Environmental Exposures and Childhood Mental Health

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Overview

1. Burden of Mental Health Disorders in Children
2. Social / Environmental Determinants of (Mental) Health
3. Environmental Exposures, Pathways, and Mental Health
4. Susceptible Periods of Growth and Development
5. Cincinnati Childhood Allergy and Air Pollution Study Findings

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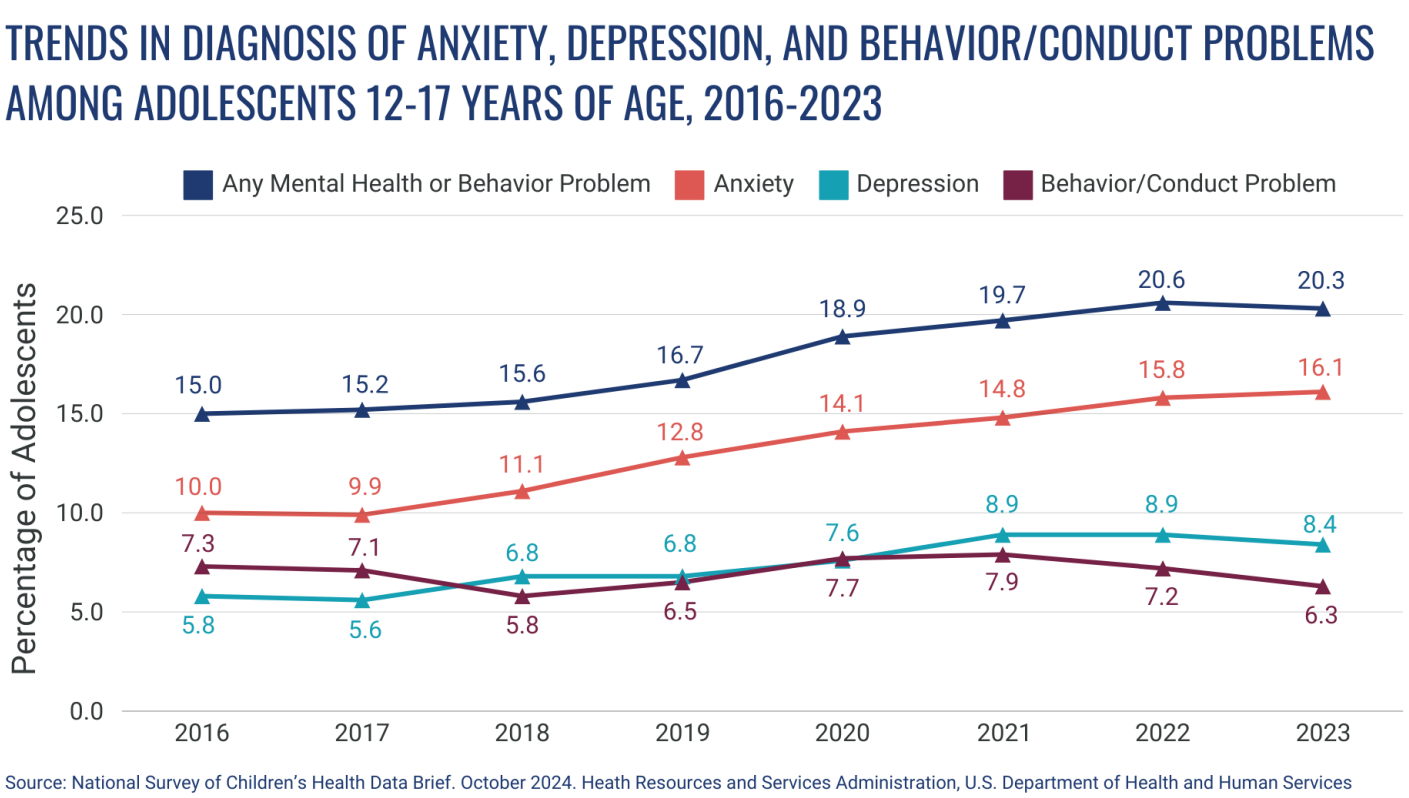
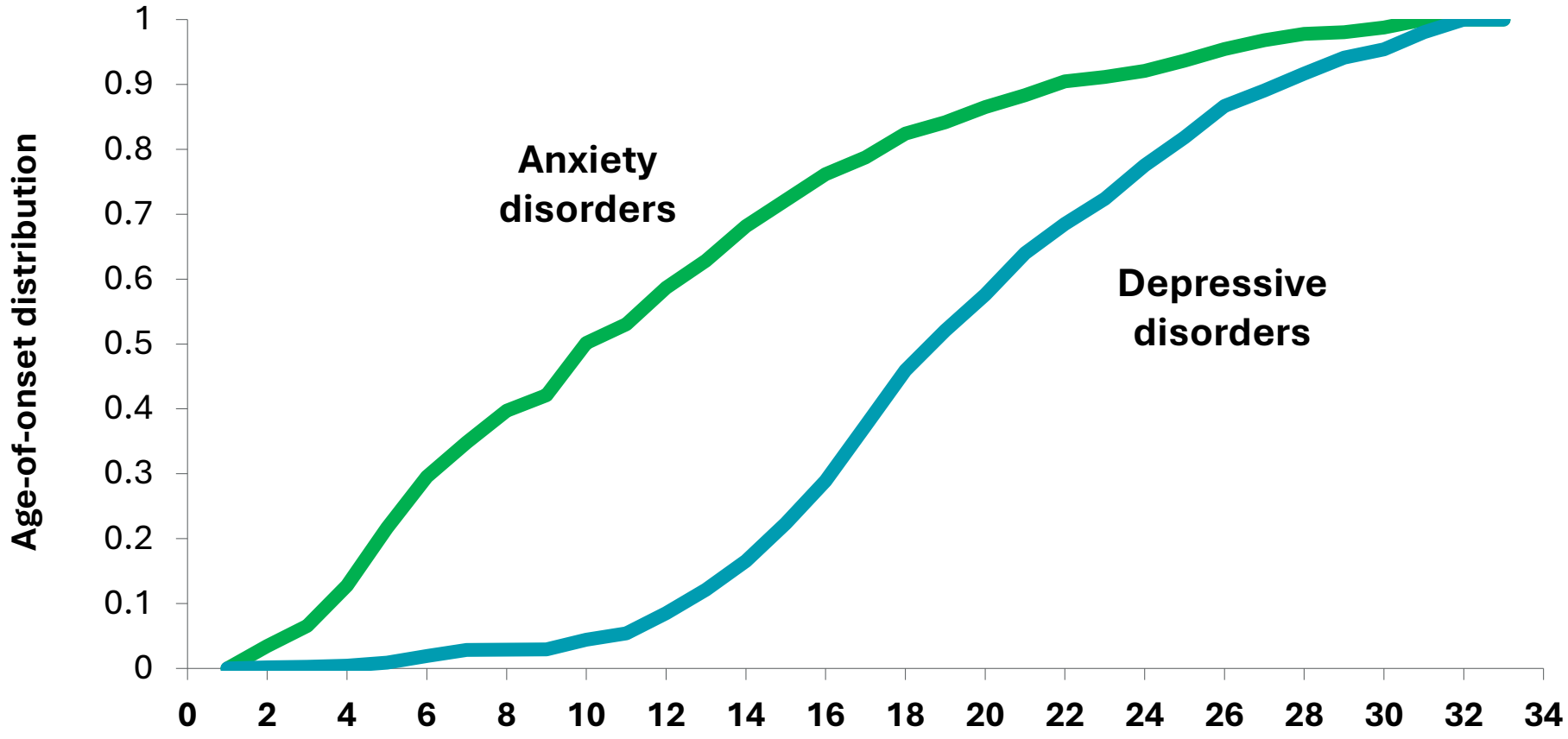
Burden of Mental Health Disorders During Childhood

