The effect of socioeconomic disadvantage on longitudinal growth of hippocampal subregion and subfield volumes in the Adolescent Brain Cognitive Development (ABCD) SM Study

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Adolescent Brain Cognitive Development SM

Introduction

- The hippocampus plays an essential role in memory and learning[1] and is comprised of distinct subregions (i.e., anterior and posterior) and subfields (i.e., CA1, CA3, CA4/DG, and subiculum) which have been shown to differentially contribute to memory function in children[2] and adults[3].
- Given the high density of glucocorticoid receptors, the hippocampus is particularly sensitive to chronic stressors.
- Indeed, past cross-sectional research with the ABCD dataset suggests socioeconomic disadvantage is associated with smaller hippocampal subregion and subfield volumes in children[4].
- However, to-date, no studies have examined the effect of socioeconomic disadvantage on the development of hippocampal subregion and subfield volumes longitudinally.
- Therefore, the proposed study, utilizes the ABCD Study dataset to investigate this effect in a large, diverse sample of children.

Methods: Data and Participant Characteristics

- ABCD Study Data Release 5.1[5-6] includes structural MRIs completed at Baseline (ages 9-10, mean age 9.9 years, n=11,867) and during the Year 2 follow-up (ages 11-12, mean age 11.9 years, n=7,752).
- Freesurfer hippocampal segmentation was previously completed for Baseline MRIs (n=10,695) [4].
- In the current study, Freesurfer hippocampal segmentation was completed for a subsample of the Year 2 MRIs (n=5,500).
- 577 subjects were excluded due to either not having both Baseline and Year 2 MRI data or an Area Deprivation Index (ADI) score, resulting in a final sample of 4,923.

Table 1. Sample demographics (n=4,923).

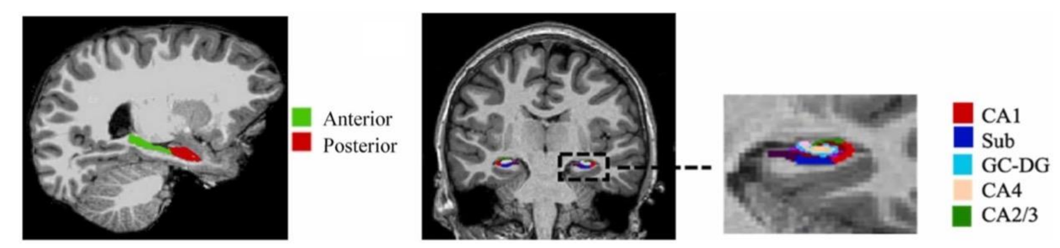
Female [n (%)]	2331 (47.35%)
Age (yrs), Baseline (M)	9.92
Age (yrs), Time 2 (M)	11.92
Area Deprivation Index (M)	38.9
Parent education [n (%)]	
At least one parent with a 4-year college degree	3101 (63%)
Family income [n (%)]	
< $50,000	1180 (24%)
$50,001 to $100,000	1341 (27%)
> $100,001	1969 (40%)
Child race/ethnicity, [n (%)]	
Asian	98 (<1%)
Black	562 (11%)
Hispanic or Latino	965 (20%)
Multi-Racial/Other	498 (10%)
White	2785 (57%)

- To investigate reproducibility, this sample was further split into a discovery sample (n= 2,462) and a replication (n=2,461) sample based on ADI, sex, and site ID.
- Discovery sample: *Mean* ADI = 38.9, 47.1% female.
- Replication sample: *Mean* ADI =38.9, 47.6% female.

Methods: Measures and Statistical Analyses

Hippocampal Subregion and Subfield Volumes:

- Freesurfer v7.4.1 was used to segment hippocampal subregions and subfields using T1 and T2-weighted scans.
- The anterior hippocampal subregion was measured using the hippocampal head volume, and the posterior hippocampal volume was comprised of the body and tail volumes.
- The FS60 parcellation that includes CA1, CA3 CA4, DG, (CA4 and DG were combined) and the subiculum was used to segment hippocampal subfields.



Area Deprivation Index:

- The Area Deprivation Index (ADI), comprised of 17 socioeconomic variables, was used to assess socioeconomic disadvantage[7,8] at Baseline.
- The ADI uses the subjects home address to assess factors such as income, education, employment, and housing quality[9].

