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Enhanced neural function in highly aberrated eyes following perceptual learning with adaptive optics

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ABSTRACT

Highly aberrated keratoconic (KC) eyes do not elicit the expected visual advantage from customized optical corrections. This is attributed to the neural insensitivity arising from chronic visual experience with poor retinal image quality, dominated by low spatial frequencies. The goal of this study was to investigate if targeted perceptual learning with adaptive optics (AO) can stimulate neural plasticity in these highly aberrated eyes. The worse eye of 2 KC subjects was trained in a contrast threshold test under AO correction. Prior to training, tumbling 'E' visual acuity and contrast sensitivity at 4, 8, 12, 16, 20, 24 and 28 c/deg were measured in both the trained and untrained eyes of each subject with their routine prescription and with AO correction for a 6 mm pupil. The high spatial frequency requiring 50% contrast for detection with AO correction was picked as the training frequency. Subjects were required to train on a contrast detection test with AO correction for 1 h for 5 consecutive days. During each training session, threshold contrast measurement at the training frequency with AO was conducted. Pre-training measures were repeated after the 5 training sessions in both eyes (i.e., post-training). After training, contrast sensitivity under AO correction improved on average across spatial frequency by a factor of 1.91 (range: 1.77–2.04) and 1.75 (1.22–2.34) for the two subjects. This improvement in contrast sensitivity transferred to visual acuity with the two subjects improving by 1.5 and 1.3 lines respectively with AO following training. One of the two subjects denoted an interocular transfer of training and an improvement in performance with their routine prescription post-training. This training-induced visual benefit demonstrates the potential of AO as a tool for neural rehabilitation in patients with abnormal corneas. Moreover, it reveals a sufficient degree of neural plasticity in normally developed adults who have a long history of abnormal visual experience due to optical imperfections.

1. Introduction

Visual experience continually alters structural and functional properties of the visual system to optimize perception. Changes on a structural and cellular level in the visual system following abnormal visual experience were first documented by Hubel and Wiesel in their seminal work (Hubel & Wiesel, 1959, 1962, 1963a, 1963b, 1965, 1970). Functional changes were studied psychophysically and characteristic changes in the properties of the visual system were noticed after prolonged observation of either contrast, orientation, spatial frequency (Blakemore & Campbell, 1969) and size (Blakemore & Sutton, 1969) of retinal images. For instance, Blakemore and Campbell (1969) demonstrated a marked reduction in contrast sensitivity following the exposure to a single spatial frequency (SF) of high contrast. Progressing from visual exposure to the single spatial frequency and contrast, Webster and Miyahara (1997) showed a rapid alteration in the contrast and spatial frequency response of the visual system after exposure to natural images. Another interesting example of plasticity is from Yamauchi and et al. (2000) who synthetically altered a person's chromatic environment for an extended period of time. They noticed that the visual system shifted its response significantly in the hue direction required to compensate for the chromatically altered environment. Such plastic mechanisms are continuously in action in normal vision and are critical in maintaining optimal and minimally varying perception, despite the variations in luminance, color, spatial scales and blur of the visual environment.

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Normal visual input during a critical period of neural development in early postnatal life lays the foundation of an efficient plastic mechanism in the visual system (Huttenlocher, 2002). Amblyopia is an example of anomalous neural plasticity that occurs due to abnormal visual stimulation during the critical period of development. Amblyopes typically demonstrate reduced visual performance on account of the deficits in their neural processing. Levi and Polat (1996) investigated the limit to plasticity in amblyopic adults by testing whether perceptual training can improve this abnormal neural processing. They were able to invoke substantial plasticity with training, resulting in a 46% average improvement in Vernier acuity. Another interesting aspect of their finding was that the adult visual system retained a certain degree of neural plasticity, which was otherwise thought to be absent after post-natal life.

Optical factors represent a major factor altering neural processing in normally developed adults. Abnormal visual input due to optical limitations can be considered as those arising from refractive error like myopia or astigmatism, higher order aberrations from eyes with abnormal cornea or scatter, chromatic aberration and decrease in retinal illuminance in aging eyes. The implicit role of neural plasticity can be invoked to partly explain the gradual improvement in vision with time following refractive (Kohnen, Bühren, Kühne, & Mirshahi, 2004; Pesudovs, 2005) and cataract surgery (Delahunt, Webster, Ma, & Werner, 2005; Montés-Micó & Alió, 2003). Similarly, clinicians also often use a multiple step procedure to achieve full correction of astigmatism, allowing the neural plasticity to adjust for perceived spatial distortions due to the correction (Sawides et al., 2010; Vinas, Sawides, de Gracia, & Marcos, 2012). Presbyopia is a unique example of an optical anomaly that has been shown to benefit from a perceptual learning paradigm or "*repeated practice on a demanding visual task*", defined by Polat and et al. (2012). For the rest of this article, we will adopt the same definition–"repeated practice on a visual task"–to refer to perceptual learning. The benefit gained in presbyopia from such a paradigm demonstrates the ability of the visual system to enhance its ability to detect and discriminate blur in images, even in adults and without a change in the optics of the eye.

