A multi-modal MRI approach to studying air pollution exposure and adolescent neurodevelopment

Presented By:
Megan M. Herting, PhD
Assistant Professor
Department of Preventive Medicine

HEI Brain Health and Air Pollution Symposium
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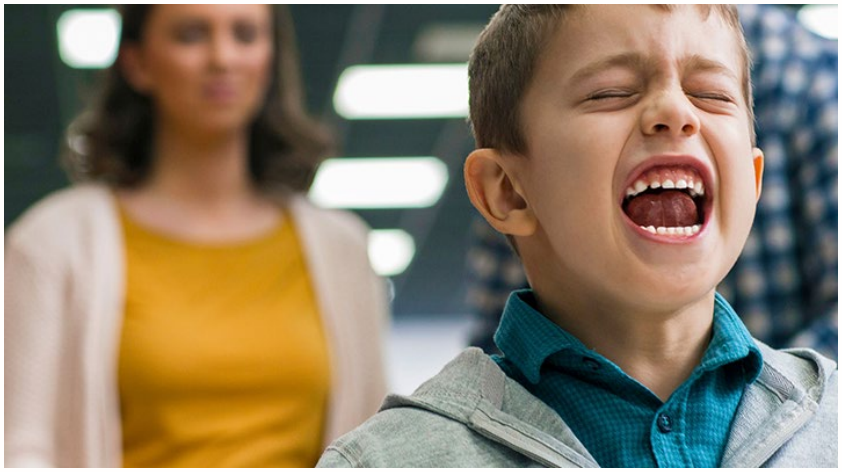
Neurotoxicant effects on child behavior

- Developmental delays
- Risk for Autism
- Lower IQ
- Greater behavioral problems



Remaining questions:

- Source(s) and exposure(s) characteristics
- Confounders/covariates
- Heterogeneity of effects (sex, socio-economic, etc.)
- Brain Mechanism(s)
- Which periods of exposure are most important?
- Are the effects long-lasting?

Timing: Prenatal vs. Postnatal?

ELSEVIER

Environmental Research

Volume 158, October 2017, Pages 798-805

Prenatal particulate air pollution exposure and body composition in urban preschool children: Examining sensitive windows and sex-specific associations

Yueh-Hsiu Mathilda Chiu [a, b], Hsiao-Hsien Leon Hsu [a], Ander Wilson [c], Brent A. Coull [d, e], Mathew P. Pendo [f], Andrea Baccarelli [g], Itai Kloog [h], Joel Schwartz [e], Robert O. Wright [a, i], Elsie M. Taveras [j, k, 1], Rosalind J. Wright [a, b, i]

N=267;
5 years

Int. J. Environ. Res. Public Health **2014**, *11*, 6827-6841; doi:10.3390/ijerph110706827

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Article

Multilevel Analysis of Air Pollution and Early Childhood Neurobehavioral Development

Ching-Chun Lin [1], Shih-Kuan Yang [1], Kuan-Chia Lin [2], Wen-Chao Ho [3], Wu-Shiun Hsieh [4], Bih-Ching Shu [5] and Pau-Chung Chen [1,6,7,*]

N=533;
18 months

ELSEVIER

Environment International

Volume 131, October 2019, 104927

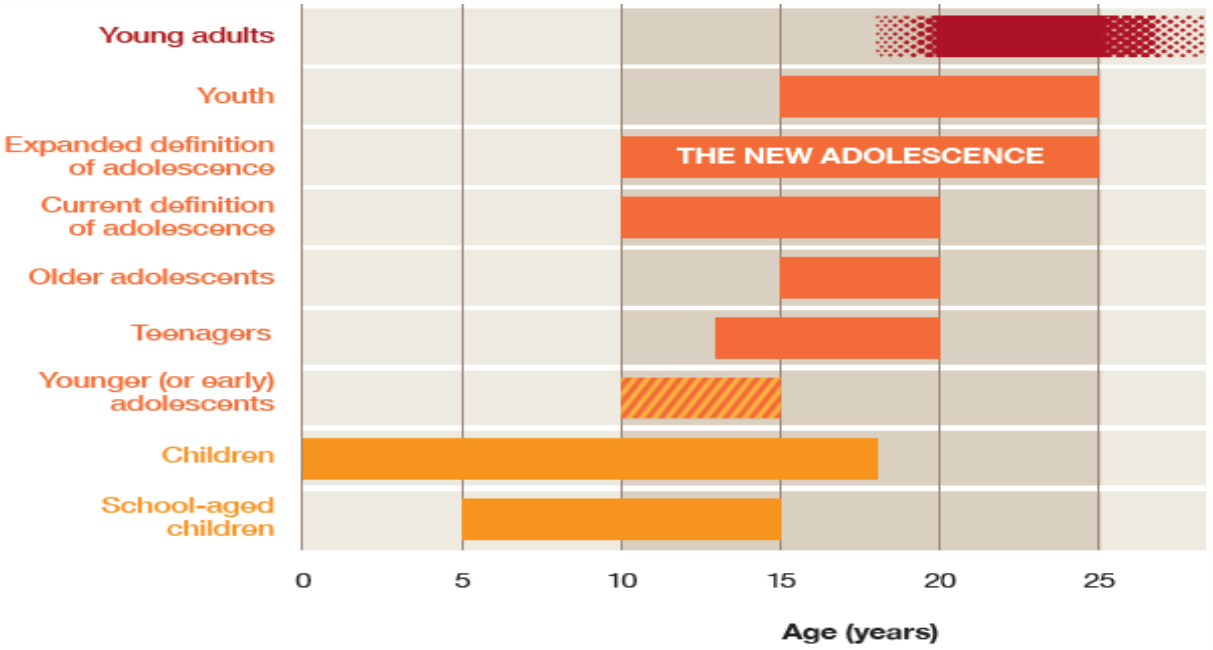
Prenatal and postnatal exposure to air pollution and emotional and aggressive symptoms in children from 8 European birth cohorts

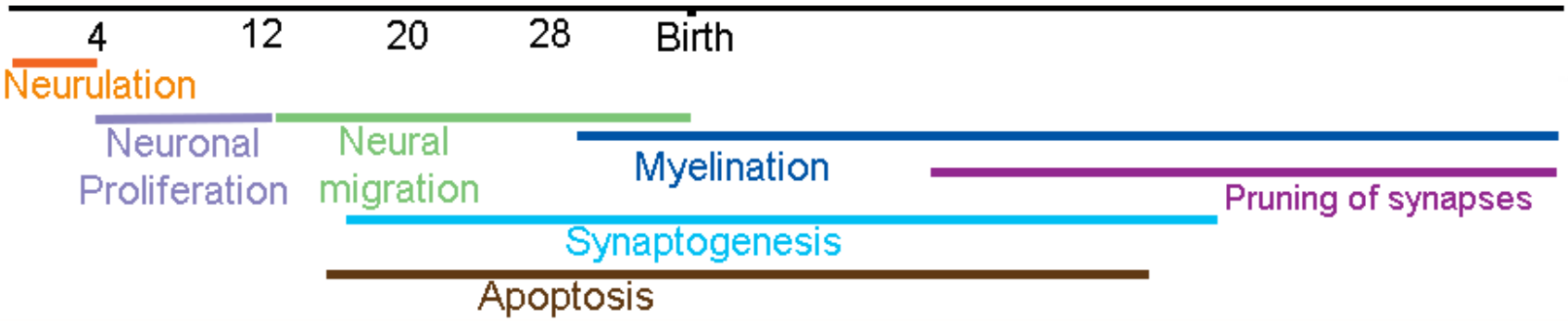
Ainhoa Jorcano [a, b, c], Małgorzata J. Lubczyńska [a, b, c], Livia Pierotti [a, b, c], Hicran Altug [d], Ferran Ballester [c, e, f], Giulia Cesaroni [g], Hanan El Marroun [h, i, j], Ana Fernández-Somoano [c, k, l], Carmen Freire [c, m], Wojciech Hanke [n], Gerard Hoek [o], Jesús Ibarluzea [c, p, q, r], Carmen Iñiguez [c, s], Pauline W. Jansen [h, j], Johanna Lepeule [t], Iana Markevych [u, v, w], Kinga Polańska [n], Daniela Porta [g] ... Mònica Guxens [a, b, c, h]

