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Objectively Measuring Observer Attention in Severe Thyroid-Associated Orbitopathy: A 3D Study

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Objective: Measure the attentional distraction of facial deformity related to severe thyroid-associated orbitopathy using three-dimensional (3D) images and eye-tracking technology.

Methods: Observers recruited at an academic tertiary referral center viewed 3D facial images of patients with severe thyroid-associated orbitopathy (TAO) and controls without TAO. An infrared eye-tracking monitor recorded their eye movements and fixations in real time. Multivariate Hotelling's analysis, followed by planned posthypothesis testing, was used to compare fixation durations for predefined regions of interest, including the eyes, nose, mouth, central triangle, and remaining face without the central triangle between severe TAO patients and controls.

Results: One hundred sixteen observers (mean age 26.4 years, 51% female) successfully completed the eye-tracking experiment. The majority of their attention was directed toward the central triangle (eyes, nose, mouth). On multivariate analysis, there were significant differences in the distribution of attention between control and severe TAO faces ($T^2 = 49.37$; $F(5{,}922) = 9.8314$, $P < 0.0001$). On planned posthypothesis testing, observers attended significantly more to the eyes (0.77 seconds, $P < 0.0001$, 95% confidence interval [CI], 0.51, 1.03 seconds) and less to the nose (−0.42 seconds, $P < 0.0001$, 95% CI, −0.23, −0.62 seconds) in severe TAO patients. There was no significant difference in time spent on the mouth, the total time spent on the central triangle, or time spent in the remaining face between the two groups.

Conclusion: Severe TAO distracted observer attention toward the eyes compared to control patients. These data lend insight into how TAO may alter observers' perceptions of these patients. Future studies should investigate how these changes in observer gaze patterns may reflect the social perception of TAO patients.

Key Words: Thyroid-associated orbitopathy, facial deformity, eye-tracking, scanpath, 3D.
Level of Evidence: NA

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INTRODUCTION

Thyroid-associated orbitopathy (TAO) is an autoimmune phenomenon characterized by a constellation of signs and symptoms that result from the inflammation and enlargement of the orbital soft tissues.[1,2] TAO is considered to be the most common extrathyroidal manifestation of Graves' disease (GD), an autoimmune thyroid disorder that affects nearly 1% of women in the United States.[3] Some studies estimate that up to half of GD patients go on to develop TAO.[4] However, TAO may develop in the absence of GD or even hyperthyroidism.[5] The pathophysiology of TAO is complex and remains to be fully elucidated.

The encumbering effects of TAO on patients are multifaceted, with functional and aesthetic complications. Numerous studies have shown the psychosocial morbidity from TAO to be significant, including depression and anxiety; general dissatisfaction with appearance can last for up to 10 years despite few long-term functional impairments after treatment.[6–14] However, whereas the patient perspective has been well explored, society's perception of TAO is not completely understood. Previous eye-tracking studies have objectively shown that facial deformities lead to attentional distraction in the casual observer.[15–17] Meanwhile, observers also rate those with facial lesions as less attractive, with a lower perceived quality of life, and are less comfortable communicating with them.[18–20] It has also been shown that central and large lesions produce greater social penalties compared to peripheral and small lesions.[21] Taken together, this body of literature provides a foundation for the study of TAO from the perspective of the casual observer.

Furthermore, the facial perception literature has predominantly relied on two-dimensional (2D) stimuli. Some have advocated for the use of 3D facial images in eye-tracking because they have been shown to facilitate

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greater accuracy in facial detail and expression.[22–25] In addition, 3D images contain volumetric properties otherwise missing in their 2D counterparts. Because a central feature of severe TAO is the forward displacement of the eyes, a 3D photo can capture a more accurate representation of what an observer might encounter in real life. Therefore, we elected to use 3D stimuli in our experiment.

To the best of our knowledge, this study is the first of its kind to explore observer attention in those with physical ocular changes, a principal element of the central triangle, using a 3D approach. We hypothesized that severe TAO would redirect observer attention toward the eyes of patients as compared to normal control faces. We further measured the time spent by observers on the central triangle overall, as well as the rest of the face, to gain insight into how they allocate visual fixation times between the two groups.