Highly aberrated keratoconus (KC) poses an analogous visual deficit as amblyopia and presbyopia, although with some key differences. This disorder is characterized by an abnormal thinning and steepening of the cornea, the optical consequence of which is a large magnitude and asymmetry in optical aberrations. This leads to severe visual disturbances, especially at middle and high SFs persisting over a long period of time before an intervention with either a corneal transplant or specialty ophthalmic lenses (Michael, Guevara, de la Paz, Alvarez de Toledo, & Barraquer, 2011). In the case of either intervention, the visual quality is usually sub-normal (Brahma, Ennis, Harper, Ridgway, & Tullo, 2000). More importantly, these subjects experience neural insensitivity arising from chronic visual experience to these optical anomalies (Sabesan & Yoon, 2009; Sabesan et al., 2013). They fail to elicit the maximum advantage from a customized correction with ophthalmic lenses, at least immediately after the correction, despite the normal optical quality conferred by the lenses (Sabesan et al., 2013). Moreover, even under complete aberration correction using adaptive optics (AO), their visual resolution remained inferior to the limits imposed by the neural system (Sabesan & Yoon, 2009).

In these highly aberrated KC eyes, habitual and severe optical blur possibly leads to lasting and robust changes in neural visual processing. For instance, they are characterized by a neural compensatory mechanism which partially compensates for the severe optical blur and improves acuity (Sabesan & Yoon, 2010). From previous reports, it has been encouraging that modest neural plasticity can lead to significant improvement in visual performance even in cases of abnormal development such as congenital cataract (Fine, Smallman, Doyle, & MacLeod, 2002) and amblyopia (Levi & Polat, 1996) following cataract removal and perceptual learning, respectively. It is important to differentiate the "passive" visual improvement in congenital cataract, which resulted from routine viewing with an improved retinal image input, from the benefits seen from an 'active' perceptual learning in amblyopia. In the latter, subjects undertook repeated training in a specific psychophysical task which resulted in visual improvement, while their routine visual diet remained unchanged. KC initializes mostly in puberty in normally developed adults and therefore is less likely to be affected by limitations in visual processing due to abnormal development. Therefore, it is plausible that 'passive' routine exposure to near-diffraction limited ocular optics achieved either via habitual wavefront-guided correction (Sabesan et al., 2007, 2013; Marsack, Parker, & Applegate, 2008; Marsack et al., 2014) or via AO might help restore visual processing in KC to a normal level when achieved and maintained over extended periods of time. Similarly perceptual learning in a psychophysical task can also elicit a visual improvements and efficiently target specific visual functions using the appropriate task. Thus, a hybrid active-passive approach combining routine viewing under optical correction methods along with perceptual learning might help re-instate the neural processing in KC subjects. The time-scale of such *re-adaptation* might be longer in the KC eyes that are affected by relatively larger native higher-order aberrations. The optical performance of the correction is a key factor that may regulate this improvement. Clinically, whether the visual performance improves with customized ophthalmic lenses over time and the timecourse therein remains unknown. If the visual system retains its normal plasticity, one can expect to see such an improvement upon a clinical intervention that improves optical quality. Nevertheless, while "passive" routine exposure to improved optical quality is likely to play a role in the rehabilitation of KC patients, whether "active" perceptual learning can trigger such plasticity and restore visual functions in KC subjects is unknown. Here, we directly address this question by evaluating the impact of a perceptual learning paradigm in KC subjects and by following the time-course of changes in visual performance. Importantly, this paradigm was undertaken upon conferring near-diffraction limited optical quality with AO on KC eyes, thus stimulating the visual pathways which otherwise may lie dormant under habitual viewing. The present study therefore addresses the underlying fundamental question of whether such neural plasticity is retained in adult visual systems altered by optical factors and can be triggered by perceptual learning paradigms.

2. Methods

2.1. Subjects

Two KC subjects (40 and 48 yo) were enrolled in this study. Keratometric readings from corneal topography maps were used to classify them as moderate and advanced respectively (Zadnik, Barr, Gordon, & Edrington, 1996). The University of Rochester Research Review Board approved this research, and each subject signed an informed consent form before participation in this study. All procedures involving human subjects were conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2. Setup

Paralysis of accommodation and dilation of the pupil in all subjects were achieved with 1% tropicamide ophthalmic solution. A large-stroke adaptive optics vision simulator was employed in this study and has described in detail elsewhere (Sabesan & Yoon, 2009,