I, Mostafa A Youssif, hereby submit this original work as part of the requirements for the degree of Doctor of Philosophy in Communication Sciences and Disorders.

It is entitled:
Vestibular Evoked Myogenic Potential (VEMP) in children with Enlarged Vestibular Aqueduct (EVA)

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This work and its defense approved by:

Committee chair: Robert Keith, PhD

Committee member: David Brown, PhD

Committee member: Fawen Zhang, PhD
Vestibular Evoked Myogenic Potential (VEMP) in children with Enlarged Vestibular Aqueduct (EVA)

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By

Mostafa A Youssif

M.D. Sohag University, 1999
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Committee Co-Chairs: Robert W. Keith, Ph.D.
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David Brown, Ph.D.
Enlarged vestibular aqueduct (EVA) syndrome is considered one of the most common congenital anomalies of the inner ear which is radiologically detectable and associated with hearing loss. It is a minor dysmorphology belonging to the family of Mondini dysplasias. Although there are many studies about the effect of EVA on audiological function, there are only a small number of studies on its effect on the vestibular system especially in children. In spite of the frequent studies emerging in the last few years which proved that vestibular disorders in children are not as rare as thought, the data about one of the most important tests in vestibular assessment, vestibular evoked myogenic potential (VEMP) test, and its response characteristics at different ages in children are scant.

This study was designed to collect normative data for VEMP response parameters in children from the age of 3 to 12 years and to examine the effect of age on these parameters. The differences between VEMP responses in normal children and children with EVA were investigated in an attempt to evaluate the effect of EVA on the saccular function. The VEMP test was conducted on 39 normal children and on 28 children with EVA. The results revealed that P1 and N1 latencies in normal children are shorter than published normal latencies in adult. The VEMP response was absent in 10% of children with EVA. Moreover, there was a direct correlation between the vestibular aqueduct (VA) diameter and VEMP threshold. Based on these results, using a specific normative data for VEMP test in children is recommended when assessing the pediatric population. In addition, the saccular function should be investigated using
VEMP test in children with EVA. However, further studies using other vestibular tests are recommended to investigate the effect of EVA on different vestibular functions.
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Cincinnati Children Hospital Medical Center and Dr Lisa Hunter, PhD

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DISCLAIMER

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I- INTRODUCTION
1. Statement of the problem and Research rational

Pediatric vestibular dysfunction is often under-diagnosed due to the challenges that are posed when evaluating children. This is primarily due to the lack of sophisticated and standardized tests available to assess the pediatric vestibular system. Children, because of vocabulary limitations, may find it difficult to express their experiences with vertigo or disequilibrium.

The diagnosis of vertigo in childhood is difficult due to a number of age-related factors. It is mainly relay on observations reported by family members. parents who can provide important information about the history of the symptoms and the associated signs such as nystagmus, gait disorders, alterations in consciousness, and motor skill changes (S. H. Erbek et al., 2006). The evaluation of vertigo in children also requires evaluation of clinical signs and diagnostic tests. Audiometry, tympanometry and electronystagmography (ENG) are the most helpful diagnostic tests (Ravid, Bienkowski, & Eviatar, 2003). With advances in technology, many new techniques can be applied to testing the vertiginous child. In addition to the traditional vestibular test battery (i.e. electronystagmography & audiometric evaluation), tests of peripheral vestibular function have become less invasive and more conducive to testing young children. Most notably, Vestibular Evoked Myogenic Potential (VEMP) has been found to be tolerated in very young children and even in newborns (Chen, Wang, Wang, Hsieh, & Young, 2007; Kelsch, Schaefer, & Esquivel, 2006).
VEMP s are myogenic potentials recorded by surface electrodes following repeated high-intensity auditory stimulation. It is thought to assess the saccule, the inferior vestibular nerve pathway, and the vestibulocollic reflex (Colebatch, Halmagyi, & Skuse, 1994).

The differential diagnosis of vertigo in children is broad ranging from disorders of the central nervous system including traumatic, infective and malignant disorders through different otological disorders. It also includes unexplained conditions such as benign paroxysmal vertigo, migraine and psychosomatic disorders (Choung, Park, Moon, Kim, & Ryu, 2003; Ravid et al., 2003).

Enlarged vestibular aqueduct (EVA) is one of the most common congenital inner ear deformities. EVA is considered to be a minor dysmorphology belonging to the family of Mondini dysplasias. It is clinically important because it is usually accompanied with hearing impairment and/or vestibular dysfunction (Elverland & Mair, 1983).

The EVA comprises abnormalities not only in the structure of the inner ear, but also in the physiology of the auditory and vestibular systems. The clinical picture is variable; hearing loss ranges from mild to profound, varying from fluctuating to stepwise progressive or sudden. Vestibular disturbances range from mild imbalance to episodic vertigo.

While there are many reports on clinical and histopathological findings in EVA, only a few studies on the vestibular function in patients with EVA have been published. The exact status of the functional structures, degree of abnormality in
critical tissue and organs and how they are affected over time by the defective pattern are not known (Sheykholeslami, Schmerber, Habiby Kermany, & Kaga, 2004). Grimmer and Hedlund (2007) reported that about half of the patients with EVA have vestibular symptoms. The same percentage was found in pediatric patients.

This study was designed to investigate vestibular function, especially saccular function, in children with EVA by means of the VEMP test.

2. Aims of the work:

1- To collect normative data for the VEMP test in children at different age groups.
2- To study the effects of age on different VEMP response parameters in children.
3- To study the effect of an enlarged vestibular aqueduct on the saccular function in children via VEMP test.

3. Research question and hypothesis

3.1. Research question:
Does an EVA affect saccular functions and hence the VEMP response in children?

3.2. Research Hypothesis:

Null Hypothesis 1:
There is no difference in VEMP latencies, between normal children (control group) and children with EVA (study group).

Research hypothesis 1:
There is a difference in VEMP latencies, between normal children (control group) and children with EVA (study group).
Null Hypothesis 2:
There is no difference in VEMP amplitude between normal children (control group) and children with EVA (study group).

Research hypothesis 2:
There is a difference in VEMP amplitude between normal children (control group) and children with EVA (study group).

Null Hypothesis 3:
There is no difference in VEMP threshold measured in dBnHL between normal children (control group) and children with EVA (study group).

Research hypothesis 3:
There is a difference in VEMP threshold between normal children (control group) and children with EVA (study group).
II- REVIEW OF THE LITERATURE
1. Enlarged vestibular aqueduct (EVA)

1.1. Definition and Anatomical background

Enlarged vestibular aqueduct (EVA) syndrome is known as one of the most common congenital anomalies of the inner ear which is radiologically detectable (Lowe & Vezina, 1997). It was first reported in 1978 by Valvassori and Clemis when they introduced the term ‘large vestibular aqueduct syndrome’ (LVAS). However, Okamoto et al. (1998) suggested to change this term into a more descriptive term ‘large endolymphatic duct and sac syndrome (LEDS). To be consistent, the simple term Enlarged Vestibular Aqueduct (EVA) will be used in this dissertation.

The vestibular aqueduct (VA) is the bony canal extending from the medial wall of the vestibule towards the cerebellar face of the petrous pyramid. It contains a vein, an artery and the endolymphatic duct. The diameter of the vestibular aqueduct is 0.62 mm on average when measured in the mid portion between the external aperture and the common crus (Valvassori & Clemis, 1978).

Enlargement of the vestibular aqueduct is considered to be a minor dysmorphology belonging to the family of Mondini dysplasias. As regards to the definition of the Enlarged vestibular aqueduct; Valvassori and Clemis, in their first description of EVA, defined it as a vestibular aqueduct anteroposterior diameter greater than 1.5 mm. Zalzal, Tomaski, Vezina, Bjornsti, and Grundfast (1995) defined EVA as a vestibular aqueduct anteroposterior diameter over 1.4 mm. However, the definition of an EVA differs among the studies (Antonelli, Nall, Lemmerling, Mancuso, & Kubilis, 1998; Arcand, Desrosiers, Dube, & Abela, 1991;
In fact, there is no universally adopted definition of an EVA (Arjmand & Webber, 2004). Recently, Boston et al. (2007) studied 107 children with SNHL in attempt to define EVA based on audiologic and computed tomography (CT) correlation, and accordingly they defined EVA as greater than 1.9 mm at the operculum and/or greater than 0.9 mm at the midpoint in children (Figure 1).
Figure 1: Measuring the vestibular aqueduct (VA) in the axial plane. In this normal VA, the width at the operculum (*) was measured between the tips of the white arrows and found to be 1.4 mm. The midpoint width was measured between the tips of the black arrows in the coronal VA midpoint plane (line marked “MP P”), which is halfway between the coronal plane of the posterior wall of the crus commune or vestibule (line marked “CC-V P”) and the coronal plane of the operculum’s edge (line marked “O P”) and was found to be 0.6 mm (Boston et al., 2007)
1.2. Etiology, Genetics and pathogenesis of EVA

The enlargement of the vestibular aqueduct is often thought to be the result of a developmental arresting during the fifth week of gestation (Jackler, Luxford, & House, 1987). Most authors suggest that enlargement of the bony aqueduct is due to an abnormal expansion of the endolymphatic duct and sac during embryogenesis and described the hearing loss as congenital (Gussen, 1985; Kodama & Sando, 1982; Okumura, Takahashi, Honjo, Takagi, & Mitamura, 1995; Temple, Ramsden, Axon, & Saeed, 1999). In contrast, the data of Pyle (2000) suggest that EVA might result from a postnatal and early childhood maldevelopment.

EVA is frequently found in association with other inner ear abnormalities, the most common being an abnormally large vestibule, an enlarged semicircular canal, or a hypoplastic cochlea (Emmett, 1985; Govaerts et al., 1999; Valvassori & Clemis, 1978).

Enlarged vestibular aqueduct can be an isolated nonsyndromic (Abe et al., 1999) or a part of a syndromic forms of SNHL, such as the Pendred’s syndrome (PS) (Cremers et al., 1998; Scott et al., 2000), the Branchiootorenal (BOR) syndrome (Stinckens et al., 2001) and distal renal tubular acidosis (dRTA) (Berrettini et al., 2002). Phelps, Mahoney, and Luxon (1997) have demonstrated that large vestibular aqueduct is a frequent (82%) finding in Pendred’s syndrome.

Concerning the genetics of EVA, it has been postulated to be inherited as an autosomal recessive trait (Griffith et al., 1996). Recently, the locus for nonsyndromic SNHL associated with EVA has been mapped to the same
chromosomal region as the PS locus, 7q31 (Coyle et al., 1996; Sheffield et al., 1996), and it has been reported that the gene responsible for PS, the PDS, is also mutated in patients with EVA associated with nonsyndromic SNHL (Everett et al., 1997; Scott et al., 2000; Usami et al., 1999).

1.2.1. Familial Enlarged Vestibular Aqueduct Syndrome

There are only a few studies which reported familial cases of EVA. Griffith et al. (1996) reported on an enlarged vestibular syndrome in two brothers with healthy parents and assumed that the inheritance pattern was recessive inheritance of chromosomes, or that their mother was a germ carrier. In agreement with Griffith et al., Goh, Shim, Roh, Wang, and Chon (2001) reported the EVA in two sisters with healthy parents and suggested the autosomal recessive inheritance also a pattern of inheritance.

1.2.2. Pathogenesis of hearing loss in EVA

The increased cerebrospinal fluid pressure causing hair cell damage was suggested as the cause of the hearing loss in EVA by Okamoto et al. (1998). Other studies postulate that hyperosmolar fluid may reflux into the cochlea causing damage to the auditory hair cells (Jackler & De La Cruz, 1989; Lemmerling, Mancuso, Antonelli, & Kubilis, 1997).

1.2.3. Pathogenesis of Vestibular dysfunction in EVA

The vestibular dysfunction in EVA may have a similar etiology as the hearing dysfunction, and some argue that reflux of the hyperosmotic fluid into the basal end of the cochlear duct may directly elicit vertigo (Jackler & De La Cruz, 1989; Naganawa, Ito, Iwayama, Fukatsu, & Ishigaki, 1999; Okumura et al., 1995).
Degeneration of vestibular hair cells due to osmotic and chemical imbalance may be another mechanism of injury (Everett et al., 2001). In addition, the Sheykholeslami findings of abnormal VEMP in three patients with EVA who previously had undergone vestibular testing with normal results suggest possible saccular dysfunction (Sheykholeslami et al., 2004).

1.3. Audiological findings in EVA

The prevalence of EVA in children with nonsyndromic SNHL is 32% (24% of ears) when an EVA was defined as 2 mm or greater at the operculum and/or 1 mm or greater at the midpoint (Boston et al., 2007).