MATERIALS AND METHODS

Participants

The Johns Hopkins Medicine and the University of Michigan Institutional Review Boards approved this study. Participants capable of normal eye movements were recruited as observers at a large academic medical center. A study surveyor stood at the entrance of the institution's outpatient center, medical education building, and public health building. The recruited observers included patients, visitors, staff, and students. We excluded individuals under the age of 18 years, as well as those who reported having an affective psychiatric condition, such as schizophrenia or autism, due to established differences in the way people with these conditions direct attention toward faces.[26,27] Participant demographics are shown in Table I. Observers were incentivized to participate using a raffle of nominal value, and they were naïve with respect to the purpose of the study.

TABLE I.
Study Participant Demographics

Variable	No. (%) (n = 116)
Age, mean (SD), years	26.4 (7.7)
Female	59 (51)
Male	57 (49)
Asian	43 (37)
African American	15 (13)
White	44 (38)
Hispanic or Latino	12 (10)
Other	2 (2)
Less than high school	1 (1)
High school/GED	2 (2)
Some college	6 (5)
2-year college degree	2 (2)
4-year college degree	77 (66)
Master's degree	17 (15)
Doctoral degree	11 (9)

GED = General Equivalency Diploma; SD = standard deviation.

Eye-Tracking Instrument

Visual scanpaths were recorded with an SMI iView X RED (SensoMotoric, Inc., Needham, MA) eye-movement monitoring system that utilizes a remote infrared camera. The eye tracker is a real-time digital image processor that tracks the center of the observer's pupils and measures their size from an infrared video image of the observer's eyes. Eye position was recorded as x and y values as though the observer were visualizing a grid in the plane of the facial image. Coordinates and pupil diameter were sampled at a rate of 60 Hz.

Stimulus Material

Eight color photographs were selected from a series of stereoscopic images captured at the University of Michigan oculoplastic surgery clinic (Ann Arbor, MI) with a FinePix REAL 3D W3 digital camera (Fujifilm Co., Tokyo, Japan). All photographs were of patients who had given informed consent that their photographs may be used for research purposes. They included normal controls (4) as well as patients with severe TAO (4). The definition of "severe TAO" was adapted from the European Group of Graves' Orbitopathy classification of "moderate to severe disease," and modified to be specifically defined as patients without sight-threatening disease and two or more of: eyelid retraction > 2 mm, severe soft tissue involvement, exophthalmos > 4 mm above normal for race and gender, or constant diplopia.[5] All photographs were of patients in frontal view and in repose. We used StereoPhoto Maker version 5.10 (http://stereo.jpn.org/eng/stphmkr) software to convert the Multi Picture Object files into a format compatible for 3D presentation (JPEG). All images were cropped to a uniform size of 1,152 pixels in width by 896 pixels in height using the same software. Three-dimensional images were generated stereoscopically using a pair of offset 2D images. Photographs were presented in a random order for each participant.

Procedure

Prior to starting the experiment, subjects were asked to fill out a brief digital demographics survey. Informed consent was obtained at this time. Subjects were then familiarized with the experiment equipment. They were told that there would be a calibration step in the beginning, followed by a series of images of faces. They were instructed to gaze freely upon the faces as though they were sitting across from them in a public setting. No specific task was assigned for facial viewing.

Participants examined life-size facial images at a conversational viewing distance of 60 cm with a pair of circularly polarized 3D glasses or clip-on lenses (LG AG-F210 Cinema 3D, LG Electronics U.S.A. Inc., Englewood Cliffs, NJ) for those who wore corrective glasses normally (Fig. 1). The observer's eye movement recordings were calibrated using a 9-point algorithm. After calibration, eight 3D images were projected on a 27-inch LED screen (LG Cinema 3D Monitor D43 Series, LG Electronics U.S.A. Inc.) at a resolution of 1280 × 1024 pixels for 10 seconds per image. At the beginning of each session, observers were asked if the images appeared blurry for quality control. They were notified of their progress periodically in order to reduce observer fatigue.

