Consequences of UHL on Language and School Performance

Judith E. C. Lieu, MD MSPH

Phonak Unilateral Hearing Loss in Children Conference

October 23, 2017

Children's HOSPITAL • ST. LOUIS
BJC HealthCare

Washington University in St. Louis Physicians

“Historically, the involvement of hearing health professionals in the management of children with unilateral hearing loss has been limited. The conventional approach was to identify the cause of the hearing loss and to assure the parents that there would be no handicap.”

Oyler, Oyler & Matkin, 1987

Prevalence of UHL in Children

- Prevalence of UHL increases with age
- Newborns—about 1 in 1000[1]
  - ~1/3 of children with congenital hearing loss
- Adolescents—about 1 in 5[2]
  - 19.5% with hearing thresholds >15 dB
  - 2.5% with hearing thresholds >25 dB

[1]Lieu, Seminars Hearing, 2010
[2]Shargorodsky et al, JAMA 2010

Overview of Consequences

- Speech-language outcomes
- Educational outcomes
- Behavior
- Quality of life
- Possible explanations

Speech-Language Consequences Infants & Toddlers

- Delay in 1st 2-word phrase by parent recall[1,2]
  - 23.5 months (18-48), n = 31
  - 18.5 mo (109 UHL) vs 15.4 mo (95 sibs), p=.008
- Delay in auditory behavior & preverbal vocalizations[3]
  - 34 infants with UHL (median age 9.4 mo)
  - 331 infants with normal hearing (median age 9.0 mo)I
  - Auditory behavior (IT-MAIS) delayed in 21% UHL vs 4% NH, OR 3.86
  - Preverbal vocalization (PRISE) delayed 41% UHL vs 3.6% NH, OR 8.64

[1]Kiese-Himmel, 2002; [2]Lieu et al, 2010

[3]Kishon-Rabin et al, 2015

Speech-Language Consequences Preschool children I

- Delayed language development at age 4-6 years compared to normal hearing peers[1] (n=58)
- Lower communication, motor skills and adaptive behavior scores in 10 children with mild HL/UHL compared to 74 with normal hearing[2]
  - Similar comprehension & expressive language scores compared to 19 children with mod-profound BHL

[1]Borg et al, 2002; [2]Vohr et al, 2012

Speech-Language Consequences Preschool children II

- Communication development (2015)[1]
  - Early identified children with mild BHL and UHL (median age ID = 4.2 mo)
  - 24 mild BHL and 31 UHL compared to 45 NH
  - Assessed at 12, 24, 36, and 48 months old
    - PEACH, ELF, CHILD, MacArthur-Bates, MLU, CDI
  - Only CHILD scores worse at age 3 & 4 years

[1] Fitzpatrick et al, Am J Audiol 24:349–353

Speech-Language Consequences School-aged children

- Few differences compared to controls on battery of 6 standardized language tests[1] (n=25 cases)
- Language & auditory development[2]
  - 21 children with profound UHL compared with 42 with NH (5-15 yo)
  - Lower scores on morphology, syntax, vocabulary in children with profound UHL
  - Similar performance on short term and working memory

[1]Klee & Davis-Dansky, 1985

[2] Sangen et al, 2017

Speech-Language Consequences School-aged children

- UHL in Children, 6-12 year olds
  - 74 children with UHL vs. 74 sibling controls
  - Higher odds of speech-language therapy
    - 42% of children with UHL
    - OR 2.6, 95% CI 1.3-5.4
  - Lower scores on oral language skills
    - Language comprehension 91 vs 98, p=0.003
    - Oral expression 94 vs 101, p=0.007
    - Oral composite 90 vs 99, p<0.001

Lieu et al, *Pediatrics* 2010

Multivariable Regression
Oral Composite

Variable	Parameter estimate	SE	T value	P value
Intercept	13.7	7.7	1.8	0.08
UHL	-5.7	1.7	-3.3	0.001
Full sum IQ	0.6	0.06	10.3	<0.001
Age	1.7	0.4	4.3	<0.001
Female sex	3.8	1.7	2.2	0.03
Poverty level	-4.3	1.3	-3.4	0.001

Effect size ~0.3 - 0.4 SD

Adjusted $R^2 = 0.56$

Cognition Scores

Standardized scores (SD)	Right UHL	Left UHL	Controls
Vocabulary*	48.7 (11.6)	46.8 (10.8)	51.6 (10.2)
Verbal IQ*	101.6 (16.9)	100.1 (15.6)	105.5 (14.6)
Performance IQ	100.3 (15.5)	99.1 (13.0)	102.6 (14.5)
Full IQ*	101.2 (16.0)	99.6 (14.2)	104.5 (14.3)

Effect size ~ 0.2-0.3 SD

*$p < .05$ for any UHL compared to controls

Multivariable Regression
Cognition scores

Variables	Parameter estimate	SE	t value	P value
Full IQ				
Intercept	85.8	3.7	23.2	<.0001
UHL	-4.1	1.9	-2.1	.038
Maternal education	5.9	1.1	5.5	<.0001
Verbal IQ				
Intercept	85.3	3.9	22.0	<.0001
UHL	-4.5	2.0	-2.2	.028
Maternal education	6.3	1.1	5.6	<.0001

Nested Longitudinal Study

- Longitudinal study over 3 years, n=46
- Outcomes
  - Cognition—WASI
  - Language—OWLS
  - Achievement—WIAT-II-A
  - Behavior—CBCL
  - Hearing—audiogram
  - School records—IEP, speech therapy