1.3.1. Laterality and gender:

It was reported that bilateral syndrome took place twice as often as unilateral and there were more female patients than male patients, at the rate of 2:3 (Valvassori & Clemis, 1978). Govaerts et al. (1999) reported bilateral involvement in 80% of cases with equal gender affection.

1.3.2. Type and course of hearing loss with EVA:

According to the literature, EVA is closely related to progressive or fluctuating sensorineural hearing loss that might be triggered by minor head trauma (Levenson, Parisier, Jacobs, & Edelstein, 1989; Temple et al., 1999; Walsh, Ayshford, Chavda, & Proops, 1999). However, (Valvassori, 1983) argued that it is accompanied by conductive hearing loss and he explained that by the opposition to the stapes movement under the increased pressure of the endolymph within the normal middle ear cavity.
Similarly, Govaerts et al. (1999) reported mixed hearing loss in 90% of cases and suggested that the conductive component is of pure cochlear origin which is pathognomonic for the disease. Boston et al. (2007) found a mixed hearing loss in only 39% of EVA ears.

The course of the hearing loss associated with EVA is mostly progressive. Boston et al. (2007) reported that progressive SNHL was more likely to occur in ears with an EVA (24%) and the rate of progressive hearing loss was greater than in ears without an EVA. Boston et al also reported that the risk of progressive SNHL increased with increasing VA size. Govaerts et al. (1999) reported that the progressive hearing loss has an average rate of 4 dB/year.

Sudden SNHL following minor head trauma was also reported in some children with EVA, causing some to recommend avoidance of contact sports or other potentially harmful activities (Bamiou, Phelps, & Sirimanna, 2000; Madden et al., 2003).

A summary of the incidence of different patterns of hearing loss accompanied with EVA in 32 patients is presented in Table 1.

<table>
<thead>
<tr>
<th>Pattern of Hearing Loss</th>
<th>Patients with EVA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital</td>
<td>37.5</td>
</tr>
<tr>
<td>Progressive</td>
<td>84.4</td>
</tr>
<tr>
<td>Sudden</td>
<td>46.9</td>
</tr>
<tr>
<td>Fluctuating</td>
<td>34.4</td>
</tr>
</tbody>
</table>

**Table 1**: Pattern of hearing loss in 32 patients with EVA (Grimmer & Hedlund, 2007).
1.4. Vestibular findings in EVA:

Grimmer and Hedlund (2007) suggested that vestibular symptoms were reported in about half of the patients with EVA with nearly equal incidence of vertigo and other vestibular symptoms in pediatric patients when compared to adult patients. The distribution of the vestibular symptoms reported in EVA patients from the same study are shown in Table 2.

<table>
<thead>
<tr>
<th>Vestibular Symptoms</th>
<th>Patients&lt;18 yrs (N=21)</th>
<th>Patients &gt; 18 yrs (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor delay</td>
<td>9.5%</td>
<td>0%</td>
</tr>
<tr>
<td>Imbalance</td>
<td>4.8%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Vertigo</td>
<td>33.3%</td>
<td>36.4%</td>
</tr>
<tr>
<td>Total vestibular symptoms</td>
<td>47.6%</td>
<td>45.0%</td>
</tr>
</tbody>
</table>

Table 2: Distribution of vestibular symptoms in adult and pediatric patients (Grimmer & Hedlund, 2007).

In agreement with the Grimmer and Hedlund (2007) study, Berrettini et al. (2005) studied vestibular symptoms in 15 patients with EVA and the results revealed that only seven (47%) complained of vestibular disturbance.

The overall incidence of vestibular symptoms in patients with EVA varies widely from 12 to 71% (Emmett, 1985; Sugiura et al., 2005). Jackler and De La Cruz (1989) reported a 30% incidence of vestibular symptoms in a series of 17 patients. However, Emmett (1985) reported 12% incidence of vestibular symptoms in a study conducted in 26 patients with EVA. Yetiser, Kertmen, and Ozkaptan (1999) reviewed ten patients with EVA and reported that three patients (30%) had episodic vertigo. The highest incidence of vestibular symptoms was reported by
Sugiura et al. (2005). They examined 17 patients with EVA, 14 of which had a Pendred mutation. Twelve of the 17 patients (71%) had episodic vertigo.

Regarding the objective vestibular tests findings in patients with EVA; Emmet et al. (1985) reported that 53% of patients showed a unilateral or bilateral caloric weakness, Berrettini et al. (2005) reported caloric weakness in 86% of patients, similarly Yetiser et al. (1999) found caloric abnormalities in 80% of the EVA patients.

The summary of the incidence of vestibular symptoms and caloric abnormalities associated with EVA in some of the studies in the last few years are shown in Table 3.

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects (N)</th>
<th>Vestibular Symptoms (%)</th>
<th>Caloric Abnormalities (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grimmer and Hedlund (2007)</td>
<td>32</td>
<td>Adult: 45.5</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pediatric: 48</td>
<td></td>
</tr>
<tr>
<td>Berrettini et al (2005)</td>
<td>15</td>
<td>47</td>
<td>86</td>
</tr>
<tr>
<td>Yetiser et al. (1999)</td>
<td>10</td>
<td>30</td>
<td>80</td>
</tr>
<tr>
<td>Jackler et al. (1989)</td>
<td>17</td>
<td>30</td>
<td>-</td>
</tr>
<tr>
<td>Emmet (1985)</td>
<td>26</td>
<td>12</td>
<td>53</td>
</tr>
<tr>
<td>Sugiura et al. (2005)</td>
<td>17</td>
<td>71</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3: Incidence of vestibular symptoms and caloric abnormalities in patients with EVA.
2. Vestibular Evoked Myogenic Potentials (VEMP) background and updates.

2.1. Introduction:

2.1.1. Historical background:

There are four nerve bundles passing through the internal auditory canal: facial nerve, cochlear nerve, superior vestibular nerve and inferior vestibular nerve. While electroneurography (ENoG), auditory brainstem response (ABR), and caloric tests were utilized to evaluate the function of the first three nerves respectively, only evaluation of the function of the inferior vestibular nerve remains unexplored. Recently, VEMP was introduced to evaluate the function of the inferior vestibular nerve and saccule. Historically, Bickford, Jacobson, and Cody (1964) demonstrated that loud sound stimuli could cause myogenic “inion response” indicative of the activation of the vestibular organs. However, it was until the revision of the recording setting by Colebatch and Halmagyi (1992) and Colebatch, Halmagyi, et al. (1994) that VEMP became a practical clinical test.

VEMPs are responses in the muscles, especially cervical muscles such as the sternocleidomastoid muscle (SCM), to sound, vibration, or electrical stimulation which is part of the vestibulocollic reflex (Figure 2). Recently, VEMP attracted the interest of clinicians and scientists as it can be used for clinical testing of the vestibular end-organs, especially the saccule and inferior vestibular nerve. Moreover, much has been published about VEMP and many clinicians use this test. At the end, VEMP is now considered as one of the most important tools for
studying the neurophysiology of the vestibular system (Toshihisa Murofushi & Kaga, 2009).

**Figure 2:** VEMP response recorded from surface electrodes over the right (R St-m) and left (L St-m) sternomastoid muscles in normal subject (Colebatch et al., 1994).

2.1.2. Generator and pathway:

As shown in Figure 3, VEMPs are generated via a disynaptic pathway and mediated by a three-neuron arc, starting from the macula of the saccule, the inferior vestibular nerve, the ipsilateral lateral vestibular nucleus, medial vestibulospinal tract, and ending with the motoneurons of the ipsilateral SCM muscle (T. Murofushi, Curthoys, & Gilchrist, 1996; T. Murofushi, Curthoys, Topple, Colebatch, & Halmagyi, 1995; Uchino et al., 1997).

The VEMP response is formed by two distinct components. The first, a biphasic positive-negative wave (p13-n23), is generated predominantly by afferents originating ipsilaterally and depends on the integrity of the labyrinth and the vestibular division of the eighth nerve. This response always requires a high stimulus intensity in order to evoke the response. The second components,
biphasic negative-positive wave (n34, p44), is not always present in normal subjects. These potentials are generated by afferents originating from both ears. They are present when the cochlea and cochlear component of the eighth nerve are intact. This evidence indicates that the p13-n23 response originates from afferents traveling within the vestibular nerve whereas the later potentials (n34, p44) probably arise from cochlear afferents (Colebatch et al., 1994).

Figure 3: Sacculosternocleidomastoid (SCM) and utriculosternocleidomastoid pathways. Filled circles, inhibitory neurons; open circles, excitatory neurons (Kushiro, Zakir, Ogawa, et al., 1999).

The description of VEMP wave generators was first described in detail by Colebatch and Halmagyi (1992) and Colebatch et al. (1994) when they recorded Electromyograms (EMGs) from surface electrodes over the sternomastoid muscles in response to brief (0.1 ms) clicks presented through headphones. They found
that in normal subjects, 85 to 100 dBnHL clicks evoked reproducible changes in the averaged EMG beginning at a mean latency of 8.2 ms. There are two potential changes, the first potentials are a biphasic positive-negativity (p13-n23). These potentials were found in all of the normal subjects. The later potentials (n34-p44) were present in most but not all subjects. Colebach et al. (1994) reported that the amplitude of the response increases with an increase in the level of muscle activation. This response was absent in patients who had undergone selective section of the vestibular nerve but was preserved in subjects with severe sensorineural hearing loss: this suggests that it is generated by activation of vestibular afferents, mostly from the saccule, and not generated through cochlear activity.

2.2. VEMP measurement technique introduced by Colebach et al. (1994):

2.2.1. Stimulus:

Colebach et al. (1994) used 0.1 ms long rarefaction square wave clicks delivered by calibrated headphones. Click intensities were adjustable in 5 dB increments. The click intensity used was not related to the subjective thresholds. Hence, the same stimulus intensity was always used for both ears. The click intensities routinely used in Colebach’s experiment were either 95 or 100 dB nHL (140 and 145 dB SPL).

2.2.2. Recording technique:

EMG activity was recorded by means of surface electrodes over the upper half of the sternomastoid muscle and a reference over the upper sternum.
Colebach and his colleagues chose these sites rather than the inion, as suggested by Bickford et al. (1964) for two reasons: First, to allow greater certainty as to the specific muscles likely to be generating the response. Second, to avoid the uncertainties inevitably associated with the use of a midline recording site when investigating the effects of unilateral stimuli.

The EMG from each side was amplified using bandpass filtered (8 Hz-1.6 kHz), and simultaneous averages of unrectified and rectified EMG that were collected from 20 ms before the clicks to 80 ms afterward.

2.2.3. Sternoleidomastoid muscle activation and monitoring:

EMG activity was rectified and low pass filtered for display on an oscilloscope screen in front of the subject. A target level of EMG activity was set and the subjects were instructed to keep the levels of the EMG just above the target level for the duration of each average (about three minutes). The usual target corresponded to a mean rectified EMG activity of about 50-60 µV. In most trials the subjects were told to press their forehead against the bar in front of them to achieve the necessary bilateral muscle activation. Recordings were also made while the subjects held their heads turned to one side (predominantly unilateral muscle activation) and during bilateral muscle activation (i.e. voluntarily holding the head slightly raised when lying supine).
2.3. VEMP Response:

2.3.1. Response description (waveform):

In the experiment reported by Colebach et al. (1994) all of the normal volunteers showed short latency responses to 95 dB clicks given during tonic neck flexor activation. The initial positive/negative polarities of the waveform with peaks were termed p13 and n23 on the basis of the respective latencies. These are named P1 and N1 in the later literatures, these symbols will be used in this study. Only this early response was present in every subject.

Additional potentials (n34, p44) often followed and were reported in the same study (Figure 2). However, those later potentials were not persistent in all subjects and are believed to be of cochlear origin. Hence they are not used for clinical purposes.

2.3.2. Response threshold:

Regarding the response threshold, Colebatch et al, (1994) found that the P1-N1 response was present only with high intensity clicks and the threshold varied from 75 to 85 dB nHL between subjects. The later responses had a threshold below that for the P1-N1 response, often as low as 50 dB nHL. Similarly, Akin, Murnane, and Proffitt (2003) reported that thresholds for clicks ranged from 80 to 100 dB nHL with a mean threshold of 91 dB nHL. Welgampola and Colebatch (2001a) reported mean click VEMP thresholds of 89.6 dB nHL.

