Audiological abnormalities in patients with vitiligo

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Summary

Background. Accumulating evidence suggests that vitiligo is a systemic disease affecting the entire pigmentary system.

Aim. To investigate the subclinical abnormalities of melanin-containing cellular elements of the auditory system in patients with vitiligo.

Methods. We studied the conventional audiometric investigations and brainstem auditory evoked responses (BAERs) of 57 active patients with vitiligo and 50 healthy human subjects. The I, III and V latencies, and I–III, III–V and I–V interpeak latencies (IPL) between the groups were compared.

Results. A mild degree of sensorineural hypoacusis was found in eight patients with vitiligo (14%), whereas no controls demonstrated abnormal audiological results (\( P = 0.006 \)). A statistically significant increase in both ears of the third peak latency (\( P = 0.02, P = 0.01 \), respectively) and IPL I–III (\( P = 0.04, P = 0.008 \), respectively), and a significant increase of the fifth peak latency in the right ear (\( P = 0.04 \)) were found, compared with controls, but no differences were found for other latencies and IPLs.

Conclusions. Melanin may play a significant role in the establishment and/or maintenance of the structure and function of the auditory system and may modulate the transduction of the auditory stimuli by the inner ear.

Introduction

Vitiligo is a common, often inherited, acquired disorder resulting from destruction of functional melanocytes (MCs). It affects all ethnic groups and has a worldwide occurrence of 0.3–1.0%. Functional MCs in patients with vitiligo disappear from the involved skin by a mechanism(s) that has yet to be identified. Traditionally, there have been three hypotheses to explain vitiligo: the immune, the neural and the autocyotoxic hypotheses.1

The embryonic origin of human MCs is from the neural crest, and they are located in the epidermis, hair bulbs of the skin, the uveal tract and retinal pigment epithelium of the eye, the inner ear and the lepto-meninges.2,3 The concept of a ‘melanocyte organ’ has been proposed. The mechanism destroying the melanocyte in the skin could also affect other melanocytic organs.4 Several ocular5 and audiological abnormalities of hearing6–12 and brainstem auditory evoked responses (BAERs)9,11 have been reported in patients with vitiligo. These abnormalities suggest that vitiligo is a systemic disease affecting pigmented cells throughout the body, rather than a purely cutaneous problem.4,13,14 However, it has not yet been demonstrated that these abnormalities are related to the same mechanism(s) that lead to destruction of MCs in vitiligo.

Most patients with vitiligo are asymptomatic for audiological abnormalities.1 Therefore, we aimed to use conventional audiological tests and BAERs in order to detect electrophysiologically any subclinical auditory abnormalities of in patients with vitiligo, compared with controls.

Patients and methods

Written consent was obtained from each patient and control following a thorough explanation of the purposes and the methodology to be used in the present study.
In total, 57 active patients with vitiligo (27M, 30F) and 50 healthy, sex- and age-matched controls (26M, 24F) were randomly enrolled. Mean ± SD age was 35.9 ± 12.1 (range 14–50) for the patients with vitiligo, and 30.5 ± 10.7 (range 20–50) for the controls. There was no statistical difference for the age distribution between the vitiligo and control groups or between male and female participants.

Exclusion criteria included: a history or evidence of autologous disease, familial hearing loss, oral autotoxic drug or corticosteroid intake, chronic noise exposure, head trauma, metabolic, neurological, vascular or autoimmune disease; any systemic disease such as diabetes or hypertension; and age > 50 years.

Focal, generalized and dermatomal types of vitiligo were seen in 29 (51%), 16 (28%) and 12 patients (21%) patients, respectively. The duration of vitiligo was 5.8 ± 3.5 years (range 5–40). VIDA score was 2.1 ± 1.2. Skin types III and IV were seen in 85% of the patients.