- Mental health consequences
  - School performance
  - Substance use disorders
  - Justice system encounters
  - Unemployment
- Suicide is the 2nd leading cause of death among ages 10-24
- Measurement
  - Clinical thresholds / diagnoses
    - Medical records
  - Spectrum of mental health and severity
    - Validated assessments



Source: National Survey of Children's Health Data Brief. October 2024. Heath Resources and Services Administration, U.S. Department of Health and Human Services

Onset of Psychiatric Disorders



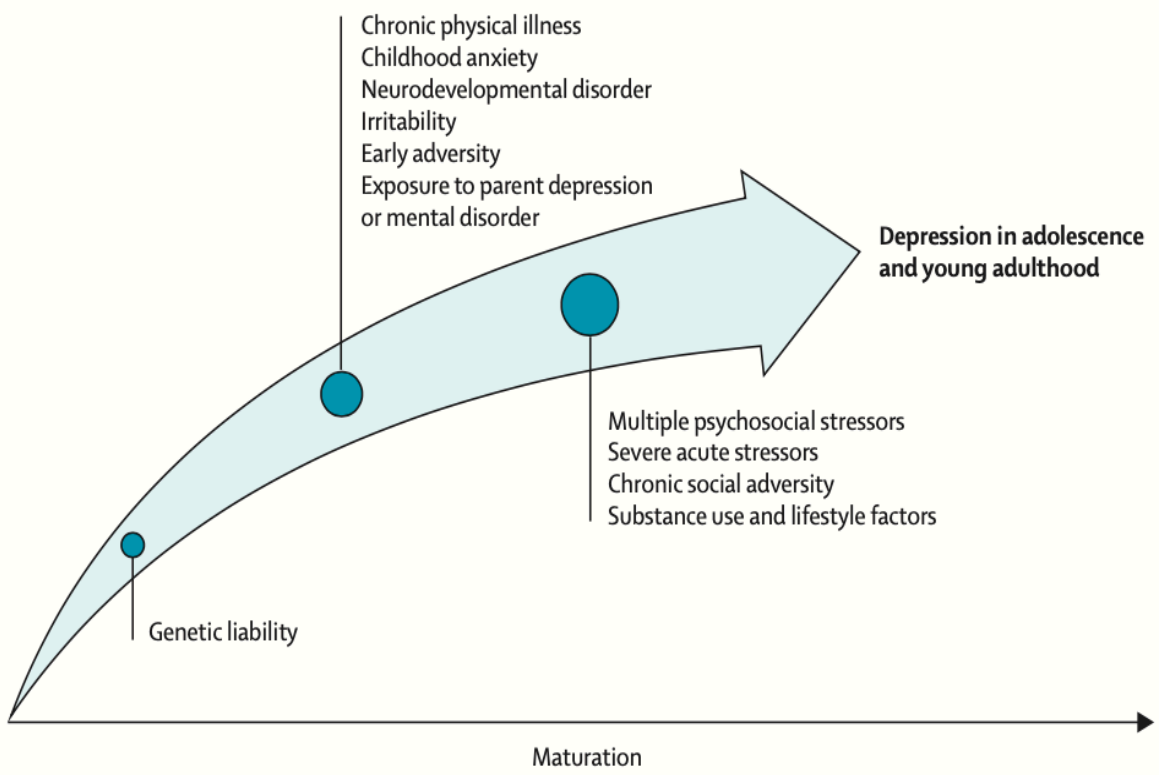
Adapted from Wehry et al. 2015. | Beesdo et al. Arch Gen Psychiatry 2010;67:47-57.
Data courtesy of Katja Beesdo, PhD, Early Developmental Stages of Psychopathology Study.

Risk Factors: Temperament, Genes & Environment

Anxiety Disorders

- **Stressful life events**
- **Parenting**
  - Overprotective/overcontrolling parenting
    - Anxious parents may fail to encourage social responsiveness.
    - Some fears may arise from modeling and vicarious learning, and verbal transmission of threat information about novel objects
- Lack of social support and **negative peer interactions**
- **Behavioral inhibition**
  - Withdraw from novel or unfamiliar social situations
  - 15% of infants are behaviorally inhibited, and half will develop **social anxiety disorder**
- Anxiety disorders are **familial**
  - Phenotypic variability explained by genetic factors ranges from 25–60%

Depressive Disorders

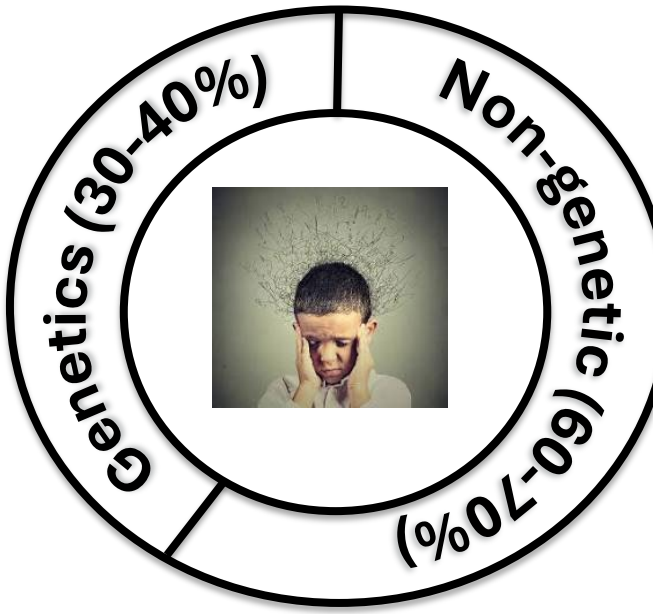


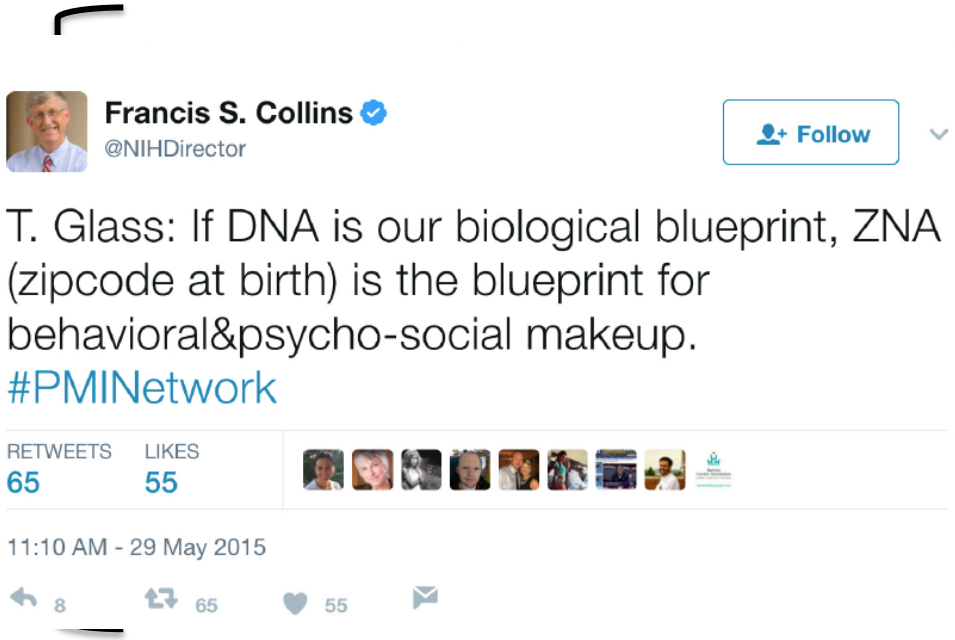
Salum et al. Rev Bras Psiquiatr 2013;35(Suppl 1) | Kagan et al. Dev Psychopathol 1999;11:209-24;
Clauss JA et al. J Am Acad Child Adoles Psychiatry 2012;51:1066-75. | Beesdo et al. Arch Gen Psychiatry 2010.
Walkup and Strawn. Depression. Rutter's Child and Adolescent Psychiatry and Psychology, 7th Edition
Thapar et al, Lancet, 2022

