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: ≈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

3-Frequency Average (dBHL) vs. Open-Set Speech Score (%)

- Black dots represent Word score.
- White circles represent Sentence score.

Graph shows a general trend where lower 3-frequency average dBHL correlates with lower Open-Set Speech 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
Speech Perception in Noise

- 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
Speech Perception in Noise for Children with ANSD

(essentially normal sound detection)

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

$r = -0.652, P=0.001$
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)

Age at Assessment (yrs)

Equiv. Language Age (yrs)
Receptive Language (PPVT)

Equiv. Language Age (yrs)

Age at Assessment (yrs)

SN (CI)
Receptive Language (PPVT)
Receptive Language (PPVT)

![Graph showing the relationship between Age at Assessment (yrs) and Equivalent Language Age (yrs) with data points for ANSD (CI).]
Receptive Language (PPVT)
Receptive Language (PPVT)

Age at Assessment (yrs)
Equiv. Language Age (yrs)
ANSD (Aided)
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