A Role of Corneal Mechanical Adaptation in Contact Lens–Related Dry Eye Symptoms

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PURPOSE. To compare corneal mechanical adaptation measured psychophysically in contact lens wearers with or without dry eye symptoms.

METHODS. Two groups of contact lens wearers were recruited. One group (symptomatic) consisted of subjects with dry eye symptoms (according to the subjective evaluation of symptoms of dryness [SeSoD] questionnaire). The second control group (asymptomatic) consisted of subjects reporting no symptoms. There were 32 (aged 20 to 42 years, 6 males and 26 females) and 29 subjects (aged 21 to 36 years, 9 males and 20 females) in the symptomatic and asymptomatic groups, respectively. Mechanical stimulus thresholds of the cornea were determined using a Belmonte pneumatic esthesiometer and the ascending method of limits. Then three stimulus intensity groups (subthreshold, threshold, and suprathreshold) were applied to the eye in random order, each 20 times. Subjects rated the intensity of the stimuli using a scale of zero to four. The rating data from the two groups were compared by Friedman nonparametric ANOVA. Adaptation was defined as the reduction in subsequent ratings compared with earlier ones.

RESULTS. No significant difference was seen in subjects' thresholds in both groups (P = 0.22). The symptomatic group rated their sensations to suprathreshold stimuli higher than the asymptomatic group. More importantly, there was significant adaptation with suprathreshold mechanical stimulation in the asymptomatic group (P = 0.006) but not in the symptomatic group (P = 0.08). There was no adaptation during threshold and subthreshold stimulus sessions in either group.

CONCLUSIONS. Adaptation was found to suprathreshold mechanical stimuli in the asymptomatic group but not in the symptomatic group. (Invest Ophthalmol Vis Sci. 2011;52:1200–1205) DOI:10.1167/iovs.10-5349

Contact lens–related dry eye symptoms have received attention from both clinicians and researchers. It was reported in an examination of optometric practices that half of contact lens wearers experience less discomfort. Since both high-oxygen-permeable silicone hydrogel and daily disposable lenses have the potential to minimize sensitivity decrease, they might potentially decrease wearing comfort because of the increased lens sensitivity awareness caused by the relatively well-preserved sensitivity. Adaptation is the decrease in sensation or in the neural response during sustained stimulation at a constant intensity. It has been demonstrated in different sensory systems, such as olfaction, audition, and the somatosensory system in the tooth pulp and skin and is believed to maintain the sensory system’s sensitivity over a wide dynamic range. In a previous report, we showed that in normal corneas there is adaptation to suprathreshold mechanical and cooling stimuli, and even though mechanical adaptation has been implicated only in sensitivity decrease in rigid contact lens wear, we hypothesized that adaptation might also play a role in the comfort of soft contact lens wear. The objective of this study was to compare the adaptation in contact lens wearers with or without dry eye symptoms using the previously used psychophysical methods. The null hypothesis was that there are no significant differences in adaptation between the two groups of subjects.

METHODS

Subjects were recruited by advertisements at the University of Waterloo. All subjects were healthy without any systemic or ocular disease history. None of them was taking medication. Subjects reported their
dryness related to contact lens wear using the single-score subjective evaluation of symptom of dryness (SeSoD) questionnaire for symptoms of ocular dryness.25,27,28

This study adhered to the Declaration of Helsinki for research involving human subjects and received clearance from the University of Waterloo, Office of Research Ethics. Informed consent was obtained from all the subjects before the experiment.

A Belmonte pneumatic esthesiometer, with computerized control of gas flow and temperature, was used to apply the mechanical stimuli. In addition, the computer collected subject responses and calculated the stimuli based on those inputs. A more detailed description of this instrument can be found in previous reports.29,30

Subjects were asked to stop using contact lenses the night before their experimental session, and at least 4 hours passed after subjects opened their eyes before the experiments began to minimize the effect of diurnal variation of ocular surface sensitivity.31,32

