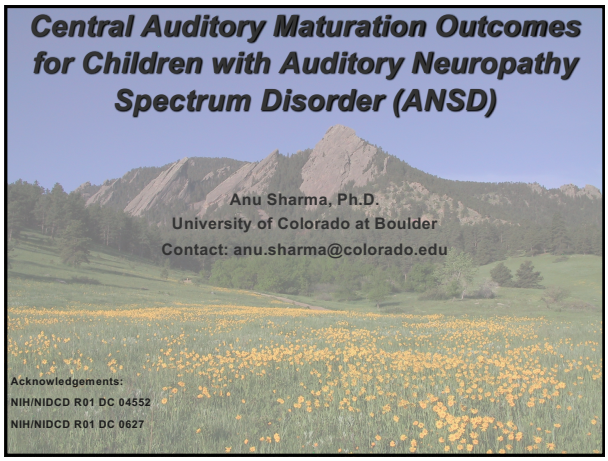
Central Auditory Maturation Outcomes for Children with Auditory Neuropathy Spectrum Disorder (ANSD)



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ANSD: DEMOGRAPHICS

Described in the literature for almost 2 decades

10-15% of all children with 'SNHL' (Talaat et al., 2009, Kirkhim et al., 200)

Up to 40% of hearing-impaired NICU graduates

ANSD: Etiology

Possible etiologies are many:

- Anoxia
- Hyperbillirubinemia / Kernicterus
- Infectious process
  - (e.g., mumps)
- Immune disorders
  - (e.g., Giullian-Barre syndrome)
- Genetic and syndromal conditions
  - (e.g., hereditary sensory motor neuropathy, Freidrich's ataxia, Charcot-Marie-Tooth syndrome, Pejvakin)
- Absent or hypoplastic VIII nerve
- Often associated with prematurity
- Exposure to Ototoxic Medications
- Unremarkable medical history

(Rance et al., Kraus et al, 2001; Madden et al, 2002)

How is ANSD diagnosed?

ANSD: Clinical Presentation

OAEs *usually* present (or were at one time)

Absent or abnormal ABR

Cochlear microphonic

Audiogram → from 'normal' to profound HL

Hearing abilities can fluctuate

Speech perception usually poor

Difficulty in noise

Absent or abnormal acoustic reflexes

Characteristics of ANSD: Summary

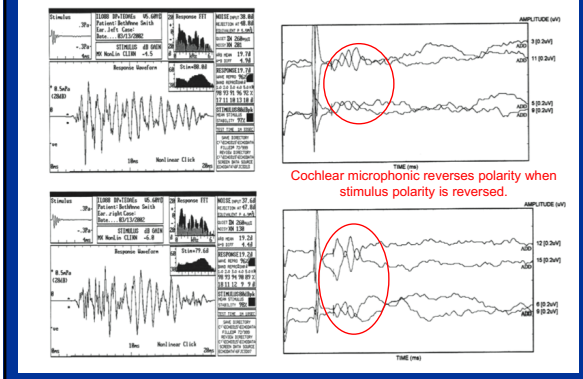
Evidence of outer hair cell function in the cochlea

- Present OAE's
- Cochlear microphonic present in ABR

Evidence of neural impairment

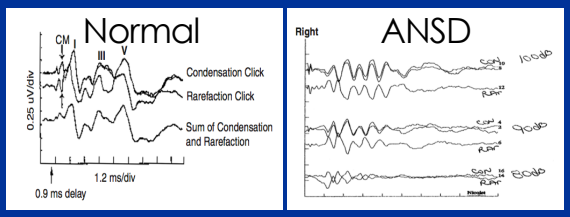
- ABR is absent/abnormal
- Acoustic Stapedial reflexes are absent/abnormal
- Audiogram ranges from normal to profound, can fluctuate
- No correlation between speech perception skills and audiogram

- High inter and intrasubject variability



ANSD: Auditory Brainstem Response

Cochlear Microphonic



Must change polarity of stimulus, as a long-ringing CM may masquerade as a normal ABR

What is the underlying mechanism that leads to the clinical findings in ANSD?

