

Hearing Loss and Healthy Aging Impact on Cognition

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Disclosures

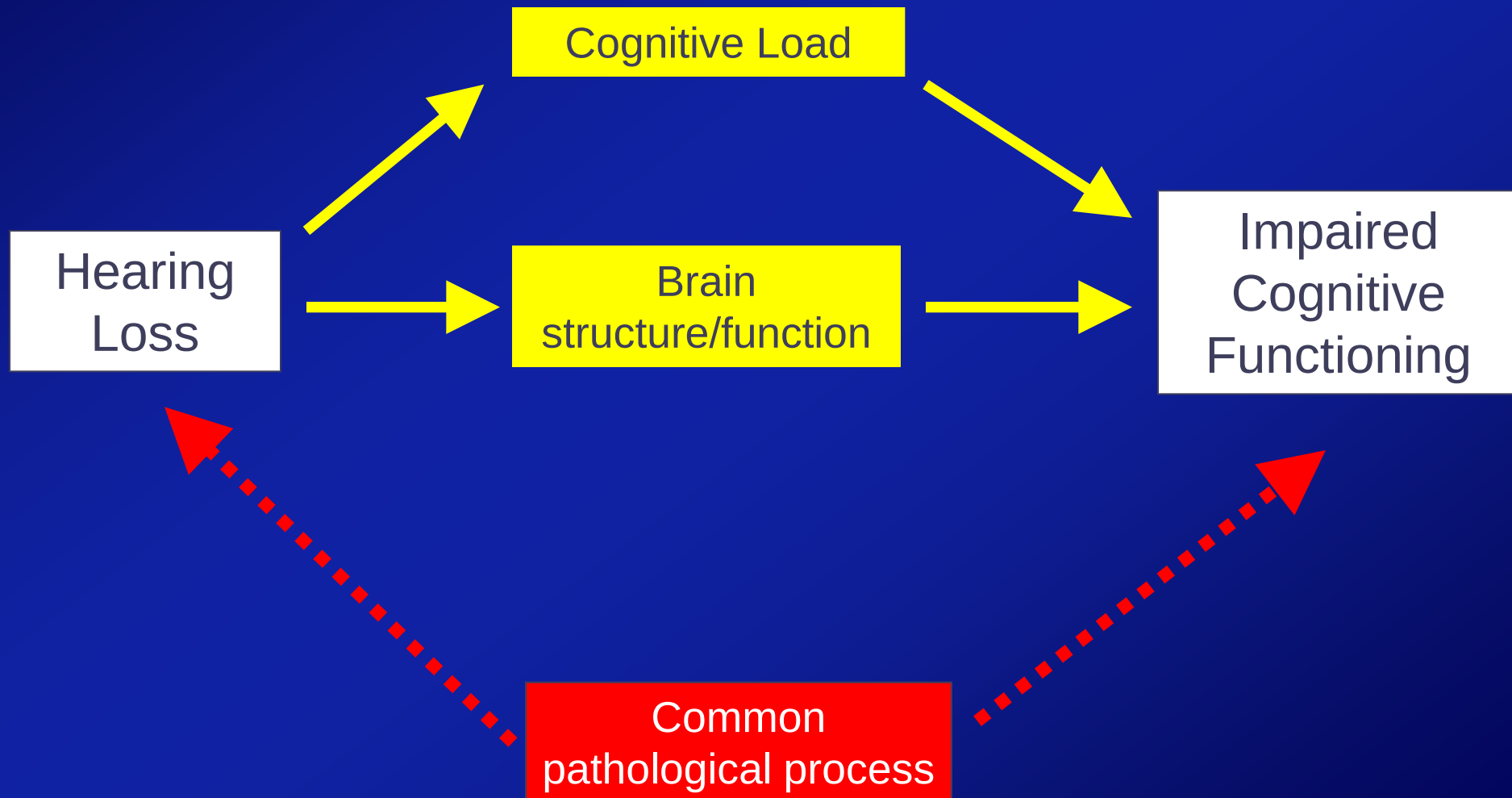
- Consultant agreements:
 - Agenebio
 - Eisai
 - Genentech
 - Janssen
 - Lilly
- Completed grants for imaging studies:
 - GlaxoSmithKline
 - Pfizer