Standardized tests
Mean = 100, SD = 15

- Multilevel regression modeling to analyze longitudinal outcomes

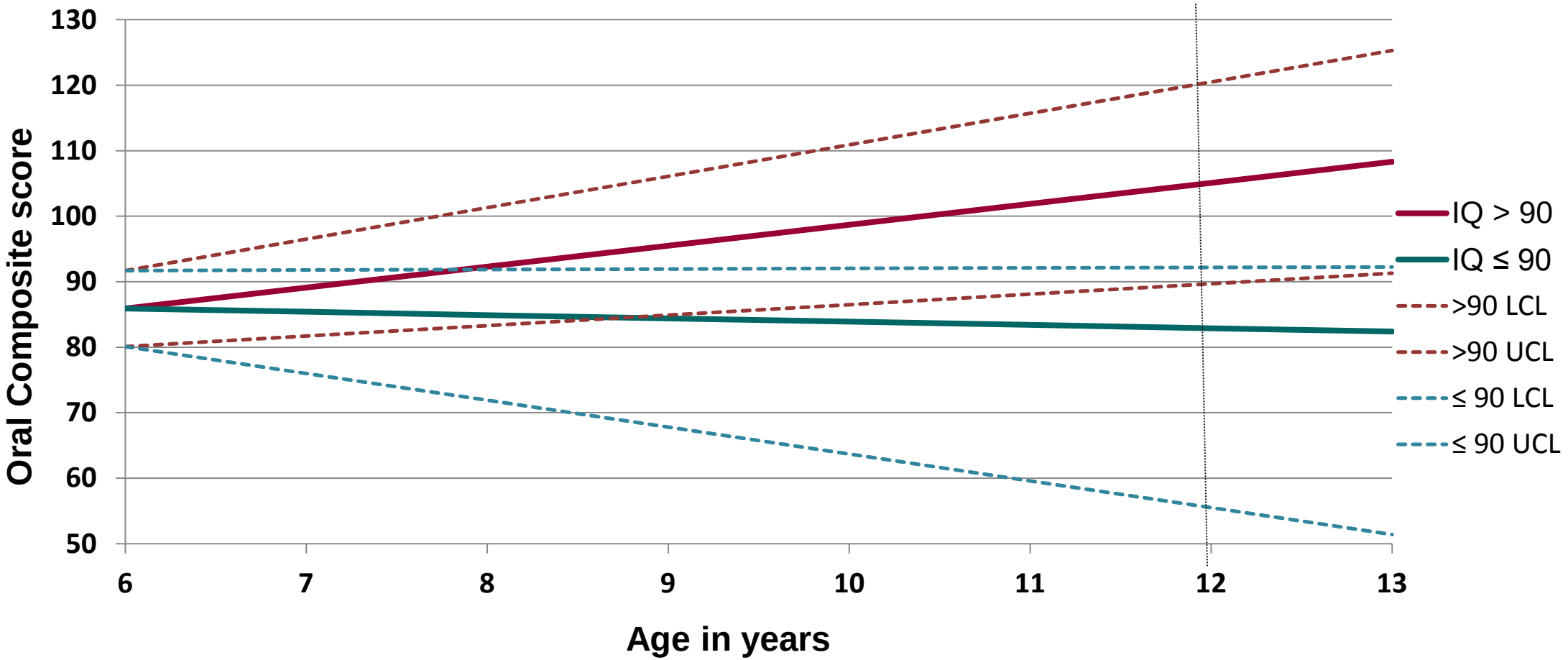
Multilevel Model: Effect of Time (Age)

Outcome n=46	**Initial Status (SE)**	**Rate of Change (SE)**	**Pseudo R^2**
Full IQ	98 (2.7)***	1.8 (0.6)**	0.11
Verbal IQ	96 (2.9)***	2.5 (0.8)**	0.13
Performance IQ	100 (2.7)***	0.3 (0.6)	0.004
Listening comp	91 (2.4)***	1.0 (0.7)	0.04
Oral expression	85 (2.8)***	2.9 (0.7)***	0.19
Oral composite	85 (2.7)***	2.5 (0.7)**	0.16
Reading	104 (2.4)***	-0.2 (0.5)	0
Math	94 (2.8)***	0.5 (0.7)	0.007
Writing	100 (3.4)***	1.4 (0.9)	0.03

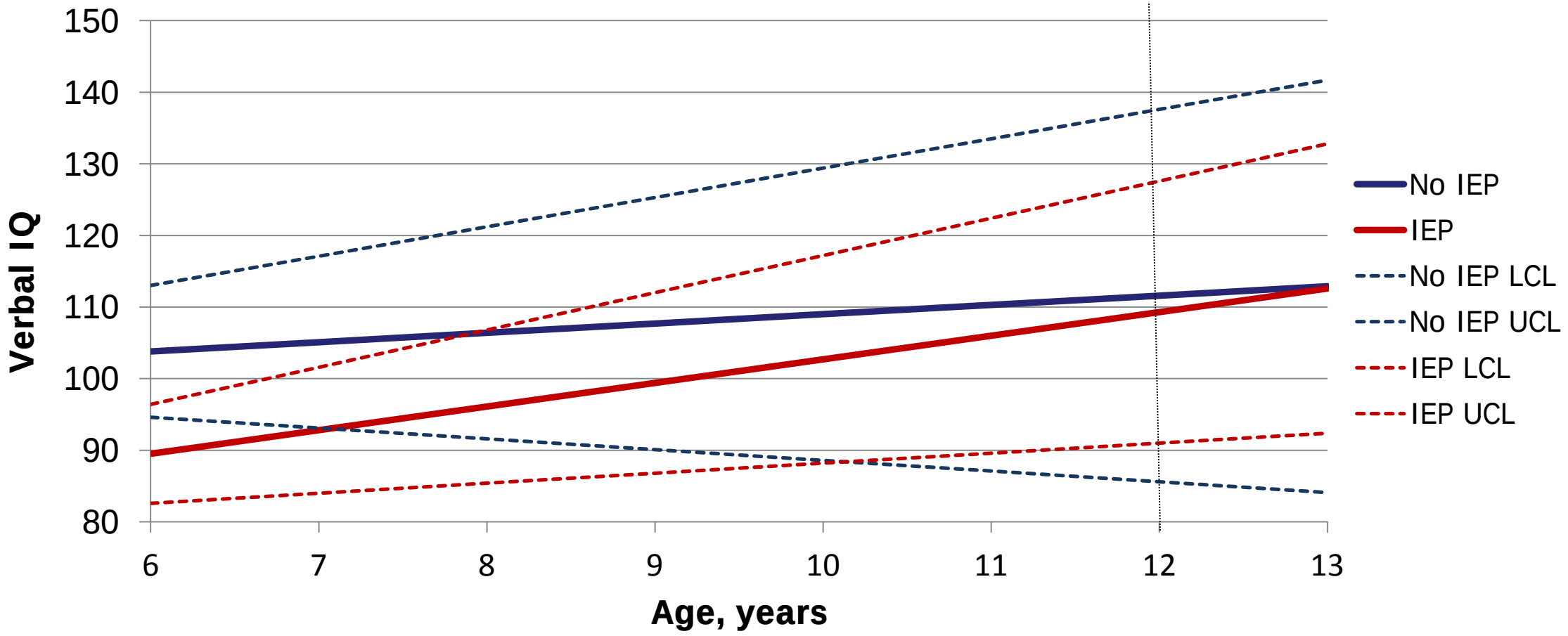
*p<0.05, **p<0.01, ***p<0.001

Lieu et al, Laryngoscope 2012

Oral Composite Score Model Interaction with Full IQ



Verbal IQ Model
Interaction with IEP



Education & Behavior
Effects of UHL

- Educational and/or behavioral problems[1]
  - 22-59% receiving additional help (1980s-1990s)
  - 24-35% grade failures vs. 3% normally
- Compared to siblings with normal hearing[2]
  - 4.4-fold increased risk of Individualized Educational Plans/Programs