Data Analysis

The regions of interest, including the eyes, nose, mouth, central triangle as a whole, and the rest of the face, were outlined using SMI BeGaze analysis software (SensoMotoric, Inc., Needham, MA). Eye-movement data were analyzed offline using Hotelling's multivariate t test, followed by planned posthypothesis testing in Stata 13 SE (Stata Corp., College Station, TX). Demographics information was collected using Qualtrics Survey Software (Qualtrics, Provo, UT).

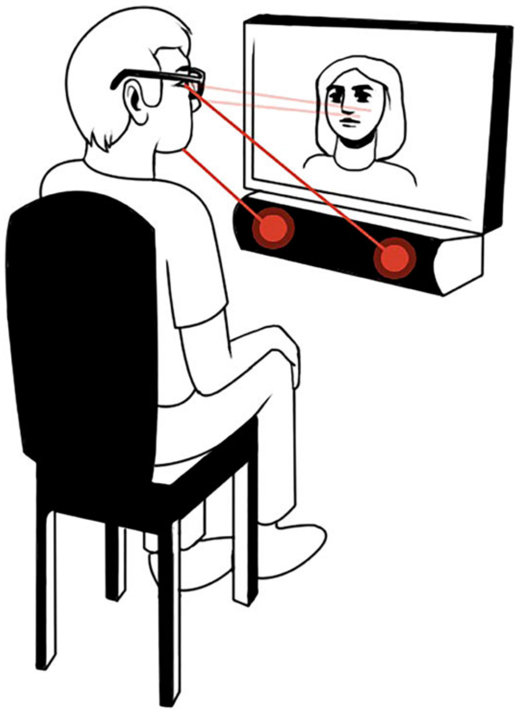

Fig. 1. Illustration of a casual observer wearing three-dimensional eyeglasses whose eyes are being tracked and recorded while gazing at a photograph of a patient. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

RESULTS

One hundred sixteen observers (mean age 26.4 years, 59 females) successfully completed the eye-tracking experiment (Table I). The majority of their attention was directed toward the central triangle (eyes, nose, mouth) for both TAO and normal control patient images. Mean fixation times for the primary areas of interest are shown in Table II. We hypothesized that observers would spend more time looking at the eyes of TAO patients compared to controls. Hotelling's multivariate t test revealed significant differences in the distribution of attention between control and TAO faces ($T^2 = 49.37$; $F(5,922) = 9.8314$, $P < 0.0001$). On planned posthypothesis testing, we found that observers attended significantly more to the eyes (0.77 seconds, $P < 0.0001$, 95% confidence interval [CI] [0.51, 1.03] seconds) and less to the nose (–0.42 seconds, $P < 0.0001$, 95% CI [–0.23, –0.62] seconds) in TAO patients. Meanwhile, there was no significant difference in time spent on the mouth ($P = 0.51$), the total time spent on the central triangle ($P = 0.07$), or time spent in the remaining face ($P = 0.06$) between the two groups (Table III). In other words, casual observers redirected their attention away from the nose and looked longer at the eyes of TAO faces.

TABLE II.
Mean Fixation Times

Region of Interest	Mean (SD), ms		No./Group
	Control	Severe TAO	
Eyes	2,148 (1,938)	2,918 (2,160)	464
Nose	1,785 (1,630)	1,365 (1,397)	464
Mouth	820 (1,076)	774 (1,053)	464
Central triangle	4,893 (2,022)	5,163 (2,359)	464
Remainder of face	2,689 (1,623)	2,638 (1,532)	464

No./Group = number of observations per group; SD = standard deviation; TAO = thyroid-associated orbitopathy.

TABLE III.
Post Hoc Comparison of Differences Between Groups

Region of Interest	No.	Mean Difference,* ms	95% CI	*P* Value
Eyes	928	770	51 to 1035	< 0.0001
Nose	928	–421	–225 to –616	< 0.0001
Mouth	928	–46	–183 to 91	0.51
Central triangle	928	270	–24 to 564	0.07
Remainder of face	928	–51	–254 to 153	0.62

*Mean difference: mean fixation times in severe TAO minus control.
CI = confidence interval; ms = milliseconds; No. = total number of observations; TAO = thyroid-associated orbitopathy.