Impact on Cognition

- Longitudinal studies showing an association between hearing loss and cognitive decline or incident dementia
- Cross-sectional studies showing an association between hearing loss and brain atrophy
- Hypothesis regarding link between hearing loss and cognitive decline
- Potential future directions for research

Hearing Loss & Cognition

Modifiable Risk Factor or *Common Cause*



Hearing Loss and Cognition

Relevant Studies

- Cross-sectional cognitive studies: Association of hearing loss and lower cognitive performance
- Longitudinal cognitive studies: Association of hearing loss and *declines* in cognitive performance AND diagnosis of *incident* dementia
- Cross-sectional imaging studies: Association of hearing loss and increased brain atrophy
- Longitudinal imaging studies: Association of hearing loss and declines in brain volume

Hearing Loss and Cognition

Relevant Studies

- Longitudinal cognitive studies, using pure tone audiometry to assess hearing:
 - Cognitive decline: Uhlmann et al., 1989; Lin et al., 2013
 - Incident dementia: Lin et al., 2011; Gallacher et al., 2012
- Cross-sectional and Longitudinal imaging studies, using pure tone audiometry to assess hearing:
 - Differences in brain volume in auditory cortices: Peele et al., 2010
 - Decline in whole brain and regional volumes: Lin et al., in press

Hearing Loss

Cognitive Decline / Incident Dementia

- **Health ABC: Health, Aging & Body Composition**
 - Prospective population-based study of ~3,000 adults 70 yrs and older
- **BLSA: Baltimore Longitudinal Study of Aging**
 - Prospective study of older adults, initiated in 1958, clinical diagnoses of adults 70 yrs and older since 1989

Hearing Loss & Cognition

Health ABC

- **Digit Symbol Substitution test (DSS)**
 - Psychomotor Speed
 - Set-Shifting (executive function)
 - Incidental Memory
 - Attention

Health ABC

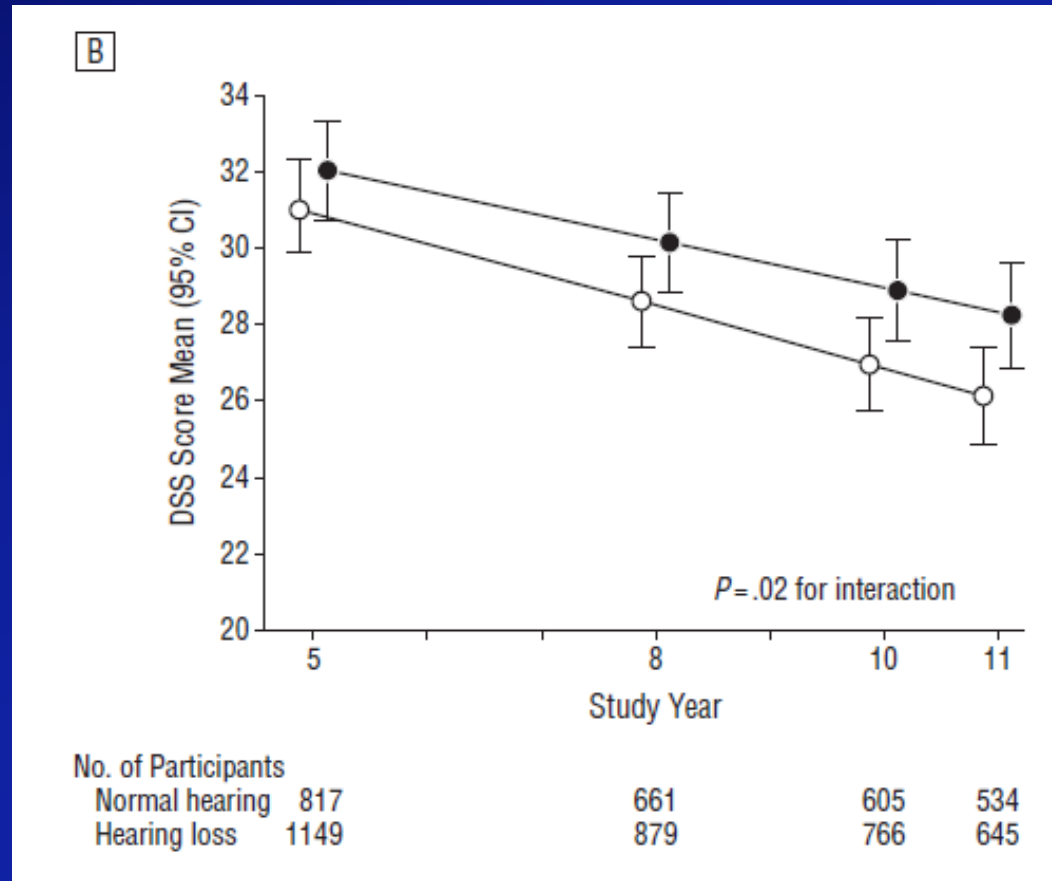
Digit Symbol Substitution Test (DSS)