The screening process consisted of clinical history, symptom questionnaire, ocular surface biomicroscopy, and tear breakup time (T-BUT) measurement. Thresholds to mechanical stimuli were estimated using an ascending method of limits,29,30 with the final threshold being the average of six “yes” responses. Based on this measurement, three stimulus intensity sessions—subthreshold, threshold, and suprathreshold—followed: The subthreshold and suprathreshold stimuli were 25% below and above threshold, respectively.25 In each session, 20 equal-intensity, 2-second stimuli were presented with 10-second interstimulus intervals. After each stimulus, subjects were asked to rate stimulus intensity using a five-point intensity scale: 0, no stimulus; 1, very mild stimulus; 2, mild stimulus; 3, moderately strong stimulus; 4, strong stimulus; 5, intense stimulus.

The responses were reported by the subject using a button box and recorded by the computer. Five sequential stimulus ratings were averaged, and there were four periods in each session during which intensity ratings were averaged. The experimental stimulation and response sequence is illustrated in Figure 1.

Friedman nonparametric ANOVA was used to evaluate the statistical significance of ratings from each averaged period (set at \( P \leq 0.05 \)). Adaptation, the reduction in subsequent ratings compared with earlier ones, was tested using post hoc paired comparisons with Holm’s sequential Bonferroni corrected one-tailed Wilcoxon matched pairs tests.33 A Mann-Whitney \( U \) test was done to compare ratings between the two groups.

RESULTS

There were 32 subjects in the symptomatic group and 29 subjects in the asymptomatic group. Demographic and lens data are listed in Table 1. A summary of responses to the questionnaire is presented in Table 2.

The two groups’ mechanical threshold, T-BUT, and wearing time are presented in Table 3. The T-BUT time for symptomatic subjects was shorter than that for the asymptomatic group \(( P < 0.05 )\), and the asymptomatic group had shorter daily wearing time than the asymptomatic group \(( P < 0.05 )\). The mechanical threshold and years of contact lens wear were not different between the two groups.

In the symptomatic group, ratings of intensity of the repeated mechanical stimulation are presented in Figure 2. There was no significant adaptation observed in any of the three sessions (subthreshold, \( P = 0.88 \); threshold, \( P = 0.61 \); and suprathreshold, \( P = 0.08 \)).

In the asymptomatic group (Fig. 3), although there was no significant adaptation in subthreshold and threshold sessions \(( P = 0.43 \) and 0.2, respectively), adaptation was found in the suprathreshold session \(( P = 0.006 \)). Post hoc testing showed intensity ratings during period 1 being significantly higher than periods 2, 3, and 4.

Ratings of the suprathreshold mechanical stimuli in symptomatic and asymptomatic groups are shown in Figure 4. The median ratings in the symptomatic group were greater than those in the asymptomatic group in all four rating periods. The median rating of the symptomatic group to suprathreshold stimuli was approximately 2, whereas the intensity of the asymptomatic group was only 1.4 \(( P < 0.001 \), Mann-Whitney \( U \) test).

DISCUSSION

In this study, we demonstrated significant corneal adaptation to suprathreshold mechanical stimuli in the control asymptomatic (non–dry eye) group, whereas there was no adaptation to suprathreshold mechanical stimulation in the symptomatic (dry eye) group. According to our previous report, there was

![Figure 1](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932971/) The experimental sequence. Interstimulus interval is 10 seconds.

![Figure 2](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932971/) Comparison of Symptomatic and Asymptomatic Groups

<table>
<thead>
<tr>
<th>Table 1. Basic Data of the Two Groups</th>
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<tbody>
<tr>
<td><strong>Symptomatic (Dry Eye)</strong></td>
</tr>
<tr>
<td><strong>Male</strong></td>
</tr>
<tr>
<td>Subjects, ( n )</td>
</tr>
<tr>
<td>Age in years, mean ( \pm SD ) (range)</td>
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<tr>
<td>Contact lens type</td>
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<tr>
<td>Daily</td>
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adaptation to repeated suprathreshold mechanical stimulation in the normal asymptomatic population.\textsuperscript{25} We propose therefore that inability to adapt (or abnormal adaptation) in the symptomatic group is implicated in the presence of dryness symptoms.

