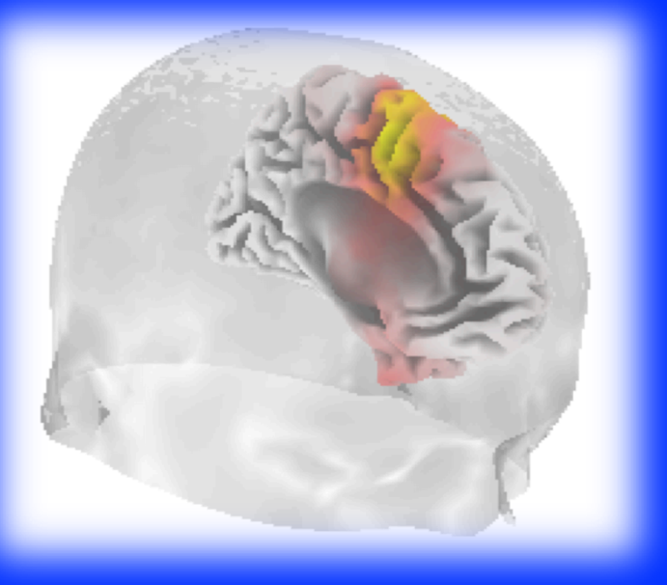
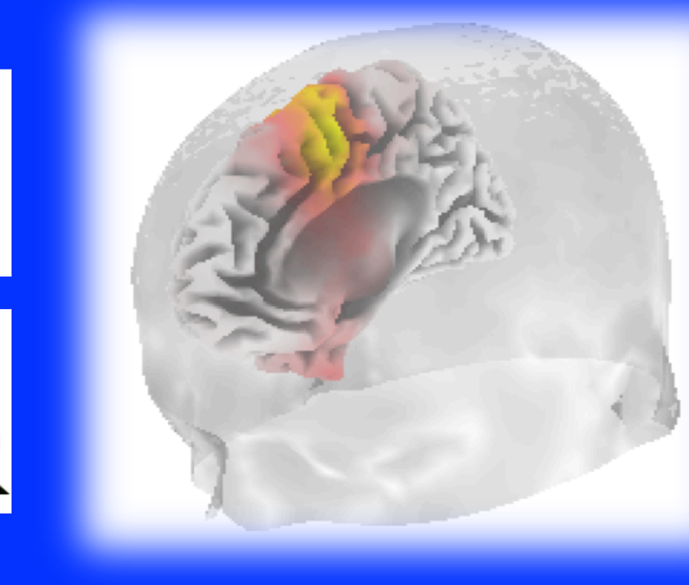


Sitting Height: An Adult Correlate of Physical and Neurocognitive Growth Dysregulation by Early Childhood Adverse Events



R·I·T NATIONAL TECHNICAL INSTITUTE FOR THE DEAF

Vincent J Samar[a,c] Sidney J Segalowitz[b] James Desjardins[b] Steven Barnett[c] Erika Sutter[c]

[a]National Technical Institute for the Deaf (NTID) Rochester Institute of Technology (RIT)

[b]Psychology Department and Centre for Lifespan Development Research, Brock University

[c]National Center for Deaf Health Research (NCDHR) University of Rochester

This research was partly supported by Cooperative Agreements U48 DP000031, U48 DP001910, and U48 DP005026 from Centers for Disease Control and Prevention (CDC). The contents of this poster are solely the responsibility of the authors and do not necessarily represent the official views of CDC.

SUMMARY

Low childhood socioeconomic status (L-CSES) exposes fetuses and children to early adverse events (EAEs), such as intrauterine growth restriction, infections, and toxicities. EAEs dysregulate metabolic growth pathways and energy metabolism, and cause deafness, especially in developing countries. EAEs cause childhood and adult obesity and poor adult physical and mental health outcomes. No simple adult biomarker of exposure to growth-dysregulating EAEs has been identified. We report four studies that suggest that sitting height reflects early-life growth dysregulation by adverse events in populations at risk for, or exposed to, EAEs (e.g., L-CSES populations). We show that adult sitting height is correlated with adult weight dysregulation and neurocognitive dysfunction of the frontal-lobe self-regulation network within L-CSES groups and groups who report EAEs. Sitting height may be a useful adult biomarker for future research on adult physical and mental health consequences of early exposure to adverse events in at-risk populations in developed and developing nations.

