Vestibular Dysfunction in Children with Sensorineural Hearing Loss: Where we Started, Where we Are, and Where we are Going

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Where we started

The association between vestibular dysfunction and sensorineural hearing loss (SNHL) has long been established.[1] Despite this known relationship, the vestibular system has been often overlooked during the evaluation of deaf children for many decades.[2] There were a number of reasons for this disconnect between knowledge and clinical practice. First, vestibular deficits are challenging for children to verbalize, making complaints rare. Likewise these children most commonly present with disequilibrium without vertigo. Second, traditional vestibular testing, such as caloric stimulation and rotational chair assessment, can be rather unpleasant for pediatric patients. Third, children are developmentally dynamic and small changes in balance are often mistakenly considered as part of a normal trajectory. Lastly, the incentive to diagnose vestibular dysfunction was generally poor given that therapeutic options to date have been quite limited.

As recently as the recent turn of the century, the vestibular function of deaf children started to draw more attention. The initial attention arose from concern regarding the potential impact cochlear implant (anterior labyrinth) surgery might have on the other half of the inner ear (posterior labyrinth). Histopathologic studies of adult temporal bones had already highlighted the potential for iatrogenic labyrinthine damage.[3,4] When bilateral simultaneous cochlear implantation (CI) was introduced, the attention grew more intense. As infants receiving bilateral implants were often pre-ambulatory, the impact of surgery on motor development naturally came under scrutiny.

In order to begin to understand the risk that CI might pose to the vestibular end organs, clinician researchers first needed to define the baseline vestibular function in children with SNHL. In 2004, Tribukait *et al*. described a series of 36 deaf children who had undergone calorics, vestibular evoked myogenic potentials (VEMPs) and subjective visual horizontal testing.[5] 70% of subjects produced abnormal results in at least one of the tests, and 30% demonstrated abnormal function across all 3 tests. Around the same time, Buchman *et al*. reported on 22 children who had undergone horizontal canal testing prior to unilateral CI and similarly found that nearly 70% of implanted ears had absent or low intensity responses to caloric irrigations pre-operatively.[6] In light of this poor baseline function, the authors surmised that only 30% of pediatric patients with SNHL seemed to truly be "at risk" for a significant decline in vestibular function after CI.

Though some insight had been gained, vestibular testing on a larger scale was still needed in this patient population. Jacot *et al*. examined a cohort of children with profound SNHL (n = 89) who underwent a thorough vestibular assessment (clinical exam, bicaloric testing, earth vertical axis rotation, off vertical axis rotation and VEMPs) both pre- and post-CI.[7] Again, pre-operative vestibular impairment was prevalent: only 50% had normal baseline vestibular function, while 20% demonstrated bilateral areflexia. Post-operatively, 10% of children with residual vestibular function at baseline went on to develop complete areflexia in the implanted ear. Moving a step beyond end organ testing, Cushing *et al*. assessed static and dynamic balance via a cross-sectional study of 41 children with cochlear implants and 14 normal-hearing controls.[8] They found that children with implants performed significantly more poorly on the balance subset of the Bruininks-Oseretsky Test of Motor Proficiency 2 (BOT-2).[9] Interestingly, implanted children showed significant improvement when tested with their processors turned on compared to when the processors were turned off. Later, Cushing *et al*. expanded the same cohort to include 119 children with unilateral cochlear implants.[10] Notably, unilateral dysfunction of the horizontal canal or the saccule was equally distributed between implanted and non-implanted ears, indicating that the dysfunction commonly preceded surgical intervention. This study also considered etiology of SNHL and uncovered a higher incidence of severe vestibular dysfunction among children with abnormal cochleovestibular anatomy or a history of meningitis. In fact, complete bilateral horizontal canal areflexia was most commonly the pre-implant state in children in whom bacterial meningitis was the cause of their deafness. More recently, reports have also identified a very high prevalence of vestibular end organ impairment and motor milestone delay in children infected with cytomegalovirus (CMV).[11]

In summary, the aforementioned work helped to highlight the prevalence of concurrent vestibular dysfunction in children with SNHL, especially those with inner ear anomalies or a history of acquired infection (meningitis, CMV). Though a small proportion of children with residual vestibular function at baseline seemed to be at risk of worsened vestibular function after CI, this sub-group remained ill defined.