DYS-SYNCHRONY

Abnormal ABR

⬇

Dys-synchronous firing of the VIII nerve

Dys-synchrony due to: IHC abnormalities

Genetic anomalies – affect synaptic transmission

VIII nerve abnormality

demyelination

ANSD: Site(s) of Lesion

Three Possible Sites of Lesion:

Inner hair cells (IHC)

IHC loss with possible degeneration of VIII nerve afferents

Synapse between IHC and VIII nerve

Genetic mutations hinder neural transmission

VIII nerve itself

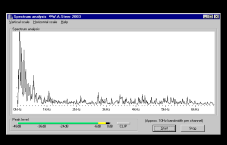
Neural fiber loss; VIII nerve absence; Demyleination

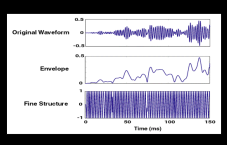
How do we distinguish the different sites of lesion?

(Starr et al, 1996)

Dys-synchrony affects 'temporal processing'

Spectral Processing	Temporal Processing
• Ability to detect frequency / pitch • Related to **place** of articulation	• Ability to detect fluctuations / changes over time • Fine grained vs. Gross • Related to **manner** of articulation and **voicing**





ANSD causes

- Inner hair cell disorder
  - Otoferlin gene, selective IHC loss

  (Varga et al., 2003; 2006, Yasunaga et al., 1999, Amatuzzi et al., 2001).
- Demyelination and/or axonal loss
  - Late-onset ANSD
  - Syndromal conditions, concomitant neuropathies

  (Rance and Aud, 2005, Sininger and Oba, 2001)
- Unilateral etiologies may be different
  - Expression of GJB2 gene for connexin 26

  (Cheng et al., 2005)

Treatment and Management

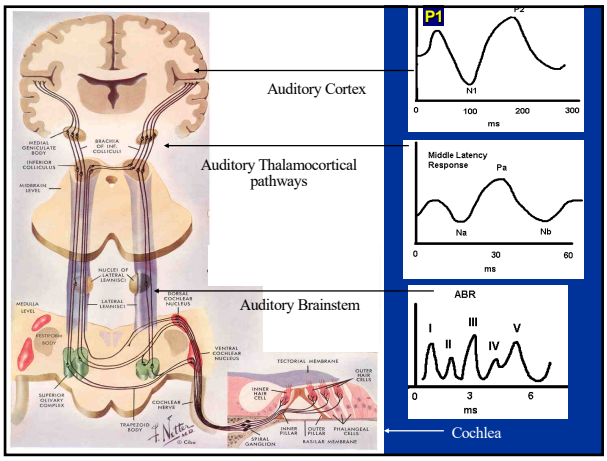
ANSD: Treatment & Management

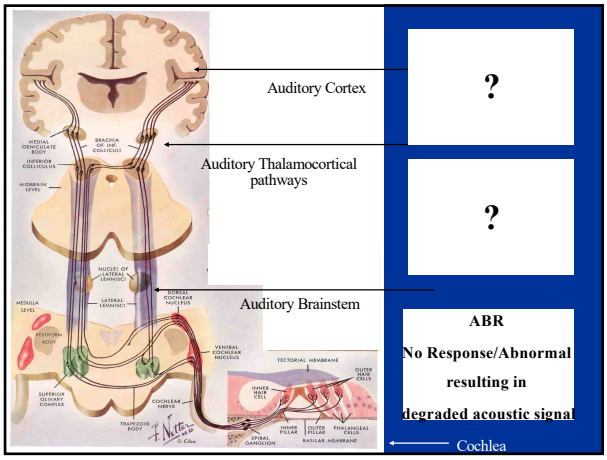
Overall, when it comes to treatment of children with ANSD:

Some benefit from HAs

Many more benefit from CIs

Why is cortical development relevant in children with ANSD?