2.3.3. Response latencies:

The mean latency of the first positivity (P1 or p13) was 13.3 (SD=1.5) ms and the first negativity (N1 or n23) was 22.6 ms (SD=2.4) (Colebatch et al., 1994).
Akin et al. (2003) reported similar findings with a mean of P1 and N1 for 100 dB nHL using click stimuli of 12 ms (SD=2.5) and 19 ms (SD=1.5), respectively. No significant latency differences have been shown between the right and left sides (Colebatch et al., 1994).

2.3.4. Response amplitude:

There is a large variability in VEMP amplitude among subjects and between different laboratories. It is affected by both, stimulus and recording factors such as stimulus level, stimulus frequency and SCM contraction. Akin et al. (2003) reported that with a 50 uV EMG target level, the P1-N1 amplitude ranged from 16 to 179 uV for a 100 dB nHL click and from 15 to 337 uV for a 90 dB nHL 500Hz tone burst. Due to this wide variability across studies, it was recommended that clinicians obtain their own normative data.

2.4. Factors affecting VEMP response

2.4.1. Effect of stimulus intensity

There is an increase in the P1-N1 peak to peak amplitude with increasing stimulus intensity (Akin et al., 2003; Lim, Clouston, Sheean, & Yiannikas, 1995; Ochi & Ohashi, 2001). On average, the P1-N1 response to 100 dB clicks is 36% larger than that to 95 dB clicks (Figure 4) and the effect of suprathreshold click intensity seemed to be linear (Colebatch et al., 1994). Similar findings were observed in the following studies using both clicks (Lim et al., 1995; Ochi & Ohashi, 2001) and tone bursts (Akin et al., 2003).
Figure 4: Effect of increasing the intensity of stimulation in a single subject. All components of the averaged response become progressively larger in amplitude as the intensity of the clicks is increased (Colebatch et al., 1994).

2.4.2. Effect of stimulus frequency

The peak to peak amplitude of P1-N1 varies with the frequency of the stimulus. Akin et al. (2003) reported that the largest P1-N1 was obtained at 500 and 750 Hz, and it is markedly reduced for 2000 Hz tone bursts. Colebatch (2001) reported larger VEMP amplitudes at 500 and 1000 Hz compared to other frequencies. These findings are consistent with the suggestion that the inferior vestibular nerve has broad, V-shaped tuning curves with best frequencies between 500 and 1000 Hz (McCue & Guinan, 1995).
2.4.3. Effect of the level of muscle activation

The amplitude of the averaged potentials after clicks of a fixed intensity is dependent on the level of tonic muscle activation. There is a linear relation between the amplitude of the P1-N1 (and the p44) peak of the evoked response and the mean level of rectified EMG before the stimulus presentation (Figure 5). This means that both the vestibular dependent and cochlear dependent components increase linearly with increasing tonic muscle activation (Colebatch et al., 1994).

![Figure 5: Three separate averages made over the right sternomastoid in one subject with bilateral clicks of 95 dB intensity during weak, moderate, and strong contractions of the neck flexors (Colebatch et al., 1994).](image)

2.3.4. Effect of sternocleidomastoid electrode location

To study the effect of SCM electrode location on VEMP response, (Sheykholeslami, Murofushi, & Kaga, 2001) compared the VEMP response with four different SCM electrode locations: the upper part of the SCM muscle at the
level of mandibular angle, the middle part of the muscle, and immediately above the sternal and clavicular origins of the SCM muscle. They found that the amplitudes of VEMP evoked at the upper and middle parts of the SCM is the largest among those recorded at the other locations while the latency of P1 and N1 showed no significant difference among the four locations. However, variations in the calculation of absolute latencies and P1–N1 intervals were greater in the upper part of SCM than in middle part of the muscle. They concluded that the optimal EVMP recording site is the middle part of the SCM muscle as it provides marked and consistent responses.

2.5. VEMP Optimal stimulation and measurement techniques

After Colebach et al’s description of the VEMP response in 1992 and 1994, many researchers have studied the optimal stimulation and measurement techniques. Young (2006) proposed that 95 dB nHL tone bursts with a frequency of 500 Hz, a repetition rate 5 Hz, rise/fall time 1 ms, plateau 2 ms, and binaural stimulation with bilateral recordings as an ideal stimulation mode for VEMPs. Shykholeslami et al. (2001) reported that the largest VEMP amplitudes are obtained when the SCM electrode is located over the midpoint of the muscle.

The typical stimulus and recording parameters of the VEMP are summarized in table 4.
Table 4: Suggested VEMP stimulus and recording parameters (Jacobson & Shepard, 2008).

### 2.5.1. Optimal electrode montage:

Akin and Murnane (2001) recommended VEMP recording with non-inverting electrodes placed at the midpoint of the SCM muscle, the inverting electrodes at the sternoclavicular junction and the ground electrode on the forehead. This electrode montage results in positive potentials measured and plotted as upward deflections (Figure 6). Similarly, Shykholeslami et al. (2001) reported that the largest VEMP amplitudes are obtained when the SCM electrode is located over the midpoint of the muscle.
Figure 6: Individual example of VEMP response using a two channel recording with non-inverting electrode placed at the midpoint of the SCM muscle, the inverting electrodes at the sternoclavicular junction and the ground electrode on the forehead (left ear blue waves and right ear red waves).

2.5.2. Monaural vs. binaural stimulation

Brantberg and Fransson (2001) reported that VEMPs by binaural stimulation provide neither different information nor less variability, as compared with VEMPs by monaural stimulation. The advantages of the binaural stimulation are that it is a more convenient mode compared with two monaural recordings when testing young, elderly, or disabled patients, who may have difficulty in keeping continuous muscle contraction during testing (S. J. Wang & Young, 2003). In addition, binaural simultaneous acoustic stimulation with bilateral recording can be utilized to compare the right-left VEMP difference, and the side difference of P1-N1 amplitude is adjusted using a relative amplitude or IAD ratio (C. T. Wang & Young, 2004).

However, Wang and Young (2004) reported that P1-N1 amplitude may be larger with monaural acoustic stimulation, whereas binaural acoustic stimulation
with bilateral recording evokes higher response rates and larger amplitudes for wave n34 and p44.

2.5.3. Head elevation vs. head rotation methods

The Head Elevation method is used frequently for obtaining the SCM contraction level which is essential for recording the VEMP responses. However, a false-negative response is sometimes reported in patients who cannot sustain SCM muscle contraction by head elevation such as: elderly, newborn, or debilitated subjects. To overcome this problem, the head rotation method was developed (Young, 2006).

During the head elevation method (supine flexion), bilateral SCM muscle activation is achieved by having patients raise their head against gravity while in the supine position. While using the Head Rotation method, unilateral activation of the SCM muscle is achieved by having patients turn their head away from the stimulated ear while either in the sitting or supine position and to ensure the SCM muscle activation, the patient sometimes is instructed to allow their chin to touch the shoulder throughout the entire test.

Each method of SCM activation has its advantages and disadvantages. The Head Elevation method has the advantage of reduced test time when combined with binaural acoustic stimulation as VEMP can be obtained simultaneously from both sides (C. T. Wang & Young, 2006). Alternatively, the Head Elevation method is sometimes associated with a false negative VEMP in patients who can not sustain sufficient level of tonic muscle contraction.
Wang and Young (2006) reported that the head rotation method is not recommended as an initial screening test for VEMPs due to the lower response rate with smaller amplitude. Therefore, when VEMP responses cannot be elicited by the head elevation method, the head rotation method should be utilized to reduce false negative results.

2.5.4. Tapping evocation or bone-conduction (BC) stimulation

In cases of conductive hearing loss with an air-bone gap measuring ≥ 20 dB, the VEMP responses are typically absent and hence the response rate of VEMPs by tone-burst method is low (Halmagyi, Yavor, & Colebatch, 1995). In these cases, two alternative stimulation methods can be used to overcome this problem: (1) tapping method and (2) bone-conduction stimulation.

In conductive hearing loss, the tapping method has a higher response rate with VEMPs than Bone conduction, which indicates that the VEMP provoked by tapping with a tendon hammer on the forehead is a vibratory input rather than an auditory input (C. T. Wang & Young, 2004). However, the limitation for the tapping method is non-uniform, thus has been replaced by the BC method which will be discussed in details in a separate section (Sheykholeslami, Murofushi, Kermany, & Kaga, 2000).
2.6. VEMP Variants

2.6.1. Bone conduction VEMP (B-VEMP)

Although air-conducted VEMPs can be recorded from subjects with profound sensorineural hearing loss, these potentials are attenuated by even mild-to moderate conductive hearing loss (Colebatch et al., 1994). Bone conduction (BC) stimuli have been used to elicit VEMPs in cases with conductive hearing loss (Yang & Young, 2007).

In the absence of conductive hearing loss, B-VEMPs are identical to the Air-conducted VEMP (A-VEMP). Furthermore, Bone-conducted stimuli are not affected by middle ear pathologies, thus B-VEMP can be used to evaluate vestibular function even in patients with conductive hearing loss (Miyamoto, Seo, Node, Hashimoto, & Sakagami, 2006).

B-VEMP measurement techniques:

**Stimulus:** In contrast to A-VEMP the maximum amplitudes for B-VEMP are obtained using 200 to 250 tone bursts with a duration of 7-12 ms and are usually absent at frequencies above 1000 Hz (Miyamoto et al., 2006).

**Bone conduction oscillator placement:** the largest average B-VEMP amplitude is obtained with the bone oscillator located 3 cm posterior and 2 cm superior to the external auditory canal (Welgampola, Rosengren, Halmagyi, & Colebatch, 2003).
B-VEMP response (Figure 7):

**Threshold:** the lowest B-VEMP thresholds are 30 to 35 dB nHL and are obtained at 200 to 250 Hz significantly lower than thresholds to air conducted clicks (131.7±4.9 dB SPL/86.7 dB nHL) and tones (114.0±5.3 dB SPL/106 dB HL) (Welgampola et al., 2003).

**Latencies:** Welgampola et al. (2003) reported that bone conducted sound resulted in evoked short latency P1, N1 responses in both SCM muscles. Ipsilateral responses occurred earlier and were usually larger. Mean (SD) P1 and N1 latencies were 13.6 (1.8) and 22.3 (1.2) ms ipsilaterally and 14.9 (2.1) and 23.7 (2.7) ms contralaterally.

**Amplitude:** in the same study, Welgampola et al. (2003) found that a 250 Hz stimuli delivered over the mastoid process, posterosuperior to the external acoustic meatus, provoked the largest amplitude responses.

Similar to VEMP in response to air conducted clicks and tones, P1-N1 responses to bone conducted stimulation were absent ipsilaterally in subjects with selective vestibular neurectomy and preserved in those with severe sensorineural hearing loss. However, P1-N1 responses were preserved in conductive hearing loss, whereas VEMP to air conducted sound were abolished or attenuated in case of conductive hearing loss.
2.6.2. Ocular VEMPs (oVEMP)

Recently, a new form of VEMP which presented as a potential test for examining vestibular function was developed. The new procedure is called ocular VEMP (oVEMP). The oVEMP was proposed only few years ago (Chihara, Iwasaki, Ushio, & Murofushi, 2007; Todd, Rosengren, Aw, & Colebatch, 2007; Welgampola, 2008) when they used the extraocular muscle activity recorded using surface electrodes instead of using the SCM muscle as in usual cVEMP.

**Recording technique:** The electrode montage obviously will be targeted to record the extraocular muscles activity so the active electrodes are placed on the face just...
inferior to each eye, and the reference electrodes placed 1 to 2 cm below. The EMG signals are amplified and bandpass-filtered between 5 and 500 Hz. The time window for analysis is 50 ms. A good response can be obtained after 100 sweeps.

**Stimulus:** Many types of stimuli were used to elicit the oVEMP response. Air conducted acoustic stimuli using a 500 Hz tone burst with high intensity levels up to 135 dB SPL are used to develop a prominent response. Some studies used bone-conducted sound or tapping and reported clearer responses (Iwasaki et al., 2007; Rosengren, McAngus Todd, & Colebatch, 2005).

**Muscle contraction:** The desired muscle contraction level can be easily achieved by instructing the subject to maintain an upward gaze during recording. The responses are the largest at this gaze position.

**Response:** Using 500Hz air-conducted tone bursts at 135 dBSPL, the oVEMP response wave is formed of an early negative deflection (mean 10.5 ms) named N1 followed by a positive deflection (mean=15.9 ms) and named P1. The response is most prominent in the contralateral contracted extraocular muscles (Chihara et al., 2007).
3. VEMP in children

There have only been a few studies about the feasibility of recording VEMPs in neonates, infants and children. Although the muscle tone of neonates and young infants is poor compared with that of grown children and adults, it is possible to record VEMPs from the sternocleidomastoid muscle during infancy and early childhood (Toshihisa Murofushi & Kaga, 2009).