N=13,182;
7-11 years

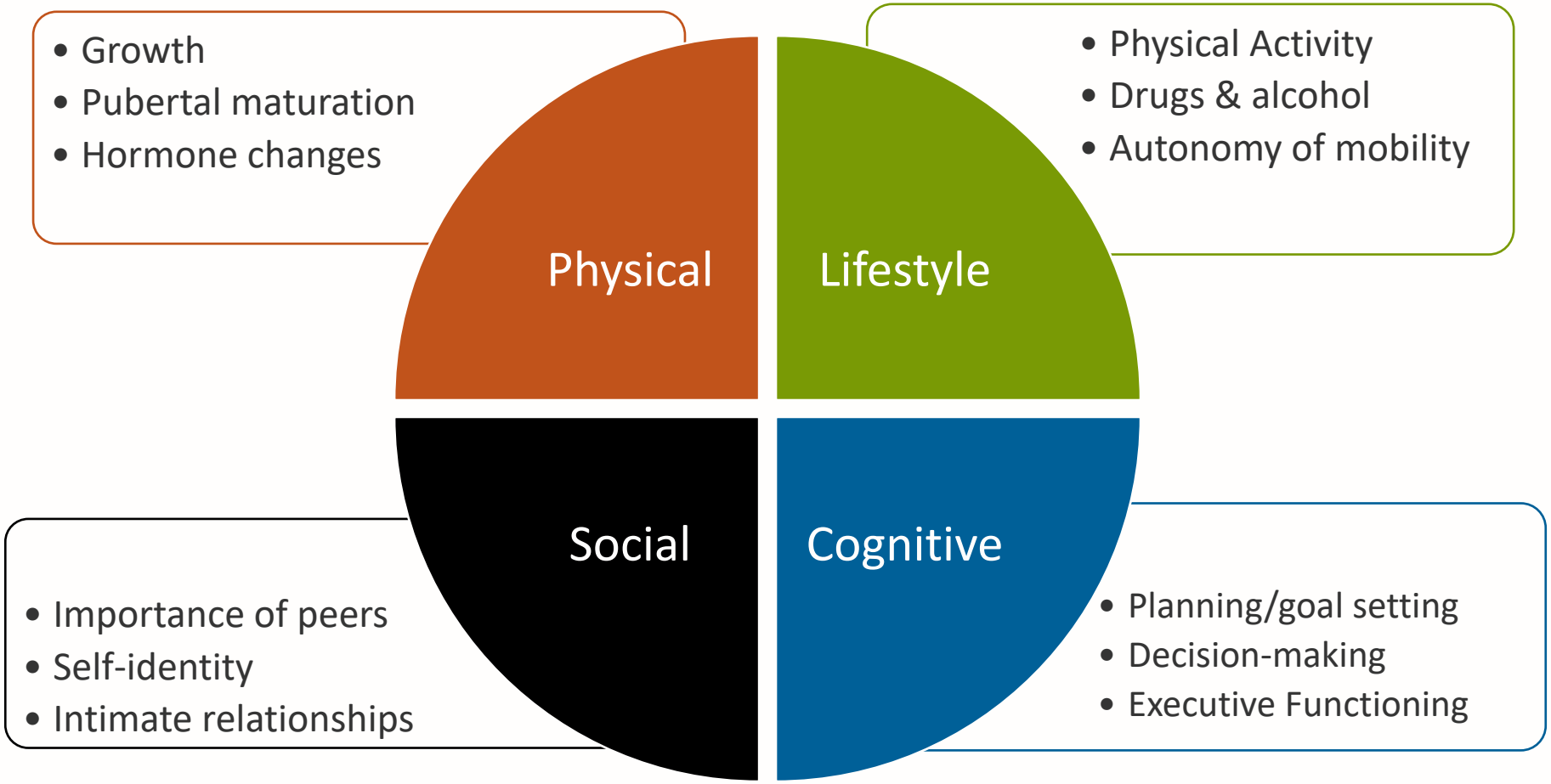
Neurodevelopment: A prolonged sensitive period

Sawyer et al., *Lancet*, 2018



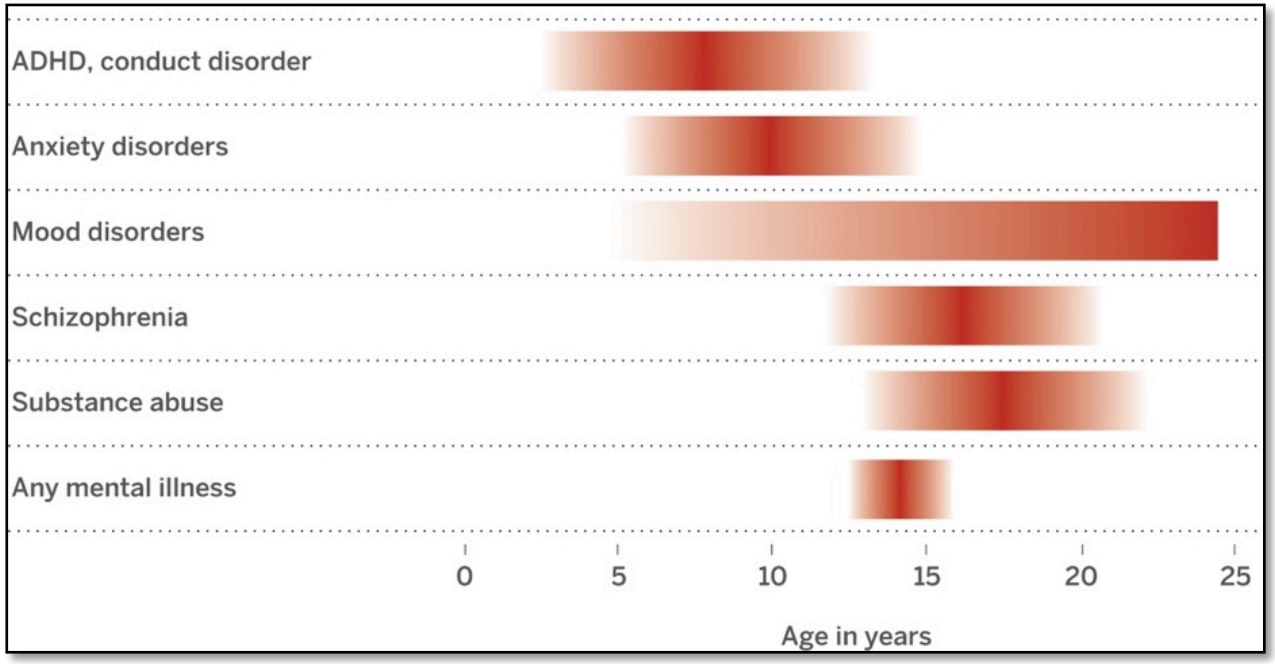


Child and adolescent development: a period of opportunity & vulnerability



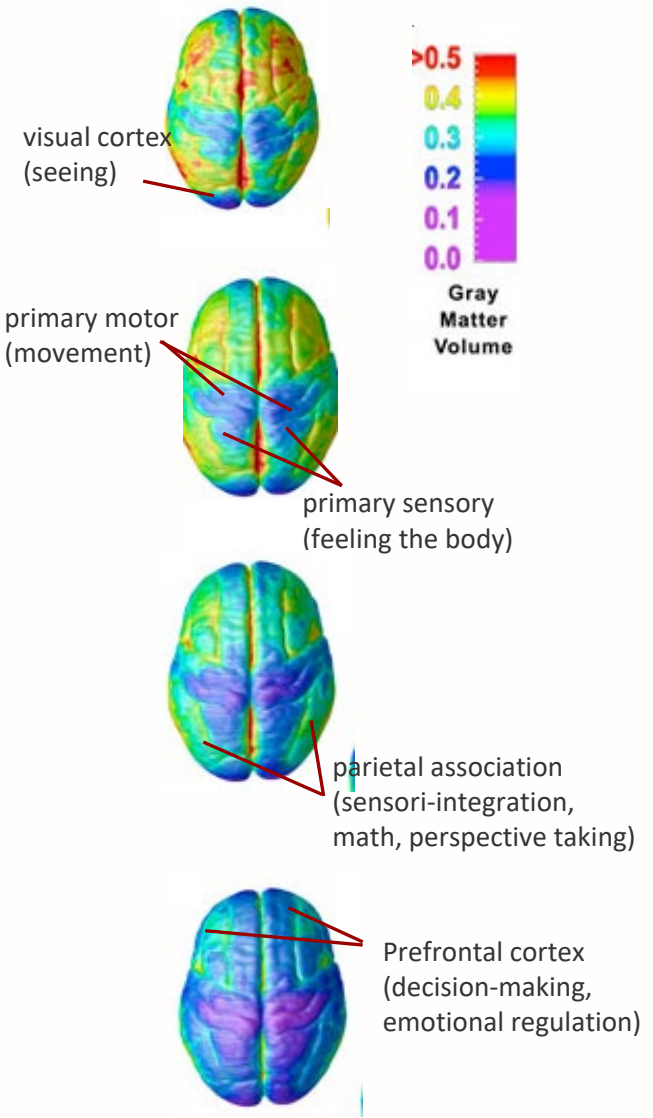
Child and adolescent development: a period of opportunity & vulnerability