Examinations

The duration, type of vitiligo, skin phototypes and Vitiligo Disease Activity (VIDA) score of vitiligo were noted on a bespoke form. Clinical and tympanometric examination was made by an autolaryngologist for exclusion of middle-ear pathologies. Autoscopic, audiometric and BAER examinations for both ears were performed for both patients and controls.

Audiometric examination Audiometry was performed using a pure-tone audiometer (clinical audiometer model AC30; Interacoustics, Copenhagen, Denmark) in a silent cabin. Pure-tone thresholds were determined for each ear at the frequencies of 250–8000 Hz for air conduction and 250–4000 Hz for bone conduction. The scale of hearing impairment was assessed according to the International Standard Organization hearing threshold parameters (normal = inability to hear at minus 10–20 dB, mild deafness = inability to hear at 27–40 dB, moderate deafness = inability to hear at 41–55 dB).

Measurement of BAERs BAERs were measured using Medelec Sapphire Software and two recording channels with filter bandpass between 100 and 3000 Hz. These were based on the American EEG Society guidelines. Recording electrodes were attached at the vertex (Cz, reference), both mastoids and at a frontal location midway between the nasion and the vertex (ground). During testing, all subjects reclined in a dark and quiet room. Monoaural rarefaction clicks (80–85 dB, 0.1 ms duration) were used as auditory stimuli. White noise at 30 dB to the contralateral ear was used. The sounds were produced by activating earphones (model TDH-39) with 0.1 ms pulses at a rate of 8–10/s and an intensity of 70 dB above sensation level for click. Analysis time was 100 ms with a system bandpass of 100–200 Hz. The I, III, and IV wave latencies, amplitudes, and I–III, III-IV and I–V interpeak latencies (ILP) were measured and compared between the groups in each ear.

Statistical analysis

All statistical tests (Student’s t-test, \(\chi^2\), Fisher’s exact probability tests) were performed using SPSS software (version 11.5; SPSS Inc, Chicago, IL, USA). The threshold of significance (\(\alpha\)) was accepted as 0.05.

Results

Sensorineural hypoacusis was found in eight patients (14%) with generalized vitiligo and VIDA score = 3 on audiological examination, who previously had no complaint of any hearing impairment. Two of the eight patients showed unilateral minimal hearing loss (≥ 30 dB) at only high frequencies (4000–8000 Hz), while the other six demonstrated bilateral hearing loss (≥ 30 dB) over a large range of frequencies (2000–8000 Hz). The findings in the control subjects were all within normal limits (\(P = 0.006\)). These patients were not statistically different from the other patients who had normal auditory function for their age range and illness duration.

A statistically significant increase in both ears for third peak latency (\(P = 0.02, P = 0.01\), respectively) and IPL I–III (\(P = 0.04, P = 0.008\), respectively), and a significant increase in fifth peak latency in the right ear (\(P = 0.04\)) were found in patients compared with controls. No significant difference for the other latencies or IPLs or in amplitude were observed (Table 1).

Discussion

The functions of MCs or melanins in MC organs are clearly unknown. MCs are present in the stria vascularis, auditory receptors or hair cells, vestibular organ and endolymphatic sac of the inner ear. It has been reported that melanin has semiconductive properties, responding to phonic, acoustic and electrical stimulation, and the ability to convert energy states into molecular rotation and vibration, as well as the reverse process. Furthermore, inner-ear melanin functions as...
Table 1 Comparison of BAERs parameters between patients with vitiligo and control subjects for left ear and right ear stimulation.