3.1. VEMP in Newborn and infants:

VEMPs can be elicited easily in healthy newborns. The fourth week after birth is the most appropriate time for early vestibular assessment (S. Erbek et al., 2007). Erbek et al. (2007) studied VEMPs in 24 newborns and they found that they all passed the audiologic evaluation, and biphasic waveforms of the VEMP were obtained in all 48 tested ears. Mean latencies of P1, N1, and P1-N1 intervals were 13.7 +/- 1.1, 20.5 +/- 1.6, and 7.1 +/- 2.1 ms, respectively. The VEMP amplitude was 22.6 +/- 18.4 mV. Erbek et al. (2007) also reported that there were no significant differences in latency or amplitude with regard to sex or side of ear tested in newborns. However, they concluded that the values of the test parameters in VEMP may change with regard to test method and age during testing in newborns and recommended that every vestibular laboratory should have its own normative data for each VEMP parameter for newborns.

In newborns between 2 to 5 days, Chen et al. (2007) found that VEMPs were present in 40%, prolonged in 35%, and absent in 35% of the tested ears and
suggested that the results reflected variation in maturation of the sacculo-colic reflex at birth.

Sheykholeslami, Megerian, Arnold, and Kaga (2005) reported that reproducible biphasic VEMPs were recorded from the SCM in all infants they examined (12 healthy infants and children, ages 1-12 months) using loud and short-tone burst sounds. They concluded that the VEMP has characteristics that differentiate it from the postauricular response and the Jaw reflex and the overall morphology of the neonatal VEMP is quite similar to that of adults. The major neonatal differences are a shorter latency of the N1 peak and higher amplitude variability. They suggested that recording of the VEMP in neonates with various audio-vestibular problems provides useful information about vestibular function in this population and may provide information that leads to better care and rehabilitation for neonates at risk of developmental and motor system delay.

Kaga (2005) studied the developmental changes in VEMPs in infants and children which are shown in Figure 8. He further reported that in normal infants and children, air-conducted sound evoked a biphasic response (P1 and N1 peaks) in VEMPs that were of larger amplitude and shorter latency than those in adults. Kaga (2005) explained this difference in VEMPs on the side of the stimulated ear is due to developmental changes in the distance of the pathway between the saccule and the SCM and changes in the strength of muscles. However, it was found that neonatal VEMPs varied in amplitude, with consistent timing for peak P1 but shorter peak N1 latencies than those in adult VEMPs.
Young, Chen, Hsieh, and Wang (2009) studied VEMP in full-term newborns younger than 2 weeks (45 full-term newborns aged 2-13 days), to investigate the development and maturation of the sacculo-collic reflex in early life. They found that the majority of healthy full-term newborns demonstrate VEMPs by day 5, with a mean P1 latency of 13.3 ±0.8 ms. They also suggested that these criteria can be used to evaluate the development and maturation of the sacculo-collic reflex in newborns, which is responsible, at least in part, for detecting changes in head position in relation to gravity. A summary of the characteristics of VEMP responses in newborns during postnatal days is presented in Table 5.
### Table 5: Characteristics of VEMP responses (mean and SD) in newborns during postnatal days (Young et al., 2009).

<table>
<thead>
<tr>
<th></th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (ears)</td>
<td>6</td>
<td>32</td>
<td>20</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Response rate</td>
<td>0</td>
<td>72%</td>
<td>65%</td>
<td>92%</td>
<td>85%</td>
</tr>
<tr>
<td>p13 Latency (ms)</td>
<td>15.7(3.4)</td>
<td>14.2(2.6)</td>
<td>13.3(0.8)</td>
<td>13.4(0.5)</td>
<td></td>
</tr>
<tr>
<td>n23 Latency (ms)</td>
<td>20.5(3.0)</td>
<td>20.2(3.3)</td>
<td>18.6(1.7)</td>
<td>18.8(0.8)</td>
<td></td>
</tr>
<tr>
<td>Raw amplitude (µV)</td>
<td>17.7(10.4)</td>
<td>23.2(19.5)</td>
<td>23.2(15.0)</td>
<td>42.4(22.7)</td>
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<tr>
<td>Corrected amplitude</td>
<td>0.45(0.26)</td>
<td>0.60(0.49)</td>
<td>0.48(0.28)</td>
<td>0.50(0.20)</td>
<td></td>
</tr>
</tbody>
</table>

#### 3.2. Difficulties in recording VEMP in infant and young children

Sheykholeslami et al. (2005) reported some difficulties they experienced during VEMP recordings in infants: 1) there was difficulty in maintaining the desired electromyographic (EMG) activity of the SCM during the period of data acquisition, which required several interruptions of the recording session and restarting data collection after achieving the same level of muscle contraction. 2) The recording sessions were much longer for infants partly because of the difficulty mentioned above and partly because of the time necessary to educate parents and have their help during the test. 3) Finally, it was necessary to have a technician in the room to position the patients and control the muscle contraction level.

#### 3.3. VEMP in older children

Kelsch et al. (2006) were the earliest to study the normative data for VEMP in children. In this study, VEMP test was performed in 30 children aged 3 to 11
years to accumulate normative data and to examine the feasibility of testing in young children. The study focused on optimal test parameters, reproducibility, and subject compliance in a pediatric population. VEMP testing was performed with alternating clicks at three intensities (80-, 85-, and 90-dB nHL) using averaged, unrectified electromyograms recorded by surface electrodes on the sternocleidomastoid muscle ipsilateral to the stimulus. They found that, of the 30 children completing VEMP tests, bilateral reflexes were recorded for all subjects with symmetric responses in 28 subjects (93%). The mean peak latencies for P1 and N1 waves were 11.3 ms (±1.3 ms) and 17.6 ms (±1.4 ms), respectively, the mean P1-N1 amplitude (± SD) was 122 µV (±68 µV). In addition, the results revealed significantly shorter N1 mean peak latency in the left of the younger children age group (ages 3–5) in comparison to other groups, with an absolute shorter mean latency N1 in the right ear of the same age group.

Finally, Kelsch et al. (2006) concluded that VEMP is a well-tolerated test for screening vestibular function in young children, performed with minimal test time and reproducible results. Mean latencies in this study suggested a shorter initial negative peak (N1) than in adult studies, consistent with prolongation seen in previous researches on the effects of age. A stimulus level of 90 dB nHL clicks was adequate for uniform response rates. The average test time was 15 minutes with two researchers testing, and subjects were highly compliant.

This study has provided solid data for normative values in children; however, the authors noted several important limitations. First, to demonstrate the significance in bilateral N1 latencies between pediatric age groups, a larger
number of subjects is required. Next, response thresholds were not established and additional study in this area could investigate how to undertake this task while decreasing the labor required of the subjects. Finally, uncertified electromyograms were used by the authors in this study and future studies could utilize rectified curves in order to normalize data to enable institutional comparison.

In a larger study done by Valente (2007), the maturational effects of vestibular system were investigated in two age groups (younger group of age 3-6 years and elder group of age 9-12. N = 30 per group) of children with normal hearing sensitivity. This study was conducted using rotary chair (RC), computerized dynamic posturography (CDP), and vestibular evoked myogenic potential (VEMP) measures. Data obtained from each pediatric group was compared with clinic and/or published adult normative data for each measure. Valente reported significant age effects on VEMP latencies and the other vestibular test used in the study; demonstrating significant maturational effects from preschool age through adulthood. She also suggested that adult normative data may not be appropriate when interpreting pediatric test results.

A summary of VEMP results in the Valente study is shown in Figure 9. In these results a significant differences was noted between child latencies (both groups) and clinic adult normative values. When results obtained from the younger group were analyzed, latencies for both P1 (p13) and N1 (n23) appeared earlier than they appeared with adults, for both click and 500 Hz tone burst stimuli. When results obtained from the older group were analyzed, results mirrored the above,
and latencies of both P1 and N1 appeared sooner than they appeared with adults for both types of stimuli.

Figure 9: VEMP latencies as a function of age and stimulus (Valente, 2007).

3.4. VEMP in children with congenital hearing loss

Colebatch et al. (1994) reported that P1-N1 responses were present in all three adult patients with pronounced sensorineural deafness and no symptoms or signs of vestibular disease while, the P1-N1 response was abolished in patients who had undergone selective vestibular nerve section. Hence they proposed that VEMPs are of vestibular origin and that the saccule is probably an acoustically sensitive organ. Similarly, Sheykholeslami et al. (2005) reported that 67% of the
children with congenital profound hearing loss showed normal VEMPs and suggested that VEMP testing may be a new tool to illuminate vestibular activity in deaf infants and children.

3.5. VEMP in children with cochlear implantation (CI)

Jin, Nakamura, Shinjo, and Kaga (2006) examined the saccular function before and after CI in a group of 12 children. Preoperatively, six children had normal and one child had decreased VEMP. Postoperatively, with CI switched off, the VEMP was lost in 11 children and only one child still had measurable VEMP, yet with reduced amplitude. Interestingly, when the CI was switched on, four children had reproducible VEMP again (Figure 10).

Jin et al. (2006) revealed that the saccule of most children with cochlear implants can easily be damaged, as shown by the absence of vestibular-evoked myogenic potentials (VEMPs). Also, in most of the children, the vestibular nerve was seemingly not stimulated by the cochlear implant. These results suggest that electrical stimulation at a comfortable listening level can stimulate the cochlear nerve; however, this stimulation did not spread to the vestibular nerve in the children. In some children with Mondini dysplasia or vestibulocochlear nerve abnormality, the vestibular nerve was assumed to be stimulated when the cochlear implant device was on, as shown by a VEMP response to electrical stimulation.
Figure 10: Changes in VEMPs before and after cochlear implantation. A. Before surgery. B. Switched off cochlear implant (CI) after surgery and switched-on CI after surgery (Jin et al., 2006).

In a later study, Jin et al. (2008) demonstrated that VEMPs evoked by cochlear implants may be related to an electrical current intensity at a comfortable level (C level), particularly in channels that are closer to the apical turn of the cochlea. So the patients who showed no VEMPs with the cochlear implant switched on may require higher current intensities to elicit clear VEMPs (if they need to be recorded). However, it is difficult to increase the current intensity in such children because they feel pain or facial nerve stimulation when the current intensity is higher than the C level.

3.6. VEMP in children with enlarged vestibular aqueduct (EVA)

There are very few studies about VEMP in EVA children. The first study about the characteristics of VEMP response in children with EVA was reported by Sheykholeslami et al. (2004) in which they studied VEMPs in three patients with
EVA. They reported greater amplitude and lower threshold for EVA patients compared to normal. However, this was a case study which included only three patients, and the results revealed lower VEMP thresholds than normal in two cases and the presence of VEMP waves in the third case which have large air bone gap and VEMP was not expected. Merchant et al. (2007) reported VEMP as one of the tests that can help to identify a non-middle ear source for air-bone gap in patient with EVA, thereby avoiding negative middle ear exploration as the large vestibular aqueduct may act as a third mobile window in the inner ear, resulting in an air-bone gap at low frequencies.
III- Methods
1. Subjects:

Sixty nine subjects between 3 years and 12 years 11 months of age who participated in this study were divided into two groups:

1.1. Control group (Group A):

The control group included thirty-nine children with normal hearing and no vestibular symptoms such as: dizziness, balance disorder, disequilibrium or clumsiness, or delay in developmental landmarks, such as walking. Subjects were included or excluded by using a balance questionnaire designed for this study (Appendix 1). Forty-one children were recruited for this group but one child refused to do any testing after the bedside tests and was excluded from the study. Another child was excluded due to the history of penetrating head trauma complicated by meningitis.

**Inclusion criteria for the Control group:**

1. Average hearing threshold for the frequencies 0.5, 1, 2 and 4 kHz less than 20 dB HL.
2. Type (A) tympanogram with a compliance peak between -150 to +100 daPA and a normal immittance of 0.2-2.5 mmhos as showed by acoustic immittance test (Jerger, 1970).
3. No complaints of vestibular symptoms in the form of vertigo, unsteadiness, frequent falling or delayed walking (Answer “No” for all 6 questions in part one in the balance questionnaire shown in Appendix 1).
1.2. Study group (Group B): 

Twenty eight children with EVA: either with or without vestibular symptoms.

_Inclusion criteria for Study group:_

1. Children from Cincinnati Children’s Hospital Medical Center, diagnosed with EVA as defined by Boston et al. (2007), based on radiological finding, as one that is $\geq 2$ mm at the operculum and/or $\geq 1$ mm at the midpoint of the vestibular aqueduct.