- Heightened risk taking paired with a mis-match in timing of maturation of emotion, reward, and regulation systems
- 50% of all lifetime mental illness begins by age 14
- 75% of all lifetime mental illness by age 24



Lee et al., *Science*, 2014

Interconnections & efficiency of neural systems occur in a systematic fashion



Gogtay et al., PNAS, 2004

5 years

25 years

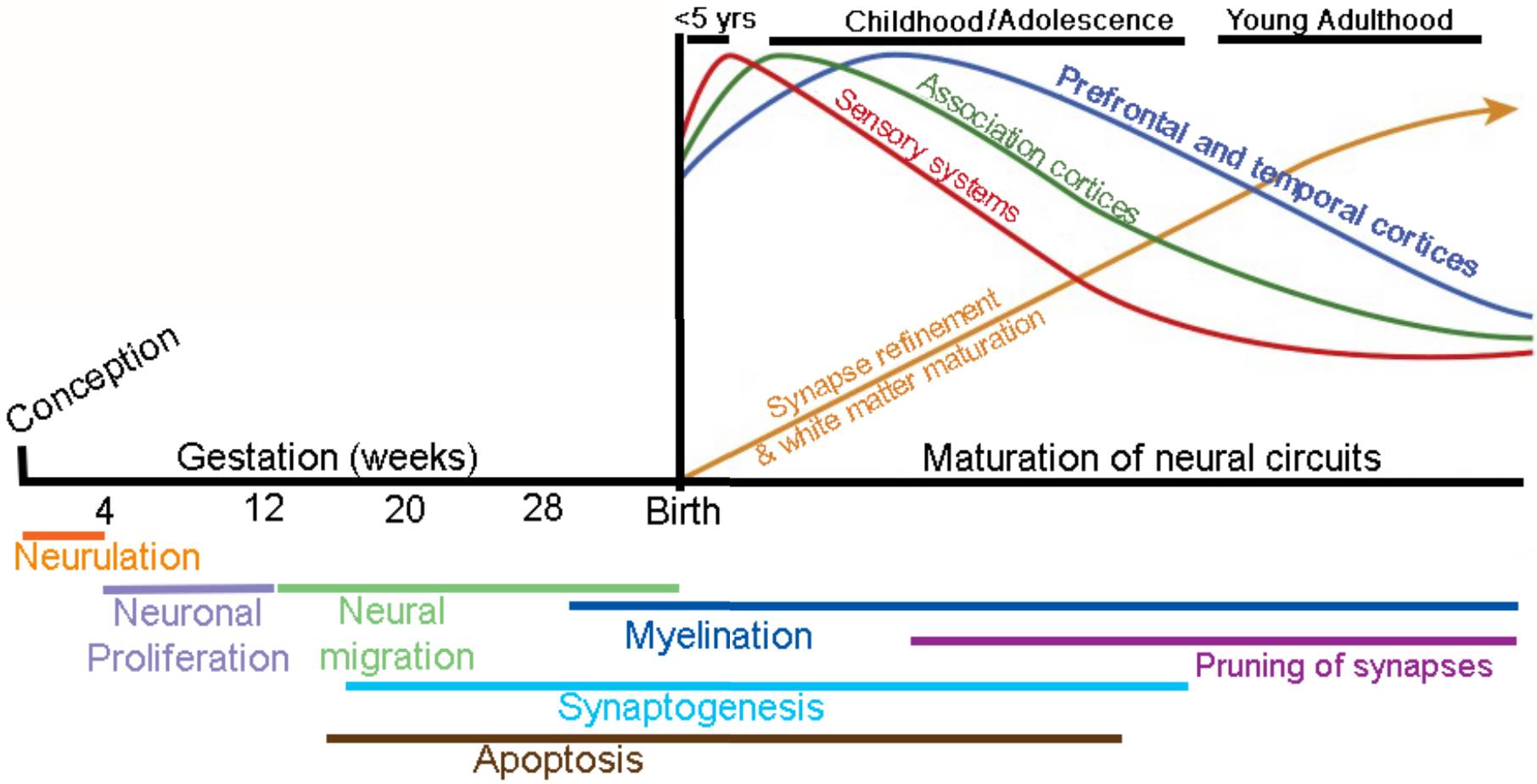
Early childhood: sensory and motor regions involved in speaking, listening, and perceived emotions

Mid-to-Late childhood: association brain regions to sensory integration and conceptual frameworks of social, emotion, and cognitive concepts

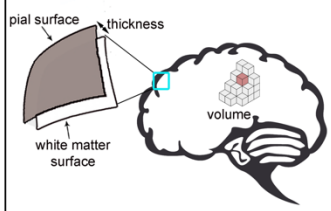
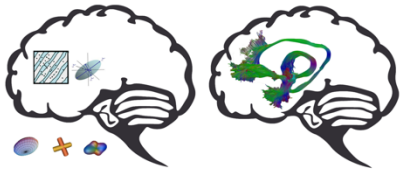
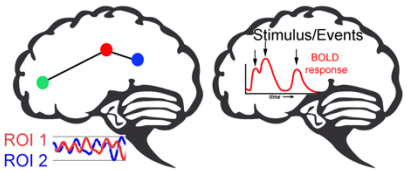
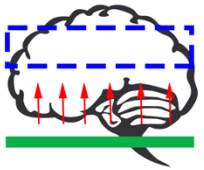
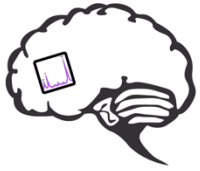
Early-to-Mid adolescence: emotional & reward processes, sensitivity to social identity

Late adolescence to adulthood: improved emotional regulation, long-term planning, and abstract thinking

Does air pollution exposure impact brain structure and function in humans?



Outdoor Air Pollution-MRI Studies

	Structural MRI (sMRI)	Diffusion MRI (dMRI)		Functional MRI (fMRI)		Arterial Spin Labeling (ASL)	Spectroscopy (MRS)
MRI Technique	tissue composition 	water diffusion 		blood-oxygen-level- dependent (BOLD) signal 		tissue perfusion 	proton frequencies 
		diffusion modeling (e.g. DTI, ball & stick, NODDI)	tractography	resting-state correlations	task-based brain activity		
Measures	volume; surface area; cortical thickness; density (VBM)	water restriction/ orientation (e.g. FA, ICVF)	white matter fiber bundles	timecourse correlations	signal change between task conditions	cerebral blood flow	metabolites
Biomarkers							
Functionality	gray or white matter size & shape	white matter microstructure	*structural* connectivity between regions	*functional* connectivity of brain regions	brain function	brain blood flow	brain metabolites

- Peterson 2015
- Pujol 2016a
- Pujol 2016b
- Mortamais 2017
- Guxens 2018
- Alemany 2018
- Mortamais 2019
- Beckwith 2020

- Pujol 2016a
- Pujol 2016b
- Malgorzata 2020

- Pujol 2016a
- Pujol 2016b

- ?

