Hearing Disorders in Childhood IAPO 2018 Up to Date

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The frontier of hearing disorders in childhood has expanded rapidly with the development of new research technologies, especially in genetics. The expansion of hearing screening programs and the wider access of hearing impaired children to hearing electrophysiological evaluation centers, have been determinant in the early definition of the audiometric profile and in the etiological orientation. Cytomegalovirus and Zika virus have occupied an important place in the prevalence of childhood deafness in Brazil. In addition to early diagnosis, timely rehabilitation and the possibility of cochlear implantation have provided a future with greater opportunities for children with hearing disorders.

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LANGUAGE DEVELOPMENT AND DEAFNESS

Sulene Pirana

Language is fundamental for intellectual development and social relations. When rehabilitation is possible at a very early stage, the introduction of linguistic stimuli, whether through oral language or through sign language, allows cognitive development to travel its natural path. There is no harm when development takes place through sign language; there even seems to be greater facilitation when the child appropriates one language, making the learning of a second language, for example in the oral mode, more effective.

AUDITORY PROCESSING

Berenice Dias Ramos

We hear with our ears but we listen with our brains. Sound, after being detected by the inner ear, undergoes numerous physiological and cognitive processes to be decoded and understood. Auditory processing (AP) is a set of specific abilities of the central auditory nervous system on which the individual depends to understand what he/she hears. These mechanisms and processes of the auditory

system include skills such as lateralization and spatial location of sound; speech understanding in noise; understanding of a message, even when it is distorted or fragmented; ability to choose stimuli presented to one ear, ignoring information presented to the opposite ear; recognition of different stimuli presented simultaneously to both ears; ability to discriminate and identify small changes in stimuli such as differences in frequency, intensity or duration and ability to detect and perceive modulations and minimal intervals in a sequence of sounds. Normal children may have greater difficulty than adults to hear in environments with complex and fluctuating noises due to the slow maturation of the various mechanisms responsible for binaural hearing. Two conditions further aggravate this difficulty: otitis media, which is highly prevalent in the first years of life, and the permanent environmental noise arising from the always-on television, a habit increasingly common in modern homes.

AUDIOLOGIC EVALUATION OF CENTRAL AUDITORY SYSTEM

Ana Alvarez

The Audiologic Evaluation of Central Auditory System assesses auditory abilities and provides a measure of maturity and developmental status of the Central Auditory Nervous System. The interpretation of the results reveals the intimacy of the hearing-brain relationship, evidencing signs and symptoms of language and learning disorders, as well as pointing to possible cognitive deficits in attention and memory. Reading and even Mathematics difficulties, for example, can display typical results and be paired with distinct profiles of alterations.

VIRAL CAUSES OF HEARING LOSS: CYTOMEGALOVIRUS AND ZIKA VIRUS

Miguel Angelo Hyppolito

The two most important viral agents as cause of sensorineural hearing loss (SNHL) are Cytomegalovirus (CMV) and Zika virus. Contamination by Zika virus is caused by the bite of infected Aedes *aegypti* mosquitoes or through sexual contact with people who have contracted Zika. The relationship between Zika virus infection and hearing loss was the subject of research during the last outbreak in 2016 in Brazil. The studies started from the observation that a group of adult patients who were positive for Zika virus had been experiencing transient symptoms of tinnitus, dizziness and hearing loss. Currently, the concern is also focused on newborns whose mothers had symptoms of the disease in early pregnancy. These babies have a high risk of developing microcephaly particularly if the mother had symptoms between the second and fourth month of gestation, a critical period for neurogenesis. Suspicion of auditory dysfunction refers to brain calcifications and to evidence for neuronal damage or cochlear nerve damage. To date, monitoring does not confirm late hearing loss or elucidate the exact mechanism of hearing loss in children with microcephaly. However, children at risk should have their hearing monitored and be followed up at preschool and elementary school.

SNHL is one of the most common problems that occur at birth. Genetic and environmental causes are present and the most common environmental cause of

congenital SNHL is CMV infection, with an estimated overall birth prevalence of approximately 0.3-2.4%. Infection is predominantly asymptomatic at birth, since 90% of infected infants will show signs of congenital infection later. Among CMV-infected children, SNHL occurs in 22-65% of those who are symptomatic, and in 6-23% of those who are asymptomatic, whose onset is late and progressive. The gold standard for the diagnosis of congenital CMV infection is the isolation of the virus from urine or saliva samples in the first two weeks of life. Thus, asymptomatic children who present SNHL late after two weeks of age are less likely to be diagnosed. Ganciclovir therapy initiated in the neonatal period in newborns infected with CMV and central nervous system involvement should be instituted early to six months of age in order to prevent auditory deterioration. In addition, there should be monitoring for neutropenia. The recommendation points to the collection of saliva from all children who fail in neonatal hearing screening performed at maternity.

