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The relationship between anisometropia and amblyopia

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ABSTRACT

This review aims to disentangle cause and effect in the relationship between anisometropia and amblyopia. Specifically, we examine the literature for evidence to support different possible developmental sequences that could ultimately lead to the presentation of both conditions. The prevalence of anisometropia is around 20% for an inter-ocular difference of 0.5D or greater in spherical equivalent refraction, falling to 2–3%, for an inter-ocular difference of 3D or above. Anisometropia prevalence is relatively high in the weeks following birth, in the teenage years coinciding with the onset of myopia and, most notably, in older adults starting after the onset of presbyopia. It has about one-third the prevalence of bilateral refractive errors of the same magnitude. Importantly, the prevalence of anisometropia is higher in highly ametropic groups, suggesting that emmetropization failures underlying ametropia and anisometropia may be similar.

Amblyopia is present in 1–3% of humans and around one-half to two-thirds of amblyopes have anisometropia either alone or in combination with strabismus. The frequent co-existence of amblyopia and anisometropia at a child's first clinical examination promotes the belief that the anisometropia has caused the amblyopia, as has been demonstrated in animal models of the condition. In reviewing the human and monkey literature however it is clear that there are additional paths beyond this classic hypothesis to the co-occurrence of anisometropia and amblyopia. For example, after the emergence of amblyopia secondary to either deprivation or strabismus, anisometropia often follows. In cases of anisometropia with no apparent deprivation or strabismus, questions remain about the failure of the emmetropization mechanism that routinely eliminates infantile anisometropia. Also, the chronology of amblyopia development is poorly documented in cases of 'pure' anisometropic amblyopia. Although indirect, the therapeutic impact of refractive correction on anisometropic amblyopia provides strong support for the hypothesis that the anisometropia caused the amblyopia. Direct evidence for the aetiology of anisometropic amblyopia will require longitudinal tracking of at-risk infants, which poses numerous methodological and ethical challenges. However, if we are to prevent this condition, we must understand the factors that cause it to develop.

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1. Introduction and rationale

The majority of human ametropes can be characterised as isoametropic, in that the refractive status of their two eyes is very similar. For example, in the large-scale study by Qin et al. (2005, their Fig. 3A), at least 85% of those aged up to 70 years had right and left eye ocular refractions which were matched to within 1 dioptre. In a minority of humans, however, there are significant interocular differences in refractive error (anisometropia), which can be accompanied by an interocular difference in visual acuity that is optically uncorrectable, at least initially (amblyopia). The co-occurrence of these two anomalies, with no additional abnormality, is labelled 'anisometropic amblyopia'. Anisometropia, therefore, is a special case of an emmetropization failure that is commonly accompanied by a serious neurological deficit. Le Cat (1713, reviewed in Ciuffreda et al., 1991) is credited with providing the first accurate description of amblyopia, and anisometropic amblyopia has been identified clinically since 1743 when George Louis Leclerc, Count de Buffon, proposed a treatment for this condition which is as relevant now as it was when it was first proposed: refractive correction and occlusion of the better eye. Anisometropic amblyopia continues to be treated by refractive correction alone or in combination with patching or other therapies that differentially stimulate the two eyes (Ciuffreda et al., 1991; Simons, 2005; Shotton et al., 2008; Taylor et al., 2012).

Although anisometropia and amblyopia are often discovered at the same time, for example during a school vision screening, it is widely held that the anisometropia is a precursor to, and indeed the cause of the amblyopia. However, definitive evidence that anisometropia universally precedes development of the amblyopia is lacking, and the simplicity of this cause and effect relationship continues to be challenged (Almeder et al., 1990; Barrett et al., 2005; Lempert, 2000, 2003, 2004, 2008a, 2008b; Lempert and Porter, 1998; Smith and Hung, 1999). In light of the general uncertainty about the aetiology of anisometropia and anisometropic amblyopia, an examination of the literature is timely as part of the continuing effort to refine approaches to vision screening and clinical care. This review examines the human and non-human primate literature concerning the co-occurrence of these two conditions in an attempt to gain insight into their origins and the underlying relationships between them. It is timely because it coincides with a recent surge in the number of published articles on the topic, from around 1000 per decade between 1960 and 2000 to around 1900 during the last decade (a PubMed search conducted on July 1st 2012 using the term 'anisometropic amblyopia' yielded 7046 citations, Fig. 1). Anisometropic amblyopia is also of major significance from a clinical perspective. In 1980 it was estimated that each year in the USA 1.2 million office visits for medical eye care were related to amblyopia and its associated conditions (National Society to Prevent Blindness, 1980). Given that