- Pujol 2016a
- Brunst 2019

Herting et al., *Frontiers in Public Health*, 2019

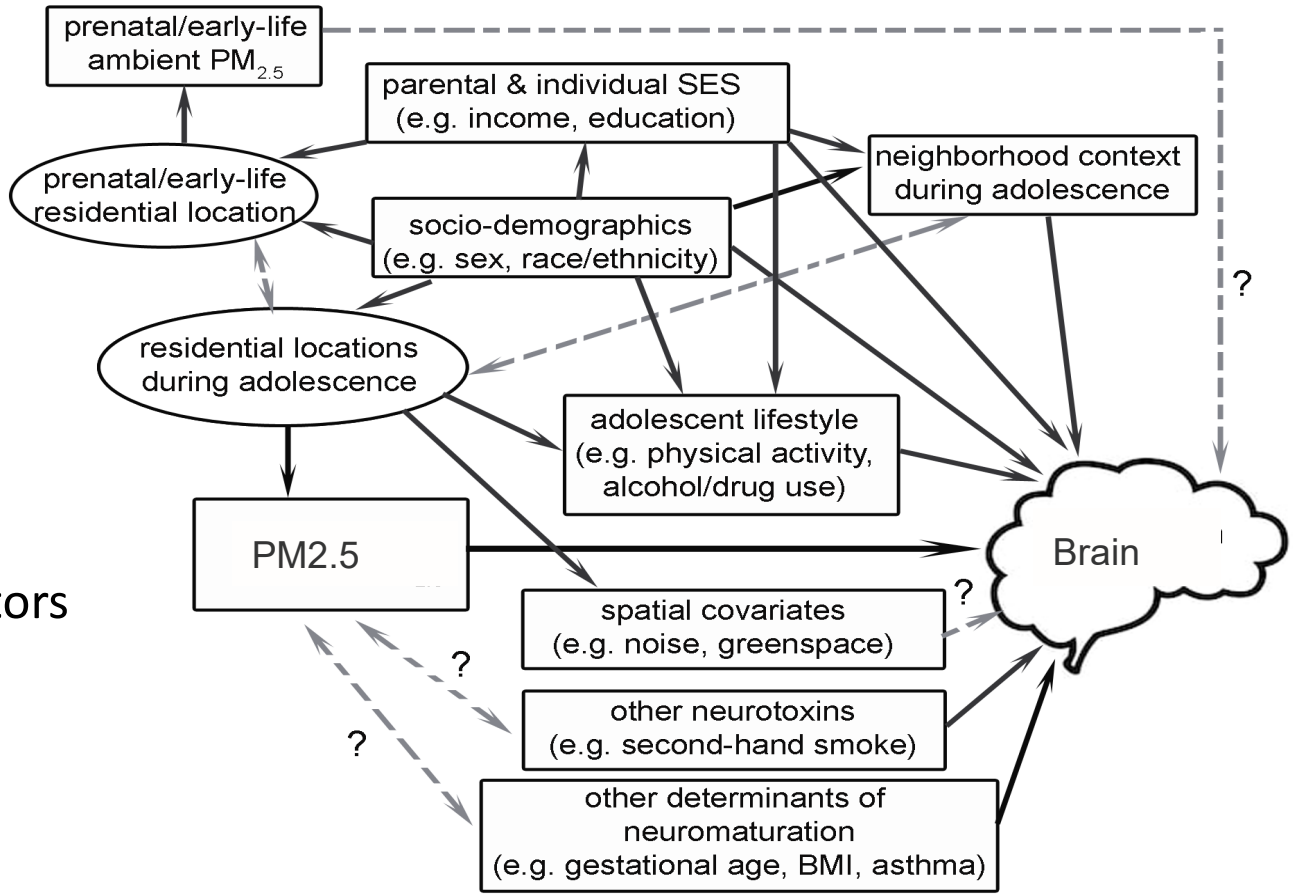
Outdoor Air Pollution and MRI studies

Columbia Center's Birth Cohort	BREATHE Cohort	Generation R Cohort	CCAAPS
• New York Boroughs • 40 children • PAHs	• Barcelona, Spain • 263 children • School/home, traffic-related, Cu	• Rotterdam, The Netherlands • 2,900 children • NO2, $PM_{2.5}$, PM_{10}, and PM Components	• Cincinnati, OH • 135 children • Elemental carbon attributable to traffic (ECAT)

- Generalizability and reproducibility
- Sources and lifetime of exposure(s)
- Identifying susceptibility risk factors

Covariates, Confounders, Mediators, Moderators

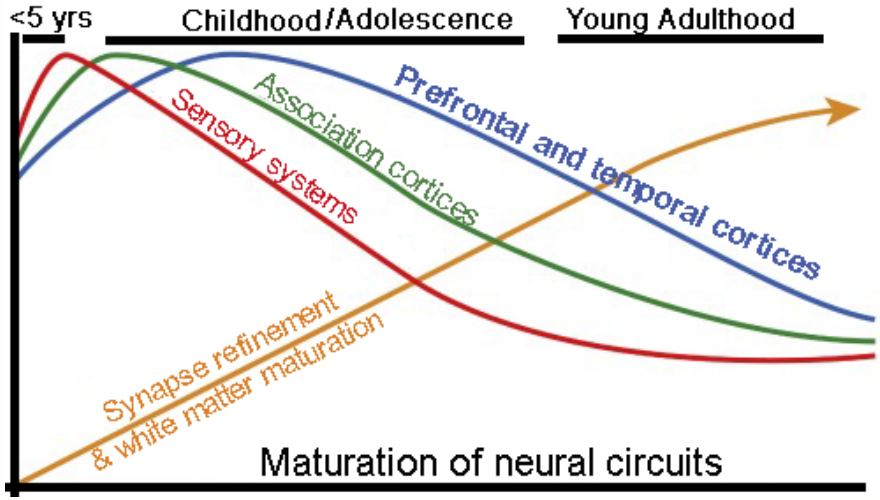
- Community factors
- Genetics
- Parental/family factors