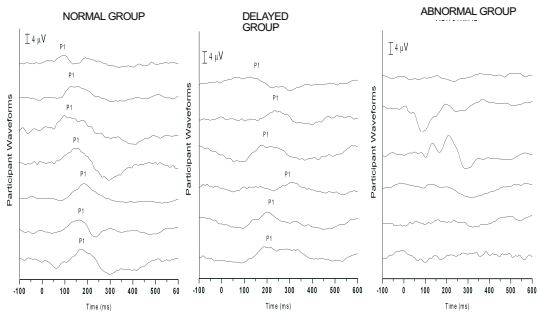
Neuroplasticity in Children with Auditory Neuropathy Spectrum Disorder (ANSD)

21 Children with ANSD fitted with hearing aids.

24 Children with ANSD fitted with cochlear implants.

Sharma et al., (2011); Cardon and Sharma (2013)

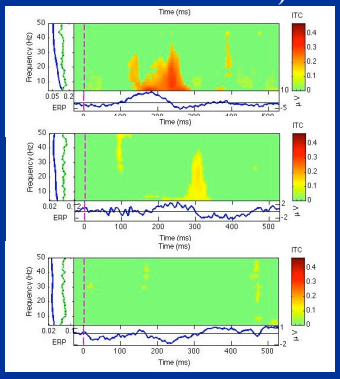
ANSD CHILDREN FITTED WITH HEARING AIDS FELL INTO 3 DISTINCT GROUPS.



P1 development reflects underlying levels of cortical dys-synchrony.

Sharma and Cardon, 2015; Cardon and Sharma 2013

Cortical Phase Synchrony (Inter-Trial Coherence) in ANSD



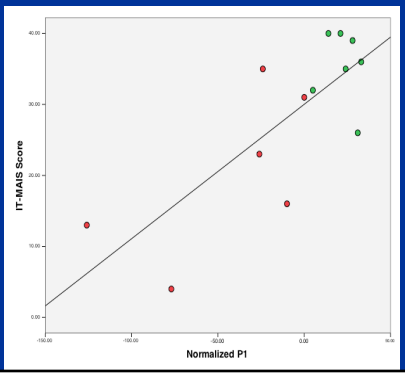
NORMAL P1

DELAYED P1

ABNORMAL P1

Nash and Sharma 2014; Nash Gilley and Sharma, 2014

Relationship between cortical maturation and behavioral auditory skill development.



r=0.8 p<0.05

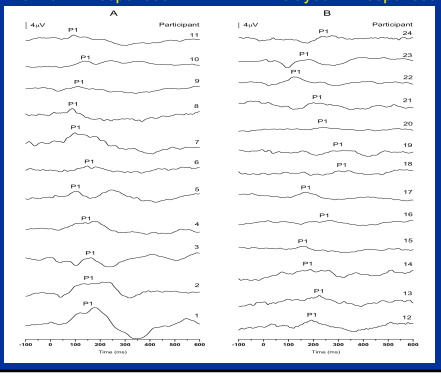
R^2=0.6

P1 responses in ANSD: post cochlear implantation

n=24

Normal P1 responses

Delayed P1 responses



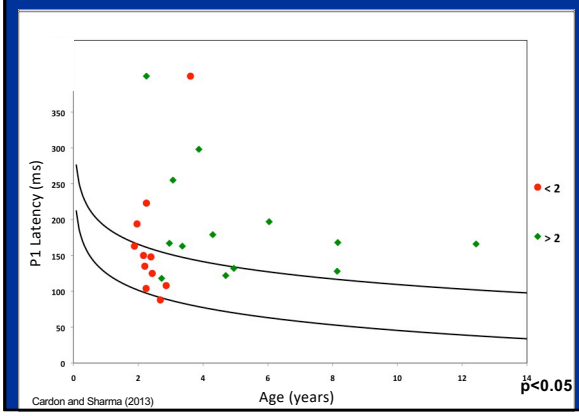
Cardon and Sharma, 2013

No ANSD child fitted with a cochlear implant showed abnormal cortical maturation.

Cochlear implantation provides some degree of benefit to most children with ANSD.

Cardon and Sharma, 2013

Is there a Sensitive Period for Cochlear Implantation for ANSD?



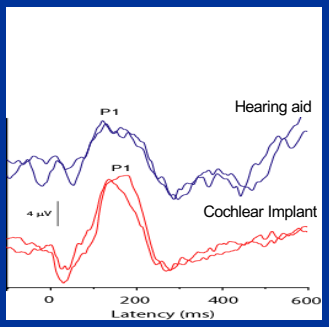
Cardon and Sharma (2013)

Preliminary data suggest a brief sensitive period of 2 years for cochlear implantation in children with ANSD.