Slide courtesy of J. Strawn

Social Determinants of (Mental) Health

- Conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life
  - Significant contributors to health outcomes





Individual-level

- Socioeconomic disadvantage
  - arly life & childhood adversity
  - utrition
  - buse & neglect
  - dverse childhood experiences ACEs)
  - iscrimination

er social factors

- ocial capital
- eighborhood characteristics and resources
- Physical environment

Andreassen et al. World Psychiatry 2023.

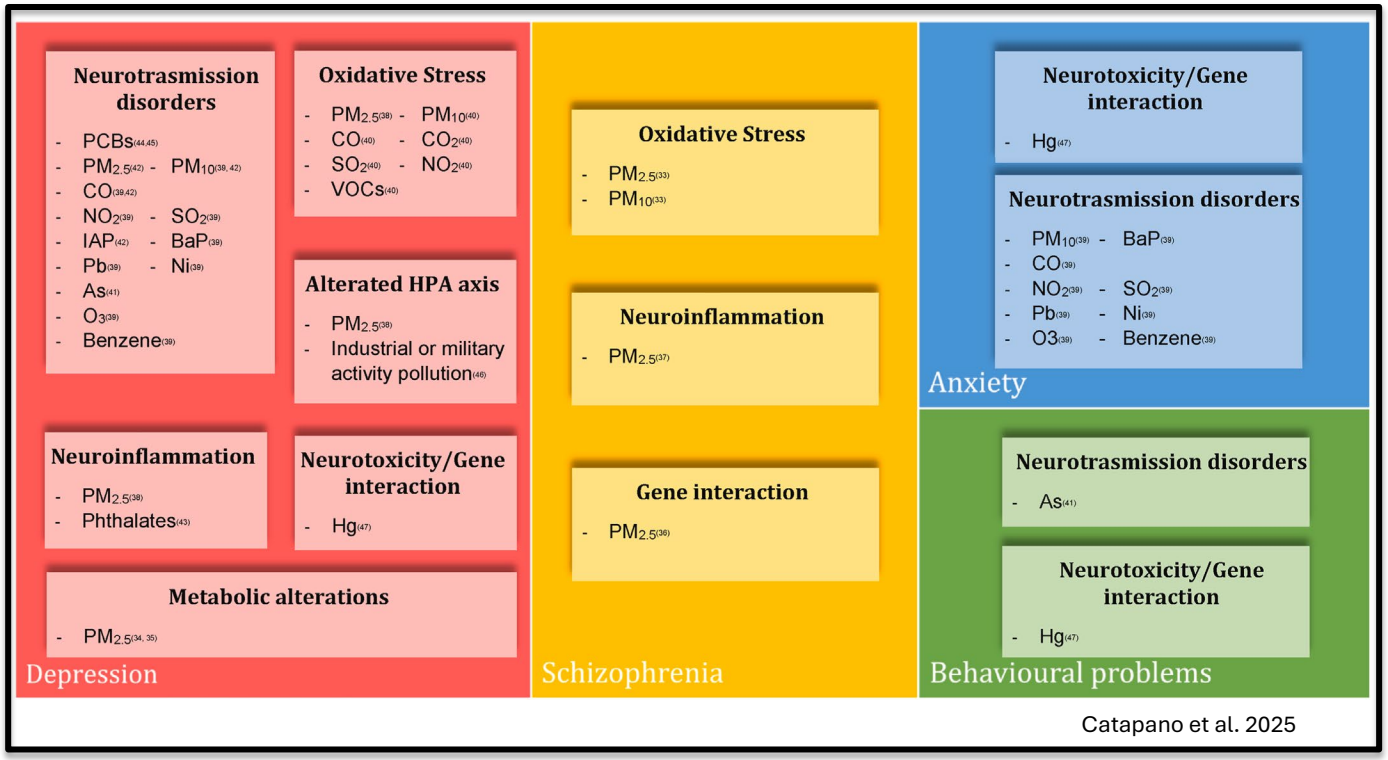
Cumulative Impacts of SDoH

- “Totality of exposures to combinations of chemical and non-chemical stressors and their effects on health, well-being, and quality of life outcomes”
- Environmental exposures and the context in which they occur (e.g. community characteristics, chronic stress) are important risk factors and predictors of mental health outcomes
  - Air pollution, greenspace, temperature
  - Neighborhood characteristics
    - Population density, households in poverty
    - Crime, access to care, pharmacies, food deserts

Tulve et al. The Lancet Regional Health – Americas. 2024

Environmental Exposures Linked to Mental Health

- Metals
  - Pb, Mn, As, Hg
  - Substitution for minerals required for neuronal signaling
- Organic solvents
  - Lipophilic → concentrate in white matter
  - ROS
- Phthalates
  - Neuroinflammation (IL-6, CRP)
- PCBs
  - Altered dopamine metabolism
- Pesticides
  - Inhibit acetylcholinesterase → disrupted neurotransmission



Catapano et al. 2025

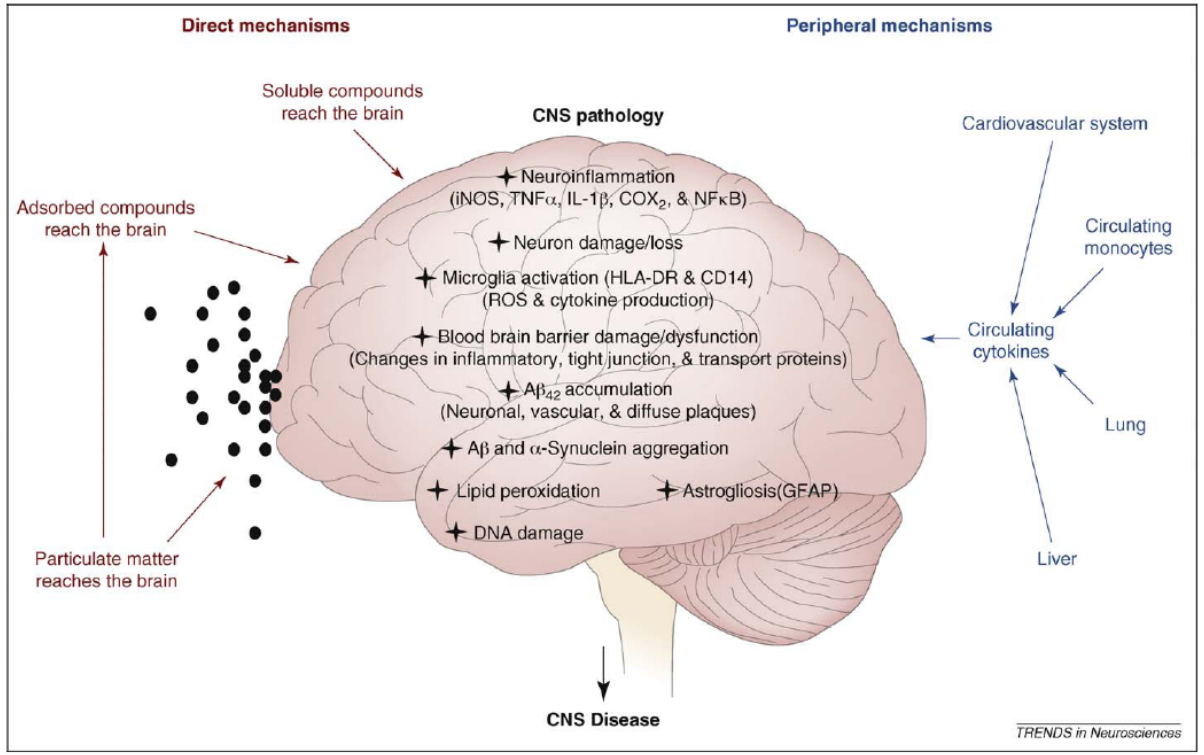
- Temperature
  - Increased stress response, disrupted thermoregulation
- Greenspace
  - Modifier: Air quality, stress, social integration