Pubertal Status:

- Pubertal status at Year 2 was assessed using the 5-item Pubertal Development Scale and Menstrual Cycle Survey[10]. Scores were summed across the 5 items.

Statistical Analyses:

- Linear mixed-effects (LME) models were conducted to test relations between ADI at Baseline and Year 2 hippocampal subregion and subfield volume using the R lme4 and lmerTest package[11].
- Fixed effect covariates included Baseline hippocampal subregion and subfield volume, sex assigned at birth, age at Year 2, pubertal status at Year 2, and time between the two MRI scans (in months).
- Random effect of site ID was also included in each model.
- Separate models were run for the discovery and replication sample. Findings that did not replicate are noted with an asterisks in the results section.

Results: Descriptive Statistics

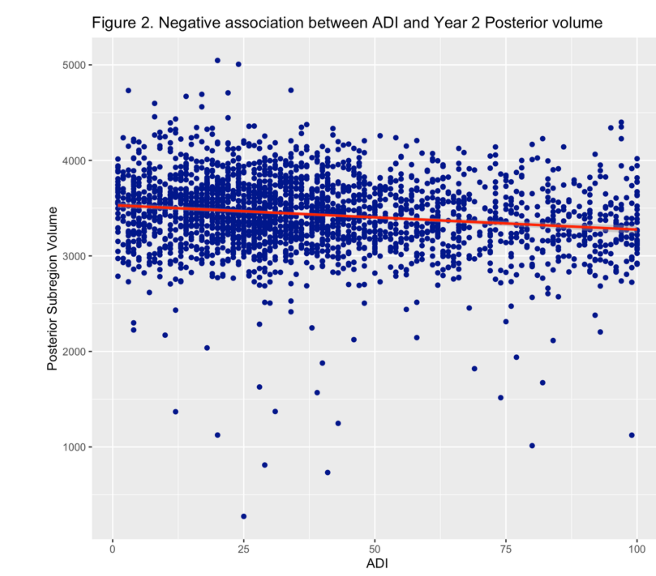
Table 2. Discovery sample and replication sample descriptive statistics for hippocampal subregion and subfield volumes

	Discovery Sample		Replication Sample	
	Baseline	Year 2	Baseline	Year 2
	M (SD)	M (SD)	M (SD)	M (SD)
Anterior	3274.7 (411.27)	3313.6 (434.38)	3273 (433.22)	3321.2 (441.34)
Posterior	3437.6 (392.75)	3428.1 (412.36)	3434 (401.45)	3428.6 (397.88)
CA1	1232 (158.73)	1256 (171.64)	1233.1 (166.04)	1259.9 (173.01)
CA3	411.1 (61.85)	407.5 (63.44)	410.1 (63.97)	407.7 (63.6)
CA4/DG	999.4 (122.12)	995.4 (128.83)	999.5 (128.45)	997.4 (127.89)
Subiculum	805.7 (101.57)	813.02 (592.43)	805.6 (104.74)	814.8 (105.29)

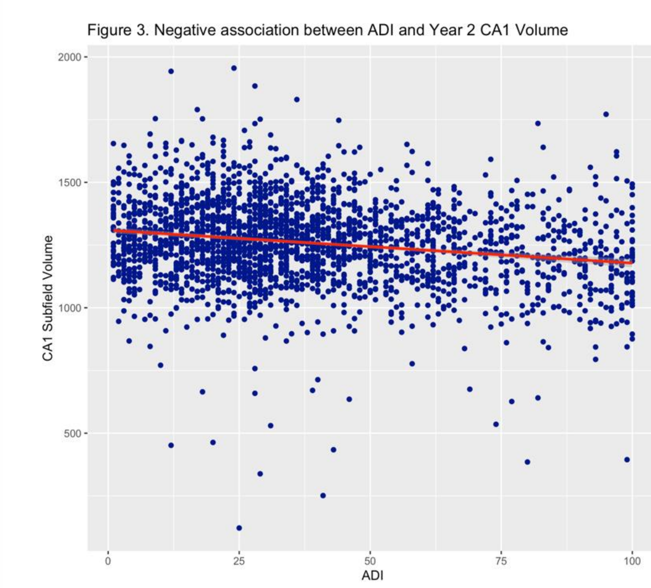
Notes. Volumes are in mm³ units.