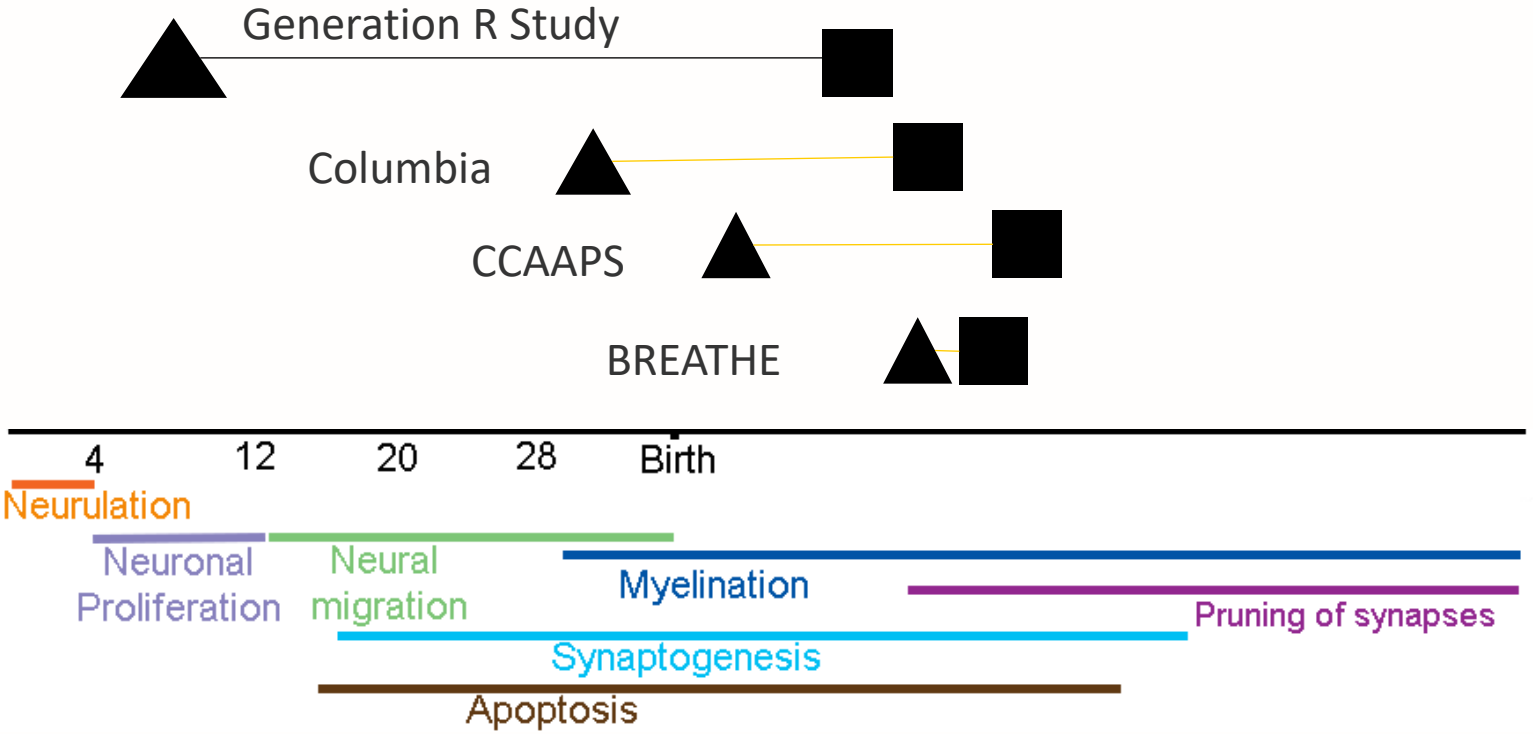


Timing Effects

Exposure

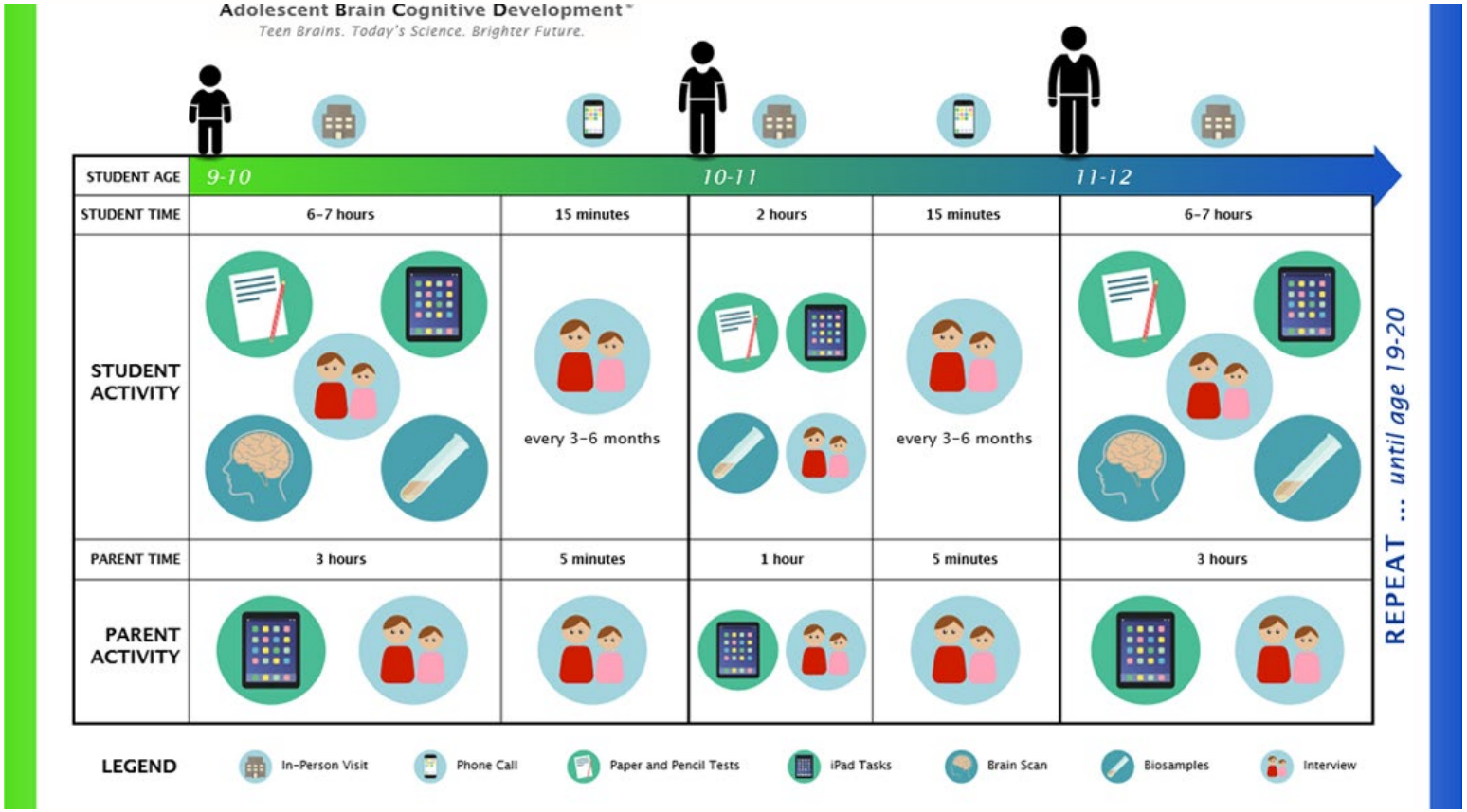
Brain Scan





Adolescent Brain Cognitive Development Study®

- Largest long-term study of brain development and child health in the U.S.
- 11,873 children ages 9-10 years from 21 research sites across the country
- Annual cognitive and behavioral assessments; brain MRI every 2 years for 10 years