Air Pollution and the Central Nervous System

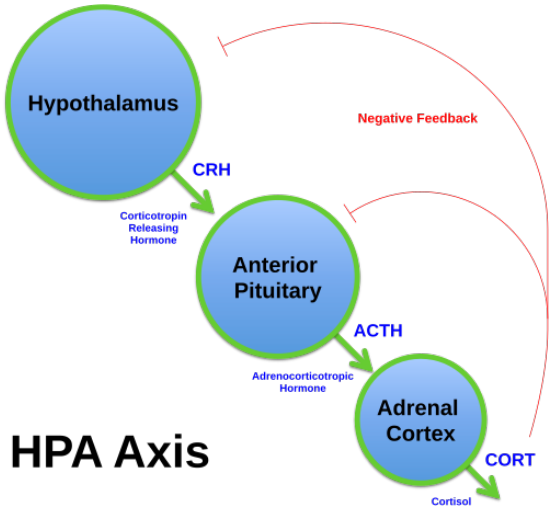
- Air pollutants
  - $PM_{2.5}$
  - Traffic-related air pollution
    - Ultrafine particles (UFP, $PM_{0.1}$)

- Mechanisms
  - Direct: Particles and absorbed compounds direct exposure to the brain
  - Indirect mechanisms
    - Inflammatory response in peripheral organ systems
    - Disruption of hypothalamic-pituitary-adrenal (HPA) axis

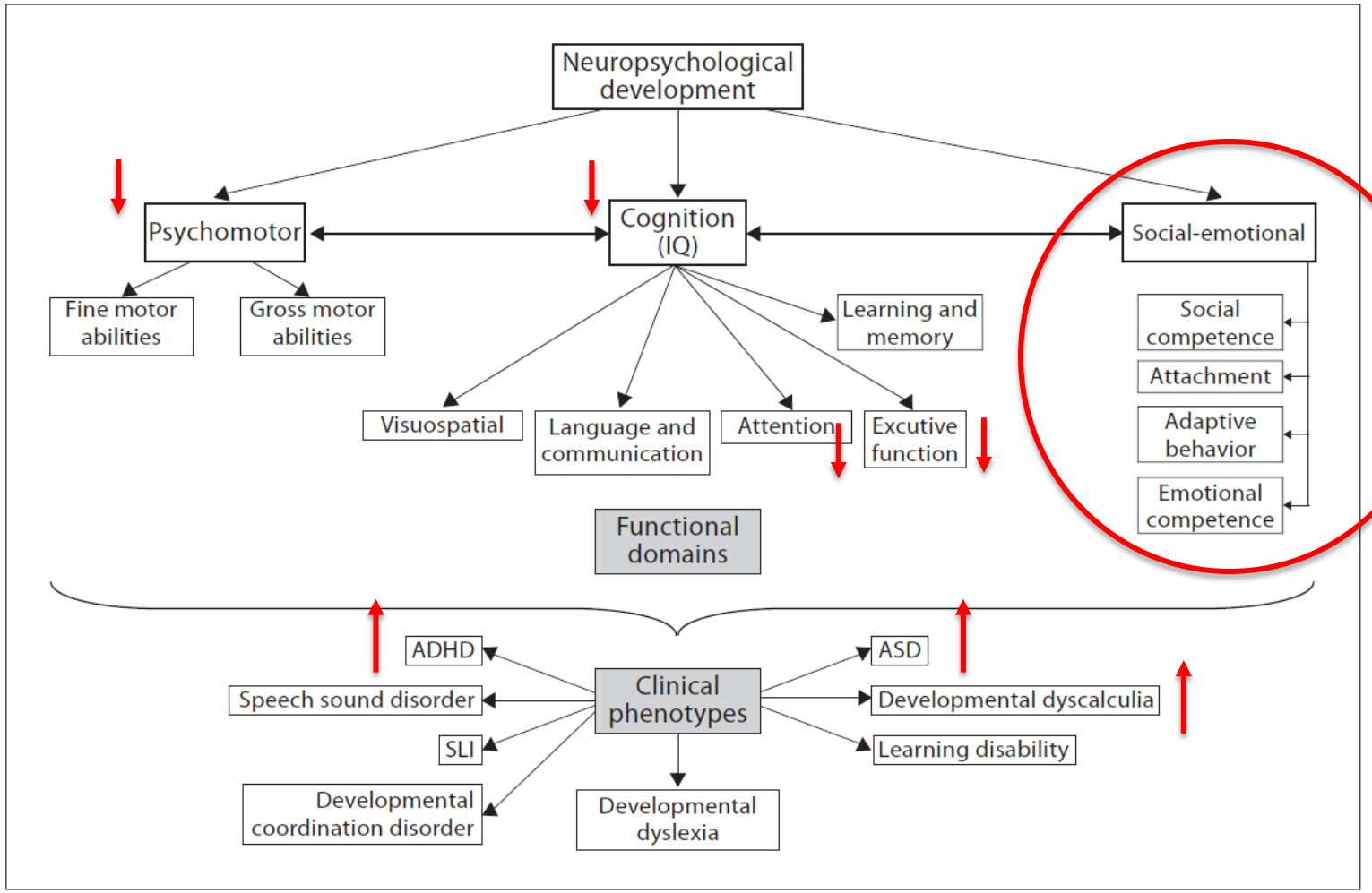
- Exposure to neurotoxicants during brain maturation can manifest as functional impairments later in life



Block and Calderon-Garciduenas. *Trends in Neurosciences*. 2009;32:506-516.