2. Children with Type (A) tympanogram or children with ventilation tube with an air-bone gap of 10 dB or less.

_Exclusion criteria for groups A and B:_

1. Abnormal middle ear function (e.g. Cholesteatoma, perforated tympanic membrane, etc.).
2. Developmental Delays (e.g. Down syndrome, neuromuscular disorders, inability to ambulate or stand unassisted).
3. Any neurological or medical problem that can affect balance.
4. Children unable to complete the testing.

Both control and study groups were divided by age into three subgroups; subgroup (1) which included children between ages 3 to 6 years 11 months; subgroup (2) from age 7 to 9 years 11 months, and age subgroup (3) from age 10 to 12 years 11 months.

The subjects in the control group were recruited from children of friends and family of Cincinnati Children’s Hospital Medical Center (CCHMC) employees. The children in this study group were recruited to participate by identifying those with a
previous diagnosis of EVA or who were newly diagnosed through the Ear and Hearing Center at CCHMC. Previously identified patients’ parents and caregivers were contacted by a study investigator. Parents of the participants completed an informed consent prior to participating in the study. The children’s signed assent was obtained from participants who were 9 years of age or more. This study was approved by the Institutional Review Board (IRB) at CCHMC.

1.3. Subjects demographic data:

**Group (A):**

Thirty nine children completed the study in the control group (group A): Subgroup 1 (between 3-6 years) consisted of 15 subjects (8 females & 7 males) with a mean age 5.1 years; Subgroup 2 (between 7-9 years) consisted of 13 subjects (5 females & 8 males) with a mean age 8.3 years; Subgroup 3 (between 10-12 years) consisted of 11 participants (7 females & 4 males) with a mean age 11.2 years. A summary of the details of group (A) are presented in Table 6.

<table>
<thead>
<tr>
<th>Age subgroup</th>
<th>Number of subjects</th>
<th>Minimum (years)</th>
<th>Maximum (years)</th>
<th>Mean (years)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>subgroup 1 (3-6 yrs)</td>
<td>15</td>
<td>3.9</td>
<td>6.9</td>
<td>5.1</td>
<td>.97</td>
</tr>
<tr>
<td>Subgroup 2 (7-9 yrs)</td>
<td>13</td>
<td>7</td>
<td>9.9</td>
<td>8.3</td>
<td>.95</td>
</tr>
<tr>
<td>Subgroup 3 (10-12 yrs)</td>
<td>11</td>
<td>10.2</td>
<td>12.9</td>
<td>11.2</td>
<td>.89</td>
</tr>
</tbody>
</table>

**Table 6:** Subjects of the control group, (N) number of subjects, (SD) standard deviation.
Group (B):

The twenty eight children with EVA were divided into 3 age subgroups; Subgroup 1 (between 3-6 years) consisted of 5 subjects (4 females & 1 male) with a mean age 5.8 years; Subgroup 2 (between 7-9 years) consisted of 11 participants (2 females & 9 males) with a mean age 8.4 years; and; Subgroup 3 (children age between 10-12 years) consisted of 12 participants (7 females & 8 males) with a mean age 11.2 years. The total number of ears diagnosed with EVA in this group was 48 ears. A summary of the details of group B is presented in Table 7.

<table>
<thead>
<tr>
<th>Age subgroup</th>
<th>Number of subjects</th>
<th>Number of ears with EVA</th>
<th>Minimum (years)</th>
<th>Maximum (years)</th>
<th>Mean (years)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup 1 (3-6 yrs)</td>
<td>5</td>
<td>9</td>
<td>3.7</td>
<td>6.5</td>
<td>5.8</td>
<td>1</td>
</tr>
<tr>
<td>Subgroup 2 (7-9 yrs)</td>
<td>11</td>
<td>16</td>
<td>7.1</td>
<td>9.8</td>
<td>8.4</td>
<td>.84</td>
</tr>
<tr>
<td>Subgroup 3 (10-12 yrs)</td>
<td>12</td>
<td>23</td>
<td>10.3</td>
<td>12.6</td>
<td>11.2</td>
<td>.66</td>
</tr>
</tbody>
</table>

Table 7: Subjects of the study group; (N) = number of subjects, (SD) = standard deviation.
2. Equipment

The equipment used in this study to assess the auditory and vestibular system in children with normal hearing and children with enlarged vestibular aqueduct are described below:

- Hearing threshold was assessed using a clinical audiometer (Grason Stradler Inc. 61 Clinical Audiometer) in a sound treated room.
- Middle ear function was assessed using impedance tympanometry (Grason-Stadler Inc. TympStar).
- The saccule and inferior vestibular nerve pathway was assessed via vestibular evoked myogenic potentials (Intelligent Hearing Systems Smart EP).

3. Procedure:

All subjects were subjected to:

3.1. **Balance questionnaire**: A detailed subjective balance and vestibular history was taken using the balance questionnaire presented in Appendix 1. The questionnaire was filled in by at least one of the subjects’ parents who attended the testing session.

3.2. **Otological examination**: Visual inspection of the subject’s ear canal and tympanomeric membrane was conducted using otoscopy to rule out occluding wax, any foreign body or abnormality of the tympanic membrane.

3.3. **Audiological assessment**: for the control group: pure tone audiometry was done to get the hearing threshold at frequencies .5, 1k, 2k, and 4Hz, and the speech reception threshold (SRT). In young children, less
than 6 years or with unreliable audiometric results, distortion product otoacoustic emissions (DPOAEs) was done to supplement the hearing test.

For the study group (group B): the last audiological assessment data, which was done not more than three months prior to the experiment date, was used for data analysis.

3.4. **Clinical vestibular tests (bedside vestibular tests):**

3.4.1. **Romberg test**, each subject was asked to stand still with legs slightly apart and arms across his/her chest for 30 seconds and then this was repeated with their eye closed for another 30 seconds. For safety, the examiner’s arms were around the child without touching, the degree of sway with their eye’s open was compared to the sway with their eye’s closed.

**Sharpened Romberg test:** The subject is asked to do the same thing but stand with feet heel-to-toe.

*Abnormal response:* marked sway, stepping or falling with eye closed was considered as a positive response.

3.4.2. **Fukuda Stepping Test:** in this test the child stands with both arms extended 90 degree in front and then they march in place for 50 steps with their eye’s closed (eye bands are for young or unreliable children).

*Abnormal response:* deviation of the subject of more than 45 degrees compared to the original position was considered as positive response.
3.4.3. **Head Thrust test:** in this test the head of the child was tilted 30 degree forward to put the lateral SCC in the horizontal plain. The child was asked to fixate his/her eyes on a target (a sticker on the examiner nose). The examiner then introduced a rapid passive movement by moving their head 15 to 20 degree to one side and then to the opposed side with observation of the child’s eyes.

*Abnormal response:* catch up saccade (re-fixation) was considered as a positive response.

3.5. **Vestibular evoked myogenic potentials (VEMP).**

The VEMPS were evoked by using a 500 Hz tone burst stimulus (rise/fall time 1 ms, plateau time 2 ms and rate of 5.1 per second). The stimulus was presented at 107dB nHL to detect clear repeatable waves and then repeated with decrement in 10 dB steps until the VEMP was unrecognizable, and then increased in 5 dB steps until the response reappeared. The responses to 200 stimuli were averaged and band-pass filtered between 30-3000 Hz for each repetition. The response was measured ipsilaterally using surface electrodes with the non-inverting electrode on the midpoint of sternocleidomastoid muscle, and the inverting electrode in the upper sternum and the ground on the forehead. Electrode impedances were kept less than 5 kOhms. These parameters were chosen as they have been shown to provide the most robust VEMP responses at the lowest sound intensities (Cheng & Murofushi, 2001; Wu et al., 1999; Welgampola & Colebatch, 2001: Akin et al., 2003).
Head rotation in sitting position method with ipsilateral recording was used as a default method to obtain SCM contraction (Figure 11). However, head elevation method in supine position with ipsilateral recording was used in cases where the child failed to keep the desired contraction in the first method (Figure 12). Ozdek, Tulgar, Saylam, Tatar, and Korkmaz (2009) reported no significant difference in the VEMP response between the two methods in children. The manufacturer (Intelligent Hearing Systems, Inc) supplied an EMG contraction feedback device which allowed the child to view an animated cartoon if they were holding the designated contraction. If the child failed to hold the contraction, the cartoon would pause and wave averaging stopped till the contraction return to the desired level.

For each tracing, the latencies of the first positivity (P1) and the following negativity (N1), the P1-N1 peak to peak amplitude and the asymmetry ratio (AR) between right and left ear were measured. The threshold for each ear was identified. Threshold was defined as the lowest intensity level where the VEMP response could be visually identified and replicated (Ochi & Ohashi, 2003). An absent reflex was considered when no recognizable tracing could be identified at the maximum stimulus level (107 dB nHL). The average time range for testing was between 30 to 45 minutes including the subject preparation, instruction, collection of an average of 6 to 8 VEMP responses from each ear to obtain the threshold and a rest of 1 to 2 minutes between each run.
Figure 11: Head Rotation in sitting position method.

Figure 12: Head Elevation in supine position method.

4.1. Data analysis:

All statistical analyses were performed using SPSS 16.0 (SPSS Software, SPSS, Chicago, IL). Before any analysis was conducted, the distribution of the data was evaluated using means with standard deviations and medians with ranges (for continuous data).

The first step in data analysis for this study was to describe the VEMP response in normal children (control group) and the relationship between age and each VEMP parameters (threshold, latencies, amplitude and asymmetry ratio). The mean (M) and the standard deviation (SD) for each VEMP parameter for the overall normal subjects and for the three age subgroups were measured to describe the VEMP response. The Pearson product-moment correlation coefficient was applied to evaluate the relationship between age and the VEMP response parameters, with $p < 0.05$ as a limit for statistical significance. Analysis of variance (ANOVA) was used to investigate the differences in the VEMP response parameters between the three age subgroups. Post hoc comparisons were performed using the Tukey “honestly significant differences” test, with the criterion for statistical significance set at $p < 0.05$.

The second step in this study was to compare between normal children (Control Group A) and children with EVA (study group B). The Independent sample $t$ test was used to test the differences in the mean values for each VEMP parameters (Latency, Amplitude and Threshold) between the two groups.
Further analysis for the VEMP response in children with EVA was done in the form of studying the relationship between vestibular aqueduct diameter and VEMP response parameters (latency, amplitude and threshold). Pearson product-moment correlation coefficient was used for this purpose with $p < 0.05$ as a limit for statistical significance.

4.2. Power considerations

The power considerations were based on a detectable difference in outcomes between groups. Data to support the power calculations are from published research on values obtained in children with no balance issues (Valente, 2007). If we assume that the control group will have a mean (SD) latency value for P1 of 13.3 (1.5) ms, 20 subjects per group (Group A vs. Group B) will have 80% power to detect a difference in the mean value for this test of 1.4. Power calculations here are based on the assumptions of using a 2-sided t-test at an $\alpha$ level =0.05.
VI- RESULTS
1. VEMP response in normal children (control group)

1.1. Descriptive data for the overall subjects in control group (3-12 years old):

Descriptive data showing the mean and standard deviation for ear specific (right and left ears), gender specific (male and female) and overall subjects in control group for VEMP parameters: threshold, P1 and N1 latencies, peak to peak amplitude and the asymmetry ratio (AR) are presented in Table 8.

<table>
<thead>
<tr>
<th></th>
<th>Threshold (dB nHL)</th>
<th>P1 Latency (ms)</th>
<th>N1 Latency (ms)</th>
<th>Amplitude (µV)</th>
<th>AR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Right (n=39)</strong></td>
<td>91.9±4.1</td>
<td>12±1.5</td>
<td>17.6±2</td>
<td>102±46</td>
<td></td>
</tr>
<tr>
<td><strong>Left (n=39)</strong></td>
<td>92.5±5.1</td>
<td>11.9±1.1</td>
<td>17.6±1.8</td>
<td>112±64</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p=.592</td>
<td>p=.671</td>
<td>p=.949</td>
<td>p=.452</td>
<td></td>
</tr>
<tr>
<td><strong>Male (n=38)</strong></td>
<td>91.2±4.9</td>
<td>11.9±1.2</td>
<td>17.7±1.9</td>
<td>118±66</td>
<td>22.2±18</td>
</tr>
<tr>
<td><strong>Female (n=40)</strong></td>
<td>93.1±4.2</td>
<td>12±1.5</td>
<td>17.5±2</td>
<td>97±41</td>
<td>11±7</td>
</tr>
<tr>
<td></td>
<td>p=.07</td>
<td>p=.651</td>
<td>p=.570</td>
<td>p=.101</td>
<td>p=.029</td>
</tr>
<tr>
<td><strong>Overall (n=78)</strong></td>
<td>92.2±4.6</td>
<td>11.9±1.3</td>
<td>17.6±1.9</td>
<td>107±56</td>
<td>17±15</td>
</tr>
</tbody>
</table>

Table 8: The overall Left-Right & Gender specific VEMP parameters: Threshold, Latency, Amplitude and Asymmetry ratio (AR). Data are expressed as mean ± SD, n = number of ears.