[1]Lieu, Arch *Otolaryngol Head Neck Surg* 2004

[2]Lieu et al, *Pediatrics* 2010

Behavioral Outcomes—Longitudinal

- >20% scored ≤ 3rd percentile for Competency scales
  - Activities, Social, School, and Total
- 24% had academic area of weakness or executive function problems per teachers
- ~50% continued to have Individualized Educational Plans throughout the 3 years

Lieu et al, Laryngoscope 2012

UHL and Adolescents

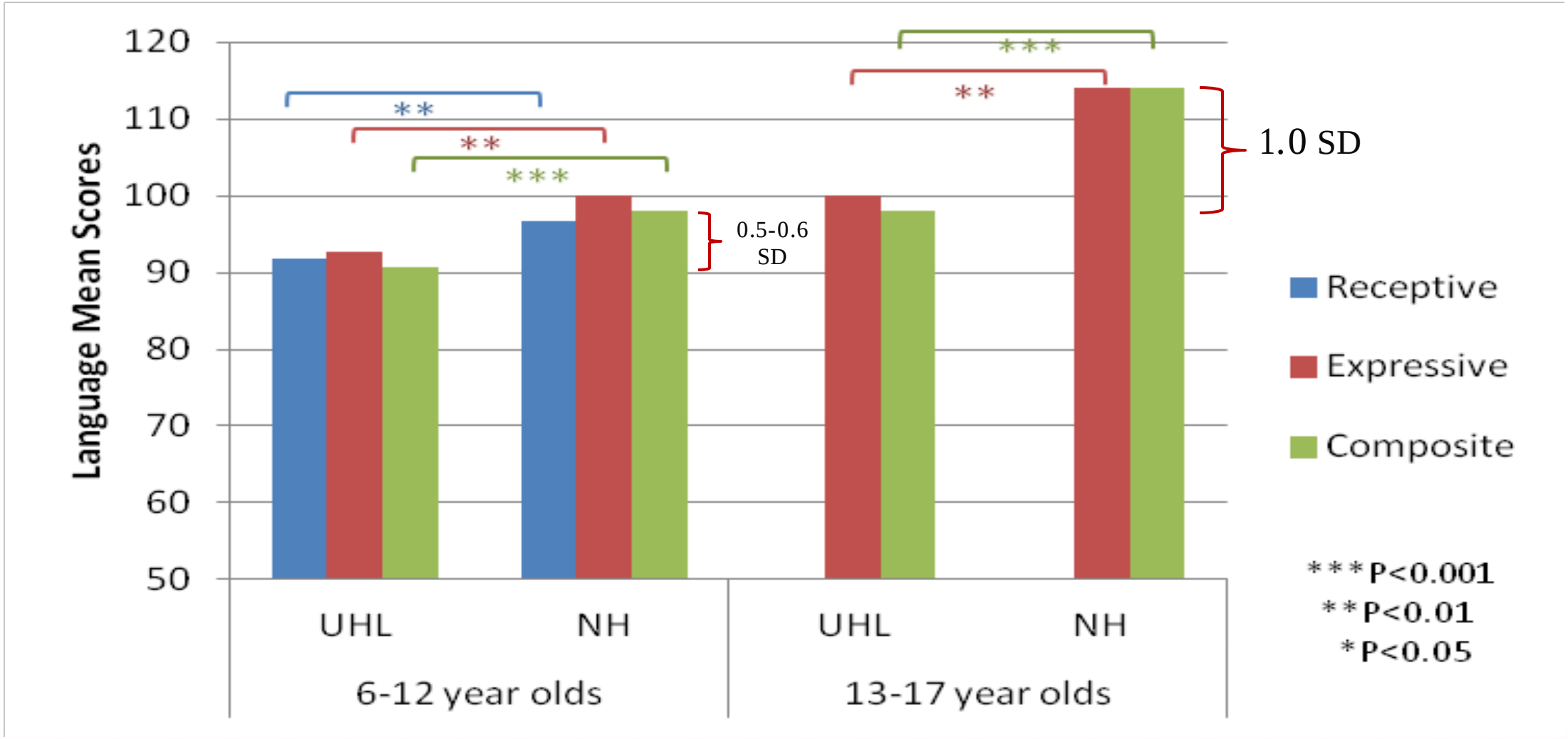
Outcome	UHL n=20	NH n=13	Diff	P value
Full scale IQ	98 (15)	112 (15)	14	0.017
Verbal IQ	101 (16)	113 (12)	12	0.032
Performance IQ	95 (15)	107 (16)	12	0.037
Core language score	98 (16)	114 (10)	16	0.001
Expressive language score	100 (16)	114 (10)	14	0.006

