatitis patients displayed a significant response to the visual cues depicting other people itching & scratching. Their ratings of itch and the overall number of scratching episodes recorded *during watching itch videos* were significantly higher in comparison with healthy volunteers (in the same settings), even when only a mock itch stimulus was applied.
- The intensity of itch, the extension of the skin areas scratched and the number of scratching episodes in areas extended bilaterally was increased significantly in atopic dermatitis when a mock itch stimulus (aq. isotonic saline) was delivered *during exposure to itch videos*.
- These results suggest that central activation could be involved in "contagious" itching that may be linked to the "mirror neuron" system (in the prefrontal cortex) and therefore the central mechanisms of itch processing in the brain may be crucial for understanding the amplified response seen in atopic dermatitis.