DISCUSSION

Human eyes serve a cardinal purpose in communication. Physical changes to the eyes, as in TAO, can perturb their day-to-day function in social interactions. The TAO patient experience has been well documented. Through interviews, Estcourt et al. found the development of an altered identity to be a major theme for patients. This identity often resulted from perceived prejudicial judgment, misinterpretation of facial expressions, and a diminished self-image.[10] Given that the onset of TAO is primarily between the third and fifth decades of life,[28] the associated psychosocial effects can have a profound impact on both the personal and professional lives of those with TAO.

Whereas TAO can lead to visual impairment, numerous studies suggest that the changes in appearance also have significant and long-term consequences on patient quality of life. Kahaly et al. showed that TAO patients had higher rates of depression and anxiety compared to the general German population.[7] Similar findings have been reported in Taiwanese, Korean, Iranian, and American cohorts, suggesting similar psychological effects span multiple cultures.[8,9,11,12] One long-term follow-up study further showed that even after 10 years had elapsed since diagnosis, over half of patients still considered their eyes to be abnormal, and over a third of patients remained unhappy with their appearance.[14]

Unlike in earlier eye-tracking studies, the TAO deformity represents a distortion of organic features within the face as opposed to an overt lesion in the traditional sense. It is a disease process that can be characterized by proptosis, eyelid retraction, strabismus, soft tissue erythema and edema, and asymmetry of the eyes. Given the fundamental role of the eyes in human identity and social interaction, it is no wonder that patients cite experiences of being stared at and ineffective communication, leading to feelings of social isolation.[7] Eye-tracking technology allows us to gain insight into how TAO affects observer attention. Eye movements and fixations are established surrogates for visual attention.[16,29] As such, eye-tracking serves as an important tool for understanding the visual processing of faces with deformity.

To the best of our knowledge, this is the first experiment to characterize the casual observer's perception of faces with the TAO deformity. Humans visually regard faces in a predictable distribution, focusing on the central triangle which comprises the eyes, nose, and mouth.[30] This finding has been replicated in multiple facial recognition studies, signifying a highly conserved evolutionary process.[15,23] A typical pattern of facial processing has been further supported by magnetic resonance imaging studies showing consistent brain activation outside the fusiform gyrus.[31,32] Thus, any deviation from this pattern suggests an abnormality in the face that distracts the viewer's attention. In this study, we showed that observers view severe TAO faces differently than they do control faces. In faces with the severe TAO deformity, they spend more time gazing at the eyes and less time gazing at the nose as compared to control images, indicating an attentional bias toward the eyes.

In comparison to other facial abnormalities, our findings are in line with previous studies that looked at attentional bias in observers for facial paralysis, nasal deformity, and cleft lip. One study showed that severe facial paralysis (House-Brackmann grades IV–VI) independently increased fixation on the mouth by 164 milliseconds as compared to normal faces.[33] Similarly, Godoy et al. showed that observers spent, on average, 658 more milliseconds on a crooked nose than they did on a normal nose.[16] Dindaroglu et al. further demonstrated comparable differences in upper lip fixation when studying how laypeople gazed on photos of cleft lip patients.[34]

Perhaps more telling are the social penalties suffered by those with facial deformity. For example, both patients with facial paralysis and those with crooked noses are perceived as less attractive by society, and diminished attractiveness has been strongly associated with depression.[18,35] Although the effect may have been amplified by the 3D nature of our experiment, it stands to reason that severe TAO also confers a social penalty given an increased fixation on the abnormal eyes by 770 milliseconds. However, future studies are needed to better characterize what those penalties are.