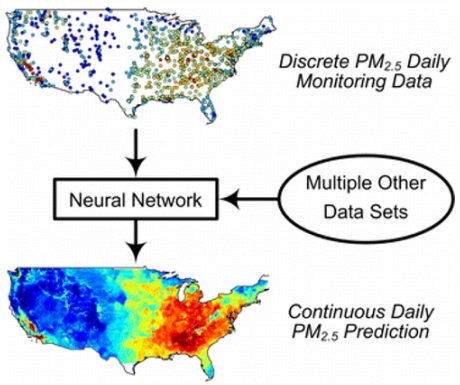


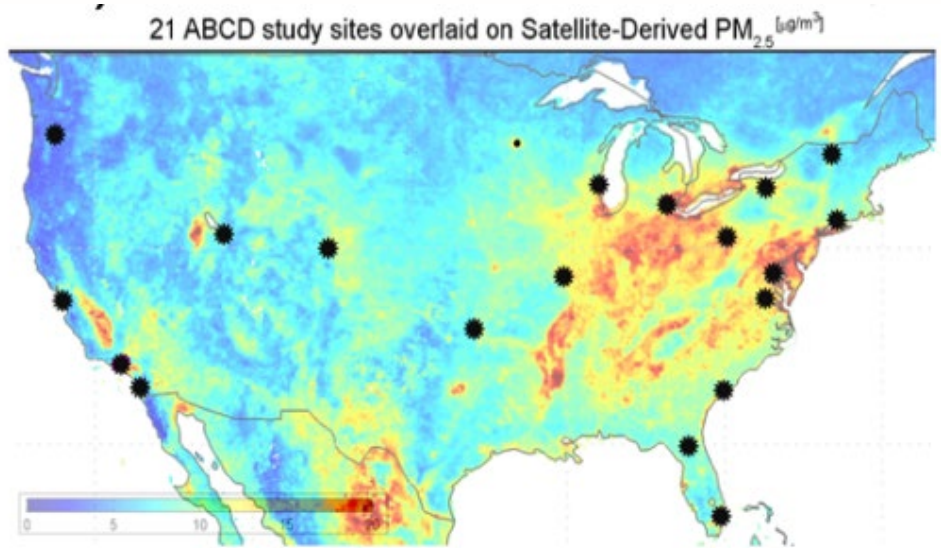
https://abcdstudy.org/

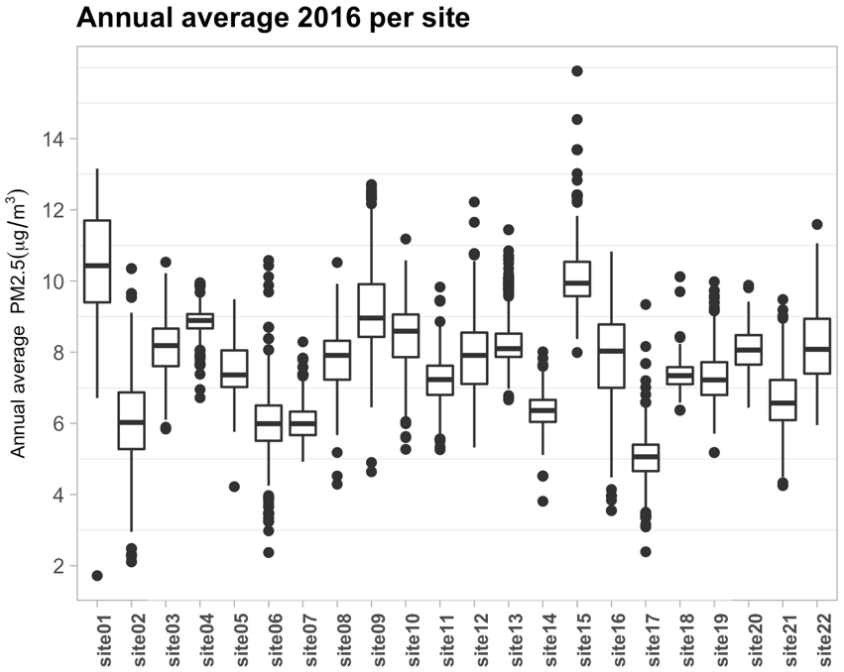
ABCD-Environment

P30ES007048-23S1

CV R^2: 0.89

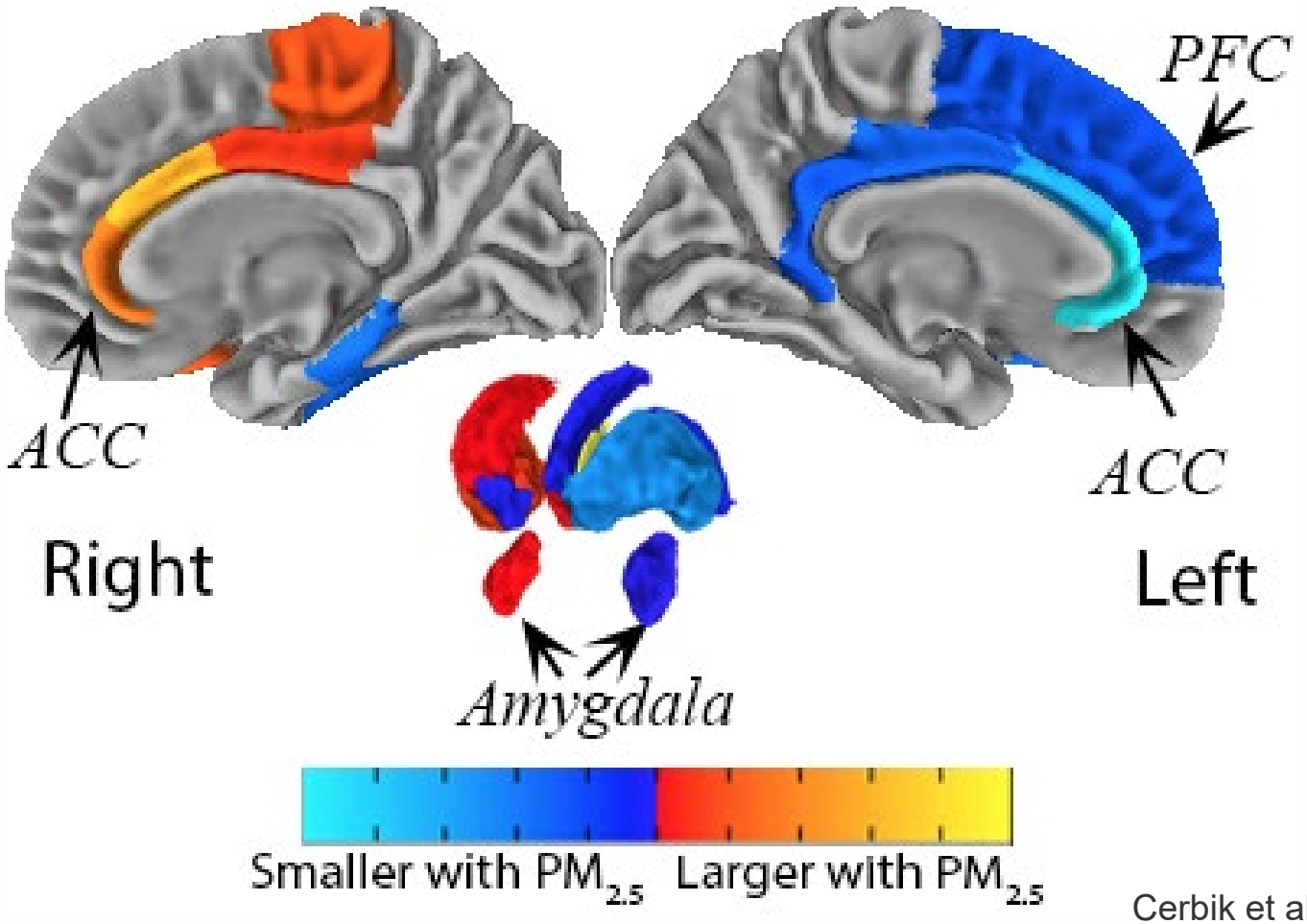






Cserbik et al., *Under-review*

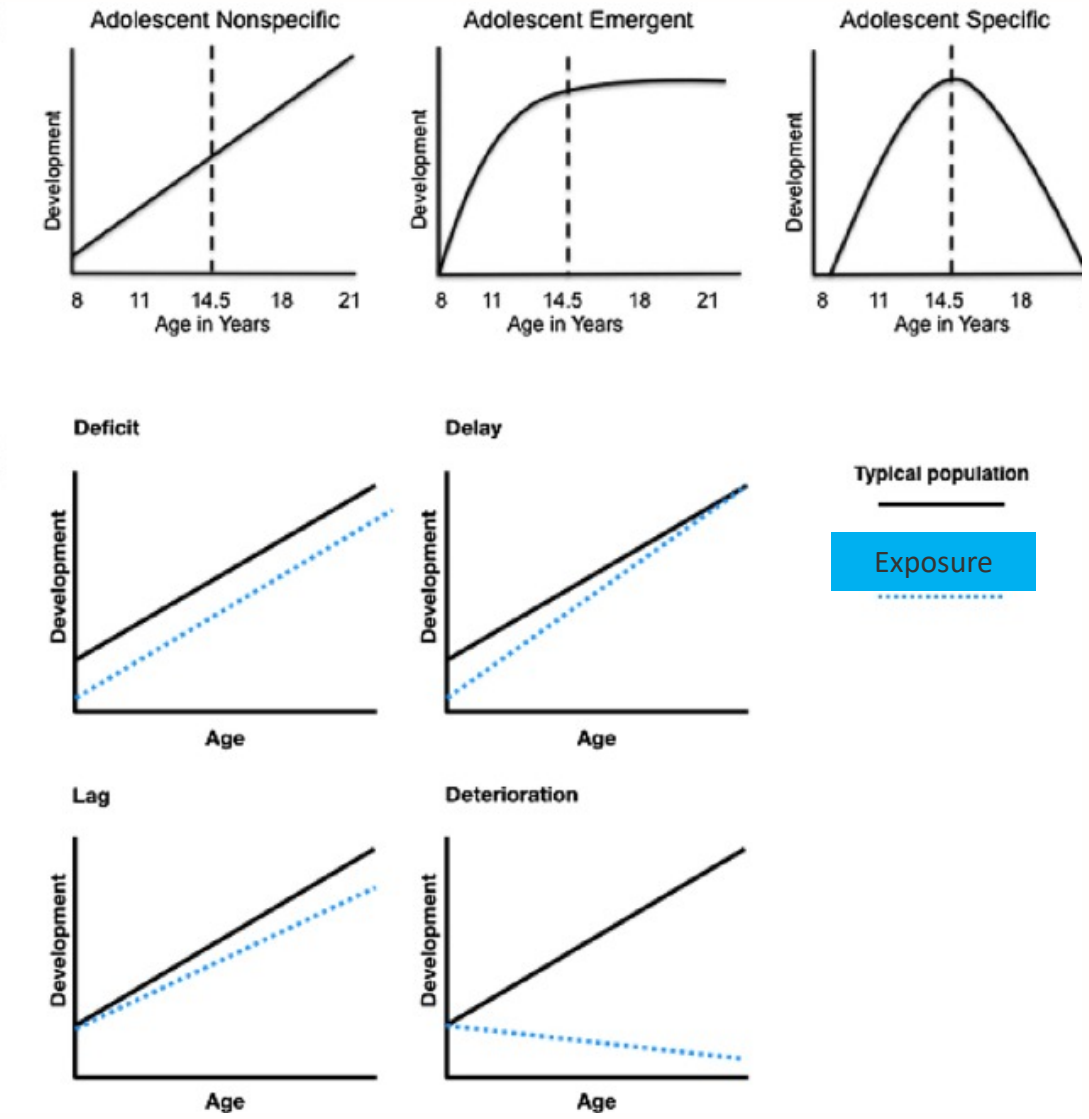
Ambient $PM_{2.5}$ Exposure and Brain Structure at 9-10 years