Cardon and Sharma, 2013

Can we use central auditory system neuroplasticity to help with clinical decision making in newborns and infants?

P1 biomarker of auditory cortical maturation



Sharma et al., JAAA (2005)

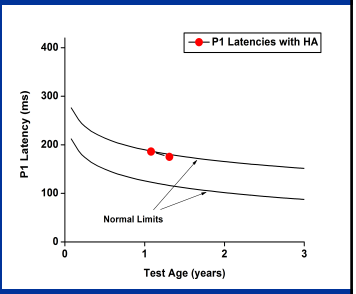
How do we determine candidacy and benefit from a hearing aid and/or a cochlear implant?

We are exploring the use of the P1 CAEP to assist in management of children with ANSD.

Cardon, Campbell and Sharma JAAA, June 2012

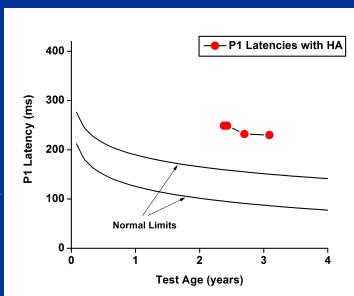
Benefit From Hearing Aid Use

- IT-MAIS Score: 32
- IT-MAIS Age: 1.08
- PTA Unaided: 62
- PTA Aided: 40
- HA Fit Age: .77
- Etiology: prematurity (27 week), low birth weight, hyperbilirubinemia, chronic lung disease, ototoxic meds



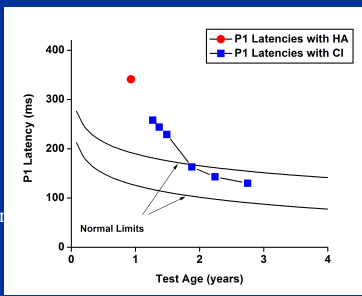
No Benefit From Hearing Aid Use

- IT-MAIS Score: 4
- IT-MAIS Age: 1.08
- PTA Unaided: 83
- PTA Aided: 57
- HA Fit Age: 2.38
- Etiology: family history no known risk factors



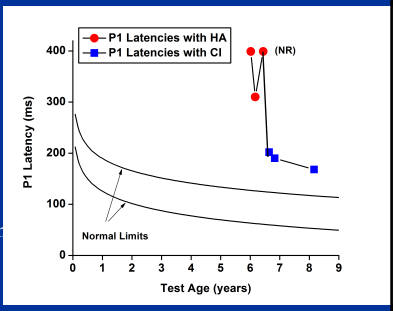
Benefit From CI Use

- IT-MAIS Score:
- IT-MAIS Age:
- PTA Unaided: 105
- PTA Aided: 85
- HA Fit Age: .90
- CI Fit Age: 1.27
- Etiology: twin - no other known risk factors



Persistently Delayed Post-implant

- IT-MAIS Score: 9
- IT-MAIS Age: 6.83
- PTA Unaided: 95
- PTA Aided: 65
- HA Fit Age: 6.12
- CI Fit Age: 6.62
- Etiology: seizures, fam
  history of hearing loss

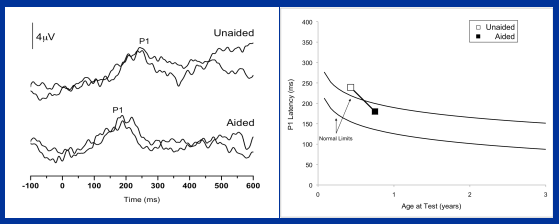


ANSD: Case SC

- Born full term and healthy. Needed oxygen for a minute after birth. No other complications.
- Absent ABR with robust cochlear microphonic.
- DPOAE's absent
- Severe hearing loss bilaterally
- Hearing aid fit age: 0.68 years

Cardon, Campbell and Sharma JAAA, June 2012

ANSD: Case SC



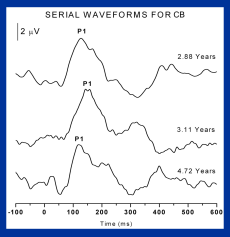
IT MAIS: 39/40̊ with hearing aid experience