1	2	3	4	5	6	7	8	9
$\vee$	$\sqsubset$	$\div$	$\wedge$	$\times$	$\lrcorner$	$\sqsubset$	$\vdash$	$\sqsubset$

[illegible][illegible][illegible][illegible]

Hearing Loss & Cognition

Adjusted **DSS** scores by years of follow-up and hearing loss status in 1,966 adults > 70 years followed for 6 years



**32% greater
rate of
cognitive
decline in DSS
scores in
HL vs. NH in
Health ABC**

Adjusted for age, sex, race, education, study site, smoking status, hypertension, diabetes, and stroke history

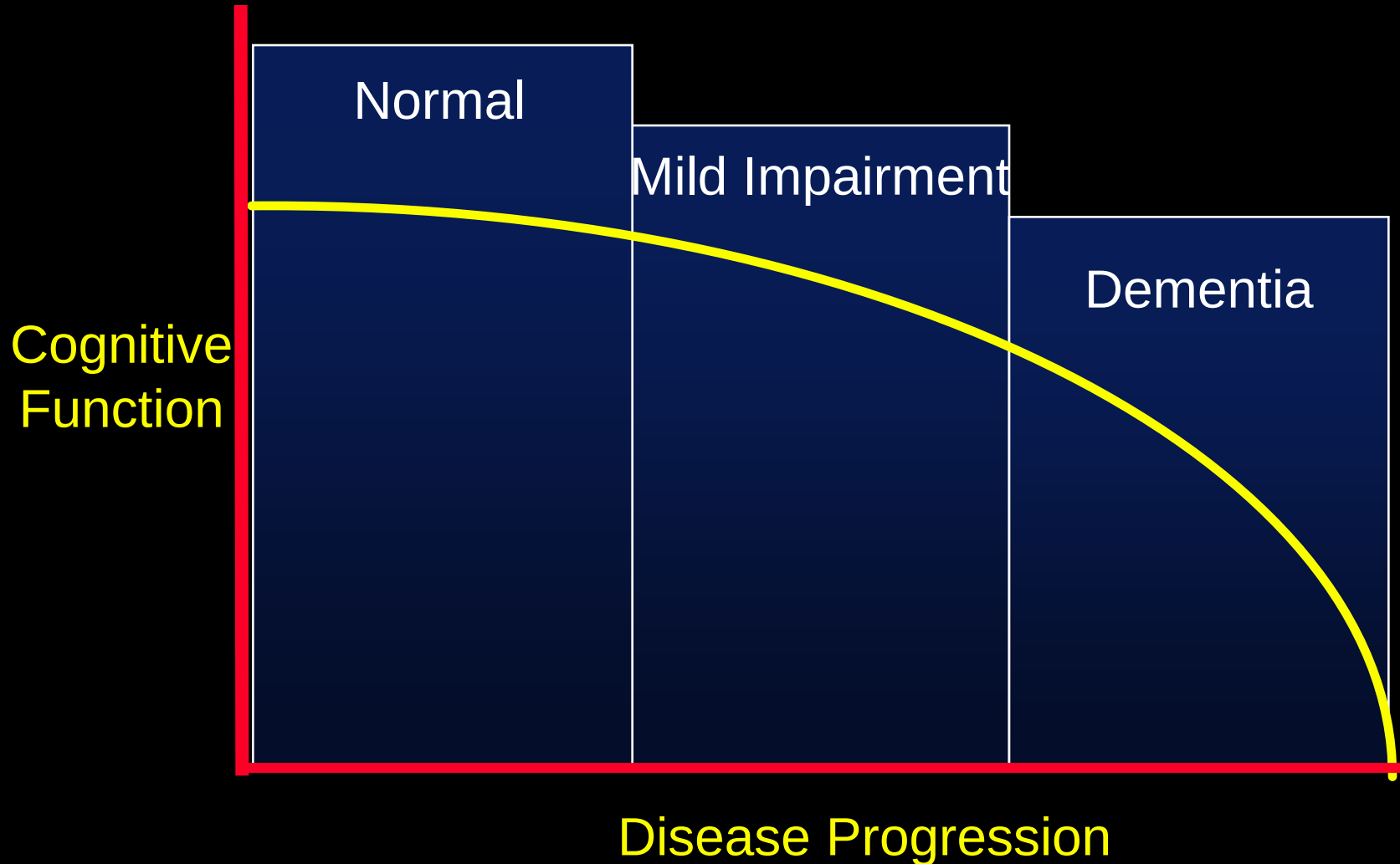
Lin et al. JAMA Int Med. 2013

Hearing Loss & Incident Dementia

Dementia Syndrome

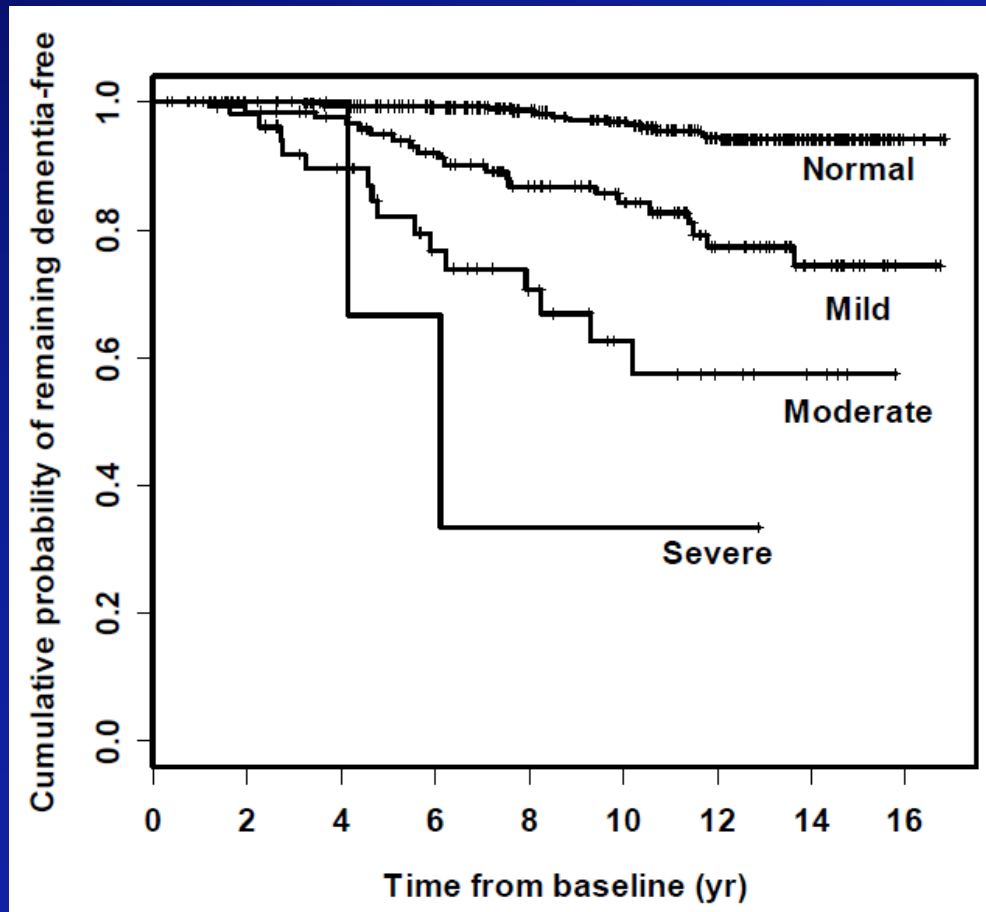
- Progressive decline in mental abilities to the point where an individual can no longer maintain their independent function without assistance
 - Must be a decline from a previous higher level
 - Impairs two or more domains of cognition (e.g., memory and language)