<table>
<thead>
<tr>
<th></th>
<th>Left ear</th>
<th></th>
<th>Right ear</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$l_1$ (ms)</td>
<td>$l_{III}$ (ms)</td>
<td>$l_V$ (ms)</td>
<td>$l_{III-V}$ (ms)</td>
</tr>
<tr>
<td>Patients (n=57)*</td>
<td>1.70 ± 0.18</td>
<td>3.90 ± 0.24</td>
<td>5.68 ± 0.36</td>
<td>2.21 ± 0.22</td>
</tr>
<tr>
<td>Controls (n=50)*</td>
<td>1.67 ± 0.19</td>
<td>3.78 ± 0.16</td>
<td>5.62 ± 0.23</td>
<td>2.13 ± 0.19</td>
</tr>
<tr>
<td>$t$</td>
<td>1.00</td>
<td>2.28</td>
<td>1.06</td>
<td>2.02</td>
</tr>
<tr>
<td>$P$</td>
<td>&gt;0.05</td>
<td>0.02</td>
<td>&gt;0.05</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Ie, $I_{III}$, $I_V$, wave latencies; $A_I$, $A_{III}$, amplitudes; $I_{e,III}$, $I_{e,III-V}$, $I_{e-V}$, interpeak latencies. *Mean ± SD. Significant results are in bold.

Table 2 Features of the sensorineural hypoacusis in patients with vitiligo.

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of patients</th>
<th>Mean age (years)</th>
<th>Sex (M/F)</th>
<th>Mean duration (years)</th>
<th>Type</th>
<th>Ear affected (n)</th>
<th>Frequency range (Hz)</th>
<th>Hearing loss (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tosti et al.</td>
<td>8 / 50 (16%)</td>
<td>36.3</td>
<td>5 / 3</td>
<td>7.3</td>
<td>Generalized</td>
<td>Bilateral (3)</td>
<td>2000–8000</td>
<td>≤ 40–60</td>
</tr>
<tr>
<td>Orecchia et al.</td>
<td>4 / 50 (8%)</td>
<td>25</td>
<td>1 / 3</td>
<td>8.2</td>
<td>Generalized (3)</td>
<td>Unilateral (5)</td>
<td>4000–8000</td>
<td>≤ 40–60</td>
</tr>
<tr>
<td>Nikiforidis et al.</td>
<td>4 / 50 (8%)</td>
<td>N/A</td>
<td>N/A</td>
<td>5.3</td>
<td>Acral (1)</td>
<td>Bilateral (3)</td>
<td>2000–4000</td>
<td>35–60</td>
</tr>
<tr>
<td>Ozuer et al.</td>
<td>2 / 50 (4%)</td>
<td>43.2</td>
<td>N/A</td>
<td>8.2</td>
<td>Generalized</td>
<td>Bilateral (1)</td>
<td>4000</td>
<td>55</td>
</tr>
<tr>
<td>Sharma et al.</td>
<td>34 / 180 (18.9%)</td>
<td>35.2</td>
<td>N/A</td>
<td>= 5</td>
<td>Generalized</td>
<td>Bilateral (4)</td>
<td>2000–8000</td>
<td>30 to 40</td>
</tr>
<tr>
<td>Aydogan et al.</td>
<td>8 / 57 (14%)</td>
<td>31.4</td>
<td>4 / 4</td>
<td>4.8</td>
<td>Generalized</td>
<td>Bilateral (2)</td>
<td>4000–8000</td>
<td>&gt;30</td>
</tr>
</tbody>
</table>

N/A, data not available.
third and fifth peak latency and I–III IPL are related to the pathology of the superior olivary nucleus (SON) and upper brainstem or inferior colliculus, and to abnormal synaptic activity and transmission of the action potential from the auditory nerve to the cochlear nucleus and from the cochlear nucleus to the SON and inferior colliculus. Vitiligo may also be associated with a delayed synchronization of action potentials in these nuclei.\textsuperscript{11}

Indeed, in albino people, abnormal BAERs have been reported, which indicate SON abnormalities.\textsuperscript{24}

Patients with vitiligo with audiological changes are usually asymptomatic, therefore we consider these changes to be of more interest to neurophysiologists and biologists than to clinicians. However, the presence of these alterations in a proportion of patients confirms that vitiligo can sometimes represent a systemic disease and modulate the transduction of the auditory stimuli by inner ear. Investigations of abnormalities of the audiological and brainstem auditory pathways in patients have been verified by postmortem histopathological studies.

### References