1.2. Descriptive data and comparison between the three age subgroups:

Table 9 shows the mean and standard deviation for the VEMP parameters: threshold, P1 and N1 latencies, peak-to-peak amplitude, and asymmetry ratio (AR). In addition, it shows the comparison between the three age subgroups using an analysis of variance (one-way ANOVA test).
<table>
<thead>
<tr>
<th>Age subgroup</th>
<th>Number of subjects</th>
<th>Threshold (dB nHL)</th>
<th>P1 (ms)</th>
<th>N1 (ms)</th>
<th>Amplitude (µV)</th>
<th>AR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>subgroup 1 (3-6 yrs)</td>
<td>15 (n=30)</td>
<td>92.3±4.1</td>
<td>11.6±1.3</td>
<td>16.9±1.8</td>
<td>118±58</td>
<td>22±16</td>
</tr>
<tr>
<td>Subgroup 2 (7-9 yrs)</td>
<td>13 (n=26)</td>
<td>90.8±4.4</td>
<td>12±1.3</td>
<td>18.1±2</td>
<td>102±65</td>
<td>16±12</td>
</tr>
<tr>
<td>Subgroup 3 (10-12 yrs)</td>
<td>11 (n=22)</td>
<td>93.7±5.2</td>
<td>12.3±1.2</td>
<td>18±1.8</td>
<td>98±38</td>
<td>13±16</td>
</tr>
<tr>
<td>Overall (Total)</td>
<td>39 (n=78)</td>
<td>92.2±4.6</td>
<td>11.9±1.3</td>
<td>17.6±1.9</td>
<td>107±56</td>
<td>17±15</td>
</tr>
</tbody>
</table>

**Table 9:** The VEMP parameters: latency, amplitude, threshold, and asymmetry ratio (AR) and comparison between age subgroups. Data are expressed as mean ± SD, *p < 0.05.

### 1.3. Age correlation:

Table 10 shows the correlation between age and VEMP parameters: threshold, P1 and N1 latencies, peak to peak amplitude and asymmetry ratio (AR) for the three age subgroups as well as the overall subjects in the control group using the Pearson correlation test.
### Table 10: Age correlation for the age subgroups and the overall subjects in the control group.

*Correlation is significant at the 0.05 level (2-tailed),
**Correlation is significant at the 0.01 level (2-tailed).

<table>
<thead>
<tr>
<th>Age subgroup</th>
<th>Number of subjects</th>
<th>Threshold (dB nHL)</th>
<th>P1 (ms)</th>
<th>N1 (ms)</th>
<th>Amplitude (μV)</th>
<th>AR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>subgroup 1 (3-6 yrs)</td>
<td>15 (n=30)</td>
<td>-0.308 (p=.098)</td>
<td>0.451* (p=.012)</td>
<td>.429* (p=.018)</td>
<td>.102 (p=.591)</td>
<td>-2.61 (p=.438)</td>
</tr>
<tr>
<td>Subgroup 2 (7-9 yrs)</td>
<td>13 (n=26)</td>
<td>-.138 (p=.501)</td>
<td>0.234 (p=.250)</td>
<td>.267 (p=.187)</td>
<td>.025 (p=.903)</td>
<td>.564 (p=.056)</td>
</tr>
<tr>
<td>Subgroup 3 (10-12 yrs)</td>
<td>11 (n=22)</td>
<td>.360 (p=.100)</td>
<td>-.073 (p=.748)</td>
<td>-.030 (p=.896)</td>
<td>-.006 (p=.978)</td>
<td>-.050 (p=.890)</td>
</tr>
<tr>
<td>Overall (3-12 yrs)</td>
<td>39 (n=78)</td>
<td>.077 (p=.502)</td>
<td>.312** (p=.005)</td>
<td>.320** (p=.004)</td>
<td>-.123 (p=.284)</td>
<td>-.231 (p=.196)</td>
</tr>
</tbody>
</table>


1.4.1. Gender and ear difference:

No significant right-left or gender differences were demonstrated in the VEMP response parameters: threshold, N1 & P1 latencies, and peak-to-peak amplitude (Table 8). Since no significant differences were detected in left-right and gender categories, ear and gender data were combined for all other analyses.

1.4.2. Response rate and threshold:

All the participants in the control group showed clear and repeatable VEMP waves in both ears with a response rate of 100%. The mean threshold for the overall subjects in this group was 92.2±4.6 dB nHL. In studying the correlation between age and VEMP threshold for the overall subjects (between age 3 to 12 years old).
years), the Pearson correlation test revealed that there is no statistically significant correlation (r=0.077, p=0.502). Further analysis for different age subgroups also revealed no statistically significant correlation between age and VEMP threshold in the 3 age subgroups (Table 10). Moreover, analysis of variance using a one-way ANOVA test revealed no statistically significant difference in the mean VEMP threshold between the three age subgroups (F=2.576, p=0.083) as shown in Table 9.

1.4.3 Latencies:

The mean P1 and N1 latencies for the overall subjects were 11.9±1.3 ms and 17.6±1.9 ms, respectively (Table 9). As shown in Table 10 and Figure 13; there was a statistically significant positive correlation between age and both P1 and N1 latencies (p = 0.005 & p = 0.004 respectively) for the overall subjects which means that there is progressive increase in VEMP latencies for both P1 and N1 waves with age increase. For the age subgroups, only Subgroup 1 (age 3-6 yrs) showed a significant correlation between age and P1 and N1 latencies (p=.012 & p=.018). However, there was no statistically significant correlation between age and other elder age subgroups (subgroup 2 and subgroup 3).

In comparison between the three age subgroups’ mean latencies for waves P1 & N1 (Table 9, Figures 14&15), a one-way ANOVA revealed no statistically significant differences for P1 latencies (p=0.093) between the three age subgroups. However, there was a statistically significant difference in N1 latencies among subgroups (F=3.726, p=0.029*). Tukey HSD post hoc pair wise
comparisons showed that the N1 latency of subgroup 1 was significantly shorter than subgroup 2 & subgroup 3.

**Figure 13**: Scatter plots presenting all individual P1 & P2 latency for the control group.
Figure 14: Mean and 95% confidence interval for P1 latency for the three age subgroups.

Figure 15: Mean and 95% confidence interval for N1 latency for the three age subgroups.
1.4.4. Amplitude and asymmetry ratio:

There was large variability between subjects in P1-N1 peak to peak amplitude ranging from 27 μV to 333 μV. The overall mean peak to peak amplitudes were $107 \pm 56 \mu V$ and the mean asymmetry ratio (AR) was $17 \pm 15\%$ (Table 9).

Pearson product-moment correlation test was used to study the correlation between age and VEMP amplitude and AR for the overall subjects between 3 to 12 years old. The results revealed no statistically significant correlation (Amp: $r=-0.123$, $p=0.284$; AR%: $r=-0.231$ $p=0.196$; Figure 16). Further analysis for the different age subgroups also revealed no statistically significant correlation between age and VEMP Amplitude or AR for the three age subgroups (Table 10). Moreover, as shown in Table 9, the analysis of variance revealed no statistically significant difference between the three age subgroups in regards to the mean VEMP amplitude ($F=0.946$ $p=393$) or the AR ($F=1.124$ $p=0.338$).

![Figure 16](image_url): Scatter plots presenting all individual peak to peak amplitude for the control group.
2. Study group (children with EVA):

2.1. Gender, ear, and hearing loss distribution of the study group:

Twenty eight subjects (15 female and 13 male) with EVA participated in this group. Twenty subjects (71%) have bilateral EVA and 8 subjects (29%) have unilateral EVA as based on radiological criteria for the diagnosis of EVA as used in this study (VA diameter more than 1 m at mid point and/or more than 2 mm at the operculum). The total number of ears with EVA is 48. Among the 48 ears with EVA, 46 have hearing loss (either sensorineural, conductive or mixed hearing loss) and two ears have normal hearing (Table 11). The mean PTA and vestibular aqueduct diameter for overall ears in this group as well as the age subgroups are presented in Table 12.

<table>
<thead>
<tr>
<th></th>
<th>Subgroup 1</th>
<th>Subgroup 2</th>
<th>Subgroup 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ear side</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>4 (45.5%)</td>
<td>7 (44%)</td>
<td>11 (48%)</td>
<td>22 (46%)</td>
</tr>
<tr>
<td>Left</td>
<td>5 (55.5%)</td>
<td>9 (56%)</td>
<td>12 (52%)</td>
<td>26 (54%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2 (22%)</td>
<td>12 (75%)</td>
<td>10 (43.5%)</td>
<td>24 (50%)</td>
</tr>
<tr>
<td>Female</td>
<td>7 (78%)</td>
<td>4 (25%)</td>
<td>13 (56.5%)</td>
<td>24 (50%)</td>
</tr>
<tr>
<td><strong>Type of hearing loss</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNHL</td>
<td>0</td>
<td>5 (31%)</td>
<td>10 (43.5%)</td>
<td>15 (32%)</td>
</tr>
<tr>
<td>CHL</td>
<td>1 (11%)</td>
<td>1 (6%)</td>
<td>0</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Mixed</td>
<td>8 (89%)</td>
<td>10 (63%)</td>
<td>11 (47.8%)</td>
<td>29 (60%)</td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
<td>0</td>
<td>2 (8.7%)</td>
<td>2 (4%)</td>
</tr>
</tbody>
</table>

*Table 11: Ear, gender and type of hearing loss frequency distribution of the ears with EVA in study group. SNHL= Sensorinearal Hearing Loss, CHL= Conductive Hearing Loss.*
Table 12: PTA and Vestibular aqueduct diameters of the ears with EVA for the overall subjects and for the age subgroups. Data are expressed as mean ± SD, n = number of ears.

2.2. VEMP response in children with EVA (study group):

VEMP response was absent in 5 out of 48 ears with EVA examined in this group, with a response rate of 90%. The mean and standard deviation for the overall subjects and the 3 age subgroups of the study group for the different VEMP response parameters: threshold, P1& N1 latencies, P1/N1 peak to peak amplitude and AR are presented in Table 13.

Table 13: VEMP parameters: latency, amplitude, threshold, and asymmetry ratio (AR) are compared across the age subgroups. Data are expressed as mean ± SD.
3. Comparison between VEMP parameters in normal children and in children with EVA:

3.1. Difference in VEMP latencies, between normal children (control group) and children with EVA (study group):

Independent sample t-test revealed no statistically significant difference between control group and study group (subjects with EVA) in VEMP N1 latency for the overall all group as well as the three age subgroups, similarly no difference was found in regards to the P1 latency (Table 14, Figures 17 & 18).

<table>
<thead>
<tr>
<th>Age subgroup</th>
<th>Control group Latency (ms)</th>
<th>Study group latency (ms)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup 1 (3-6 yrs) P1</td>
<td>11.6±1.3</td>
<td>11.8±1.93</td>
<td>0.434</td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>16.9±1.8</td>
<td>0.405</td>
</tr>
<tr>
<td>Subgroup 2 (7-9 yrs) P1</td>
<td>12±1.3</td>
<td>11.7±1.3</td>
<td>0.444</td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>18.1±2</td>
<td>0.256</td>
</tr>
<tr>
<td>Subgroup 3 (10-12 yrs) P1</td>
<td>12.3±1.2</td>
<td>12.17±1.33</td>
<td>0.673</td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>18±1.8</td>
<td>0.186</td>
</tr>
<tr>
<td>Overall (3-12 yrs) P1</td>
<td>11.9±1.3</td>
<td>11.96±1.2</td>
<td>0.857</td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>17.6±1.9</td>
<td>0.207</td>
</tr>
</tbody>
</table>

Table 14: Comparison in mean P1 and N1 latencies between control and study groups for overall subjects and each age subgroup. Data are expressed as mean ± SD, *p < 0.05. No statistically significant differences were found.
Figure 17: Mean P1 latencies for both the control and the study age subgroups.

Figure 18: Mean N1 latencies for both the control and the study age subgroups.
3.2. Difference in VEMP amplitude between normal children (control group) and children with EVA (study group):

Independent sample t-test revealed no statistically significant difference between the control group and the study group (subjects with EVA) in VEMP amplitude for the overall all group subjects (p=0.981) as well as the three age subgroups (subgroup 1: p=0.306, subgroup 2: p=0.317, subgroup 3: p=0.312; Table 15 & Figure 19).