Neurodevelopmental Outcomes Associated with Air Pollution



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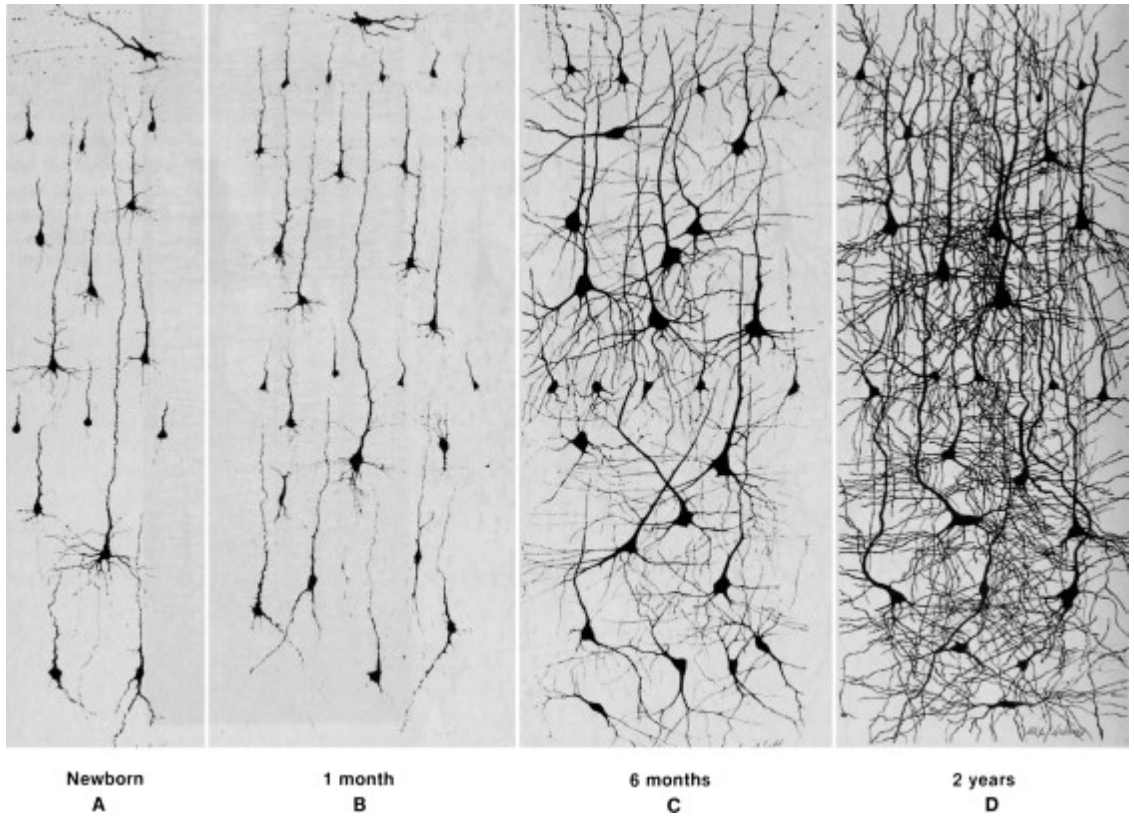
Forns et al. A Conceptual framework in the Study of Neuropsychological development in Epidemiological Studies. *Neuroepidemiology*. 2012;38:203-8.

Gestation and Early Childhood

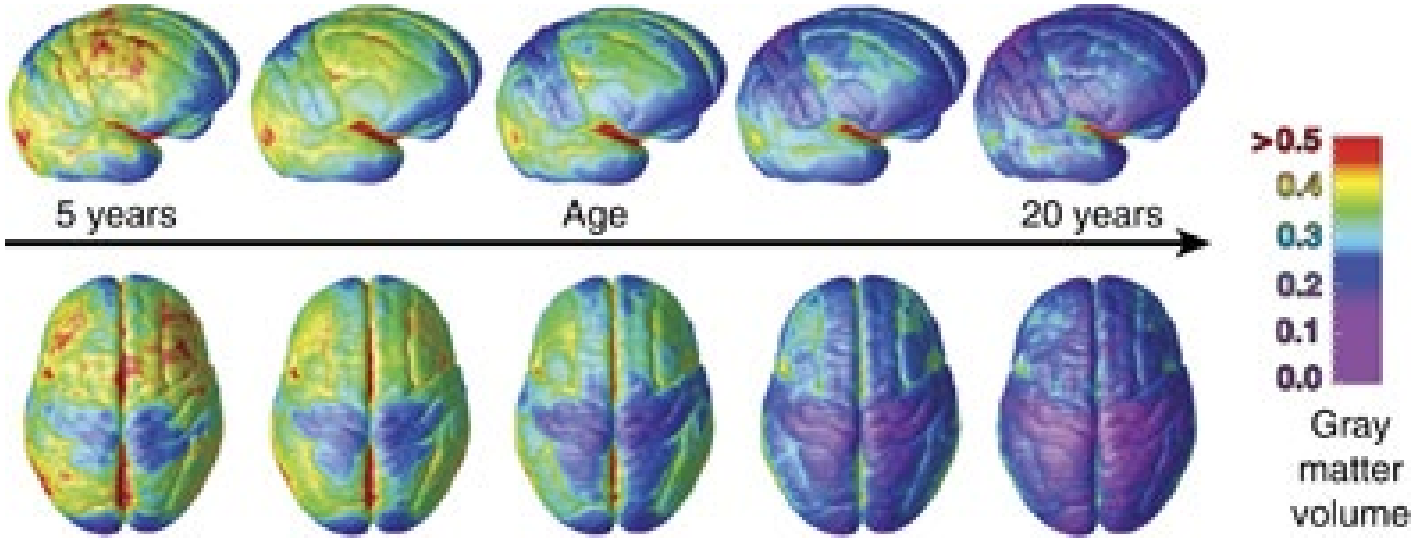
- Neuronal development
  - Rapid period of growth and connectivity through ~ 2 years followed by pruning
- Gray matter
  - Neuronal cell bodies (‘brain cells’)
    - Volume increases from mid-gestation through ~ 6 years followed by slow decrease
    - Subcortex peaks in adolescence
  - Muscle control, sensory perception, memory, emotions, decision-making
- White matter
  - Myelinated axons (‘brain connections’)
    - Rapid increase through early childhood with continued growth through ~ 30 years
    - Accelerated decline > 50 years
  - Signaling

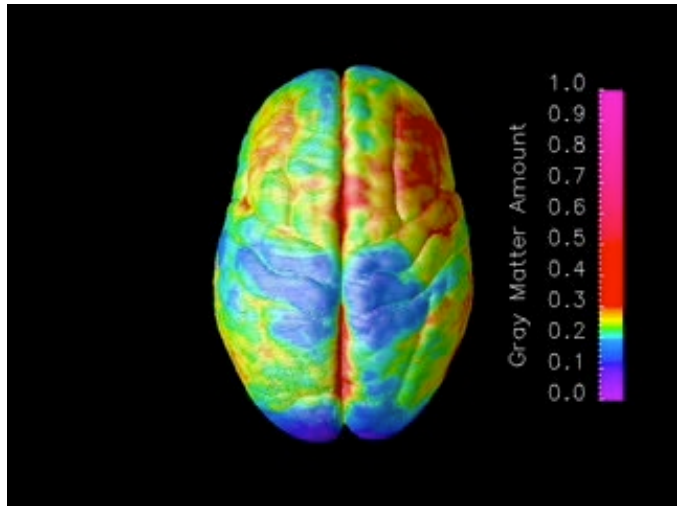


Neuronal development in cerebral cortex, Courchesne et al. Neuron. 2007

Adolescence

- Prefrontal cortex undergoes myelination and synaptic pruning
  - Loss of gray matter (↑ efficiency)
  - Decision-making, impulse control, planning
- Limbic system activity increases
  - Emotion and reward processing