INTRODUCTION

- **Early Adverse Events (EAEs)**
  - Examples: malnutrition, illness, infection, toxicities, pregnancy complications, social deprivation, chronic stress.[1,2]
  - EAEs follow a social gradient: Low childhood socioeconomic status (L-CSES) increases risk of exposure to EAEs.[3]
  - EAEs are known to restrict and dysregulate body and brain growth, and energy metabolism.[1,2,4]
    - EAEs are therefore major risk factors for poor childhood and adult physical and mental health outcomes.
      - Examples: obesity, metabolic syndrome, diabetes, cardiovascular disease, cancer, lowered IQ, depression[5]
      - EAEs also often cause early childhood deafness.[6]
  - No simple anthropometric adult biomarker of the impact of EAEs on an individual's childhood and adult health exists, but height and its components have been proposed as possible biomarkers.[7]

HYPOTHESIS

- *Since height is largely established by early adulthood, adult height or a height component is a useful biomarker for exposure to EAEs specifically in populations at high risk for EAEs, but not in populations at low risk for EAEs*
  - *Test implications:*
    - *Adult height or a component will positively correlate with BMI in L-CSES groups or groups with EAE histories.*
    - *Adult height and its components will be uncorrelated or negatively correlated with BMI in H-CSES groups or groups with no history of EAEs.*

RATIONALE

- EAEs initially inhibit early-life body and brain growth (stunting)[8]
- Transient EAEs metabolically program catch-up growth, a compensatory increase in growth velocity following an EAE.[8]
  - More severe growth inhibition results in a greater amount of catch-up growth in height, weight, etc.[9,10]
- **Intrapopulation Variation in Height (H), Leg Length (LL), Sitting Height (SH)**
  - High CSES (H-CSES) populations: EAE rates are typically low, so height variation is largely determined by genetics.
  - L-CSES populations: EAE rates are high, so height variation is strongly affected by age of occurrence of EAE, EAE severity, EAE type, and opportunity for catch-up growth, in addition to genetics.
    - EAEs differentially and independently affect leg length and sitting height.[11,12]
      - Leg length: Sensitive to environmental factors and diet, especially during infancy
      - Sitting height: Sensitive to environmental factors, illness, stress after infancy and before puberty
- **Intrapopulation Variation in Weight (W), BMI**
  - H-CSES populations: EAE rates are low, so weight variation is strongly determined by genetics, diet, and exercise.
    - Weight is roughly proportional to Height^2, making BMI (W/H^2) theoretically independent of height.
    - Population studies confirm that height (hence its components) is uncorrelated or negatively correlated with BMI[13]
  - L-CSES populations: EAE rates are high, so an affected individual's weight is often additionally determined by dysregulated energy metabolism due to catch-up growth, which adds substantially to population variation in weight.
    - Under catch-up growth, weight grows disproportionately faster than height due to accelerated accumulation of fat mass ("preferential catch-up fat")[3] to an extent that depends on EAE severity.[9,10]
      - Hence BMI is expected to positively correlate with height specifically in populations at high risk for EAEs.

RESEARCH APPROACH

- Determine if adult height or a height component positively correlates with BMI only in L-CSES groups. If so, that length measure is a candidate for an adult biomarker of the severity of early growth dysregulation by EAEs.
- Validate a candidate height-related biomarker against an independent measure of functional variation in a body system known to be susceptible to dysregulation by EAEs during childhood.
  - The brain's mediofrontal self-regulation network (MSRN) is dysregulated in children at risk for EAEs.[4]
  - Impaired MSRN function during a behavioral response inhibition task can be studied with EEG measures.
- Show evidence that EAEs specifically explain the correlation of a candidate biomarker with BMI within L-CSES groups
- Include deaf and hearing participants to achieve a high sampling rate for individuals with a history of EAEs