Where we are

Bilateral simultaneous CI has indeed become the standard of care for infants with bilateral profound congenital SNHL in a significant number of pediatric centers. Fortunately, the feared vestibular consequences of this treatment rarely materialize into clinically relevant motor delays as evidenced by the complete absence of reported cases describing complete *clinical* loss of vestibular function in children. Regardless, vestibular testing is still important in deaf children for a number of reasons. For one, the possibility of vestibular decline after surgery remains, so it is helpful to document a starting point if the child is old enough to undergo testing. Secondly, identification of concurrent vestibular dysfunction can facilitate earlier diagnosis of certain etiologies, such as Usher or Pendred Syndrome, which may not be clinically apparent at a young age. Lastly, vestibular dysfunction can lead to falls, which in turn may contribute to cochlear implant failure. Recently, Wolter *et al*. performed a retrospective case review to further investigate this relationship

between diminished balance function and implant device failure.[12] Vestibular testing was either reviewed or obtained prospectively in 22 children with a history of cochlear implant failure and compared to vestibular assessments previously acquired in 165 implanted children without a history of failure. A significantly larger proportion of children in the failure group were found to have abnormal horizontal canal, saccular and balance function. Bilateral horizontal canal areflexia in particular stood out as the biggest risk factor, increasing the odds ratio of implant failure by 8 times. Proactive referral to physiotherapy is thus advisable for implanted children with documented vestibular impairment or etiologies known to be highly associated with vestibular deficiencies.

Presently, pediatric otologists have a rather extensive battery of tests at their disposal to complement physical examination when looking for vestibular end-organ dysfunction. The horizontal canals can be assessed via caloric irrigation, rotational chair testing, or video Head Impulse Testing (vHIT). The saccule can be evaluated with the cervical VEMP test, while ocular VEMP testing and subjective visual vertical assessment (SVV) can be employed to investigate utricular function. Unfortunately, time, resources as well as available expertise are often restricted, so comprehensive vestibular testing is not always feasible. In truth, the effective assessment begins with simply asking about the child's attainment of motor milestones and considering the vestibular system in the complete evaluation of the child. For clinical testing, the best vestibular assessment is the one that a clinician can realistically complete on a routine basis in a limited amount of time. At The Hospital for Sick Children in Toronto, we favor a 3-component vestibular assessment that screens: 1) the horizontal canals and vestibulo-ocular reflex (VOR), 2) the otoliths, and 3) static and dynamic balance.

The VOR can actually be screened in very young infants prior to CI. Infants under 6 months of age are unable to suppress the VOR after passive rotation. The absence of nystagmus with passive rotation should thus alert the clinician to an abnormality with the VOR. In slightly older children, suppression becomes a confounder and so head thrust testing is useful. With normal function, the VOR stabilizes gaze in space by compensating head rotation with equal and opposite eye movements. When the VOR is deficient, the eyes move with the head, and a catch-up saccade is needed to re-fixate the target. The bedside head thrust is limited by the clinicians ability to generate high enough accelerations to elicit the weakness and by the fact that only overt saccades are detectable in real-time. Overt saccades occur after the head movement and are an indirect measure of VOR function. Recently, we have begun to employ objective video head impulse testing (vHIT) in the clinic to augment our VOR screen. vHIT uses video-oculography to quantify eye movements during head thrust testing. With vHIT, head acceleration and amplitude can be measured and fed-back to the tester. Importantly, covert saccades, those that are imperceptible to the naked eye, can also be detected, thereby increasing the sensitivity of the test. The presence of corrective saccades on vHIT has been shown to confer 100% sensitivity and 100% specificity for uncovering abnormal horizontal canal function in children.[13] Furthermore, vHIT has demonstrated good test-retest and inter-rater reliability in the pediatric population.[14]

A complete assessment of otolith integrity would include cervical and ocular VEMP testing in order to assess the saccule and utricle respectively. However, not all clinicians have access to VEMPs. It must also be considered that the positioning required to perform VEMP testing can be challenging to obtain in younger children.[15] Though our preference is to obtain VEMPs when able, we've also been working with the Subjective Visual Vertical (SVV) test in clinic. This test evaluates for a discrepancy between the bilateral utricular inputs by comparing what the participant thinks is vertical to what is actually vertical. Conventional methods are expensive, but there is a newer method using a smartphone-based application that is fastened to the bottom of a bucket. Testing is done in the dark, and the bucket is rotated to the left or right. Participants are then instructed to turn the bucket until the red line displayed by the application appears vertical. The application calculates the difference between true and perceived vertical and averages this difference across a number of trials. This method is not only quick and easy to learn, but has also been validated in children by Brodsky *et al*.[16] In this validation study, the test provided a positive predictive value of 80% and negative predictive value of 94% for detecting peripheral vestibular loss.