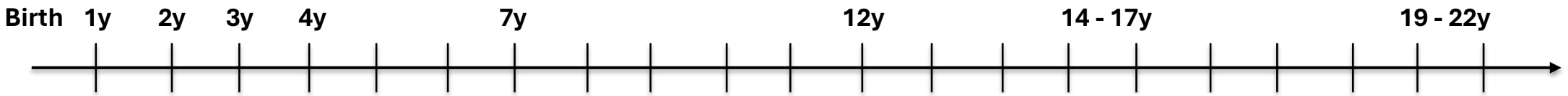
Gogtay et al., 2004, PNAS

Slide courtesy of H. Marusek

Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS)

- Determine if children exposed to traffic-related air pollution are at increased risk for
  - Allergic diseases and asthma
  - Adverse neurodevelopmental outcomes

- Longitudinal cohort of infants (n = 763) born 2001-2003 in greater Cincinnati, OH, USA
  - Birth record address < 400 m major road or > 1500 m from major road



ECHO Environmental influences on Child Health Outcomes — A program supported by the NIH | CREW Children's Respiratory and Environmental Workgroup

C4 – Cincinnati Combined Childhood Cohorts (CCAAPS + HOME Study)

Home walkthrough – Dust collection

Questionnaire, allergy testing, biospecimens, spirometry

Questionnaire, spirometry, neurobehavioral battery, MRI

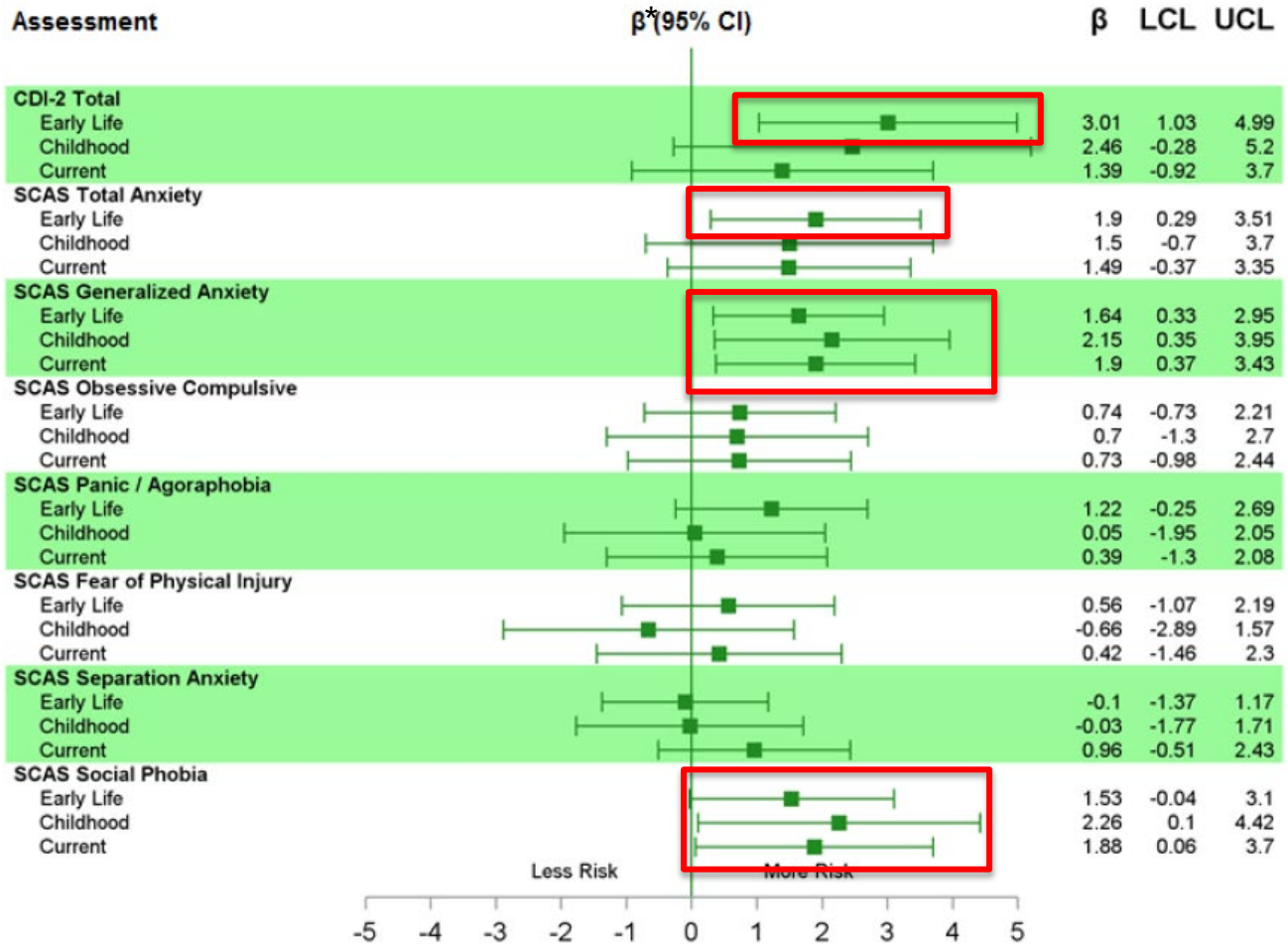
Questionnaire, allergy testing, biospecimens, spirometry

Neurobehavior, mental health, MRI

Addresses → Environmental exposure assessment & Community Characteristics at Homes, Schools, Daycares, etc

Childhood Exposure to TRAP and Symptoms of Depression and Anxiety at Age 12 y

- Early (6m) exposure to TRAP is significantly associated with child-reported depression (CDI) and anxiety (SCAS)
- Childhood and current exposure to TRAP is significantly associated with generalized anxiety and social phobia



*Adjusted for maternal age at delivery, average household income from birth through 12y, maternal depression, PRQ relational frustration, race, cotinine

Yolton K, Khoury JC, Burkle J, LeMasters G, Cecil K, Ryan P. Lifetime exposure to traffic-related air pollution and symptoms of depression and anxiety at age 12 years. Environ Res. 2019.

RESEARCH ARTICLE

Reduced gray matter volume and cortical thickness associated with traffic-related air pollution in a longitudinally studied pediatric cohort

Travis Beckwith[1,2☯*], Kim Cecil[2☯], Mekibib Altaye[3], Rachel Severs[4], Christopher Wolfe[3], Zana Percy[5], Thomas Maloney[2], Kimberly Yolton[6], Grace LeMasters[5], Kelly Brunst[5], Patrick Ryan[3☯]

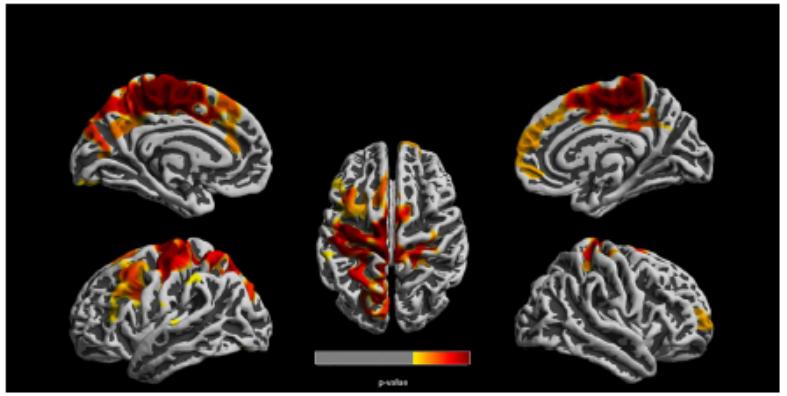


Fig 1. Statistically significant clusters using threshold free cluster enhancement. Clusters represent reduced cortica thickness in the high ECAT group compared to the low ECAT group. Clusters were corrected for multiple comparisons using a familywise error rate of $p \leq 0.05$.