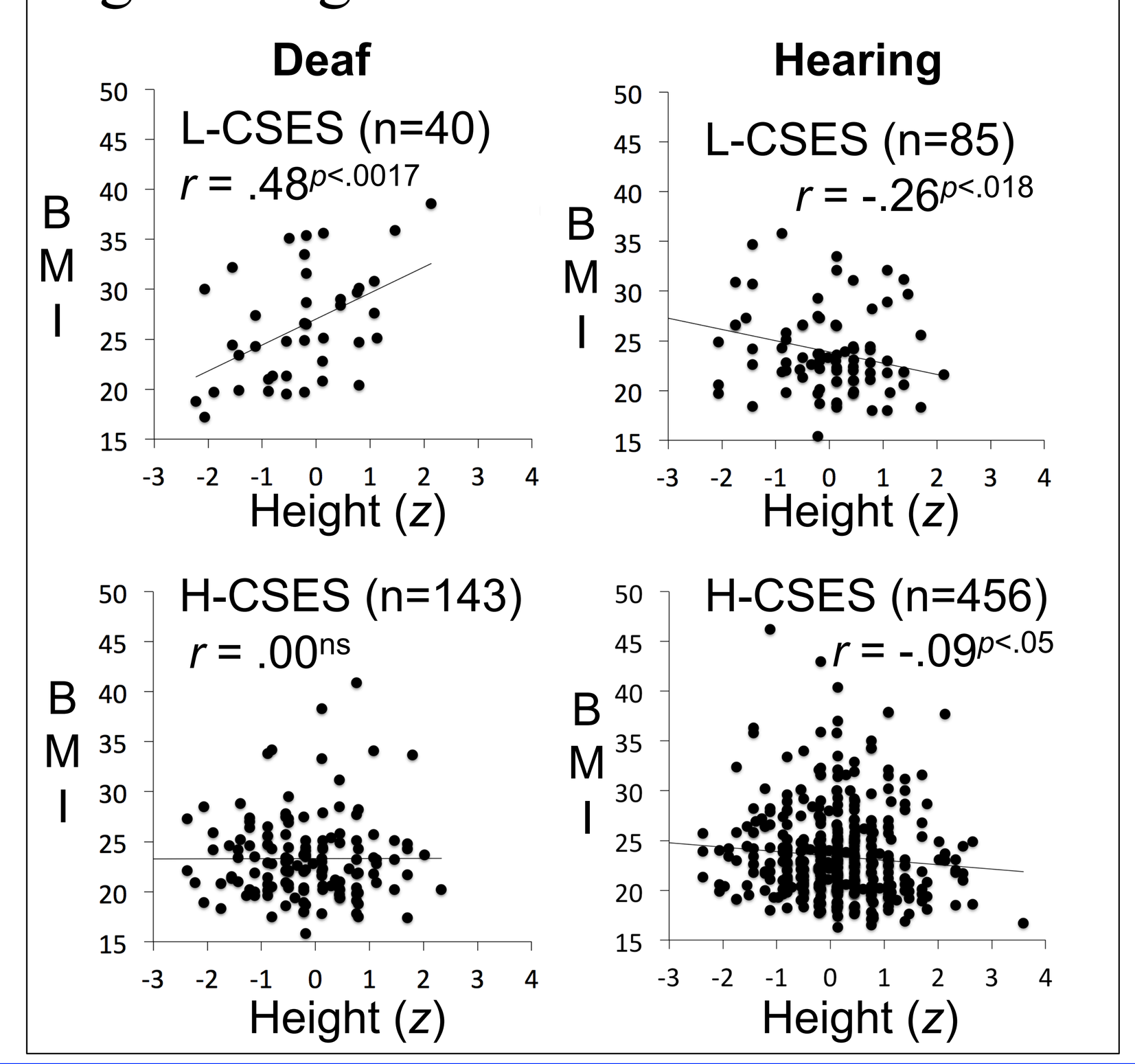
STUDY 1

- **Purpose**: Test the hypothesis using self-reported height & weight in deaf and hearing young adults.
- **Participants** (NTID and RIT students)
  - 198 Deaf (mean/sd age of onset, 2.6/3.1) & 573 hearing freshman
    - mean (SD) age = 18.2 (0.9); 78.8 white/non-Hispanic; 65% male
- **Measures** (data from anonymous self-report written English NCDHR 2008 College Health Survey[14])
  - SES (Parent Education): L-CSES: high school or less, 17.4%; H-CSES: college or more, 82.6%
  - Self Report: Height (H) – z-scores calculated within gender; weight (W); calculated BMI (W/H^2)
- **Results**
  - Deaf
    - L-CSES: Height positively correlated with BMI
    - H-CSES: Height did not correlate with BMI
  - Hearing
    - L-CSES: Height negatively correlated with BMI
    - H-CSES: Height negatively correlated with BMI

