Hearing Research 320 (2015) 1–10

Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

Review

Eye color as a risk factor for acquired sensorineural hearing loss: A review

Mario A. Mujica-Mota [a], Jonah Schermbrucker [a], Sam J. Daniel [a, b, *]

[a] McGill Auditory Sciences Laboratory, Montréal, Québec H3H1P3, Canada
[b] The Montreal Children's Hospital, Department of Otolaryngology-Head and Neck Surgery, Montréal, Québec H3H1P3, Canada

ARTICLE INFO

Article history:
Received 23 July 2014
Received in revised form
1 December 2014
Accepted 8 December 2014
Available online 19 December 2014

ABSTRACT

Eye color may be an indicator of inner ear melanin content and has been associated with hearing loss. There is controversy as to whether eye color has an effect on acquired causes of sensorineural hearing loss. This review was conducted to analyze the literature evaluating the relationship between eye color and causes of sensorineural hearing loss. Six databases were searched to identify eligible studies. Included articles were independently assessed for quality by two authors. Eighteen articles were eligible for review. Eye color was not found to have an effect in the non-exposed population or in presbycusis. In noise-induced sensorineural hearing loss, light-eyed patients had more significant loss following noise exposure, although the variability reported due to eye color was modest ($r^2 = 0.01–0.14$). Two out of three studies reported that dark eye color is associated with cisplatin ototoxicity. In one study, green-eyed patients were found to be at higher risk of radiation-induced hearing loss. Eye color does not appear to play a role in hearing loss in non-exposed individuals or presbycusis. It is possible that dark-eyed individuals, with greater inner ear melanin content, are better protected against noise-induced hearing loss. Evidence suggests that melanin can be protective against radiation-induced sensorineural hearing loss, but may predispose individuals to cisplatin ototoxicity. Future studies are required to support these conclusions.

1. Introduction

A relationship between pigmentation abnormalities and hearing loss in humans has long been known. Petrus Waardenburg noted that many deaf patients possessed white forelocks (a form of partial albinism) and light blue eyes, the result of an autosomal dominant disorder that now bears his name. (Waardenburg, 1951) Bonaccorsi later suggested that the concentration of otic melanin can be predicted based on an individual's eye color. (Bonaccorsi, 1965) He qualitatively examined the temporal bones of white subjects to assess the relationship between iris pigmentation and the pigmentation of the stria vascularis. He found that the melanin content of the stria vascularis, though independent of hair color, does correspond with iris pigmentation. Nevertheless, this finding was limited to middle aged individuals. (Bonaccorsi, 1965). Later research by Tota and Bocci (1967) assessed the correlation between eye color and susceptibility to hearing loss. The authors observed that an individual's resistance to auditory fatigue was proportional to the concentration of melanin in the eyes, with dark-eyed individuals showing the shortest hearing recovery time. Conversely, in animal models there is controversy as to whether pigmentation has an effect on normal hearing function (reviewed in Tachibana) (Tachibana, 1999) While in some studies albino guinea pigs demonstrated lower thresholds than pigmented guinea pigs (Conlee et al., 1986), opposite results were found in rats (Overbeck and Church, 1992).

Currently, it is known that human melanocytes are found in the skin, hair, eyes, inner ears, and the meninges. Otic melanocytes are

Abbreviations: ABR, Auditory brainstem response; ANCOVA, Analysis of covariance; ANOVA, Analysis of Variance; DPOAEs, Distortion product otoacoustic emissions; HL, Hearing loss; NHANES, National Health and Nutrition Examination Survey; NIHL, Noise-induced Hearing Loss; PEDF, Pigment Epithelium Derived Factor; PTS, Permanent Threshold Shift; ROS, Reactive Oxygen Species; SNHL, Sensorineural hearing loss; TEOAEs, Transient evoked otoacoustic emissions; TOAEs, Transient otoacoustic emissions; TTS, Temporary Threshold Shift

* Corresponding author. The Montreal Children's Hospital, 2300 Tupper Street, Room. B-240, Montreal, Québec H3H 1P3, Canada. Tel.: +1 514 412 4246; fax: +1 514 412 4342.

E-mail addresses: mario.mujicamota@mail.mcgill.ca (M.A. Mujica-Mota), jonah.schermbrucker@mail.mcgill.ca (J. Schermbrucker), sam.daniel@mcgill.ca (S.J. Daniel).

http://dx.doi.org/10.1016/j.heares.2014.12.002
0378-5955/

located in the stria vascularis of the cochlea (Tolleson, 2005) where it has been hypothesized that they moderate the expression of junction proteins to maintain the intrastrial fluid-blood barrier balance. (Zhang et al., 2012) Although melanocytes are found in the intermediate layer of the stria vascularis, the projections of these cells can be in close contact with strial basal or marginal cells. This characteristic has resulted in these cells being called macrophage-like melanocytes. (Zhang et al., 2012) According to work in animal models by Cable and Steel, there are two types of otic melanocytes, known as light and dark melanocytes. The authors suggest that these two cell types may simply be different functional states of the same cell, where dark melanocytes are at a later stage of differentiation (Cable and Steel, 1991).