- Bilateral, medial region of reduced cortical thickness within the posterior frontal and anterior parietal lobes associated with ECAT exposure
  - Primary motor cortex and sensory areas
  - Voluntary movements and integrating somatosensory information including touch
- Reduced gray matter volume
  - Primarily in the cerebellum
  - Involved with regulating motor function, cognition, and emotion

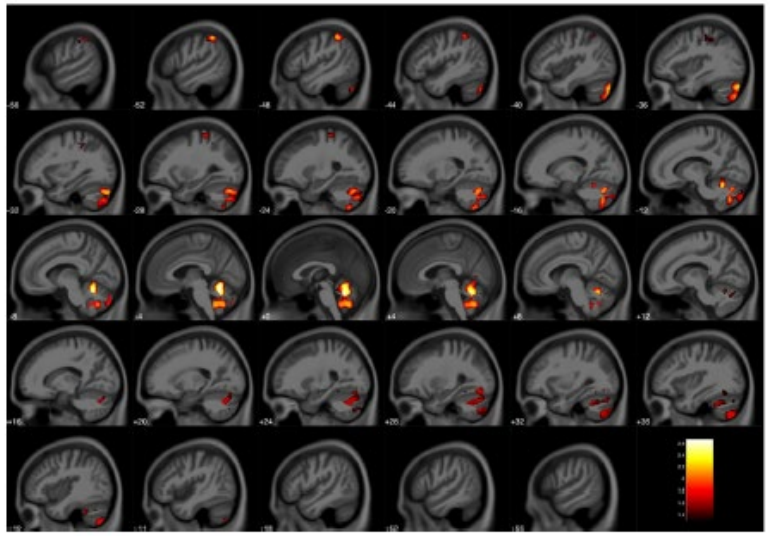
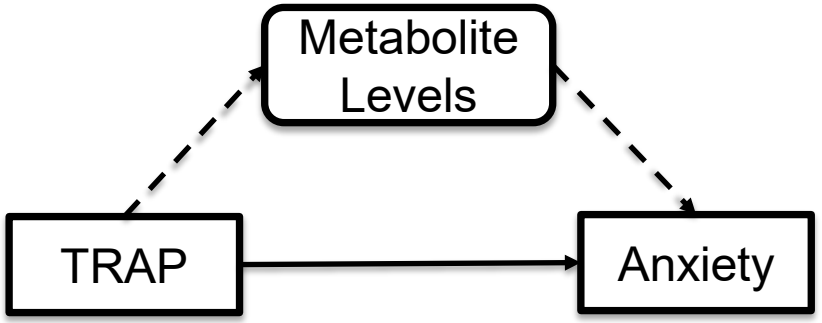


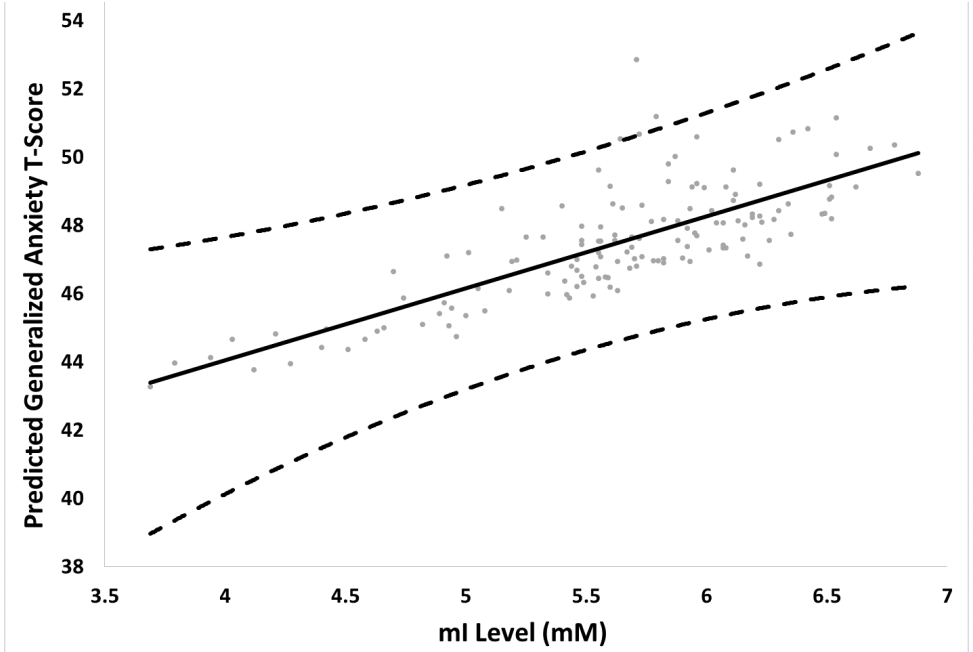
Fig 2. Reduced gray matter volume in the high ECAT group compared to the low ECAT group. Clusters were corrected for multiple comparisons using threshold free cluster enhancement with a familywise error rate of $p \leq 0.05$. Color bar represents–log(p) value.

Air Pollution, Brain Metabolism, and Anxiety

TRAP Exposure in the Past 12 Months			
Metabolite	**β ECAT**	**95% CI**	**P-value**
mI	**0.26**	**0.01, 0.51**	**0.04**
NAA	0.24	-0.13, 0.61	0.22
Cr	0.09	-0.15, 0.32	0.47
Cho	0.04	-0.02, 0.11	0.20
Glu	**0.32**	**0.03, 0.61**	**0.03**
Glx	0.52	-0.08, 1.11	0.08
GSH	0.07	-0.08, 0.21	0.38