Discussion

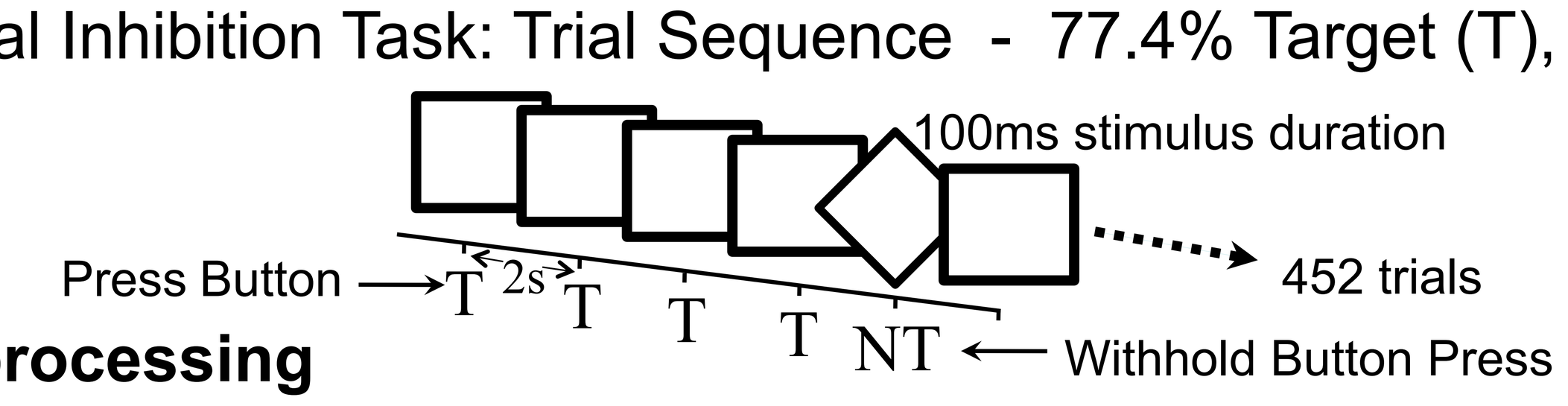
- Results from deaf group supported the hypothesis.
- Results from hearing group did not support the hypothesis.
- Possible explanations for this discrepancy to explore:
  - A college-going hearing L-CSES group may have lower or less severe EAE rates than their deaf college peers.
  - Total height may be a less reliable or specific measure than a height component (leg length or sitting height).

Fig 1. Height vs. BMI.