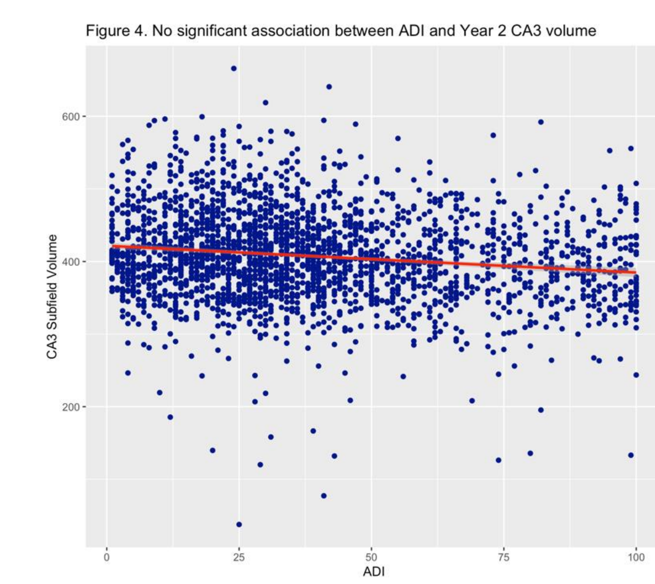
Results: Discovery Sample

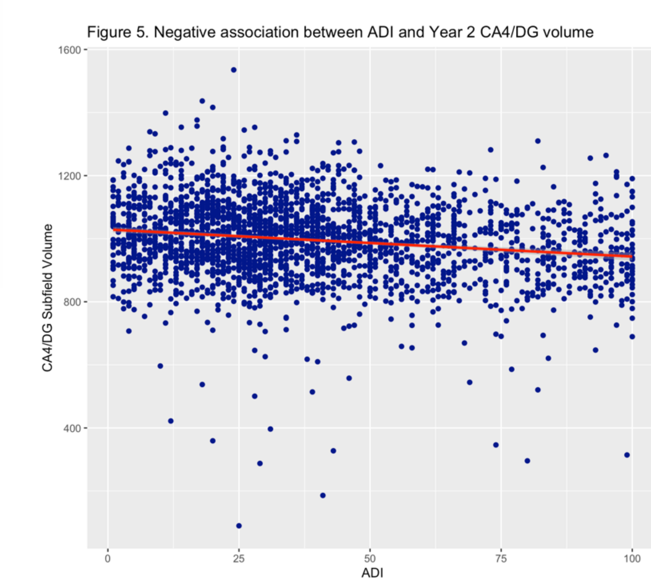
- Baseline ADI predicted smaller anterior ($b = -0.04$, $SE_b = 0.01$, $t = -2.9$, $p = 0.003$) and posterior ($b = -0.06$, $SE_b = 0.01$, $t = -3.4$, $p < 0.001$) hippocampal subregion volumes at Year 2, after controlling for hippocampal subfield volumes at Baseline.