<table>
<thead>
<tr>
<th>Age subgroup</th>
<th>Control group Amp (μV)</th>
<th>Study group Amp (μV)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>subgroup 1 (3-6 yrs)</td>
<td>118±58</td>
<td>137±48</td>
<td>0.306</td>
</tr>
<tr>
<td>Subgroup 2 (7-9 yrs)</td>
<td>102±65</td>
<td>81±49</td>
<td>0.317</td>
</tr>
<tr>
<td>Subgroup 3 (10-12 yrs)</td>
<td>98±38</td>
<td>111±40</td>
<td>0.312</td>
</tr>
<tr>
<td>Overall (3-12 yrs)</td>
<td>107±56</td>
<td>107±48</td>
<td>0.981</td>
</tr>
</tbody>
</table>

Table 15: Comparison in mean Amplitude (Amp) between control and study groups for overall subjects and each age subgroup. Data are expressed as mean ± SD, *p < 0.05. No statistically significant differences were found.
Figure 19: Mean amplitude for both the control and the study age subgroups.

3.3. Difference in VEMP threshold between normal children (control group) and children with EVA (study group):

Independent sample t-test revealed that the VEMP threshold for children with EVA was significantly higher than the VEMP threshold for normal children (p=0.048; Table 16 & Figure 20).
<table>
<thead>
<tr>
<th>Age subgroup</th>
<th>Control group Threshold (dBnHL)</th>
<th>Study group Threshold (dBnHL)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>subgroup 1 3-6 yrs</td>
<td>92.3±4.1</td>
<td>92.8±5.7</td>
<td>0.927</td>
</tr>
<tr>
<td>Subgroup 2 7-9 yrs</td>
<td>90.8±4.4</td>
<td>98.4±5.3</td>
<td>0.000*</td>
</tr>
<tr>
<td>Subgroup 3 10-12 yrs</td>
<td>93.7±5.2</td>
<td>92.4±5.2</td>
<td>0.397</td>
</tr>
<tr>
<td>Overall 3-12 yrs</td>
<td>92.2±4.6</td>
<td>94.26±5.9</td>
<td>0.048*</td>
</tr>
</tbody>
</table>

**Table 16:** Comparison in mean VEMP Threshold (dBNHL) between control and study groups for overall subjects and each age subgroup. Data are expressed as mean ± SD, *p < 0.05.

**Figure 20:** Mean VEMP threshold for both the control and the study age subgroups.
4. Correlation between vestibular aqueduct diameter and VEMP parameters

The correlation between the vestibular aqueduct (VA) diameters measured radiologically and different parameters of VEMP response was studied using Pearson product-moment correlation coefficient test. The results revealed a statistically significant correlation between VA diameter and VEMP threshold \((p=0.04)\) (figure 21). However, there was no significant correlation with the other VEMP parameters: N1 and P1 latencies and peak to peak amplitude.

![Figure 21: A scatter plot showing the correlation between the VA diameter (mm) and VEMP threshold (dB nHL).](image)
5. Bedside tests

5.1. Control group:

The bedside tests were well tolerated by all the children in the study, even as young as 3 years old. All children passed the Romberg test with 100% response rate. Two children (out of 39) failed to pass tandem Romberg with falling to either sides with a response rate of 95%. Three children showed abnormal Fukuda with a response rate of 92.3%. Two children showed abnormal Head trust test with a response rate 95%. Finally, none of the subjects in this study showed abnormality in more than one test of the four tests examined in this study.

5.2. Study group:

The results revealed that 57% (16 subjects) of children with EVA showed abnormality in at least one of the bedside tests examined in this study (Table 17). Two subjects (7%) showed excessive sway or falling in the Romberg test with response rate of 93%, eleven subjects (39%) failed to pass the Tandem Romberg test with a 61% response rate, six subjects (21%) showed an abnormal Fukuda test with a response rate of 79% and four subjects (14%) showed an abnormality in the head trust test with a response rate of 86%. Two children showed abnormalities in two tests, while only one child showed an abnormality in three tests. None showed an abnormality in the four tests.
<table>
<thead>
<tr>
<th>Bedside test</th>
<th>Control Group (n=39)</th>
<th>Study Group (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Romberg</td>
<td>0 (0%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Tandem Romberg</td>
<td>2 (5%)</td>
<td>11 (39%)</td>
</tr>
<tr>
<td>Fukuda stepping</td>
<td>3 (7.7%)</td>
<td>6 (21%)</td>
</tr>
<tr>
<td>HIT</td>
<td>2 (5%)</td>
<td>4 (14%)</td>
</tr>
</tbody>
</table>

Table 17: Frequency distribution of abnormal bedside test. HIT= Head Impulse Test.

6. Balance Questionnaire

The analysis of the balance questionnaire showed that the average age of walking in children with EVA was 14.6 months which was significantly higher than average age of walking in normal children in control group (12.6 months). In addition, fifty percent of children with EVA (14 children) reported at least one of the Vestibular symptoms presented in the balance questionnaire. The distribution of the different vestibular symptoms in children with EVA is presented in Table 18.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Subjects (N)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertigo</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Poor balance/clumsiness</td>
<td>7</td>
<td>25</td>
</tr>
<tr>
<td>Frequent falls</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>Episodes of inability to walk</td>
<td>1</td>
<td>3.5</td>
</tr>
<tr>
<td>Fear or panic</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>1</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Table 18: Frequency distribution of vestibular symptoms in children with EVA.
V- DISCUSSION
1- Normative data for VEMP in children and effect of age

1.1. Response rate and threshold of VEMP response:

The VEMP response was present in all normal subjects who participated in this study (100%), this result is in agreements with the previous studies which proved that VEMP waves can be recorded as early as the fourth week after birth (S. Erbek et al., 2007) or in young children and school age children (Kelsch et al., 2006). Similarly, the studies of VEMP response in adult showed 100% response rate up to age of 65 years (Maes et al., 2010).

The threshold of the VEMP response ranged from 80 to 105 dB nHL with a mean threshold of 92 dB nHL. This threshold is similar to the adult mean VEMP threshold for a 500 Hz tone burst (Maes et al., 2009; Vanspauwen, Wuyts, & Van de Heyning, 2006). However, other studies showed lower threshold such as Maes, (2010) who reported a VEMP threshold of 73.63±7.70 dB nHL.

In regards to the effect of age in VEMP threshold in children, the results of this study revealed no statistically significant correlation between the age and the VEMP threshold or significant differences in mean VEMP thresholds between the three age subgroups. This is the first study to report VEMP threshold in children as most of the previous studies examined VEMP at only fixed intensities and did not looked for threshold (Kelsch et al., 2006: Valente, 2007).

1.2. Latency:

Generally, the results of this study showed that there is a significant positive correlation between age and N1 (r=.312**, p=.005) and P1 (r=.320**, p=.004) latencies which means that there is a progressive increase in the wave latencies
with age increase for children between 3 to 12 years old, the rate of this increase is approximately 0.1 ms/year (the mean P1 and N1 latencies for children 10 to 12 years old were delayed compared to children 3 to 6 years old by 0.7 and 1.1 ms respectively).

However, a closer look to the age subgroups correlation data (Table 10), showed that the correlation between age and P1 and N1 latencies was most significant in the very young subgroup (age 3 to 6 years) \( r=0.451, p=0.012 \) for P1 and \( 0.429 \) \( (p=0.018) \) for N1, less correlation in the middle age subgroup (age 7 to 9 years) \( r=0.234 \) \( (p=0.250) \) for P1 and \( 0.267 \) \( (p=0.187) \) for N1, and there is no correlation between age and N1 and P1 latencies \( (r=-0.073, p=0.748 \) for P1 and \( r=-0.030, p=0.896 \) for N1) in the elder group (age 10-12 years).

The comparison between mean VEMP P1 and N1 latencies in children and published adult data revealed that the mean P1 latency (11.9±1.3 ms) did not show differences with the adult normative data in some studies such as in Akin et al. (2003): P1= 12±2.5 ms and Cheng, Huang, and Young (2003): P1= 12.49±0.94 ms. However, it was shorter than the average adult latencies reported in other studies such as Tourtillott, Ferraro, Bani-Ahmed, Almquist, and Deshpande (2010): P1= 16.0±2.2 ms, Maes et al., (2010): P1= 14.46±1.27 ms, S. J. Wang and Young (2003): P1= 14.49 ± 1.28 ms, Basta, Todt, and Ernst (2005): P1 = 16.2±2.5 ms, and Wu, Shiao, Yang, and Lee (2007): P1=14.83±0.81 ms. However, the N1 mean latency (17.6±1.9 ms) was much shorter than most of the published data for adult (24.2±2.7 ms [Tourtillott et al., 2010] 23.00±2.21 ms [Maes et al., 2010]). These findings are in agreement with the previous studies on VEMP in children which suggested that VEMP latencies may vary as a
function of age and the child latencies appear sooner (Shyekholeslami et al., 2005; Kaga 2005; Kelsch et al., 2006 and Valente et al., 2007).

However, as this study was done in pediatric hospital, no adult normative data were available from the same laboratory. Hence, further study is needed to collect these data for comparison with these pediatric normative data collected in this study to support these findings.

1.3. Amplitude and asymmetry ratio:

As regards the effect of age on the absolute peak to peak amplitude and AR, the results of this study revealed that there was no statistically significant correlation between age and absolute N1-P1 peak to peak amplitude. Similarly, there was no correlation between age and interaural asymmetry ratio. However, comparing the AR mean for the age subgroups showed progressive decrease in the amplitude difference between the two ears in elder groups than the younger one. Starting from 22±16 in children 3 to 6 years old decreased to 16±12 in children 7 to 9 years while it was only 13±16 in children 10 to 12 years. This reflects that the asymmetry in VEMP amplitude between ears decreases with age.

Similar to the normative data of the N1-P1 peak to peak amplitude in adult (Akin et al., 2003; Brantberg & Fransson, 2001; Colebatch, Rothwell, Bronstein, & Ludman, 1994; Welgampola & Colebatch, 2001b), there was a large variability between subjects in VEMP amplitude in children ranging from 27 uV to 333 uV. The mean peak to peak amplitude for the normal children was 107±56 μV. This amplitude fell within the range of the published adult normative data (102.84±44.56 μV [Cheng et al., 2003]; 126.43±67.97 μV [Maes et al., 2010]; 139.8±64.0 μV [Basta et al.,
2005]; 147.34±68.66 μV [Maes et al., 2009]; 160.71±101.11 μV [Isaradisaikul et al.,
2008]).

Similarly, the VEMP response mean AR between the two ears for normal children, using the new feedback cartoon provided in the IHS system for EMG monitoring, was within the range of the normal AR in different published studies for normative data in adults, either the studies which used the conventional EMG monitoring method for adult (by using a bar representing the muscle contraction level or a smiley face for visual feedback) such as Isaradisaikul et al. (2008): AR% = 19±17, or the studies which used feedback method using blood pressure manometer such as Maes et al. (2010): AR% = 12±10.

This acceptable VEMP amplitude and small asymmetry ratio which was found in our study indicates that the new feedback cartoon is a feasible method for EMG monitoring in children as young as three years old. However, this finding was in contrast to Valente (2007) findings which stated that monitoring the SCM contraction in children using the traditional adult method is not feasible. And she explained that this was because of a child’s limited attention span, limited space on a pediatric neck, weight of the EMG electrodes, and a child’s difficulty in monitoring neck contraction to a desired target level. Obviously, the new EMG monitoring method used in this study was able to overcome all the challenges mention in Valente (2007) study.
1.4. Gender and ear side effect on VEMP response:

No statistically significant differences in VEMP response parameters between right and left ears were observed in normal children in this study (Table 8). This result is in agreement with the adult findings (Young & Kuo, 2004). Similarly, there were no statistically significant differences between male and female for all VEMP response parameter except for the AR. the adult studies showed the same findings as regards the gender effect on VEMP amplitude and threshold (Akin et al., 2003; Brantberg & Fransson, 2001; Ochi & Ohashi 2003), as well as the gender effect on latencies (Akin et al., 2003; Basta et al., 2005).

The AR difference between male and female which was found in this study can be explained by the higher number of female subjects in the elder subgroup (10-12 years) which included 7 females versus 4 males and this group showed the lowest AR (table 9).