Cerbik et al., *Under-review*

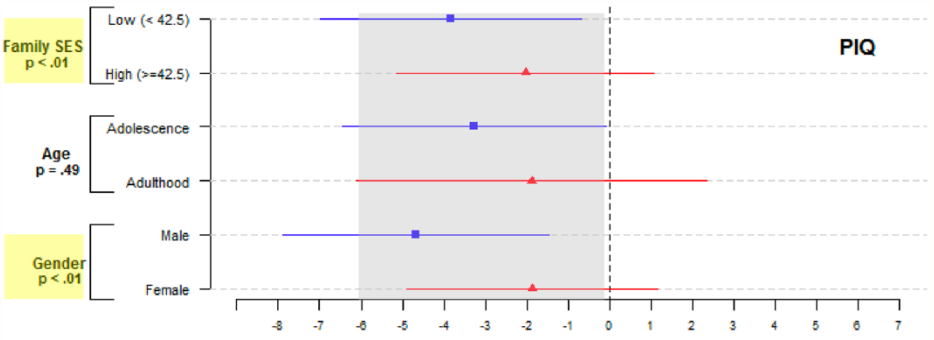
The Future: Longitudinal MRI Timing Effects

- Child and adolescent windows of vulnerability?
- Neural system and sex-specific effects?
- Long-term effects?
- May help to identify early brain MRI biomarkers of future behavioral problems

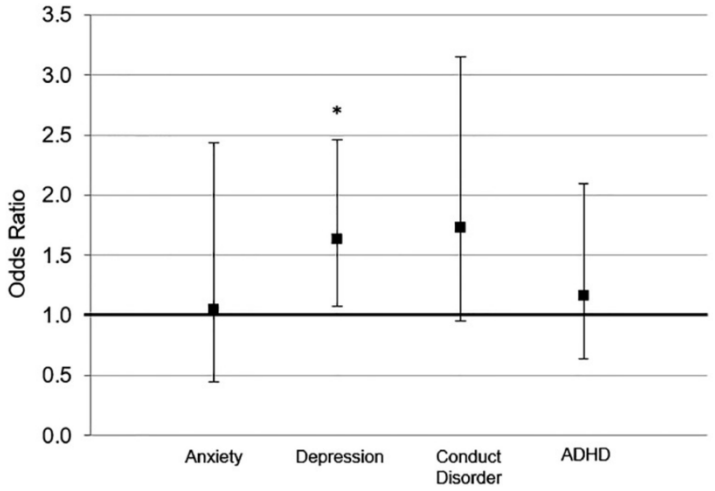


Haller et al., *DCN, 2018*

Adolescent Air Pollution Exposure Behavior Studies Suggest Long-term Effects



Wang et al., *PLOS One*, 2017

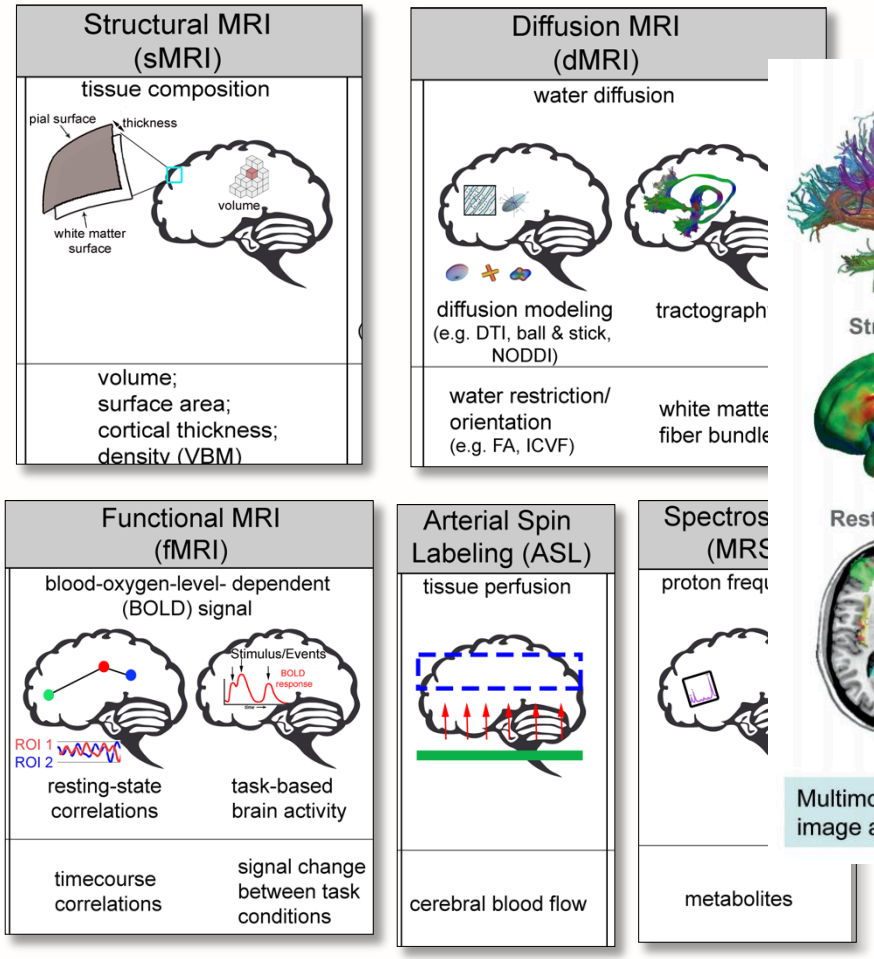


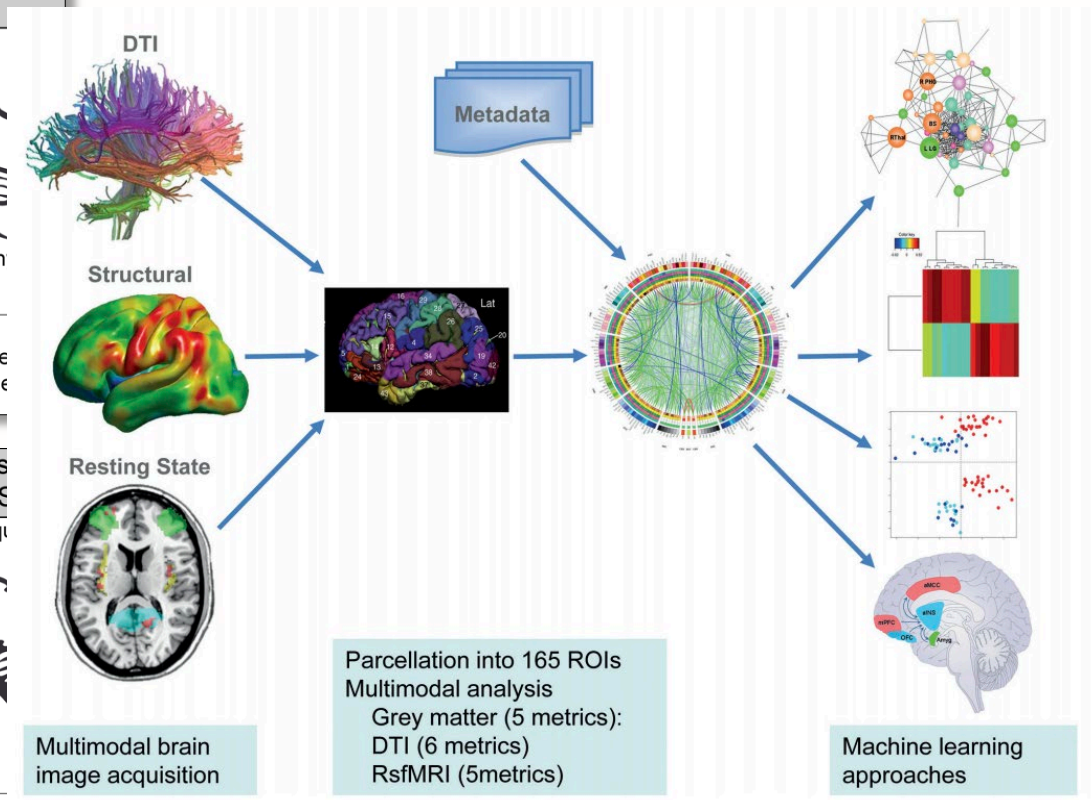
Roberts et al., Psychiatry Res., 2019

	$PM_{2.5}$ 1-year prior to baseline	$PM_{2.5}$ 2-years prior to baseline	$PM_{2.5}$ 3-years prior to baseline	$PM_{2.5}$ average over follow-up
Models[b]	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**
Base[c]	0.36* (0.12, 0.60)	0.32* (0.08, 0.56)	0.33* (0.08, 0.58)	0.30* (0.09, 0.52)
Fully Adjusted[d]	0.32* (0.06, 0.59)	0.28* (0.02, 0.54)	0.28* (0.01, 0.56)	0.26* (0.02, 0.51)