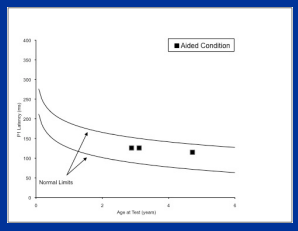
Performing well with hearing aids, will continue to monitor

ANSD: Case CB

- Premature birth; Neonatal intensive care unit (NICU) for first month of life. Ototoxic medication and mechanical ventilation in NICU.
- Absent ABR with robust cochlear microphonics bilaterally
- Absent DPOAE's and TEOAE's
- Unaided pure tone averages (PTA) of 73 and 72 dB HL in the right and left ears, respectively.
- Bilateral hearing aids at 2.88 years of age.

Cardon, Campbell and Sharma JAAA, June 2012





MLNT (E) – aided (2.88 years)	LNT (E) – aided (2.88 years)	NUCHIPS – aided (3.11 years)
Words - 40% Phonemes - 63%	Words - 40% Phonemes - 53%	Right - 84% Left - 96%

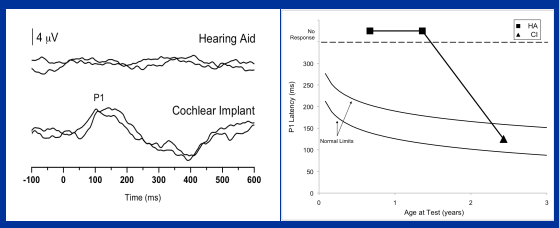
6 months after initial hearing aid fitting CB scored 84% for the right ear and 96% for the left ear on NU-CHIPS test of speech perception.

We will continue to monitor to make sure that age-appropriate acquisition of oral language and speech continues.

ANSD: Case JF

- Born at 31 weeks gestation; NICU stay for 7 weeks--jaundice treated with a blood transfusion and required mechanical ventilation.
- Absent ABR with cochlear microphonic reversal.
- Present DPOAE's and TEOAE's.
- Fit with binaural hearing aids at 0.36 years.
- JF had unaided PTAs of 38 and 70 dB HL in the right and left ears, respectively. In addition, aided testing yielded PTAs of 38 dB HL in the right ear and 41 dB HL in JF's left ear.
- Receptive language scores and use of vocabulary severely delayed.
- At 1.76 years of age, JF received a cochlear implant in the left ear.

ANSD: Case JF



P1 was absent with hearing aids and normal with cochlear implants.

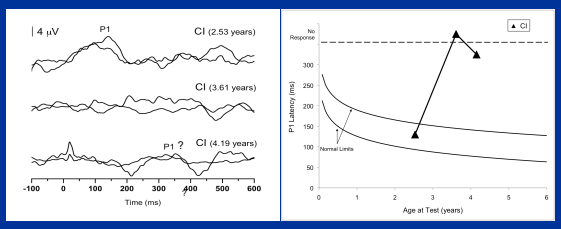
Cardon, Campbell and Sharma JAAA, June 2012

ANSD: Case RB

- RB was born full-term without complications and failed newborn screening in left ear.
- Abnormal ABR morphology with present CMs bilaterally.
- Absent TEOAEs bilaterally and limited presence of DPOAE.
- Profound rising to severe bilateral hearing loss.
- Fit with binaural hearing aids at age 1 year. Aided thresholds in the mild-severe hearing frequency range .
- RB received a cochlear implant in the right ear at 1.64 years of age.

Cardon, Campbell and Sharma JAAA, June 2012

ANSD: Case RB



Initial progress with the CI appeared to be fine.

Later reports of 'good' and 'bad' hearing days with CI.

Behavioral thresholds with CI were inconsistent and in normal-moderate range.

IT-MAIS testing performed with RB at 3.61 and 4.19 years of age yielded poor scores (14/40 and 20/40 respectively).