CITOMEGALOVIRUS

Aparecida Yulie Yamamoto

In the current era of routine immunization against type b-*Haemophilus influenzae* bacteria and with increased vaccine coverage against rubella virus, CMV has emerged as the most frequent infectious cause of non-hereditary sensorineural hearing loss in childhood. Congenital CMV infection is a significant cause of childhood hearing loss worldwide and deafness may be its only manifestation, which is progressive and can arise until the age of five. In Brazil, in the city of Ribeirão Preto, neonatal screening for congenital CMV infection and hearing involving 11,876 newborns showed an incidence of permanent deafness of 1.8 per 1000 born and CMV was responsible for 38% of the cases of permanent bilateral and or unilateral deafness. These data show the importance of tracing congenital CMV infection in those children who fail in neonatal hearing screening, allowing, when indicated, specific antiviral treatment in the neonatal period and especially early auditory rehabilitation.

ZIKA VIRUS

Mariana Leal

The most recently reported agent related to congenital sensorineural hearing loss is the Zika virus (ZIKV). The Zika virus congenital syndrome (ZIKV-CS), as it is known the set of clinical manifestations, presents phenotypically by microcephaly, craniofacial disproportion with predominantly neurological signs and symptoms, such as hypertonia/spasticity, hyperreflexia, irritability and convulsions, and ophthalmological and orthopedic changes (arthrogryposis). A total of 70 children with SC-ZIKV and microcephaly were evaluated by Leal et al in 2016[1] who reported 5.8% of hearing loss in this population, thus including congenital Zika virus infection as an indicator of risk for hearing loss, as well as other congenital infections neonates identified as STORCH (syphilis, toxoplasmosis, rubella, cytomegalovirus and herpes).

GENETIC HEARING LOSS

Joel Lavinsky

Through several genome-wide association studies (GWAS) with mice, we performed the discovery of several genes related to common and complex forms of sensorineural hearing loss, especially in noise-induced hearing loss (NIHL). Using the hybrid mouse diversity panel with 64 lines of consanguine mice, we isolated our candidate gene on chromosome 17, the Nox3 gene. We have verified in mutants that this gene is crucial for susceptibility to NIHL. Subsequently, we expanded our association study for 100 consanguine mouse lineages and studied the gene-environment interaction in the susceptibility to NIHL. We identified a polymorphism on chromosome 6, being statistically significant only after exposure to noise. It is the first objective evidence in the literature on gene-environment interaction in NIHL. Finally, we publicly provide a large-scale auditory phenotyping with more than 100 genetic lineages of mice. Recently, we applied this same methodology (GWAS) in the identification and verification of candidate genes for susceptibility to vestibular dysfunction and presbycusis. We are now advancing our knowledge on the genetic predisposition to synaptic cochleopathy, especially noise induced. The discovery of genes in common and complex forms of sensorineural deafness opens doors to identify the most susceptible individuals from a genetic point of view and to deepen the investigation of gene therapy, especially in complex diseases such as presbycusis and NIHL.

AUTISM AND LANGUAGE DEVELOPMENT

Graciela González Franco

Patients with Autism Spectrum Disorder (ASD) present a wide range of pathologies, related to behavioral disorders, hearing, language with qualitative impairment in verbal and nonverbal communication; in reciprocal social interactions, in imaginative activity, and in development. Autism develops in general before 30 months of age. The behavior of each of the children with ASD can be very different. It is primordial to diagnose correctly the otolaryngology pathologies such as conduction and sensorineural hearing loss, ventilatory, swallowing and language disorders. These require more attention and follow up in diagnostic studies, during the consultation, surgery procedures, relieve of pain and in post-surgery indications. The multidisciplinary work, communication, observation and follow up to the parents and therapists are fundamental to improve children with ASD quality of life and social inclusion.