Murphy et al.\textsuperscript{15} indicated that decreased sensitivity in lens wearers might be beneficial, resulting in less discomfort in lens wearers. Relatively well-preserved ocular surface sensitivity might result in lens wearers being more likely to sense the mechanical stimulation caused by blinking, and this might be one possible reason for discomfort symptoms in wearers of the new-generation lenses. Golebiowski et al.\textsuperscript{6} reported that newer generations of soft contact lenses did not cause significant ocular surface sensitivity change. In our experiment, mean sensitivities in both groups were about the same as those previously reported on non-lens-wearing normal subjects.\textsuperscript{30,34} This suggests that in this sample of silicone hydrogel and daily disposable lenses wearers there was no obvious sensitivity decrease compared with the conventional soft and hard contact lens wearers.\textsuperscript{35,36} Perhaps partially because of the higher oxygen permeability of the new materials.\textsuperscript{15,36}

Belmonte et al.\textsuperscript{57-58} proposed that the occurrence of symptoms was through the activation of sensory nerves innervating the ocular surface when the eye lid slid over the dry ocular surface. The increased mechanical force during blinking between the lids/lenses and globe in response to reduced tear volume and/or the reduced expression of mucins on the ocular surface has been hypothesized to partly account for symptoms in subjects with dry eye.\textsuperscript{12} Golebiowski et al.\textsuperscript{6} also speculated that the dry eye symptoms in contact lens wearers were also partially due to the mechanical forces during blinking.

Because of the relatively well-preserved ocular surface sensitivity and the gradually worsening tear film,\textsuperscript{39} there might be an increasing mechanical stimulation by contact lenses toward the end of the day. Therefore, mechanical adaptation may become more important in the comfort of lens wear at this time. If subjects adapted to this mechanical stimulation, they would be less likely to experience the uncomfortable symptoms of dry eye, and so the adapting group would be expected to behave as we found: They would have fewer symptoms.

In the symptomatic and asymptomatic groups there was significant difference in T-BUTs without lenses. This result was in accord with other studies of contact lens-related dry eye.\textsuperscript{25,40} The effect of a more easily disrupted tear film on contact lens-related dry eye has not been established, but there is a hypothesis that a thinner precorneal tear film will increase the mechanical force on the ocular surface during blinking.\textsuperscript{12} As we have demonstrated, however, suprathreshold mechanical stimulation is followed by adaptation,\textsuperscript{25} and so as long as the patients have normal adaptation, dry eye symptoms might not arise.

Difference in adaptation in the symptomatic and asymptomatic samples might reflect differences between receptor types and/or underlying sensory channels, functional differences in the central nervous system, or any combination of them. Perhaps an additional complication was the apparent dissociation between threshold and suprathreshold behavior in the two groups: Symptomatic subjects had the same sensitivity as asymptomatic subjects, but their response to suprathreshold stimulation was not to adapt.

The relationship between dry eye symptoms and corneal innervation is not clear, with little evidence of different innervation in symptomatic and asymptomatic subjects. Benitez-Del-Castillo et al.\textsuperscript{41} however, found a positive correlation between corneal nerve density and sensitivity in dry eye patients, but Hosal et al. and Tuisku et al.\textsuperscript{42,43} did not find this association. In the only study examining ocular surface innervation and pneumatic sensitivity in lens wearers, Golebiowski et al.\textsuperscript{6} did not find significant morphologic changes of the corneal nerves in contact lens wearers. It therefore appears safe to conclude that there are no distinct major neural morphologic differences between symptom groups or because of lens wear.

However, Belmonte et al.\textsuperscript{35,44} speculated that subtle injury of corneal nerve endings in lens wearers was similar to damaged corneal neurons after laser-assisted in situ keratomileusis surgery and photorefractive keratectomy\textsuperscript{45} and that the regener- ated nociceptors had increased spontaneous activity as well as longer lasting after-discharges in response to suprathreshold stimulation. We hypothesized that this altered neural functioning that was the basis of hyposensitivity, and hyperalgesia experienced by subjects after laser refractive surgery\textsuperscript{44,46} perhaps was implicated in the etiology of reported discomfort in contact lens-wearing patients reporting dry eyes.\textsuperscript{47,48} If this hypothesis was correct, it predicts a paradoxical result in our study, that symptomatic subjects with relatively lower sensitivity (higher threshold) had relatively higher ratings to suprathereshold stimuli. We were unable to demonstrate a significant difference in sensitivity between groups (Table 3), and therefore the dual nature of this hypothesis (threshold and suprathreshold effects) is not supported.