Verbal/Full IQ effect size ~0.8-0.9 SD
Language Effect size ~ 1 SD

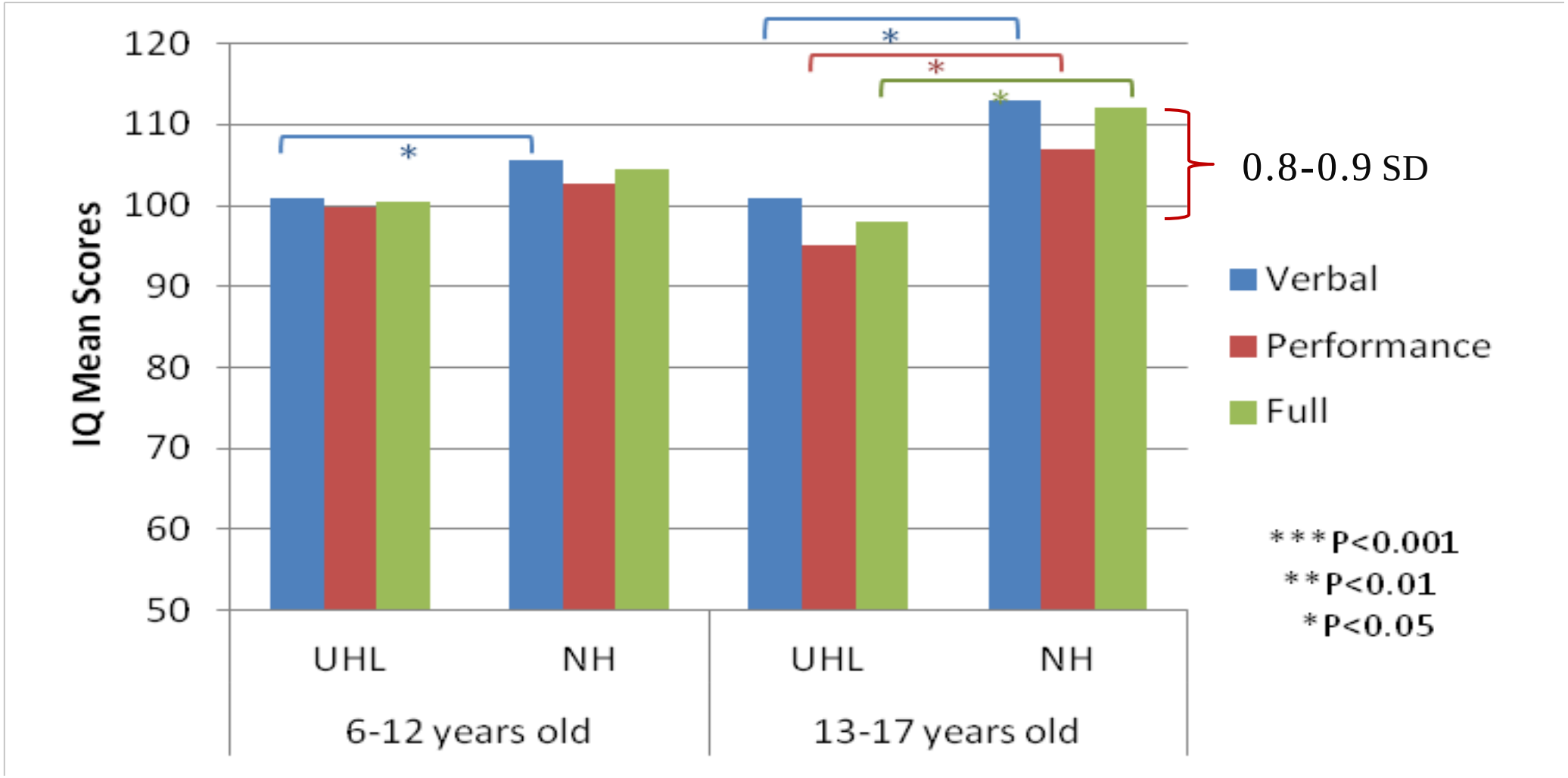
Multivariable Regression: Language Scores

Variables	Parameter estimate	SE	t value	P value
Core language				
Intercept	52.1	16	3.2	.003
Performance IQ	0.45	0.14	3.2	.003
UHL	-10.4	4.5	-2.3	.03
Health insurance	7.6	5.3	1.4	.159
Expressive language				
Intercept	55.6	16	3.4	.002
Performance IQ	0.46	0.14	3.2	.003
UHL	-8.8	4.6	-1.9	.064
Health insurance	5.5	5.3	1.0	.304

Child to Adolescent–Language Scores



Child to Adolescent–Cognitive Scores



Other Studies of Cognition

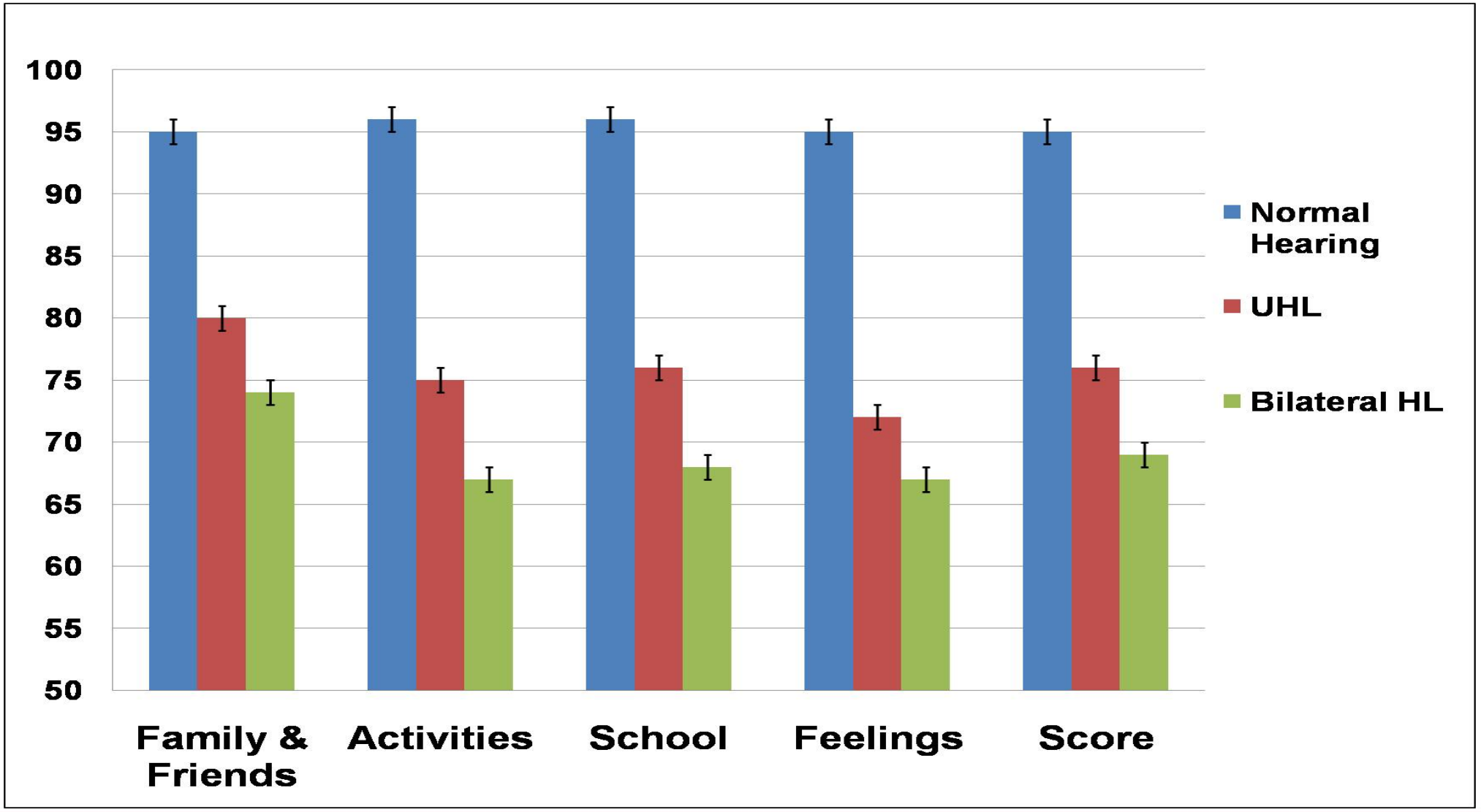
- Meta-analysis of IQ scores (2016)
  - UHL (n=173) compared to NH (n=202)
  - 6-18 year olds
    - Full IQ -6.3 (95% CI -9.1, -3.5)
    - Performance IQ -3.8 (95% CI -7.3, -0.2)
    - Verbal IQ -4.0 (95% CI -7.5, -0.4)