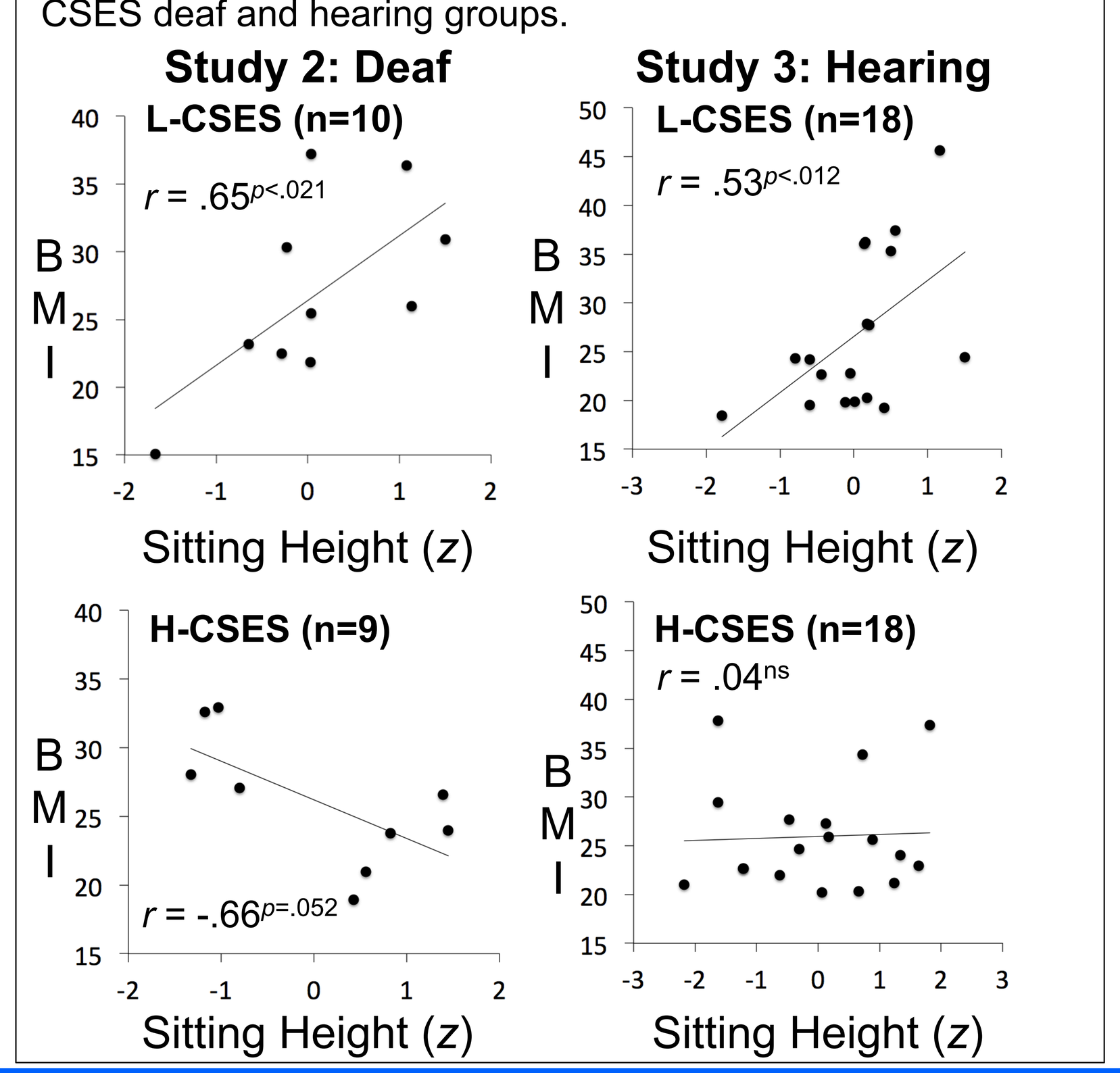
STUDIES 2 & 3

- **Purpose:** Test hypothesis with objective length and weight measures from deaf and hearing adults; Determine if height, LL, or SH correlate with EEG measures of self-regulation network function in low CSES groups
- **Participants (NTID and RIT students)**
  - Study 2: 19 Deaf (<3.5y onset), mean (sd) age: 26.4(6.2); white/non-Hispanic: 78.9%; male; 36.8%
  - Study 3: 36 Hearing, age (mean, SD): 20.9 (2.9); white/non-Hispanic: 63.9%; male; 47.2%
- **Measures**
  - SES: Median sample split - determined by composite of parents education and occupation
  - Height (*H*), Sitting height (SH), leg length (LL) – z-scores within gender; weight (*W*); BMI (W/H^2)
  - EAE History: Questions probed prenatal and childhood illness, trauma, cause of deafness
  - Go/NoGo Behavioral Inhibition Task: Trial Sequence - 77.4% Target (T), 22.6% Non-Target (NT)



- **ERP Recording/Preprocessing**
  - 64 channel EEG, avg. reference, 500hz sampling; vertical & horizontal eye leads; 1-40hz filter
  - Independent Components Analysis removed EKG/EOG/EMG yielding two MSRN measures: NoGo minus Go spectral activation surfaces (Fig. 3a) and N2-P3 amplitude (Fig. 3b)

Fig. 2. Taller SH is associated with greater BMI only in L-CSES deaf and hearing groups.