COCHLEAR NERVE DEFICIENCY

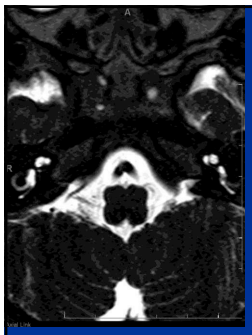
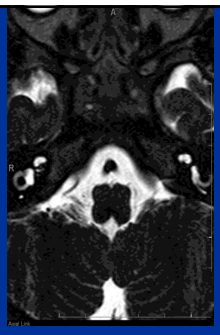
Roland, Martin, Booth, Campbell J and Sharma A (2012). (2012) Cochlear Implants International

Case: CND

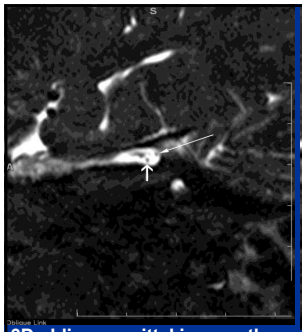
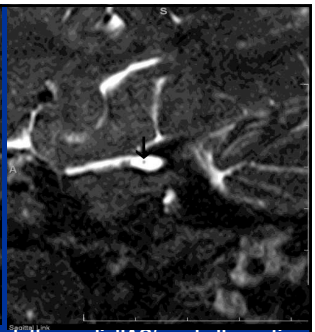
- 39 weeks gestation
- 6 week stay in neonatal ICU following delivery
- Significant Medical History:

  Hypoxia
  Mechanical Ventilation
  Left Brachial Plexus Injury
- No record of newborn hearing screening
- ABR at 22 months consistent with severe to profound sensorineural hearing loss
- Hearing aids fit at 25 months of age

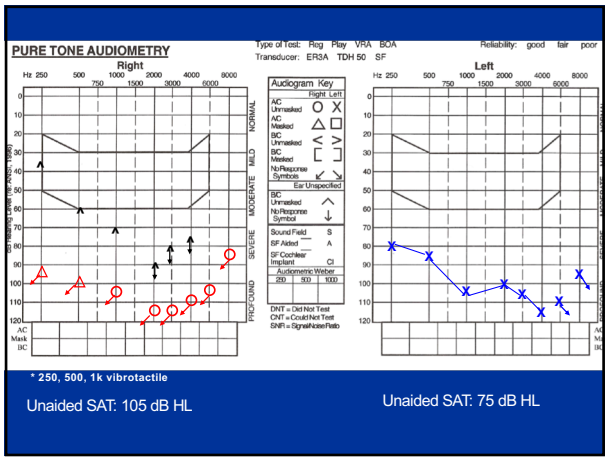
- Radiological findings (MRI) revealed "mild cochlear dysplasia; absent or severely hypoplastic cochlear nerves bilaterally"

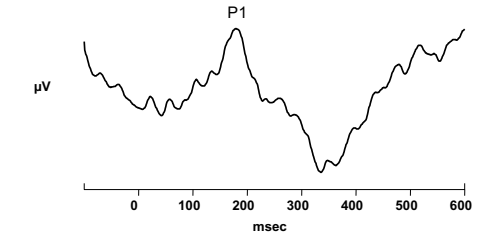
3D axial T2 weighted images through the cochlea. There is decreased partition of the cochlea with a deficient modiolus. The internal auditory canals are markedly hypoplastic.

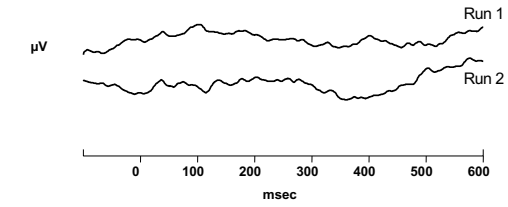
3D oblique sagittal images through the medialIAC/cerebellopontine cistern. The facial nerve was seen bilaterally (arrow). The normal vestibulocochlear complex is 2.5 times the diameter of the facial nerve. No vestibulocochlearcomplex is seen on the right and a small complex is present on the left (long arrow).



P1 response – Left Ear
(w-HA)



P1 response – Right Ear (NR)
w/HA



Child was fitted with a cochlear implant at age 3 years in the left ear.

Intra-Individual Variability

High intra-individual variability is a marker of cortical dysfunction.

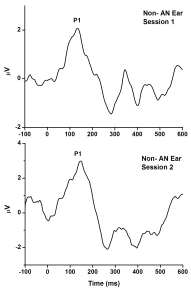
Higher than normal within-subject variability has been associated with various neurological disorders, including head injury, dementia, schizophrenia, ADHD and APD.