Purcell, Shinn, Davis, Sie. Laryngoscope 126:746–754

Quality of Life

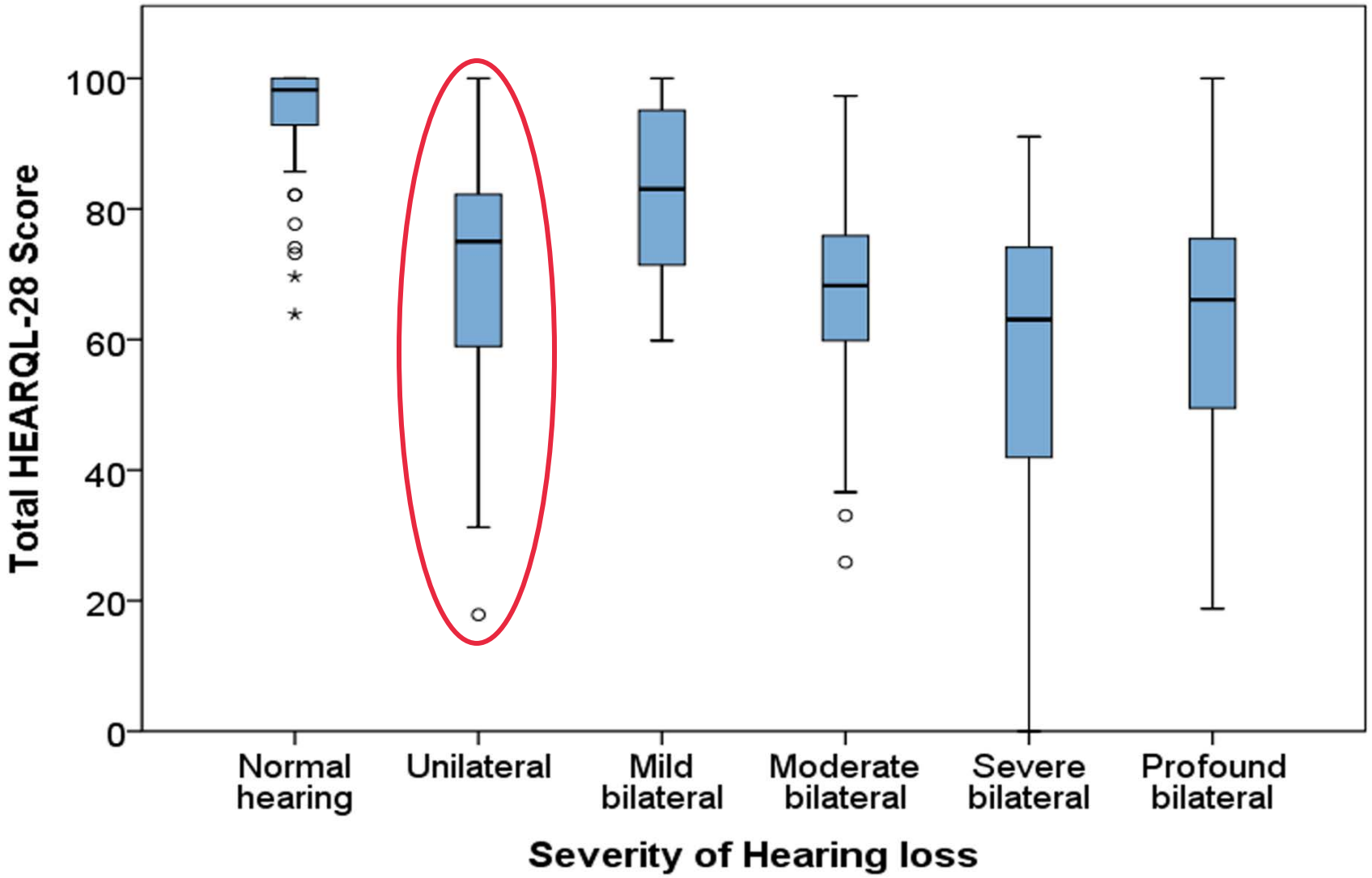
- Individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns
- Hearing Environments And Reflection on Quality of Life survey (HEAR-QL)
  - Self-reported
  - Two forms: Children and Adolescent
  - Compared children with normal hearing, UHL, and bilateral hearing loss

Quality of Life in Children, HEAR-QL



Umansky, Jeffe, Lieu, *J Am Acad Audiol*, 2011

Quality of Life in Adolescents



Rachakonda et al, *Laryngoscope*, 2014

Summary: Speech/Language Consequences

- UHL associated with delays in acquisition of preverbal behavior, speech and language in infants and preschool children
- Some school-aged children may have speech and/or language delays
- Improvement in language over time, but no “catch-up” to sibling controls
- Risk factors for delays
  - Poverty, low maternal education, male sex, low IQ, hearing severity

Summary: Educational Consequences

- ↑ Grade failures
- ↑ educational assistance (IEPs)
- ↑ Behavioral issues
- ↑ Academic weaknesses per teachers
- Risk factors for problems
  - ↓ IQ
  - Poverty, parental education
  - Severe to profound HL

MRI Studies of Brain Inter-connections

- How does UHL influence the neural development responsible for language, cognitive, and executive functioning?