Using an animal model, Steel and Barkway have hypothesized that melanocytes and melanin are crucial for normal cochlear development and interdigitation between basal and marginal cells in the stria vascularis. The absence of melanin may result in loss of the normal endocochlear potential as seen in mutant mice with neural crest defect migration and who lack melanocytes in the skin and stria vascularis. (Steel and Barkway, 1989) Further experiments on albino and pigmented animals have suggested that melanocytes, but neither melanin nor melanosomes, are required for normal hearing. Using immunohistochemistry to evaluate the development of the stria vascularis, Peters et al. (1995) found that there is a relationship between the initial interdigitation of melanocytes with marginal cells and melanin production. The authors concluded that while the melanocytes and the pigmentation production are crucial during development, melanin does not contribute to the function itself of the stria vascularis in mature rats.

Given the current understanding of melanin and hearing function, some authors have explored whether skin color, as represented by race or ethnicity, bears any relation to hearing function. Navarrete et al. (1995) found a higher melanin content in the cochlea of African–Americans compared to the cochleae of Caucasian and Native-American individuals. Similar findings were reported by Wolff, who found that cochlear pigmentation is greater in the African American group than in the Caucasian group.(Wolff, 1931) Being able to predict a person's risk of hearing loss could have applications in industry and the military, as well as in the counseling of oncology patients regarding ototoxic treatment options. Therefore, the purpose of this study was to systematically review the literature relating acquired sensorineural hearing loss to eye color in order to consolidate current knowledge. In addition, current literature was assessed to evaluate the role of other pigmentation characteristics, like skin color, in acquired sensorineural hearing loss.

2. Materials and methods

2.1. Search strategy

A systematic review was performed to identify all literature discussing acquired sensorineural hearing loss and eye color. The search was performed with the assistance of a librarian using six databases: Cochrane, Embase, Medline, PubMed, Scopus, and Web of Science. Search terms used were “eye color”, “eye pigmentation”, “iris color”, “sensorineural”, “hearing loss”, “ototoxicity”, and their combinations.

2.2. Criteria for inclusion and exclusion

Included articles mentioned in their titles or abstracts a relation between eye color and acquired sensorineural hearing loss due to infectious diseases, cisplatin or chemotherapy, radiotherapy, presbycusis, or noise-induced hearing loss. Articles were excluded when hearing loss was classified as temporary threshold shift (TTS). Articles were also excluded when the hearing loss was due to congenital causes, Waardenburg syndrome, or other syndromic causes of sensorineural hearing loss. Animal studies and systematic reviews were also excluded.

2.3. Quality assessment

The eligible articles were assessed for quality using the modified Downs and Black (DB) rating scale as it is a validated checklist for randomized and non-randomized studies. (Downs and Black, 1998) Evaluation was performed by two authors independently, with each author blind to the other's ratings. Scores were then compared using the Spearman's correlation coefficient to determine the interrater reliability. A value above 0.8 was considered acceptable for a significance level of $\alpha < 0.05$. Final scores were discussed and any study with a mean score below 12.5 was excluded due to unsatisfactory quality.

3. Results

3.1. Search results and quality assessment

Of 2321 articles identified through the search strategy and 11 additional articles from the bibliographies of reviewed articles, 30 articles were included for complete evaluation. Three articles required translation. Seven articles were excluded, either because they referred primarily to TTS or used non-objective methods to determine hearing thresholds. It has been shown that temporary threshold shifts and permanent threshold shifts (PTS) occur through distinct mechanisms (Nordmann et al., 2000). Furthermore, there is still controversy whether TTS has or does not have predictive value for future risk of developing PTS. Since a primary aim of this paper is to determine whether eye color can predict future risk of permanent sensorineural hearing loss (which by definition is PTS), TTS has been excluded from this review. Thus, 23 research publications were evaluated for quality using a modified Downs and Black scale. The selection process is summarized in Fig. 1. Eighteen studies passed the quality assessment and were included in the current review. Four were studies assessing hearing thresholds in patients without any offending exposure (Ferguson et al., 2000; Hannula et al., 2012; Le Prell et al., 2011; Roche et al., 1983), nine looked at noise-induced populations (Carlin and McCroskey, 1980; Carter et al., 1981; Cunningham and Norris, 1982; Da Costa et al., 2008; Kleinstein et al., 1984; Sallustio et al., 1998; Smith et al., 1984; Thomas and Williams, 1990; Thomas et al., 1981), three referred to cisplatin ototoxicity (Barr-Hamilton et al., 1991; Martin et al., 2007; Wendell Todd et al., 1995), one explored radiotherapy (Zuur et al., 2009), and one assessed presbycusis (Bartalena and Vaglini, 1969). Included studies ranged from 13.5 to 17.5 out of 26 possible points. Inter-rater reliability had a Spearman's r of 0.8577 ($p < 0.0001$), indicating good agreement between reviewers. A summary of the included studies can be found in Table 1.

3.2. Eye color and hearing thresholds in non-exposed population

Four studies compared the hearing threshold levels in groups of healthy individuals with different eye colors. (Ferguson et al., 2000; Hannula et al., 2012; Le Prell et al., 2011; Roche et al., 1983). While one study found that the otoacoustic emissions of dark-eyed people had larger amplitudes than those of light-eyed individuals (Ferguson et al., 2000), overall the four studies agreed that there was no significant difference in thresholds between groups. One