Progression of Cognitive Decline



Hearing Loss & Incident Dementia

Dementia incidence in 639 adults followed for >10 years by
BLSA



**Risk of incident all-cause dementia
(compared to normal hearing)^a**

	<u>HR</u>	<u>95% CI</u>	<u>p</u>
Mild	1.89	1.00 – 3.58	0.05
Moderate	3.00	1.43 – 6.30	.004
Severe	4.94	1.09 – 22.4	.04

^a Adjusted for age, sex, race, education, DM, smoking, & hypertension

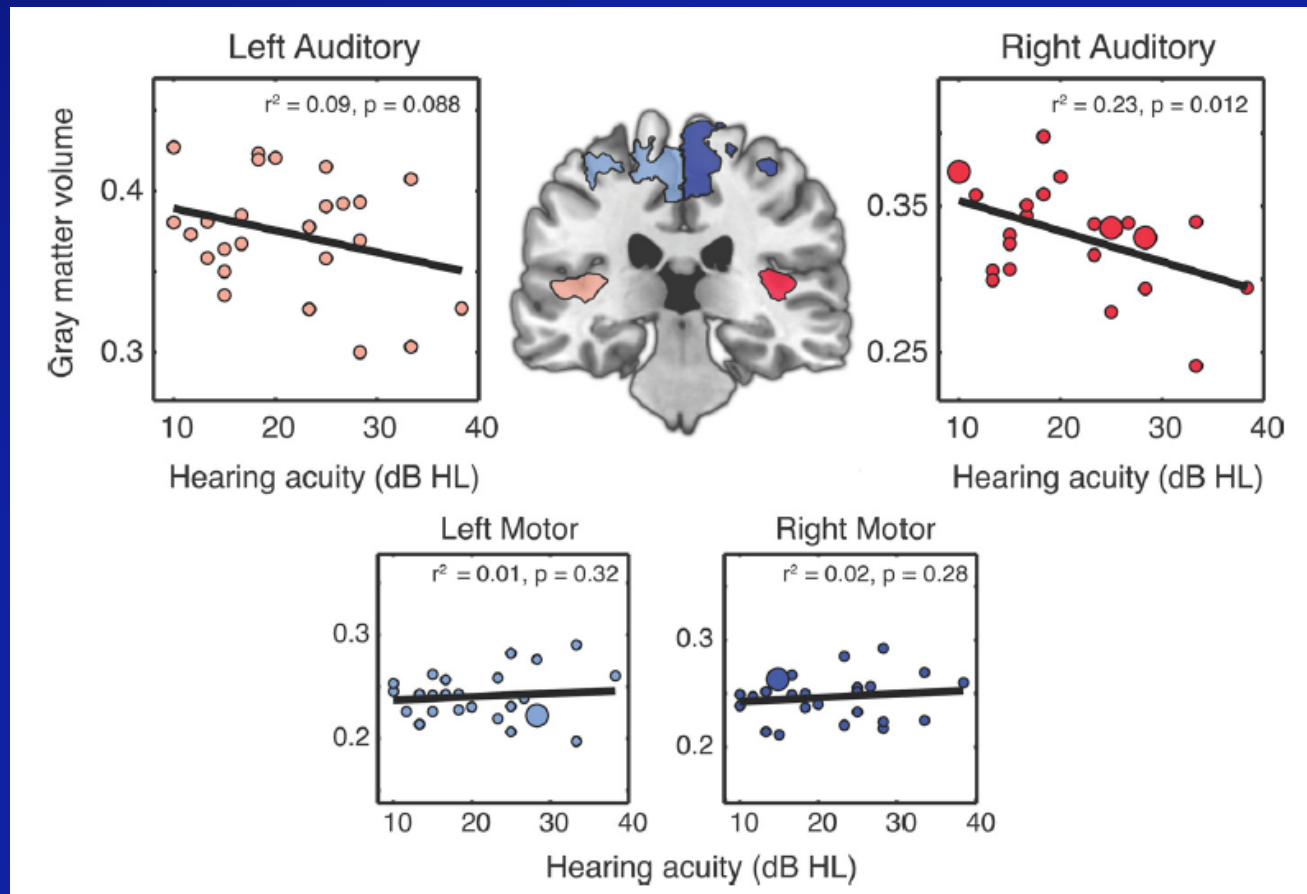
Hearing Loss & Incident Dementia

Additional Sensitivity Analyses

- The results obtained are robust to:
 - Restricting the analytical cohort to participants ≥ 65 years at baseline
 - Using age as the time scale in Cox PHM
 - Excluding participants with a prior hx of stroke or TIA at baseline (n = 19)
 - Censoring participants who developed dementia within a 2, 4, or 6 year washout period from baseline

Hearing Loss & Brain Structure

Poorer hearing is associated with reduced gray matter in the auditory cortices



Hearing Loss & Decline in Global Brain Volume

BLSA

- **Hypothesis:** Hearing loss is associated with accelerated atrophy in the superior, middle, and inferior temporal gyri with potential impact on other regions more globally
- 126 participants (56-86 years) in the neuroimaging substudy of the BLSA
 - 75 with normal hearing (NH) and 51 with hearing loss (HL)
 - Mean follow-up duration of 6.4 years