- Compared children with severe-to-profound UHL vs. NH siblings
  - 7-17 years old, normal cognition
  - White matter integrity
  - Functional connectivity within grey matter
- Diffusion tensor imaging (DTI) and Resting-state fMRI (rs-fcMRI)
  - 3.0 Tesla scanner
  - single scanning session

Diffusion Tensor Imaging

- Evaluates white matter tracts
- Measures diffusion of water molecules in brain tissue
  - Anisotropy: Faster diffusion when parallel to white matter tracts vs. perpendicular
  - Fractional anisotropy (FA)
    - 0 = equal diffusion in all directions
    - 1 = diffusion in only one axis
  - Mean Diffusivity (MD)
    - Ease of water diffusion averaged over all directions
    - Measured 0 to 1

Table 4 | DTI parameters in those with unilateral hearing loss (UHL; $n = 29$) and normal hearing (NH; $n = 20$) participants amongst six auditory regions of interest (ROI) and nine non-auditory ROIs.

	UHL	NH	*p*-value	Right UHL	Left UHL	*p*-value
AUDITORY ROIs						
MD subcortical white matter of Heschl's gyrus, right	0.637	0.591	0.048*	0.643	0.632	0.130
FA lateral lemniscus, left	0.364	0.446	0.001†	0.381	0.351	0.005*
FA subcortical white matter of Heschl's gyrus, left	0.338	0.397	0.013*	0.365	0.315	0.009*
FA lateral lemniscus, right	0.392	0.457	0.025*	0.397	0.351	0.079
NON-AUDITORY ROIs						
MD Putamen, left	0.708	0.686	0.034*	0.715	0.703	0.081
FA anterior limb of the internal capsule, left	0.575	0.607	0.030*	0.571	0.578	0.093
FA centrum semiovale, right	0.468	0.503	0.015*	0.456	0.477	0.030*

Additional columns list values for right unilateral hearing loss (Right UHL; n = 13) and left unilateral hearing loss (Left UHL; n = 16); adjacent p-value column refers to p-values of Kruskal-Wallis tests between right UHL, left UHL and normal hearing (NH). Only parameters with uncorrected p-values < 0.05 are listed.

**Trend at $p < 0.05$ level; †Significant at $p < 0.004$ for auditory ROIs and <0.003 for non-auditory ROIs.*

Rachakonda et al, Frontiers in Systems Neuroscience 8:87, 2014

Multiple Logistic Regression
DTI Parameters, UHL, and Outcomes

- Speech therapy
  - FA left middle cingulate gyrus (negative)
  - MD left middle cerebellar peduncle (positive)
  - FA left middle cerebellar peduncle (negative)
  - FA right middle cerebellar peduncle (negative)
- Individualized Educational Program (IEP)
  - MD left Heschl's gyrus (positive)
  - MD left superior temporal gyrus (positive)
  - FA left Heschl's gyrus (negative)
  - FA left superior temporal gyrus (negative)
  - MD left posterior limb internal capsule (positive)
  - MD right posterior limb internal capsule (positive)

UHL– all negative associations

Resting State fcMRI

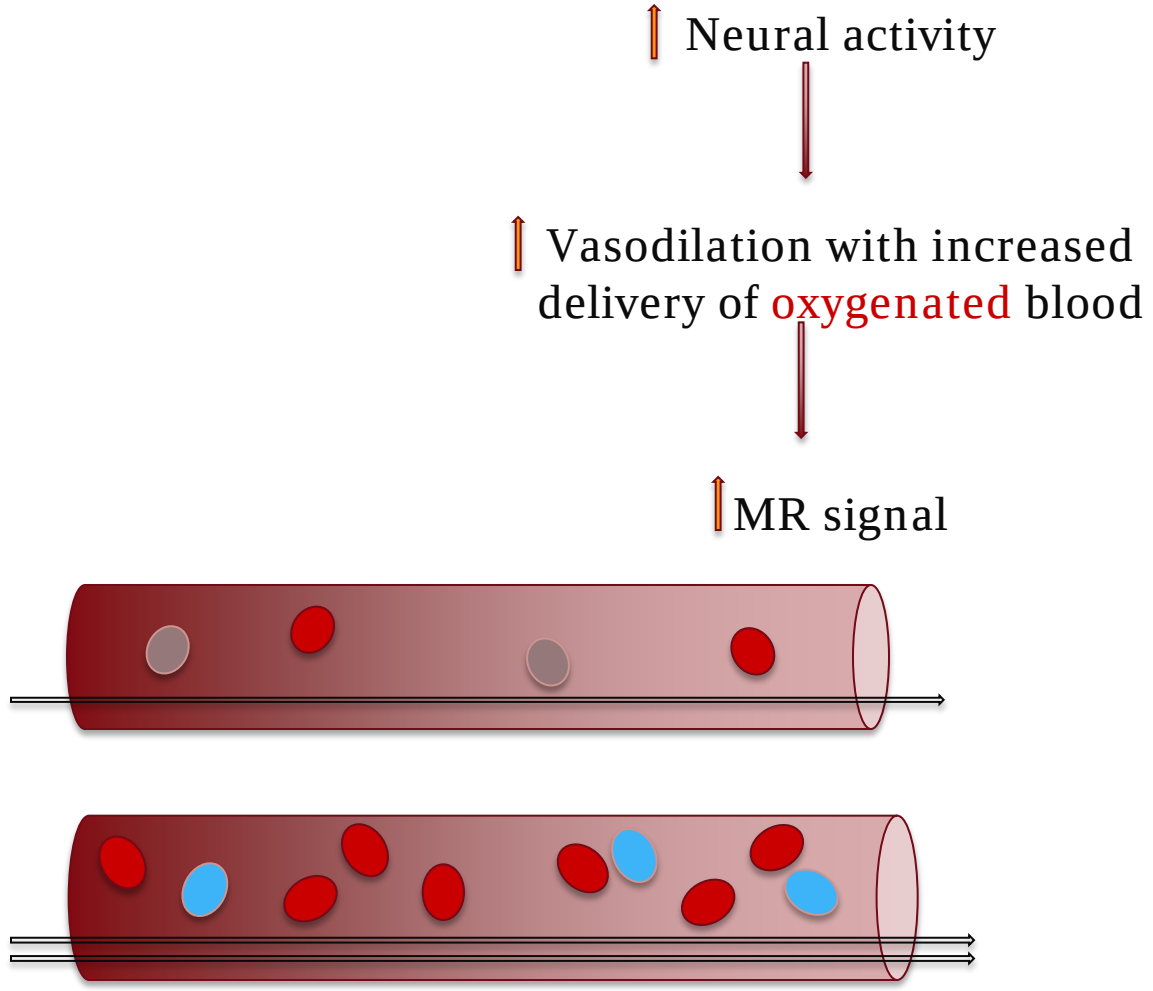
- Human brain represents 2% body mass, but consumes 20% body's energy at rest
  - Task related increase in brain metabolism is usually <5% [12]