A reviewer suggested that perhaps our results could be accounted for by nociceptors sensitization, something demonstrated in skin\textsuperscript{49-51} and the cornea.\textsuperscript{52} However, in our experiment, suprathreshold stimuli were only 25% above threshold, a modest nociceptive stimulus considering the subjects’ ratings, and because of this and the relatively short duration of our experiment we do not believe that sensitization was a primary outcome of the stimuli applied. It is possible that both adaptation and sensitization have occurred and serendipitously cancelled each other out. Ockham’s razor\textsuperscript{53} would seem to require the absence of a single mechanism (adaptation) rather

\begin{table}
\centering
\caption{Data of Average Thresholds, T-BUT, Daily Wearing Time, and Lens-Wearing History of the Two Groups}
\begin{tabular}{lcc}
\hline
 & Symptomatic & Asymptomatic \\
 & \textit{(n = 32)} & \textit{(n = 29)} \\
\hline
Mechanical threshold, mL/min & 57.9 \pm 12.0 & 46.9 \pm 24.0 & 0.22 \\
T-BUT, s & 8.0 \pm 4.3 & 12.1 \pm 6.7 & 0.02 \\
Daily wearing time, h & 9.2 \pm 1.8 & 12.2 \pm 2.3 & <0.0001 \\
Contact lens-wearing history, y & 7.5 \pm 3.7 & 7.8 \pm 2.6 & 0.82 \\
\hline
\end{tabular}
\end{table}
than proposing two coincidently oppositely signed mechanisms. Finally, sensitization (by definition) requires increased sensitivity, something we did not find in our experiment (Table 3), and therefore differences in sensitization between symptomatic and asymptomatic subjects cannot easily be invoked to account for what we found.

In addition, the change of discomfort over time that we referred to as adaptation and we have suggested is perhaps a receptoral or peripheral neural effect might also reflect differences at higher levels in the nervous system\textsuperscript{25}; even personality has been reported to play a role in the discomfort during and tolerance of dry eye\textsuperscript{54} and contact lens wear\textsuperscript{55}.

Regardless of the hypothetical neural morphologic and/or functional differences in lens wearers and in symptomatic or asymptomatic subjects, we are proposing that in lens-related asymptomatic subjects, their adaptation enables them to better adjust to mechanical stimulation. On the other hand, in symptomatic subjects, their lack of adaptation results in more awareness of the lens and therefore symptoms of discomfort.

**FIGURE 2.** (A) Subthreshold mechanical stimulation, Friedman non-parametric ANOVA, $P = 0.88$. (B) Threshold mechanical stimulation, $P = 0.61$. (C) Suprathreshold mechanical stimulation, $P = 0.08$.

**FIGURE 3.** (A) Subthreshold mechanical stimulation, Friedman non-parametric ANOVA, $P = 0.43$. (B) Threshold mechanical stimulation, $P = 0.2$. (C) Suprathreshold mechanical stimulation, $P = 0.006$. 
In this study we showed that whether contact lens wearers experienced symptoms could be differentiated by whether they adapted to suprathreshold corneal mechanical stimulation. Using this logic, a screening test for potential contact lens wearers likely to be less successful because of their lack of lower amounts of adaptation could be developed. This might be as simple as tracking patients’ responses to repeated suprathreshold mechanical stimulation for a short (few minutes long) interval. Perhaps sufficient suprathreshold mechanical stimulation could be provided just by the lenses being fitted.

In summary, using psychophysical methods, we showed that there was significant corneal adaptation to suprathreshold mechanical stimuli in asymptomatic (non-dry eye) contact lens wearers, whereas such adaptation was not found among the symptomatic (dry eye) wearers.

Acknowledgments

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References


