Air pollution and brain development: insights from population neuroimaging

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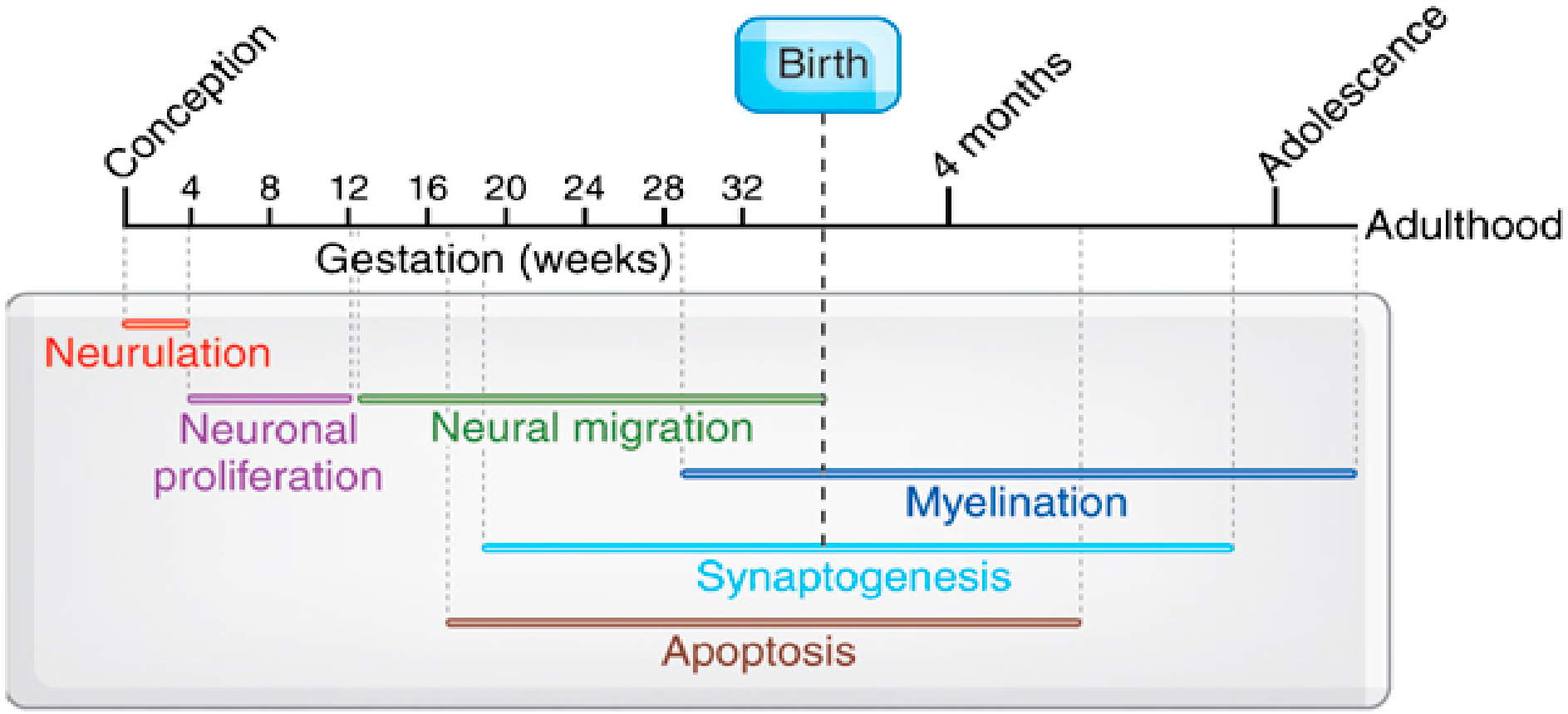
“You have only one chance to develop a brain” – Prof. Philippe Grandjean