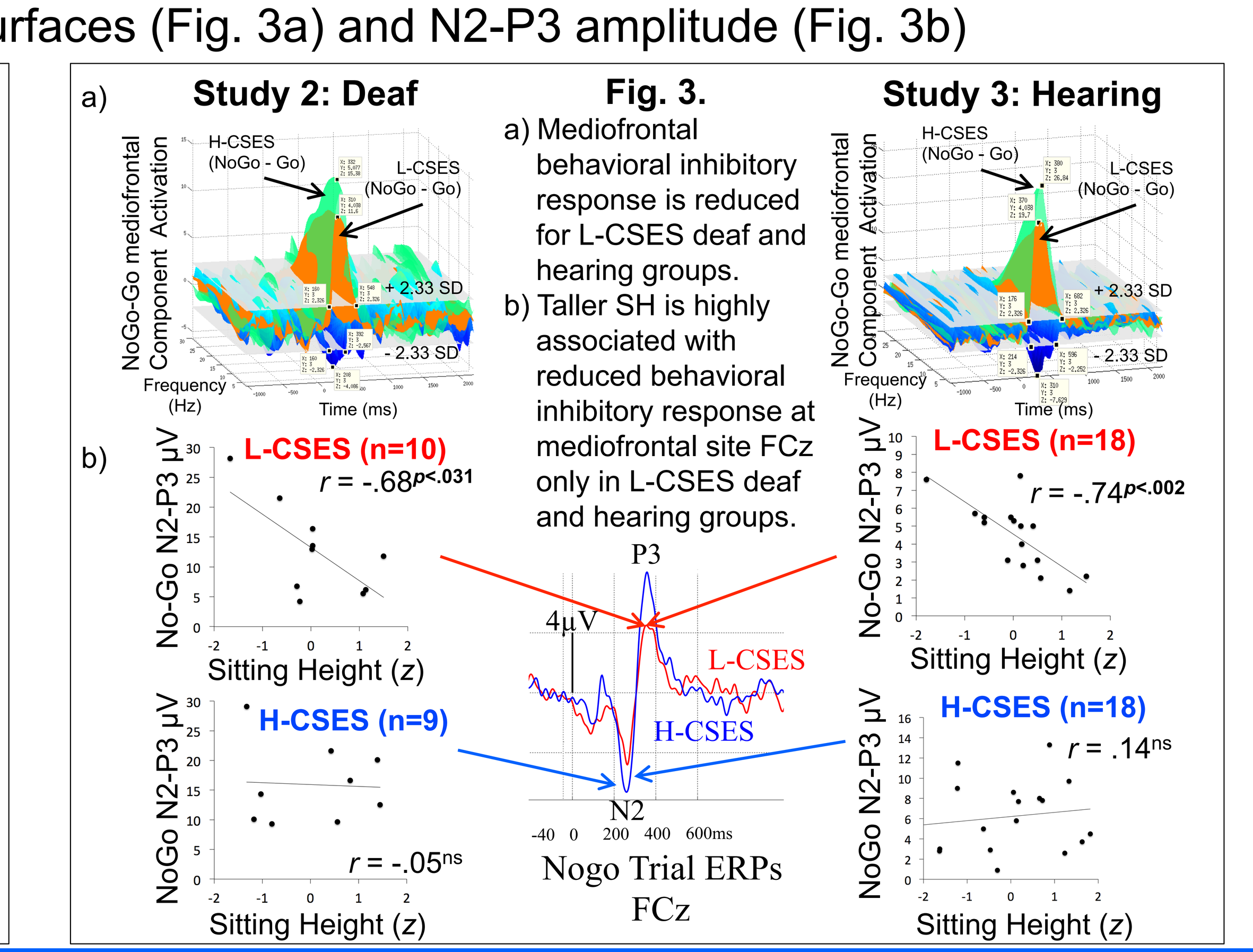


Fig. 3. a) Mediofrontal behavioral inhibitory response is reduced for L-CSES deaf and hearing groups. b) Taller SH is highly associated with reduced behavioral inhibitory response at mediofrontal site FCz only in L-CSES deaf and hearing groups.