The BOT-2 is a validated, well-recognized, yet time-consuming assessment of motor function. In an effort to make things more practical, our group recently broke the balance subset down and then created receiver operating characteristic curves to gauge the ability of each task to predict total bilateral vestibular loss.[17] We found that the single best screening tool was to apply the "one foot standing, eyes closed" task, using a 4-second cutoff. In fact, the sensitivity (90%) and specificity (84%) of this simple 4-second screen was actually equivalent to that of the entire balance subset scaled score.

Recognition of concurrent vestibular dysfunction in deaf children can contribute to etiologic diagnosis and provide valuable peri-operative information for patients heading toward CI. Present day standard of care for deaf children should therefore include a history that includes motor milestone attainment and questions about the child's balance, as well as a practical clinical screen for vestibular dysfunction. By merely applying the 4-second "one foot standing, eyes closed" screen, clinicians can detect total bilateral vestibular loss with excellent sensitivity. As mentioned, identification of this subset of patients is critical as they are potentially at significantly increased risk for implant failure.

Where we are going

Apart from physiotherapy, there has never been much available in the way of therapeutic intervention for children with vestibular dysfunction. For over a decade, though, we have recognized that cochlear implant activation is capable of conferring a benefit with respect to balance function, irrespective of end organ testing.[6,18] Until recently, the mechanisms driving this benefit had yet to be investigated. Last year, our group tested the hypothesis that electrical current from in intra-cochlear electrode array could spread outside of the cochlea to stimulate the vestibular system.[19] In this study, we were able to produce cervical and ocular VEMPs with electrical stimulation alone through cochlear implants in 35% of ears tested. More interestingly, we elicited these electric VEMPs in 25% of children

with absent acoustic VEMPs, implying that we were able to bypass dysfunctional end organs to stimulate the vestibular neural elements more directly. Although the functional implication of this finding could not be determined through our study design, we speculated that vestibular-cross stimulation might be able to provide a usable cue in the form of background activation. In order to test this second hypothesis, we then administered the SVV test to the same participants both with and without stimulation (in random order across multiple trials).[20] In addition to demonstrating that deaf children using cochlear implants have an abnormal perception of vertical, we found that cochlear implant stimulation can help correct this perception, especially when provided ipsilateral to the baseline tilt.

The logical next step after harnessing this vestibular cross-stimulation would be dedicated vestibular stimulation with an intra-labyrinthine implant. There has already been substantial work completed in animal models and prostheses have actually been implanted in adult humans with intractable Meniere's disease.[21,22] Indeed, individual canal stimulation has been shown to generate canal-specific eye movement as intended.[22] Unfortunately, unlike in animals, native vestibular and auditory function has been severely damaged.[23] More work is needed and is well under-way.

The true future of vestibular treatment will likely target the inner ear at the cellular level. The human vestibular system is phylogenetically ancient and quite similar to those found in other mammals. There is already evidence to support vestibular hair cell regeneration in mouse models using adenovectors for transfection.[24] There is even an in vitro model demonstrating gene-transfer mediated, in-vitro regeneration in the human utricle after aminoglycoside damage.[25] The mode of delivery would be rather simple as the round window is readily accessible. And in the end, we will be demanding far less from regenerated cells on the vestibular side (i.e. on/off) than from those within the cochlea. Today's paucity of treatment options for vestibular dysfunction will soon be relegated to the past as research into therapeutic intervention continues to mount on multiple fronts.

Summary

- Concurrent vestibular dysfunction is present in up to 70% of children with SNHL
- Children with inner ear malformations or acquired infectious causes (i.e. meningitis, CMV) are the most likely to demonstrate vestibular deficiencies on testing
- Vestibular and balance impairment contribute to cochlear implant failure
- Pediatric otologists and pediatricians alike should aim to employ practical strategies to screen for vestibular dysfunction in deaf children
- Future prospects for vestibular rehabilitation include cross-stimulation from cochlear implants, dedicated vestibular implants and vestibular hair cell regeneration

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