Younan et al., *J. Abnorm. Child Psychol.*, 2017

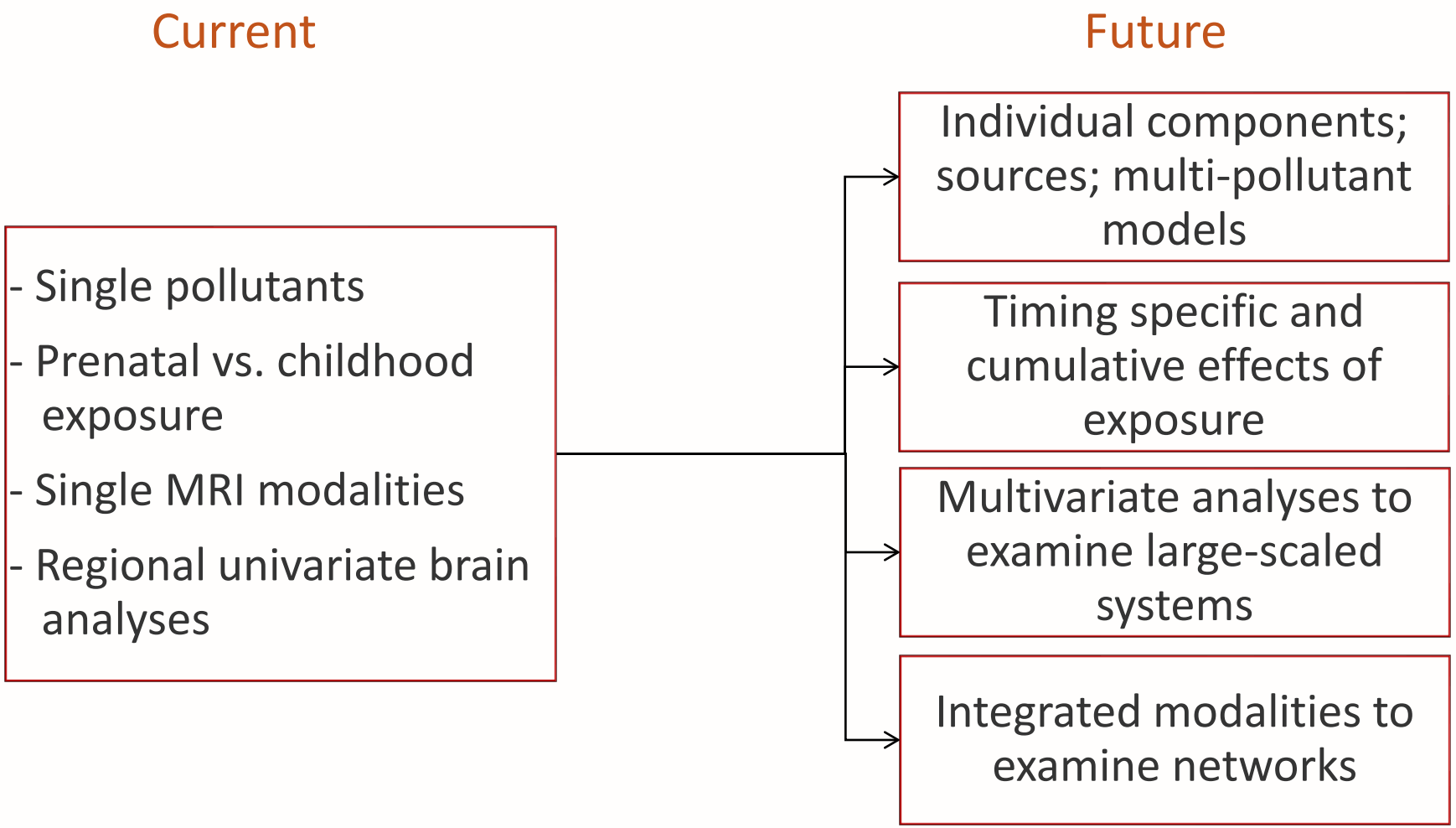
Harness the power of multi-modal MRI to understand air pollution on neurodevelopment





Mayer et al. Gut, 2019

Potential Moving Forward



Summary

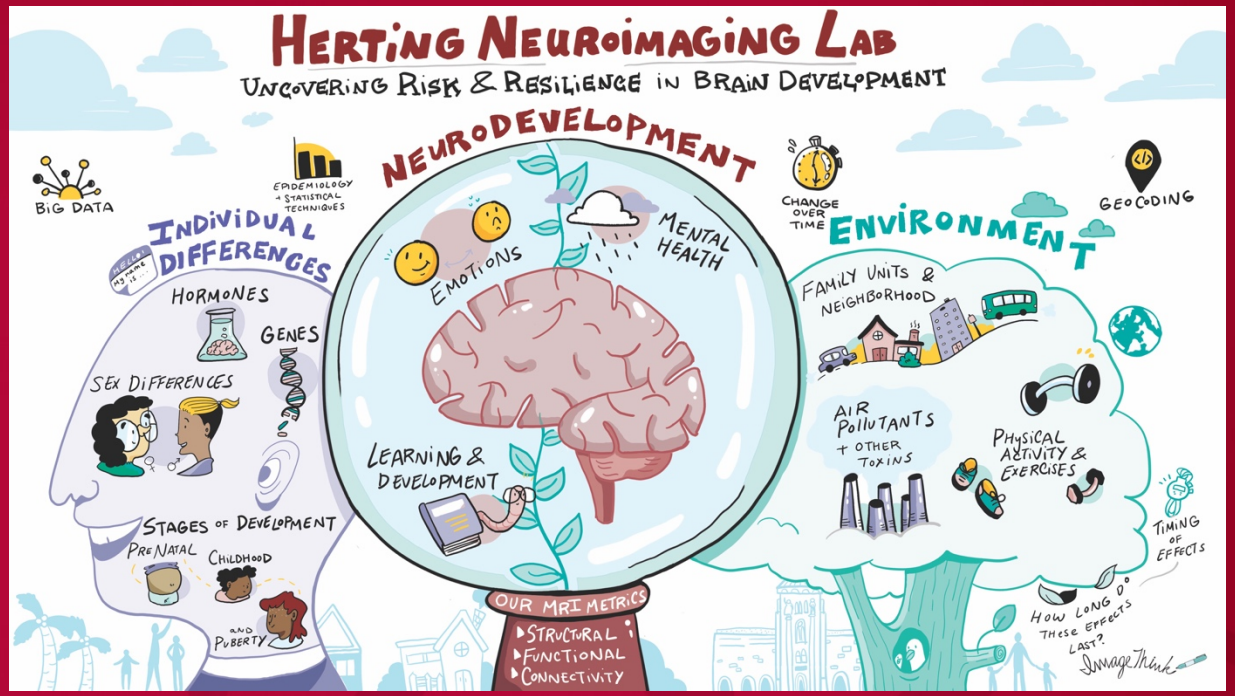
- Air pollution has been correlated with child and adolescent behavior, as well as multiple neuroimaging biomarkers of brain development
- The processes undergoing neuromaturation when the timing of exposure and the timing of brain assessment are likely important in uncovering how air pollution impacts the brain
- Identify who is at risk and identify lifestyle modifiers (e.g. social stress, physical activity, diet)
- Both new and integrated MRI methods can offer insight into brain health, with the potential to detect alterations prior to clinical onset

Herting Lab

Dora Cserbik, MS
Sandhya Prathap, MS
Claire Campbell, BS
Anisa Azad, MS
Kimberly Felix, BA
Miguel Jaime
Robert Kim, BS

ABCD-E

Rob McConnell, MD
JC Chen, MD
Joel Schwartz, PhD
Wes Thompson, PhD
Elizabeth Sowell, PhD
Daniel Hackman, PhD



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