HEARING LOSS AND HUNTER SYNDROM

Frida Scharf de Sanabria

Hunter syndrome is a rare disease belonging to the group of mucopolysaccharidoses, a metabolic genetic disorder that results in the absence or severe deficiency of one of the lysosomal hydrolases (iduronate 2 sulfatase i2s). This enzyme is responsible for the degradation of GAG glycosaminoglycans, which accumulates in cells, produces permanent and progressive cellular damage that affect the appearance and physical abilities, and causes multi organ damage: heart, brain,

ears, nose, mouth, chest, respiratory organs, spleen, liver, spinal cord, bones and joints, mental development and finally a shorter life for the patient. These children appear normal at birth, but develop a variety of symptoms and signs between two and four years old, giving the wide spectrum of clinical manifestations. It is an autosomal, recessive disease, linked to the X chromosome, transmitted by the mother to the son. This means that, in the case of the gene that causes MPS II that is found on the X chromosome, women are the carriers of the defective gene (the other chromosomes can supply a normal enzyme) and transmit it to their male children. The diagnosis is made by the clinic, family history and the detection of GAGs in urine and blood. Despite being considered intractable, its treatment is by administration of Iduronate 2 sulfatase injected for better quality of life and prognosis.

AUDITORY NEUROPATHY SPECTRUM DISORDER

Marcelo R. de Toledo Piza *and* ***Signe Schuster Grasel***

Auditory neuropathy spectrum disorder (ANSD) is characterized by a hearing loss with variable forms, from mild to severe, which can assume an upward curve with better threshold in the acute frequencies. Usually is bilateral but up to 30% are unilateral. The difficulty of speech discrimination in environments with background noise or even in silence is usually disproportionate to the degree of hearing loss, what is found in the vast majority of ANSD patients. The number of cases of this disease has increased with the greater investigation of patients with auditory complaints mainly in the noise associated with the low discrimination that these patients present even with reasonable tonal auditory thresholds. The diagnosis relies on hearing tests and should be supplemented with magnetic resonance imaging and genetic evaluation. The presence of cochlear function measured by otoacoustic emissions and or cochlear microphonism (CM) and absence of responses in brainstem auditory evoked potentials (BAEP) or potentials of extremely poor morphology are observed. Otoacoustic emissions may disappear over time, but CM remains present. Often the research of CM using the BAEP does not offer a good morphological quality of analysis, so the use of electrocochleography is the best method for research of CM and other cochlear phenomena allowing the topographic diagnosis of the lesion in the auditory system. The CM shows a large amplitude and prolonged duration which is characteristic for ANSD. Another test that can be used from birth is the immittance audiometry test with acoustic reflex, which is usually absent. ANSD may be related to perinatal factors such as neonatal anoxia, prematurity, ototoxic and hyperbilirubinemia at the level of exchange transfusion. Genetic mutations of the OTOF or OPA 1 gene are associated with ANSD. Neurodegenerative diseases such as Friedreich and Charcot-Marie-Tooth can also occur with ANSD, and in these cases, they are usually manifested in adolescence or in young adults. The treatment should always be individualized and adapted to the needs of each patient. Sound amplification devices, FM system and, in cases without improvement with these methods, the cochlear implant can be tried.

COCHLEAR IMPLANT

Ricardo Bento

The cochlear implant has become a gold standard auditory rehabilitation treatment in childhood for cases of severe to profound hearing loss according to medical and audiological criteria, and it is performed in cases of bilateral deafness as a regular indication. In recent years it has been indicated in selected cases of unilateral deafness as an non well established indication. Other types of hearing loss, conductive or mixed, especially in patients with external and middle ear malformation, have as current treatment the use of bone anchoring prostheses. In both cases and in almost all children there is a possible solution for their auditory rehabilitation.

WHEN THE COCHLEAR IMPLANT FAILS

Miguel Angelo Hyppolito

Cochlear implants (CI) have become popular and are an effective treatment for patients with sensorineural hearing loss when traditional hearing aids are not satisfactory. The parents, especially of very young children indicated to the cochlear implant present questions such as: How long can the implant last? What is the chance the implant fails? What is the chance of an infection or other serious complication? Is there a manufacturer or model with a lower occurrence of complications? If better implants become available, is it possible to upgrade them?

This information provided with exemption without any bias from the manufacturer company is scarce. Cohen *et al.*, 1998, was one of the first to demonstrate the general complication rates, excluding the failure of the electronic device, of 11.8%. Subsequent studies reflect the experience of specific CI centers, reporting complication rates of 1.8% to 4.9%. Of 4-7% of complications requiring explant and or reimplantation, failure of the electronic device is the most common cause, particularly in the pediatric population. The effectiveness of reimplantation surgery has proven to be a reality, and it can be inferred that with technological improvement, many children will be able to update their CI.