- Spontaneous neuronal activity
  - Is not random physical or physiologic noise
  - Low frequency BOLD signal

[12] Fox and Raichle, 2007 Nat Rev Neurosci

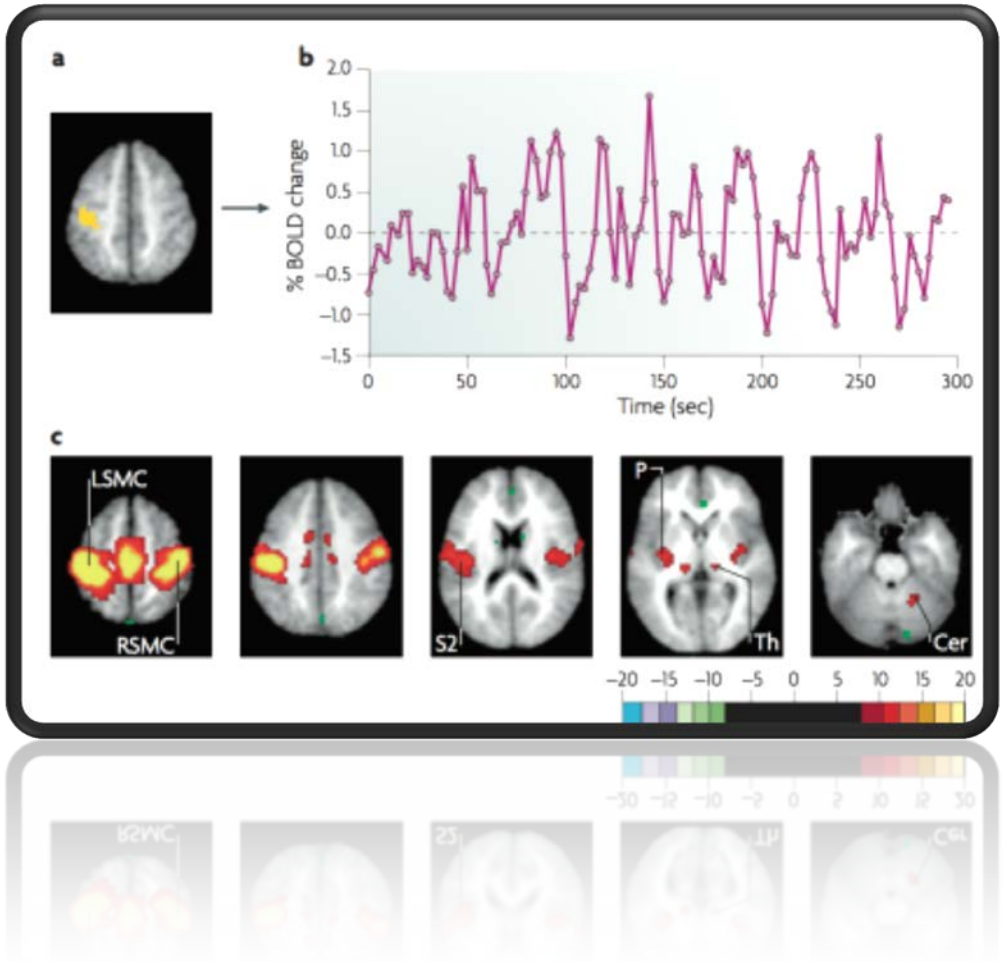
Blood Oxygen Level Dependent Signal

- Deoxygenated blood is paramagnetic and can distort surrounding magnetic field
- BOLD signal is inversely related to deoxygenated blood



Functional Connectivity

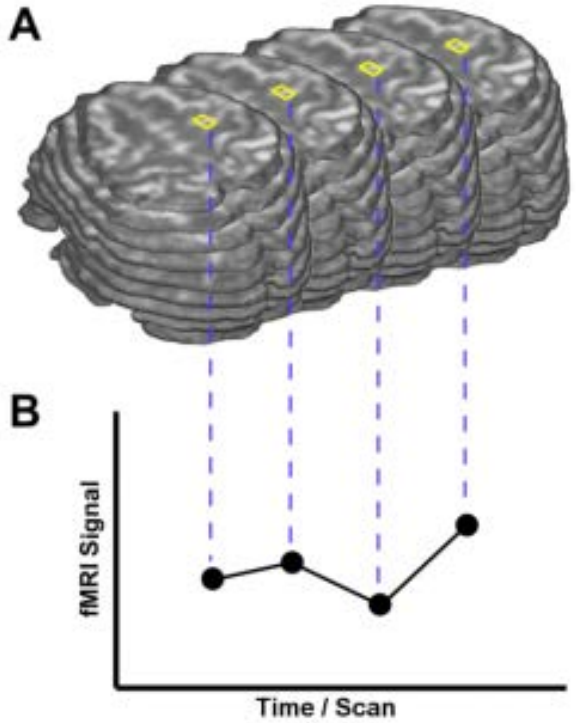
- Regions of the brain with the same BOLD time course thought to be activated together, thus, functionally linked[12]
- Low frequency BOLD (<0.1Hz) represents resting state or spontaneous neuronal activity



