An Update on Auditory Neuropathy Spectrum Disorder in Children

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Overview

- Auditory neuropathy spectrum disorder (ANSD) often described as “a newly identified form of hearing loss”
- **1984:** Kraus et al. presented children with inconsistency between auditory evoked potential and audiometric results
- **1991:** Starr et al. described ANSD in an adolescent subject
- **1999:** Rance et al. presented a group of infants with ANSD pattern
- 1671 scientific papers

**Today’s presentation**
- Provide an overview of what we have learnt
- Consider some of the current clinical challenges
- Research questions for the future
Auditory Neuropathy Spectrum Disorder (ANSD)

- Also referred to as: auditory neuropathy, auditory dys-synchrony, auditory synaptopathy…

- Hearing impairment in which cochlear outer hair cell function is “normal” but afferent neural transmission is disordered

- Indicated by the presence of pre-neural responses (OAE / CM) with absent or severely disrupted auditory neural responses (ABR)
CM/ABR assessment for a 3 mo old with ANSD
Paediatric ANSD

◆ Congenital/Perinatal
  » anoxia
  » hyperbilirubinaemia

◆ Progressive
  – Neurodegenerative disease
    » Onset physical symptoms usually in adolescence
    » Identified earlier (routinely see 1-4 yr olds in clinic)
    » Hearing difficulties often the first presenting symptom
Possible mechanisms producing the ANSD result pattern

- Cochlear damage restricted to the inner hair cells (IHC)
- IHC/auditory nerve synapse
- Auditory nerve abnormality
  - reduced neuronal population
  - disruption of neural synchrony
  - cochlear nerve deficiency
  - tumour
Axonal & Demyelinating ANSD

- **Charcot-Marie-Tooth Syndrome**
  - Progressive genetic disorder characterized by loss of muscle tissue and touch sensation (motor & sensory neuropathies)
  
- **CMT1**: demyelinating process
- **CMT2**: axonal loss

- Later stages see absent ABR but early in the disease course responses still present
Control: 90dBnHL
ANSD Clinical Profile

◆ Prevalence

– Congenital/Perinatal ANSD
  » 1 in 800-1000 children show permanent hearing loss
  » 5-15% of those present with the ANSD result pattern

– Neurodegenerative disease
  » List of diseases associated with ANSD growing
    ◆ FRDA/CMT/LHON/ADOA...
  » relatively rare
  » Friedreich ataxia most common: ≈ 1 in 20,000
    ◆ All show ANSD at some point in the disease course
ANSD Clinical Profile

- **Behavioural audiogram**
  - Level: normal hearing to profound loss
  - All configurations: $\approx 30\%$ low frequency
  - Fluctuating hearing

- **Acoustic reflexes**
  - Typically absent (regardless of hearing level)

- **Functional hearing**
  - Impaired speech perception
Speech Perception

- Consistently reported problem in both adults and children with ANSD

- Difficulties out of proportion with the behavioural audiogram
  - Abnormal speech perception in subjects with "normal hearing"
  - Subjects with elevated hearing thresholds show speech perception poorer than for SN loss of equivalent degree
Open-set Speech Perception v Hg Level for Children & Adults with ANSD

Yellin et al., 1989
Open-set Speech Perception v Hg Level for Children & Adults with ANSD

Word score
Sentence score
Why is speech perception often poorer than expected?

◆ **Signal distortion**

◆ Timing of neural conduction disrupted

◆ Impaired perception of temporal cues in speech
  - Inability to judge vowel duration
    » eg. hid vs heed
  - Inability to discriminate consonants based on timing cues
    » eg. pin vs bin
tin vs din

◆ **Degree of distortion not consistent across children**
Extreme difficulty reported in adults and children with ANSD (Kraus et al., 2000; Rance et al., 2007; 2010; 2012; Starr et al., 1998)

Some cases show normal understanding in quiet and negligible perception in “everyday” listening conditions
Speech Perception in Noise for Children with ANSD

(essentially normal sound detection)

Rance et al, 2007; 2010, 2012
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Speech Perception in Noise for Children with ANSD

(essentially normal sound detection)

Rance et al, 2007; 2010, 2012
Why is speech perception in noise a particular problem in ANSD?

◆ **Gap listening**
  – Impaired ability to use brief quiet periods in the noise to access the signal

◆ **Spatial processing**
  – Impaired ability to use inter-aural timing cues to localize sound sources
Spatial Processing

- Affected in ANSD as the neural representation of timing cues in left/right auditory nerves is degraded.
- Inter-aural difference cues [<1 msec] can’t be effectively combined in the brainstem.