1.5. The overall normative data for VEMP test in children:

At the end of discussing the normative data for VEMP response in children, a comparison between this study and two large studies with nearly the same design (which discussed in details in the review section) was done. The first study, Kelsch et al. (2006), was done on 30 children from age 3 to 11 years and its results showed lower response rate (93%) for VEMP compared with our response rate which was 100%. However, this is mostly due to that the higher stimulus intensity used in this study was 90 dB nHL, while some of the normal children in our study showed a VEMP threshold of 95 and 100 dB nHL, and probably they were missed.
in Kelsch study. Other VEMP parameters were in agreement to our study with conclusion of shorter N1 latency (17.6±1.4 ms) in children than in adult.

The second reference study on normative data on children, Valente (2007), was done on 30 children aged 3 to 6 years and 30 aged 9 to 12. The results revealed similar conclusion of shorter VEMP latencies in children than adults. However, the N1 and P1 reported latencies were longer than the current study. The main concern on Valente study was lack of no EMG monitoring for the SCM muscle contraction level. In addition, the data were collected at only one intensity level, 95 dB nHL, this is why the author considered it as a screening procedure rather than a diagnostic one.

Finally, none of the previous studies investigated the VEMP threshold in children, and according to this author, it is the first study to provide data about VEMP threshold in this age group.

1.6. The Feasibility of VEMP test in examining the vestibular function in children:

The current study revealed that VEMP test, using the new feedback monitoring carton software, is a feasible test for evaluating the vestibular functions in children as young as three years old. This new feedback method increased the child motivation and made the test like a game to play rather than a medical test. Most of the children tolerated the test very well with few complaints, usually in the form of neck ache which always relieved after rest. Only one child, a three years old girl, refused to do the test (she also refused to do any vestibular testing after she had finished the bedside tests) out of 69 children participated in this study. The average
test time was ranging from 30 to 45 minutes starting from subject preparation and test instructions till finishing an average of eight traces. Two hundred sweeps were used in this study to record each VEMP response. However, our observation showed that clear VEMP waves usually appear before 100 sweeps so our recommendation is that 100 sweeps are sufficient for getting the VEMP response in children. This will decrease the test time as well as decrease the discomfort and the neck pain the child may develop after the test.

2. Children with EVA

2.1. Hearing loss characteristics in children with EVA:

There were 28 subjects with EVA shared in this group, 20 showed bilateral involvement with percentage of 71%, this result is in agreement with Valvassori and Clemis (1978) who reported that bilateral syndrome took place twice as often as unilateral. Among the 48 ears diagnosed radiologically with EVA, there were 46 (96%) have hearing loss and only two cases with normal hearing. As regards the distribution of hearing loss, 60% had mixed hearing loss, 32% had SNHL, and 4% had conductive hearing loss (Table 11). The percentage of mixed hearing loss in this study was less than the reported percentage in Govaerts et al. (1999) which was 90%. However, the hearing loss distribution in this study cannot be generalized as this study was done on the subjects who accepted to participate in the study and not on the whole children diagnosed with EVA in CCHMC.

2.2. VEMP response in children with EVA:

There was no statistically significant difference between children with EVA and normal children for the VEMP response latencies or amplitude (Tables 14 &
However, children with EVA showed lower response rate (90%) than normal subjects (100%). In addition they had a statistically significant higher VEMP threshold (Table 16). Similarly, Zhou and Gopen (2011) reported absence of VEMP response in 8% of cases with EVA. However, in contrast to our findings, they reported lower VEMP threshold and higher amplitude.

Although our preceding expectations before this study were to find lower VEMP threshold based on the studies which were done on superior semicircular canal dehiscence (SSCD), which has the same pseudoconductive hearing loss similar to that in EVA patients (Merchant et al., 2007), and based on a case report of three adult patients with EVA and VEMP findings in those patients (Sheykholeslami et al., 2004) where lower threshold for VEMP was found in 2 cases. However, the absence of any signs of vestibular hypersensitivity such as Tullio phenomena, which is reported in most SSCD patients, support the elevated threshold findings in this study. In addition, this support that the mechanism of the air bone gap in EVA patients is due to restricted movement of the stapes as proposed by Nakashima et al. (2000) rather than due to the third window theory which proposed as explanation for the pseudoconductive hearing loss in SSCD (Rosowski, Songer, Nakajima, Brisko, & Merchant, 2004).

As regard the absolute latency for waves N1 and P1, the absence of abnormality in EVA children compared with normal are expected as all previous VEMP studies showed that VEMP latencies are rarely affected by most of inner ear abnormalities. The abnormality in latency was only reported in 30 to 70% of cases with Multiple Sclerosis where the pathology cause demyelination of the root axons
of the entry zone or of the vestibulospinal tract axons this is clearly away from the site of lesion or the pathogenesis of the EVA. This finding is in agreement with Sheykholeslami et al. (2004) findings in three patients with EVA where they did not mention any abnormality in VEMP latencies in any of the reported cases. Similarly, Merchant et al. (2007) did not mention any abnormality as regards VEMP latencies in three ears with EVA.

The AR in children with EVA compared to normal was not investigated in this study, as the subjects in our study sample had both unilateral and bilateral EVA involvement which made the overall comparison for the VEMP amplitude between the two ears is inaccurate.

2.3. Correlation between VA diameter and VEMP parameter:

There was a statistically significant positive correlation between the diameter of VA and the threshold of VEMP threshold (r=0.324, p=0.039). In addition, four of the five ears with absent VEMP had VA midpoint diameter of 4 mm or more (6.1, 5.2, 5.1, and 4 mm). Further studying of the relation between response rate and VA diameter showed that VEMP response was absent in 30% of ears with VA diameter larger than 4 mm and in 50% of ears with VA larger than 5mm. These findings suggest that the larger the enlargement of the vestibular aqueduct the higher the damage happened to the secular functions.

Other VEMP parameters, latencies and amplitude, did not show any statistically significant correlation with the VA diameter.
2.4. Correlation between degree of hearing loss (PTA) and VEMP parameters:

There was no statistically significant correlation between PTA and any of the VEMP parameters. In addition, there was no statistically significant difference in VEMP parameters between any of the three types of hearing loss (CHL, SNHL and Mixed hearing loss) as well as normal hearing subjects (Table11). This result is inconsistent with the fact that VEMP is not affected by sensorineural hearing loss (Colebatch et al., 1994). Although some of the EVA cases in this study had a conductive element (either pure conductive or mixed hearing loss), however the absence of the effect of this conductive hearing loss on VEMP response parameters is another proof that this is not a real conductive hearing loss due to a middle ear dysfunction (pseudo-conductive hearing loss).

3. Bedside tests in normal children and in children with EVA:

The results of this study showed that normal children can easily perform bedside tests with the few modifications described in the method section of this study. Romberg test was the easiest and was normal in 100% of children from age 3 to 12. Tandem Romberg, Fukuda, and Head Thrust tests were normal in 92% to 95% of normal children. However, none of them showed abnormality in more than one bedside test.

In children with EVA, 57% (16 subjects) showed abnormality in at least one bedside test, most of them were in Tandem Romberg and Fukuda stepping tests (39% and 21% respectively) while only 14 % showed abnormal HIT. This reflects that the vestibulospinal reflex (VSR) is the most functionally affected in children with EVA. While, the Vestibulocular reflex (VOR), which was examined by the HIT,
is much less affected. However, further studies using objective tests examining VOR, such as the Caloric test and Rotary chair test, are needed to quantify the effect of EVA on VOR in children.
Conclusions:

1- The study of normative data for VEMP parameters in different age groups in children showed that the P1 and N1 latencies are significantly affected by age. Thus, the specific normative data for N1 and P1 latencies should be used for children, especially for the very young children three to six years old. Other VEMP parameters (threshold, amplitude or AR) were not affected by age.

2- Children with EVA showed higher VEMP threshold than normal children. Moreover, VEMP response was absent in 10% of cases. Other VEMP parameters showed no significant differences between children with EVA and normal children.

3- There is a positive correlation between VEMP threshold and diameter of VA. In addition, VEMP response was absent in 30% of children with VA midpoint diameter of 4 mm or more and was absent in 50% of children with VA midpoint diameter larger than 5 mm. This finding can be consider as an indication of more affection of saccular functions with the more enlargement in the vestibular aqueduct in children.

4- No effect was detected for the degree of hearing loss on VEMP response in children with EVA. This finding presents another proof that VEMP is of vestibular origin. Moreover, there was no differences in VEMP response between different types of hearing loss (conductive, SNHL and Mixed hearing loss), which indicates that the conductive element of hearing loss
accompanied with EVA should not affect VEMP response, this is in agreement with the theories of the nature of this conductive hearing loss and that it is not due to abnormality in middle ear functions.

5- Although the findings of this study support the previous studies about the air-bone gap in EVA, however, our conclusion is different as regards the similarity of the mechanism of this conductive gap with the one in SSCD as lower threshold for VEMP was not reported in addition to the absence of any symptoms of vestibular hypersensitivity to high sounds (Tullio phenomena). Further studies should be done to examine the mechanism of the conductive gap in patients with EVA.

6- Bedside tests are well tolerated in young children, as young as three years old, however further studies should be done to examine their sensitivity and specificity for different vestibular disorders in children.

7- Children with EVA showed statistically significant delayed age of walking compared to normal children.

8- 50% of children with EVA had vestibular symptoms. The most common symptoms were: vertigo, poor balance/clumsiness and frequent falls.
Recommendations and future studies:

1- Specific normative data for each age group should be used in interpreting VEMP test in children.

2- In addition to audiological assessment, vestibular assessment, especially saccular functions, should be done for children with EVA as 10% of cases show abnormality in VEMP test and 57% show abnormality in at least one of the bedside tests examined in this study.

3- Another study for the adult normative data for VEMP test in Cincinnati children hospital vestibular lab is recommended to compare with the children one for more accurate examination for the differences in VEMP parameters between adult and children.

4- Future studies on the effect of EVA on other vestibular functions, part from the saccular functions which examined in this study, are highly recommended using other vestibular tests such as: Rotary chair, VNG and Posturography.

5- Further studies on the mechanism of air-bone gap in EVA are also needed.
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Appendix

Balance Questionnaire

Name of child: ___________________________

DOB: _________________________________

Sex: ___________________

Who filled in this questionnaire: ______________________

At what age did your child learn to walk? _________________

Has your child ever had an episode of any of the following (please check the corresponding yes/no box):

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vertigo (the room/or your child feels like they are spinning)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Poor balance/clumsiness</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Frequent falls</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Brief episodes of inability to walk</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Fear or panic without any obvious cause</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Rapid back and forth eye movement (nystagmus)</td>
<td></td>
</tr>
</tbody>
</table>

If you answered yes to any of the previous questions please go to Part 2.
Part 2

7- Describe your child’s balance symptoms?

8- Are your child’s balance symptoms severe enough to interfere with his/her activities?

9- Does your child experience the following that are not related to the child’s age? For example, your child may be too young to read, so that question would not apply to you. Check all that apply:

<table>
<thead>
<tr>
<th>YES</th>
<th>Does not apply (child too young)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty reading</td>
<td></td>
</tr>
<tr>
<td>Running into objects</td>
<td></td>
</tr>
<tr>
<td>Difficulty walking in low light or dark room</td>
<td></td>
</tr>
<tr>
<td>Difficulty walking on uneven surfaces (i.e. sand, gravel)</td>
<td></td>
</tr>
<tr>
<td>Becomes upset when feet leave the ground.(i.e. hanging upside down, being picked up)</td>
<td></td>
</tr>
<tr>
<td>Frequent motion sickness</td>
<td></td>
</tr>
<tr>
<td>Sensations of ringing or fullness in the ears</td>
<td></td>
</tr>
<tr>
<td>Avoids playground equipment or rides (i.e. swings, slides, merry go round, amusement parks).</td>
<td></td>
</tr>
</tbody>
</table>

If your child experiences specific instances of dizziness, then complete the following questions. If not, leave them blank.
10- How often do these instances of dizziness happen?
   ____ times per week.
   ____ times per month.
   ____ times per year.

11- How long do these instances usually last?
   ____ seconds.
   ____ Minutes.
   ____ hours.
   ____ Days.

12- Does anything trigger the dizziness?

13- What things (if any) usually increase or decrease the severity of the dizziness?

14- How is the dizziness relieved?
   ____ medication
   ____ rest
   ____ spontaneously
   ____ other (explain____)

15- Are the dizziness instances/episodes accompanied with any of the following?
   ____ Nausea or vomiting
   ____ Headache
   ____ Blurring of vision
   ____ Change in hearing
   ____ Tinnitus
   ____ Other (explain____)

16- Does your child assume any specific body position during the instances? (i.e. turns head to one side, looks to one side, lays down; etc.)