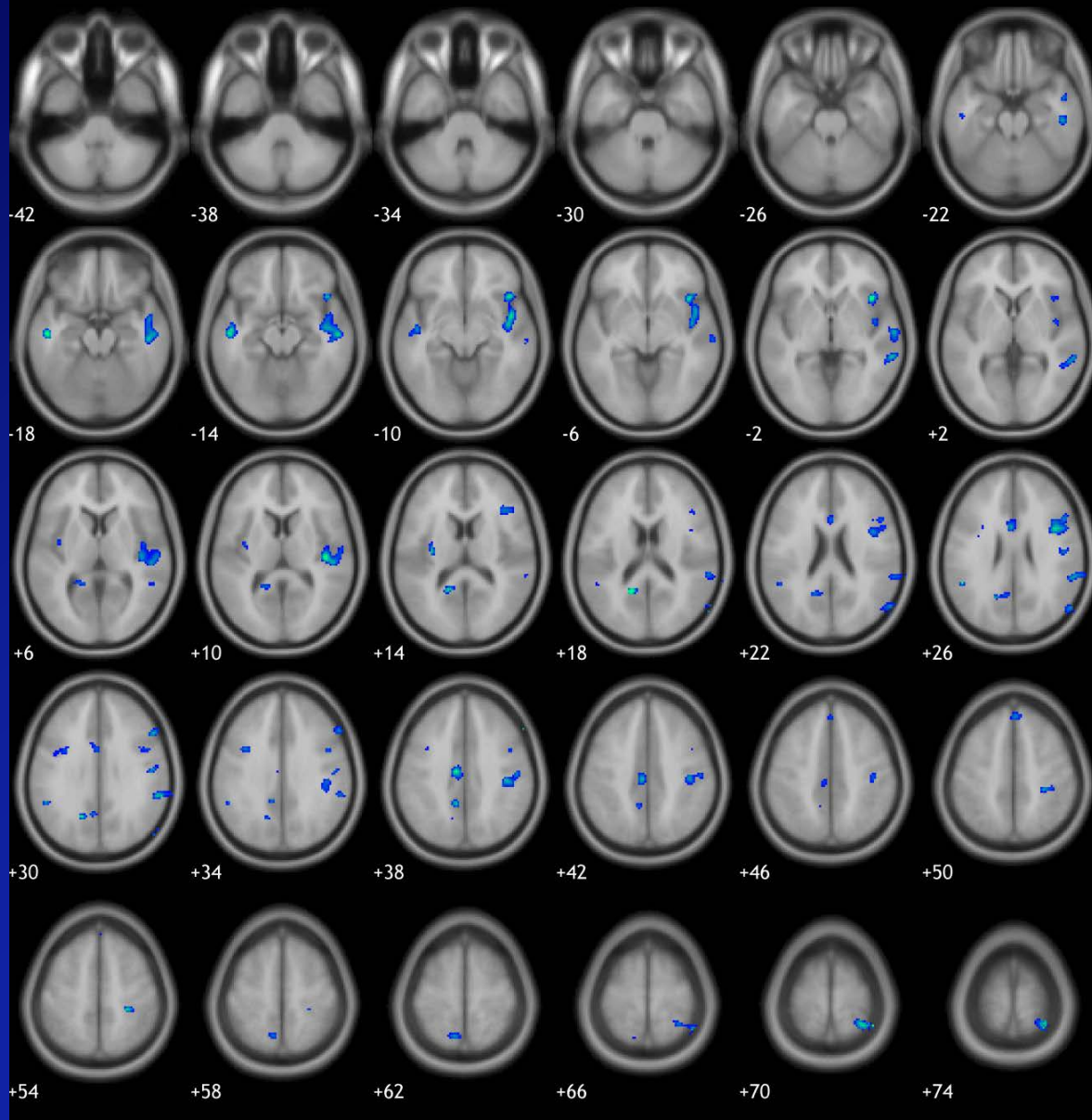
	Normal Hearing mean (SE)	Hearing Loss, mean (SE)	Difference mean (SE)
Global measures			
Whole brain	-7.21 (0.27)**	-8.33 (0.36)**	-1.13 (0.45) ⁺ p = .015
vCSF	1.30 (0.10)**	1.28 (0.14)**	-0.020 (0.18)
White matter	-4.14 (0.31)**	-4.99 (0.39)**	-0.85 (0.39) ⁺ p = .031
Gray matter	-2.63 (0.22)**	-3.38 (0.28)**	-0.76 (0.36) ⁺ p = .036
Lobar measures			
<i>Gray matter</i>			
Frontal	-0.96 (0.11)**	-1.11 (0.14)**	-0.16 (0.14)
Temporal	-0.46 (0.096)**	-0.71 (0.12)**	-0.25 (0.12) ⁺ p = .036
Parietal	-0.71 (0.051)**	-0.74 (0.066)**	-0.044 (0.081)
Occipital	-0.54 (0.057)**	-0.50 (0.073)**	0.047(0.071)
Regional Volumes			
Superior temporal gyrus	-0.20 (0.023)**	-0.31 (0.030)**	-0.11 (0.038) ⁺ p = .0046
Middle temporal gyrus	-0.15 (0.033)**	-0.30 (0.042)**	-0.15 (0.054) ⁺ p = .0065
Inferior temporal gyrus	-0.048 (0.015) ⁺	-0.12 (0.020)**	-0.067 (0.025) ⁺ p = .0093
Hippocampus	-0.019 (0.0051)**	-0.031 (0.0065)**	-0.012 (0.0082)

Estimated Annual Rates of Change in Brain Volume (cm³/year)

+ < .05; * < .01; ** < .001

Lin et al., in press

HEARING LOSS x INTERVAL ON RAVENS GM
(Hearing Loss Interval > No Hearing Loss Interval)
T contrast, $p < .005$, cluster correction ≥ 50



Voxel-Based Analyses

Difference in
mean gray
matter volume
change in those
with HL vs. NH
 $R > L$



Greater decline in
brain volume in
HL vs. NH

General Conclusions

- Longitudinal Cognitive Studies:
 - Hearing loss is associated with declines in cognitive performance over time
 - Hearing loss is associated with incident dementia
- Longitudinal Imaging studies:
 - Hearing loss is associated with increased rate of brain atrophy over time (whole brain atrophy as well as focal changes in brain regions associated with hearing)