It should be noted that our results can in part be attributed to perceived emotion expression. In a previous eye-tracking study, Eisenbarth and Alpers demonstrated that faces are encoded differently by observers based on the facial expressions. When presented with faces expressing sad and angry emotions in particular, the eyes received more attention than the mouth as compared to neutral or happy expressions.[36] This is further supported by evidence that smiling alone can increase fixation time on the mouth.[33] TAO patients are often mistaken for appearing angry due to their eyelid retraction and proptosis; our experimental findings are consistent with the patient's reported experience.[37]

We also found that there was no significant difference in the amount of time that casual observers spent on the mouth, the central triangle as a whole, and the rest of the face between the two groups. Observers primarily sacrificed time looking at the nose rather than from other parts of the face to fixate longer on the eyes of severe TAO patients. There is a general consensus that faces are viewed holistically rather than as a collection of individual parts.[38] However, visual attention allocation is a complex process that depends on features such as the saliency of the stimulus and the proximity of distractors within a given visual field space.[39–41] Given the proximity of the eyes to the nose, it follows that changes that render the eyes abnormal would make them more salient, leading to greater competition with the closest surrounding structures (i.e., the nose).

This research extends on previous eye-tracking findings through the use of 3D image stimuli. This novel methodology for exploring the visual processing of facial deformities was born out of the recognition that TAO is a process that commonly involves forward displacement of the eyes and volumetric changes of the periorbital soft tissue such as eyelid edema; as such, there are stereoscopic depth features that cannot be fully appreciated in 2D. Chelnokova and Laeng found that certain volumetric features of normal faces were attended more when comparing 3D and 2D conditions, such as the nose and cheeks. Interestingly, they found that observers attended to the central triangle differently in the 3D comparison with the order of fixation duration being the nose, eyes, and then mouth.[22,23] However, the participants in this current study attended to the central triangle with greatest duration on the eyes, followed by the nose and then the mouth. One possible explanation for this finding could be related to our comparison of severe TAO patients to controls. The prominent periorbital changes in severe TAO could have potentially clued in our participants to direct more attention toward the eyes for all subsequent images, even though they were naïve to the purposes of the study. Nonetheless, the 3D condition offers a more realistic representation of TAO and serves as a promising research tool for future facial perception studies.

There are limitations to this study. The first relates to the complexity of TAO. We measured the attentional distraction in TAO as a whole disease entity, but TAO comprises multiple aspects such as proptosis, strabismus, eyelid retraction, soft tissue swelling and redness, and eye asymmetry. We did not examine the individual aspects of TAO in this experiment due to a limited number of patient photographs and therefore cannot distinguish the extent to which each element contributes to attentional distraction. Thus, objective eye-tracking data that looks at each aspect and its contribution to attentional distraction is a logical next step.

Another limitation is that our experiment took place in a controlled environment with a static photograph, whereas social interactions are dynamic and are governed by cultural norms. For example, our findings indicate that observers spend more time viewing the eyes of TAO faces compared to those of control faces. However, this may or may not translate to social encounters. Nevertheless, these data show that severe TAO alters the way in which the casual observer gazes upon patient faces, consistent with the reported TAO patient experience. Future TAO studies might consider the use of video recordings. This would not only allow better approximation of reality but also permit the exploration of emotional expression impairment, as perceived by observers because one of the primary complaints of TAO patients is the misinterpretation of facial expressions.

Finally, it would be important to understand how objective changes in the gaze patterns of TAO faces translate to perception of TAO patients. Previous studies have shown that facial deformity leads to reduced attractiveness, a more negative affect, and a lower perceived quality of life.[19–21] Investigation of social domains in perception of TAO patients is warranted.

Despite these limitations, this pilot study demonstrates the attentional distraction caused by the severe TAO deformity. These results help explain patient concerns and pave the road for future research in the study of the perception of TAO. These results also establish 3D eye-tracking as a promising tool for surgical outcome evaluation by comparing visual processing of TAO faces before and after intervention.

CONCLUSION

Severe TAO caused attentional distraction for casual observers. These data lend insight into how this disease process may alter casual observer perception of TAO patients. This experiment also represents the first effort to use a 3D eye-tracking approach to study facial disfigurement and suggests that it is a promising tool for future research.

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