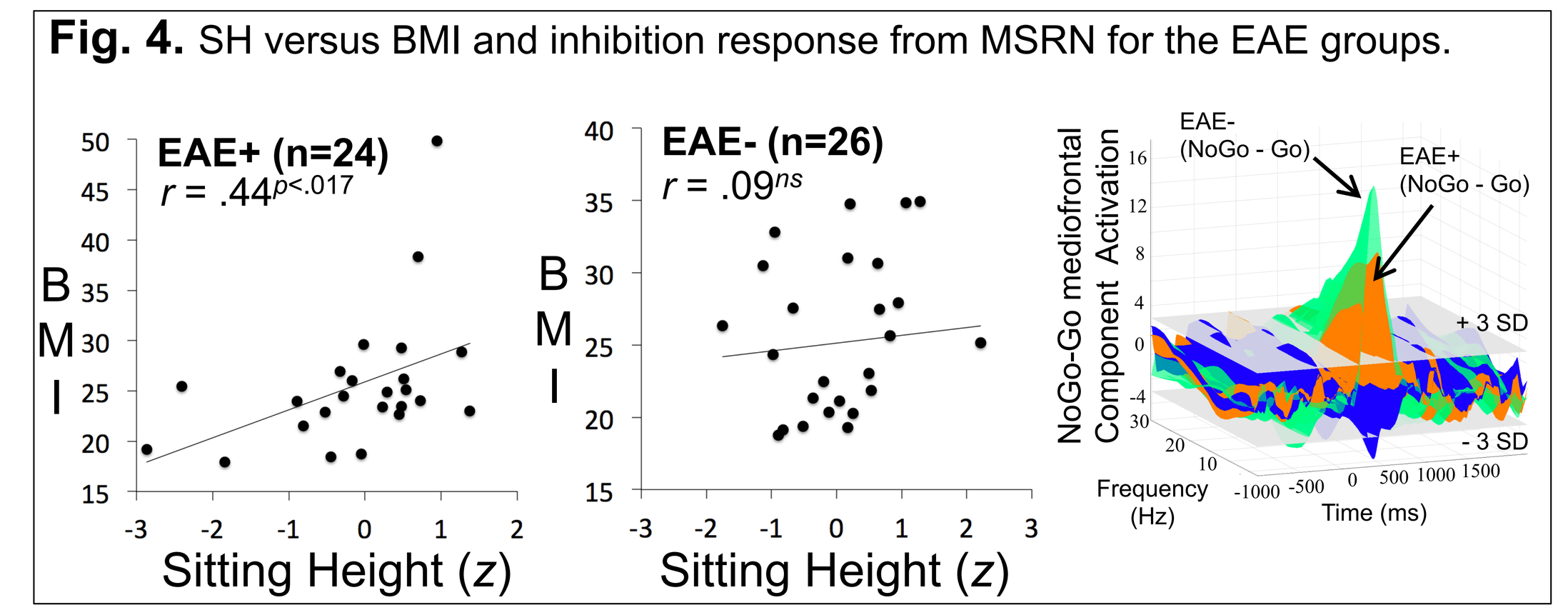
STUDIES 2 & 3

- **Results**
  - Body Measures
    - Height & LL were uncorrelated with BMI
    - L-CSES: SH positively correlated with BMI
    - H-CSES: SH did not correlate with BMI
  - Neurocognitive Measures
    - L-CSES
      - Impaired inhibitory response from MSRN
      - Taller SH correlated with greater impairment
    - H-SES: SH did not correlate with MSRN function
  - Reported EAE rates
    - Deaf (68.4%) Hearing (30.6%)
- **Discussion**
  - Studies 2 and 3 support the hypothesis that SH is a biomarker for early growth dysregulation in L-CSES groups .

STUDY 4

- **Purpose**: Confirm that a group with self-reported EAEs (EAE+) shows the SH-BMI correlation but not a group without self-reported EAEs (EAE-), approximately balanced across CSES groups.
- **Participants** (NTID students)
  - 50 Deaf (age onset <5y) mean (SD) age = 22.8 (6.1); 74% white/non-Hispanic; 52% male
    - 24 EAE+ (L-CSES, 10; H-CSES, 14)
    - 26 EAE- (L-CSES, 15, H-CSES, 11)
- **Measures**: Same as Studies 2 & 3
- **Results**

Fig. 4. SH versus BMI and inhibition response from MSRN for the EAE groups.