20% of total effect mediated by myo-inositol

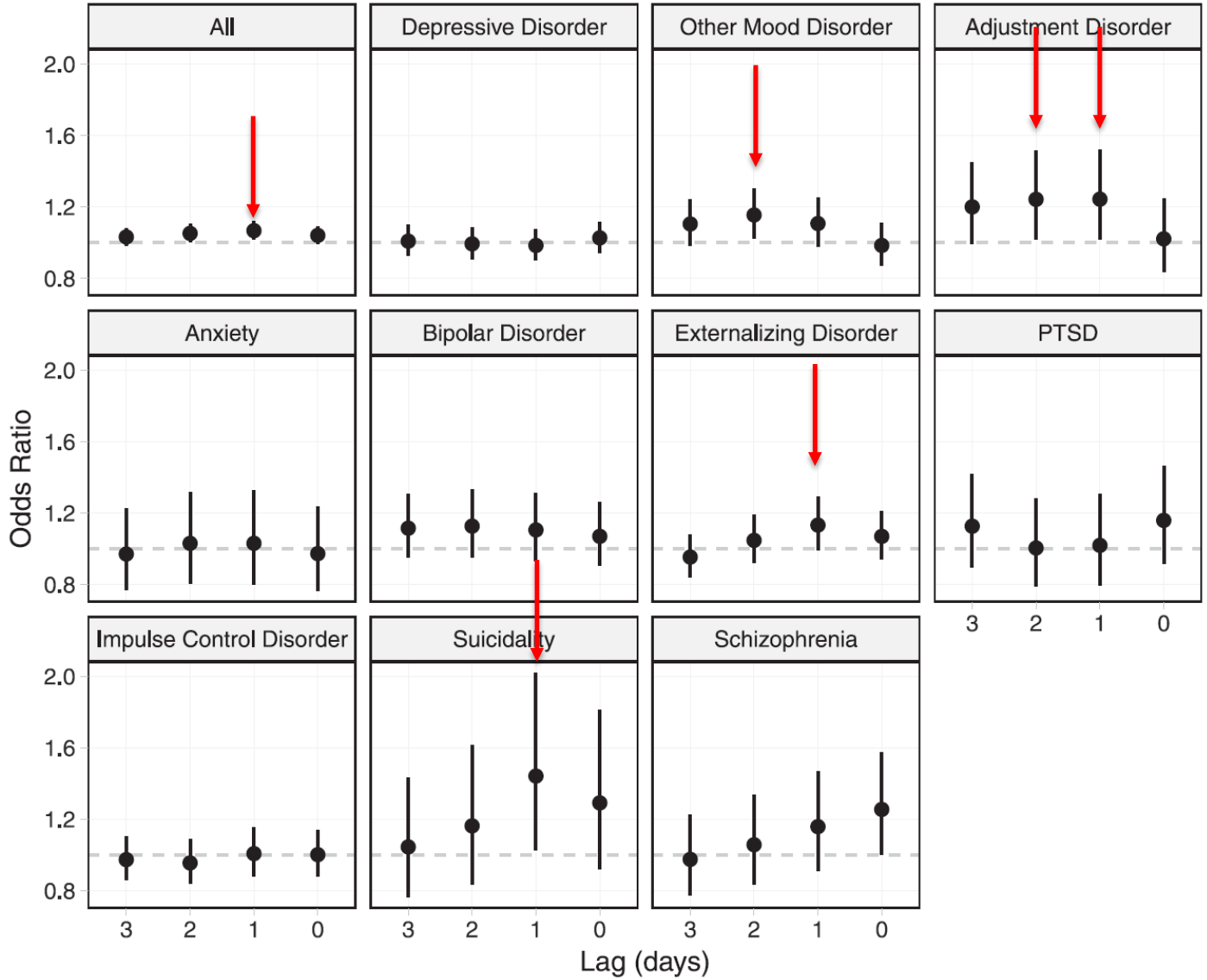


SCAS Outcome	β mI	95% CI	P-value
Generalized Anxiety	2.89	0.94, 4.83	**0.004**
Total Anxiety	3.14	0.85, 5.43	**0.007**
Social Phobia	2.52	0.34, 4.72	**0.02**

Brunst et al. Myo-inositol mediates the effects of traffic-related air pollution on generalized anxiety symptoms at age 12 years. Environ Res 2019

Acute $PM_{2.5}$ Exposure and Pediatric Psychiatric Emergency Department Visits

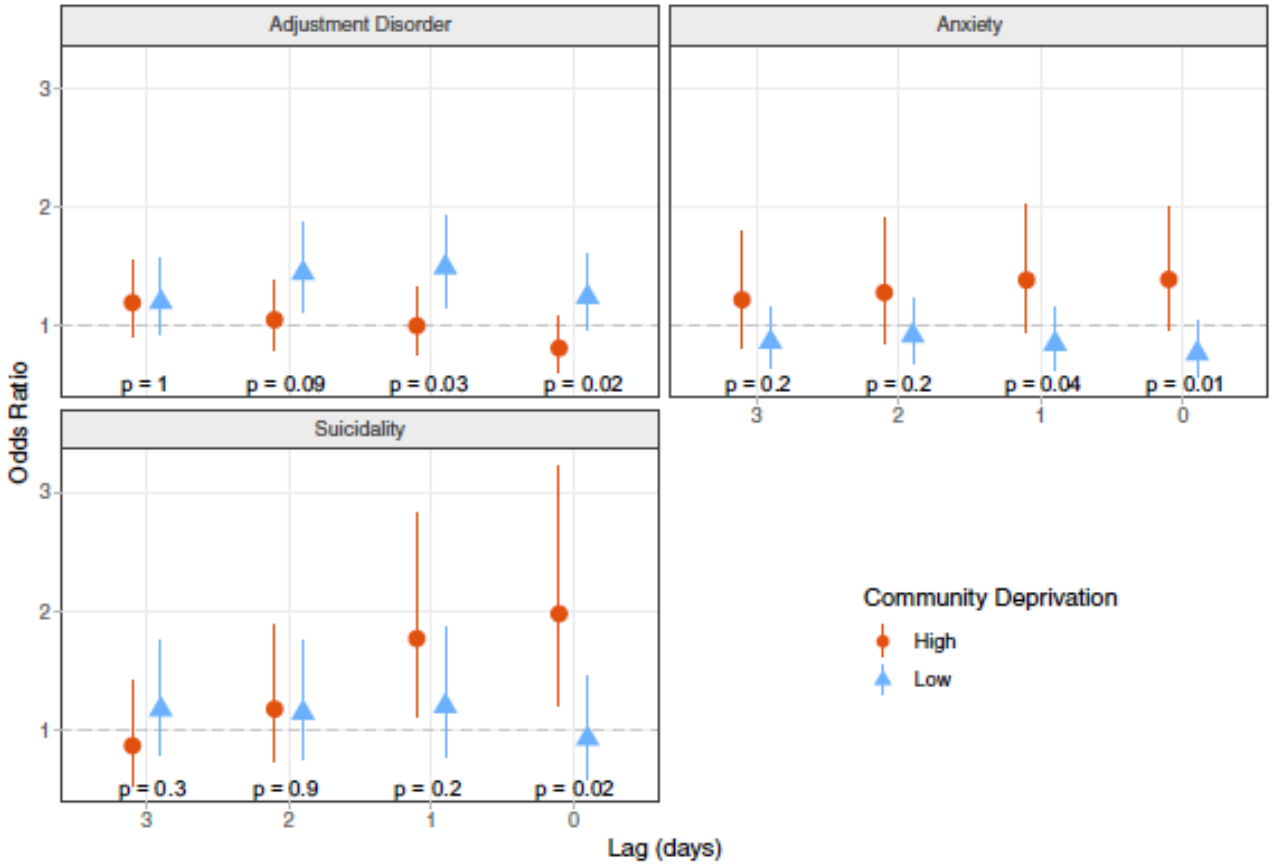
Psychiatric ED visit category	*n*
Overall	13,176
Adjustment disorder	702
Anxiety	486
Bipolar disorder	1,001
Depressive disorder	3,847
Developmental disorder	88
Externalizing disorder	1,850
Impulse control disorder	1,755
Other mood disorder	1,903
Personality disorder	142
PTSD	519
Schizophrenia	500
Suicidality	275



Brokmap C, Strawn J, Beck AF, Ryan P. Pediatric Psychiatric Emergency Department Utilization and Fine Particulate Matter: A Case-Crossover Study. *Environmental Health Perspectives*. 2019.

Community Characteristics Modify the Relationship Between Air Pollution and Mental Health

- Higher community deprivation increased risk for suicidality and anxiety
- Lower community deprivation increased risk for adjustment disorders



Brokmap C, Strawn J, Beck AF, Ryan P. Pediatric Psychiatric Emergency Department Utilization and Fine Particulate Matter: A Case-Crossover Study. *Environmental Health Perspectives*. 2019.

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