Fox and Raichle 2007 Nat Rev Neurosci

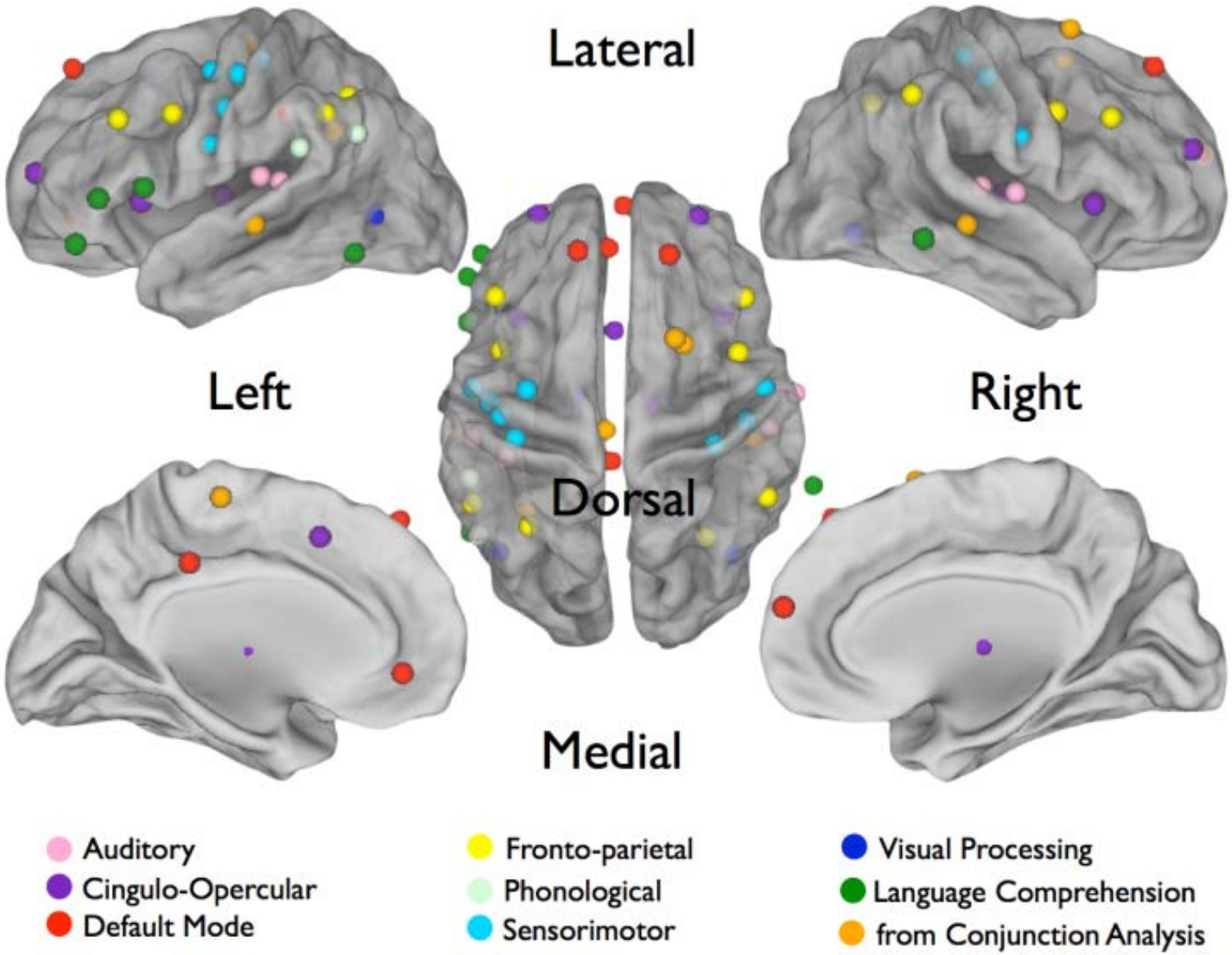
Interregional correlation analysis

- Resting state BOLD signal extracted from each ROI
- This time course correlated to time courses in each voxel of the brain (correlation seed map)
- The correlation seed map underwent Fischer transformation
- Z scores >3 ($p<0.001$) with cluster size greater than 459mm^3 (Monte Carlo simulation) used to determine statistical significance
- T-tests performed on Z-maps between controls and RUHL, LUHL and combined UHL



www.brainvoyager.com

Regions of Interest



Conclusions—fcMRI Studies

- Differences in multiple networks
  - Auditory regions—middle temporal gyrus
  - Executive function regions—inferior frontal gyrus
  - Sensorimotor regions—lips, tongue, speech
- Differences in several networks related to task-level control
  - rapid/adaptive control (fronto-parietal)
  - sustained/maintenance control (cingulo-opercular)

Tibbetts et al, 2011

Conclusions II—fcMRI Studies

- Some higher order cortical functions affected by UHL
  - Adaptive changes? There were findings to support functional changes that may show compensation for hearing loss, such as utilizing visual processes, as well as language and motor regions to increase mental rehearsal
  - Maladaptive changes? Decreased connectivity changes within executive control networks and aberrantly increased connectivity changes between anticorrelated networks
- May explain some educational and behavioral problems in children with UHL

Jung et al, Laryngoscope (in press)

Summary: Children with UHL

- High rate of speech therapy (approaching 50%)
- Language delays in infancy through adolescence, differences may widen
- Differences in verbal IQ differences do not disappear, may widen with increasing age

- Do children with UHL have permanent decrease in language and cognition (disability) or do they have slower acquisition (delay)?
- Can interventions mitigate or eliminate the consequences in children with UHL?

Acknowlegements

- Nancy Tye-Murray
- Jay Piccirillo
- Roanne Karzon
- Sandra Hale
- Lisa Davidson
- Brad Schlaggar
- Kristin Kullgren
- Kristi Kuhlman
- Pam Koprowski
- Nsangou Ghogomu
- Matt Jung
- Banan Ead
- Sarah Borton
- Stephanie Schutzenhofer
- Amy Streufert Umansky
- Lauren Wendorf Briggs
- Katherine Hoffarth
- Allison Soll
- Anita Calwas

Acknowledgements

- Funding from
  - NIH grants K23DC006638 and UL1RR024992
  - American Hearing Research Foundation
  - American Academy of Otolaryngology-Head and Neck Surgery Foundation
  - American Otological Society
- Support from the St. Louis Children's Foundation/Children's Surgical Services

Thank you!

Children's HOSPITAL • ST. LOUIS
BJC HealthCare

Washington University in St. Louis
SCHOOL OF MEDICINE