We are adapting methods which are indicators of high cortical variability in other neurological populations.

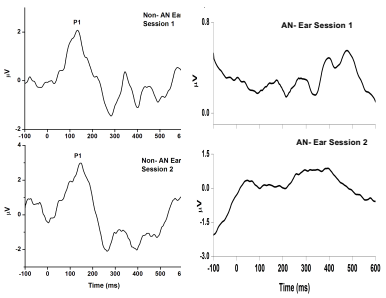
Case Study

- 9 year old child with congenital unilateral AN in left ear.
- AN ear: Normal OAE, Abnormal ABR; mild hearing loss, speech discrimination 20%, poor speech perception in noise.
- Non AN ear: Normal OAE, ABR, normal pure tone thresholds, speech discrimination 92%, good speech perception in noise.

9 yr. old with unilateral ANSD



9 yr. old with unilateral ANSD



High Density EEG study

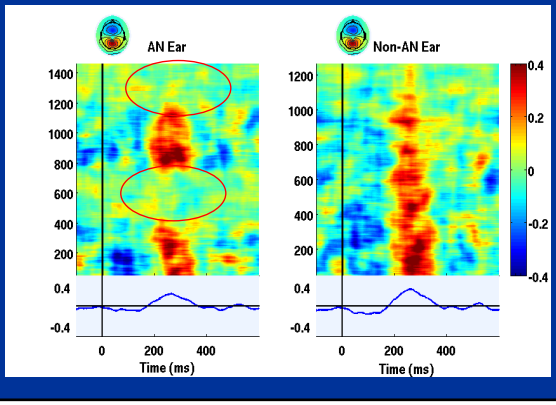
Cortical Auditory Evoked Potentials

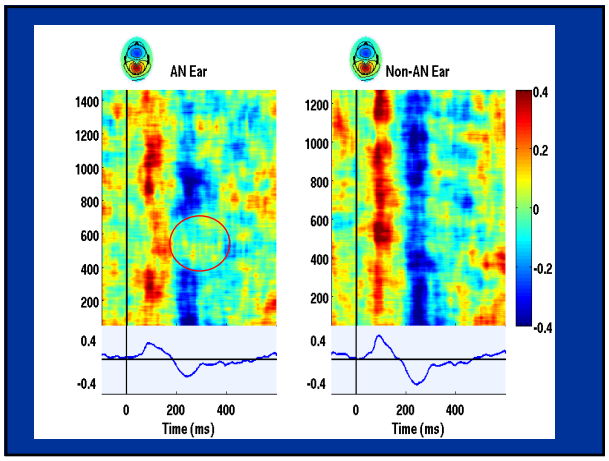
from 64 scalp electrodes

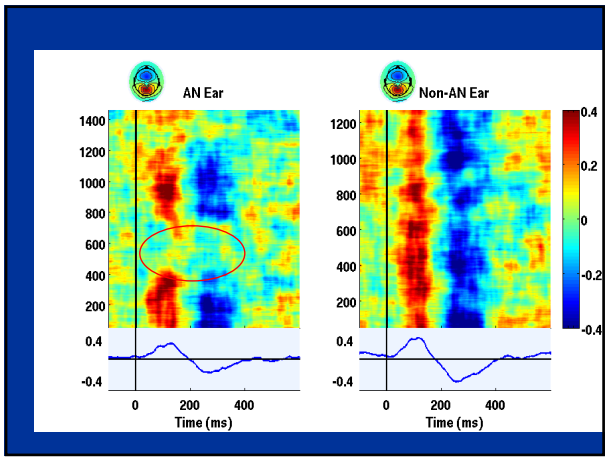
Independent Component Analysis

Each component represents a different source of activation in the brain.

The patterns tell us about the strength and consistency of activation of cortical areas.







ANSD ear showed variable strength and consistency of activation of cortical areas.

Appropriate cortical areas did not appear to be ‘engaged’ during portions of the recording.

SUMMARY

Cortical potentials provide useful information regarding central auditory development and functioning in children with ANSD.

We find that cortical potentials are useful in clinical management of ANSD.

ANSD: Last Word

Because of the high intra and intersubject variability in ANSD, each patient must be considered individually.