Listening in Spatialized Noise Test (LiSN-S)
  - Sentences in noise
  - **Spatial advantage**: The improvement in speech perception when the signal and background noise are presented from different directions.
Spatial Advantage (LiSN-S) for Children with ANSD

Rance et al. 2012
Spatial Advantage (LiSN-S) for Children with ANSD

Rance et al. 2012
Spatial Advantage (LiSN-S) for Children with ANSD

$r = -0.652, P=0.001$

Rance et al. 2012
Clinical Management of ANSD

- Children with ANSD form a heterogeneous group
  - Range of different aetiologies
  - Different clinical presentations

- Range of different management challenges

- Some questions explored in the recent literature include:
  - How should ANSD children with normal sound detection be managed?
  - Should hearing aids and CI be used in concert?
  - Should the contra-lateral ear be occluded in children with unilateral CI?
  - Can we predict cochlear implant outcomes for ANSD children in the pre-operative phase?
Management of Children with ANSD

Hearing Aids vs Cochlear Implants
Conventional Amplification

- Arguments against amplification
  » Inherent pathway limitations
  » Potential for cochlear damage

- Argument for amplification
  » Increased access to the speech signal (if sufficient gain is provided)

- Speech perception outcomes
  » 40-50% show significant benefit

Digital Speech Processing Aids

- Manipulate speech signal to make temporal cues more salient
  » Limited results/success (so far)
Cochlear Implantation

– Currently the option of choice for most individuals with ANSD

– Speech Perception Outcomes

» Most reported cases have performed at levels similar to peers with SN-loss

» Some poor results

» Teagle et al. (2010)

» 52 children with open-set scores

» 27% of cases showed speech perception scores <30%
ANSD Management: Hearing Aids / Cochlear Implants

● Melbourne Long-Term Outcome Study
  – Infant ANSD first identified in Melb (1989)
  – Tracking these individuals from infancy to adulthood

● Longitudinal data
  – Audiometry
  – Basic auditory perception (temporal/frequency processing)
  – Speech perception (quiet/noise)
  – Hearing disability ratings
  – Expressive/receptive language development
Long-term Language Development in ANSD

- **Receptive Language**
  - Peabody Picture Vocabulary Test (PPVT)
  - Determines an “equivalent language age” based on norms for normally hearing/developing children

- **Longitudinal data:** (4 yrs – 20 yrs)

- **Subjects (November 2013)**
  - Aided ANSD children (n=8)
  - Implanted ANSD children (n=6)
  - Implanted SNHL children (n=6)
Receptive Language (PPVT)
Receptive Language (PPVT)
Longitudinal Study Conclusions (Preliminary)

- Most implanted children with ANSD show long-term language outcomes equivalent to those of young implantees with SN-loss.

- Some children with ANSD managed with conventional hearing aids can perform as well as the average implantee.
Clinical Challenge

- How to predict whether a newly diagnosed baby will perform better with conventional hearing aids or CI?

- Considerations
  - **Anatomy**: if a child has no nerve then a CI will not be beneficial
  - **Sound detection thresholds**: if hg levels are in the severe/profound range the child is unlikely to benefit from amplification (same audiologic selection criteria as for SN-loss)
  - **Auditory capacity**: perceptual ability in cases with hg. levels in the mild/severe loss range determined by the degree of temporal distortion
Measuring Auditory Capacity in Infancy

- Measuring the degree of temporal processing deficit predicting long-term outcomes remains a major challenge

- Current research directions
  - Behavioural techniques
    » Conditioned psychophysics (VRA)
    » Unconditioned psychophysics
  - Eg. eye tracking technologies
Measuring Auditory Capacity in Infancy

- Measuring the degree of temporal processing deficit predicting long-term outcomes remains a major challenge

- **Current research directions**
  - Evoked potential techniques
    - Cortical Auditory Evoked Potentials
      - Acoustic Change Complex (where the response is elicited by temporal variations in the stimulus)
    - Auditory Steady State Responses
      - where the potential is elicited by fluctuations in a continuous stimulus
Summary & Conclusions

- 20+ years of experience with paediatric ANSD has led to significant advances
  - Understanding of mechanisms
  - General pattern of functional outcomes

- Results in individual children are highly variable and so the management of affected youngsters remains a challenge...
Thankyou