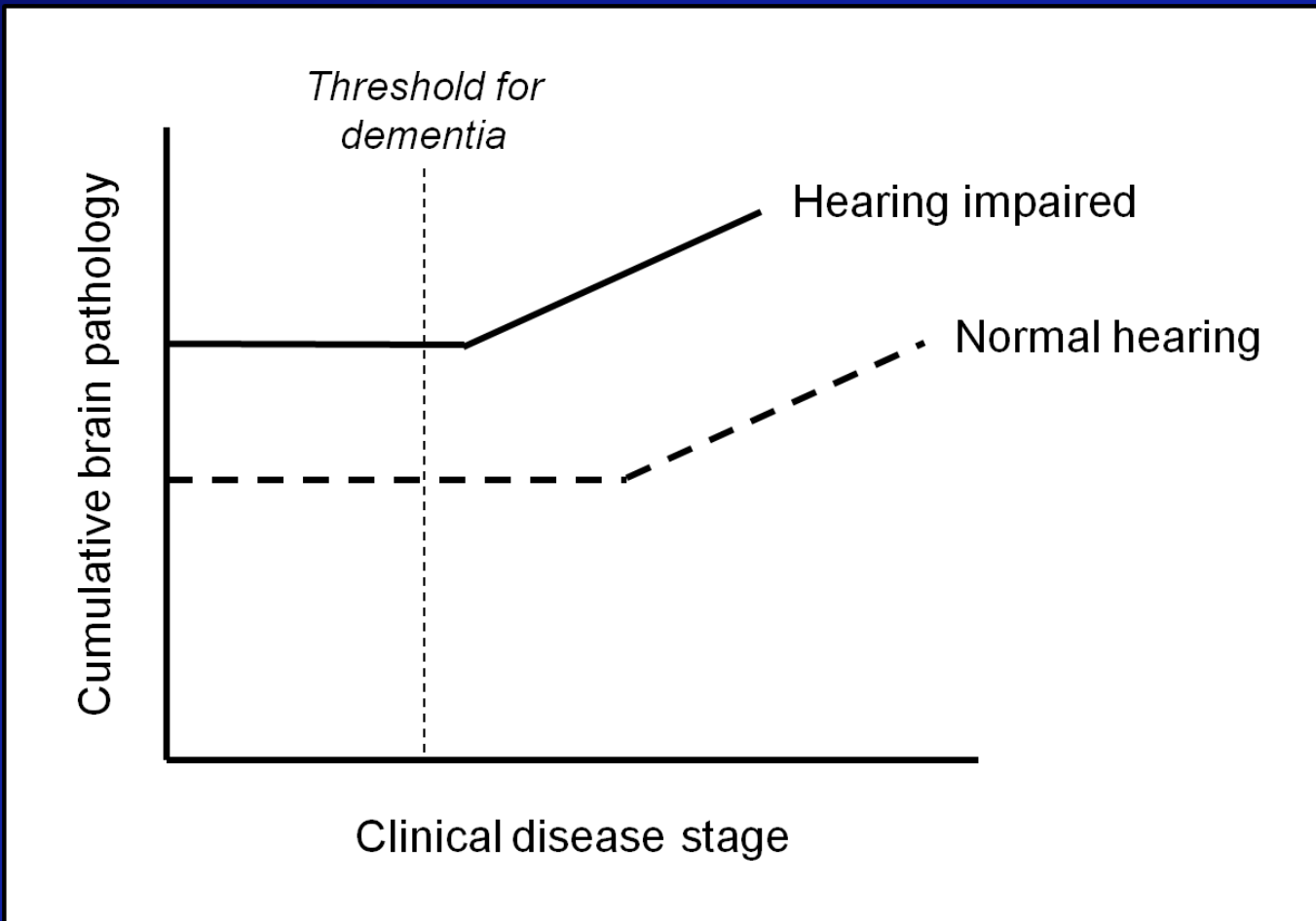
Hypothesis: Hearing Loss and Cognition

Double-Hit Theory

- Hearing loss is associated with increased brain atrophy
- In those with progressive accumulations of brain pathology (due to other causes, such as AD or microvascular disease), two pathological processes are superimposed on one another
- Two pathological processes combined:
 - Contribute to declines in cognition
 - Contribute to crossing 'threshold' for dementia at an earlier point in time

Theoretical Model – Double Hit

Potential Impact of Pathological Changes on Cognitive Decline



Future Directions

- Conduct a randomized controlled trial (randomized treatment: implementation of hearing aids in those with hearing loss)
- Outcomes to examine:
 - Cognitive performance
 - Clinical diagnoses to identify those with MCI and dementia
 - MRIs to assess brain structure
 - Measures of social engagement and QoL