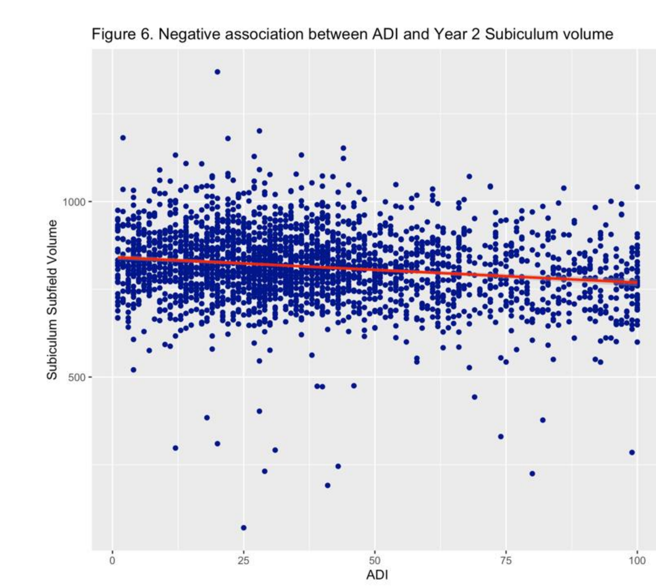


- Baseline ADI predicted smaller CA1 ($b = -0.04$, $SE_b = 0.02$, $t = -2.7$, $p = 0.007$) , CA4/DG ($b = -0.05$, $SE_b = 0.01$, $t = -3.1$, $p < 0.002$) , and subiculum* ($b = -0.05$, $SE_b = 0.02$, $t = -2.9$, $p < 0.003$), but not CA3 ($b = -0.04$, $SE_b = 0.01$, $t = -2.4$, $p > .05$), subfield volumes at Year 2, after controlling for hippocampal subfield volumes at Baseline.









Conclusions

- These findings build upon previous cross-sectional research showing associations between socioeconomic disadvantage and smaller anterior and CA1 volumes in the ABCD study sample[4].
- Results of this study provide a greater understanding of how socioeconomic disadvantage impacts growth of hippocampal subregions and subfields across development and has implications for cognitive development encompassing learning and memory processes.

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[1]Kim, E. J., Pellman, B., & Kim, J. J. (2015). Stress effects on the hippocampus: a critical review. *Learning & memory*, *22*(9), 411-416. http://www.learnmem.org/cgi/doi/10.1101/lm.037291.114
[2]Tamnes, C. K., Bos, M. G., van de Kamp, F. C., Peters, S., & Crone, E. A. (2018). Longitudinal development of hippocampal subregions from childhood to adulthood. *Developmental cognitive neuroscience*, *30*, 212-222. https://doi.org/10.1016/j.dcn.2018.03.009
[3]Shing, Y. L., Rodrigue, K. M., Kennedy, K. M., Fandakova, Y., Bodammer, N., Werkle-Bergner, M., ... & Raz, N. (2011). Hippocampal subfield volumes: age, vascular risk, and correlation with associative memory. *Frontiers in aging neuroscience*, *3*, 2. https://doi.org/10.3389/fnagi.2011.00002
[4]Botdorf, M., Dunstan, J., Sorcher, L., Dougherty, L. R., & Riggins, T. (2022). Socioeconomic disadvantage and episodic memory ability in the ABCD sample: Contributions of hippocampal subregion and subfield volumes. *Developmental Cognitive Neuroscience*, *57*, 101138. https://doi.org/10.1016/j.dcn.2022.101138
[5]Garavan H, Bartsch H, Conway K, et al. Recruiting the ABCD sample: Design considerations and procedures. *Dev Cogn Neurosci.* 2018; 32, 16-22. doi: https://doi.org/10.1016/j.dcn.2018.04.004
[6]Jernigan TL, Brown SA, & Dowling GJ. The adolescent brain cognitive development study. *J Res Adolesc.* 2018;28(1), 154. doi: 10.1111/jora.12374
[7] Kind, A. J., & Buckingham, W. R. (2018). Making neighborhood-disadvantage metrics accessible—the neighborhood atlas. The New England journal of medicine, 378(26), 2456. 10.1056/NEJMp1802313
[8]U.S. Census Bureau. (2012). 2009–2011 American Community Survey 3-year Public Use Microdata Samples [SAS Data file]. Retrieved from https://factfinder.census.gov/faces/nav/jsf/pages/searchresults.xhtml?refresh=t
[9]Kind, A. J., Jencks, S., Brock, J., Yu, M., Bartels, C., Ehlenbach, W., ... & Smith, M. (2014). Neighborhood socioeconomic disadvantage and 30-day rehospitalization: a retrospective cohort study. *Annals of internal medicine*, *161*(11), 765-774. :10.7326/M13-2946
[10]Petersen, A. C., & Brooks-Gunn, J. (1988). Puberty and adolescence. Handbook of behavioral medicine for women, (149), 12.
[11]Bates D, Mächler M, Bolker B, & Walker S. Fitting linear mixed-effects models using lme4, Journal of Statistical Software. 2015; 67(1): 1-48. doi: https://doi.org/10.48550/arXiv.1406.5823