  - Body Measures
    - Height & LL were uncorrelated with BMI.
    - Comparing EAE groups (SES approx. balanced)
      - EAE+ : SH positively correlated with BMI.
      - EAE- : SH did not correlate with BMI.
  - Neurocognitive Measures
    - EAE+ showed impaired activation of MSRN
  - Comparing SES groups (EAE approx. balanced)
    - No L-CSES SH-BMI positive correlation or MSRN response inhibition effects occurred.
- **Discussion**
  - EAEs can account for L-SES group height/SH-BMI correlations and MSRN impairment in Studies 1-3.

Conclusion

- Adult sitting height standardized within gender is a potential biomarker for early body and brain growth dysregulation in populations at risk for EAEs.

REFERENCES

1. Barker, D.J., Osmond, C., Forsen, T.J., Kajantie, E., & Eriksson, J.G. (2005). Trajectories of growth among children who have coronary events as adults. *The New England Journal of Medicine, 353,* 1802–1809.
2. Dulloo, A.G. (2009). Adipose tissue plasticity in catch-up–growth trajectories to metabolic syndrome: Hyperplastic versus hypertrophic catch-up fat. *Diabetes 58*, 1037-1039.
3. WHO (2010). *Environment and health risks: A review of the influence and effects of social inequalities*, World Health Organization
4. Hackman, D.A., Farah, M.J., Meaney, M.J., (2010). Socioeconomic status and the brain: mechanistic insights from human and animal research. National Rev. of Neuroscience, 11, 651–659.
5. Marmot, M., & Wilkinson, R. (Eds.). (2009). *Social determinants of health*. Oxford University Press.
6. Braga, M. C., & Otto, P.A. (2004). Recurrence risks for isolated cases of non-syndromic deafness. *Genetics and Molecular Biology, 27, 2,* 154-161.
7. Gunnell, D. (2002). Commentary: Can adult anthropometry be used as a 'biomarker' for prenatal and childhood exposures? *International Journal of Epidemiology, 31*, 390-394.
8. Romano, T., Wark, J.D., Owens, J.A., Wlodek, M.A. (2009). Prenatal growth restriction and postnatal growth restriction followed by accelerated growth independently program reduced bone growth and strength, *Bone, 45*, 132-141.
9. Miller, B.S., Kroupina, M.G., Mason, P., Iverson, S.L., Narad, C., Himes, J.H., Johnson, D.E., Petryk, A. (2010). Determinants of catch-up growth in international adoptees from Eastern Europe, *International Journal of Pediatric Endocrinology* 2010:107252.
10. Johnson, D.E., Guthrie, D., Smyke, A.T., Koga, S.F., Fox, N.A., Zeanah, C.H., Nelson C.A., (2010). Growth and associations between auxology, caregiving environment, and cognition in socially deprived Romanian children randomized to foster vs ongoing institutional care, *Archives of Pediatric Adolescent Medicine, 164*, 507-516.
11. Gigante, D.P., Nazmi, A., Lima, R.C., Barros, F.C., Victora, C.G. (2009). Epidemiology of early and late growth in height, leg and trunk length: findings from a birth cohort of Brazilian males, *European Journal of Clinical Nutrition, 63*, 375-381.
12. Wadsworth, M.E.J., Hardy, R.J., Paul, A.A., Marshall, S.F., & Cole, T.J. (2002). Leg and trunk length at 43 years in relation to childhood health, diet, and family circumstances; evidence from the 1946 national birth cohort. *International Journal of Epidemiology, 31, 383-90.*
13. Diverse Population Collaborative Group. (2005). Weight-height relationships and body mass index: some observations from the Diverse Population Collaboration. *American Journal of Physical Anthropology, 128,* 220-229.
14. David, T.M. (2010. A comparison of deaf/hard of hearing and hearing young adults' responses to a health risk behavior survey. *UMI 3411159.*