Tau and Peterson. Neuropsychopharmacology. 2010;35:147–168

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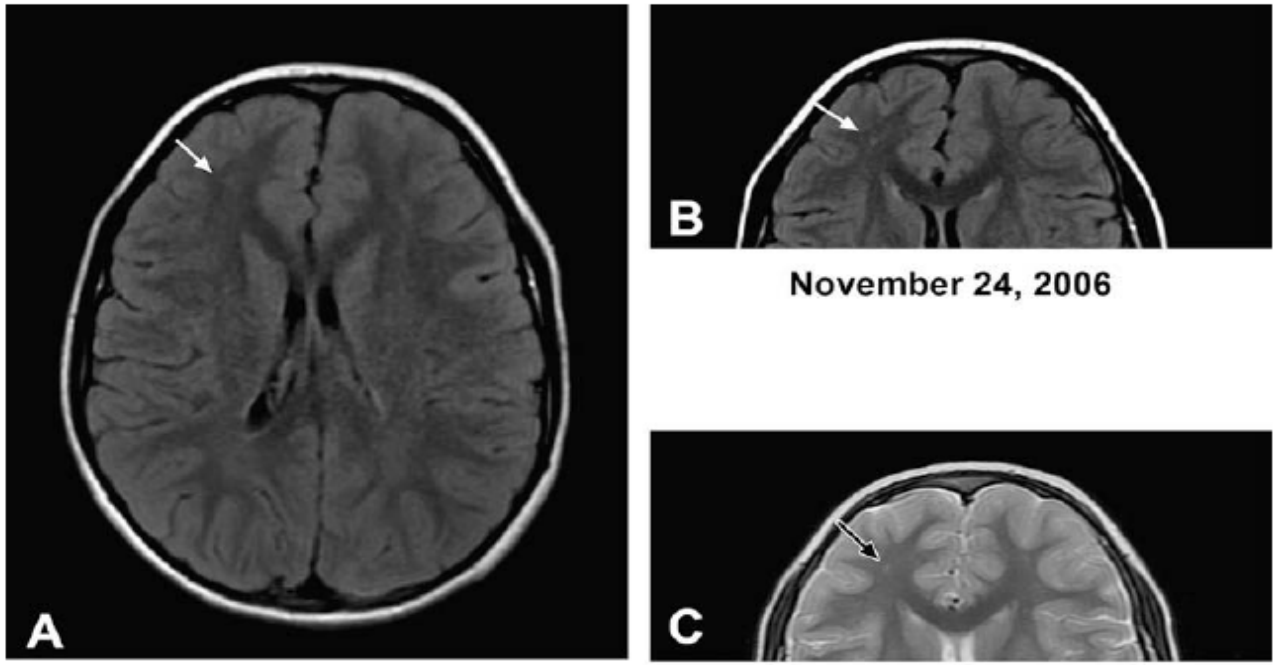
Air pollution, cognitive deficits and brain abnormalities: A pilot study with children and dogs

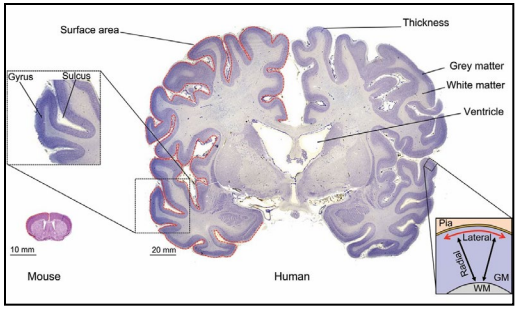
Lilian Calderón-Garcidueñas [a,b,*], Antonieta Mora-Tiscareño [a], Esperanza Ontiveros [a], Gilberto Gómez-Garza [a], Gerardo Barragán-Mejía [a], James Broadway [c], Susan Chapman [d], Gildardo Valencia-Salazar [a], Valerie Jewells [e], Robert R. Maronpot [f], Carlos Henríquez-Roldán [g], Beatriz Pérez-Guillé [a], Ricardo Torres-Jardón [h], Lou Herrit [b], Diane Brooks [b], Norma Osnaya-Brizuela [a], Maria E. Monroy [a], Angelica González-Maciel [a], Rafael Reynoso-Robles [a], Rafael Villarreal-Calderon [i], Anna C Solt [j], Randall W. Engle [c,1]

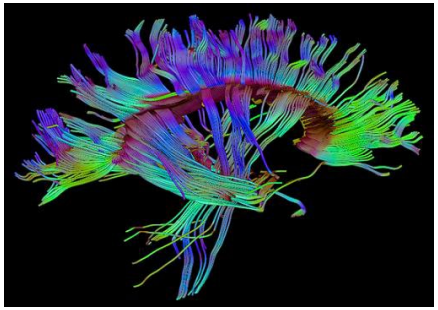
Brain Cogn. 2008;68(2):117-27

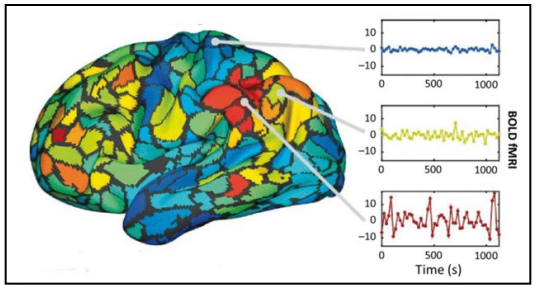


How to study brain imaging in environmental epidemiology in children?

- Magnetic Resonance Imaging
- 3 main assessments:
  - Macrostructure or brain morphology
  - Microstructure (e.g., white matter microstructure)
  - Function or brain network connectivity







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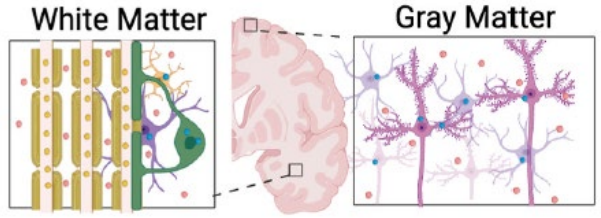
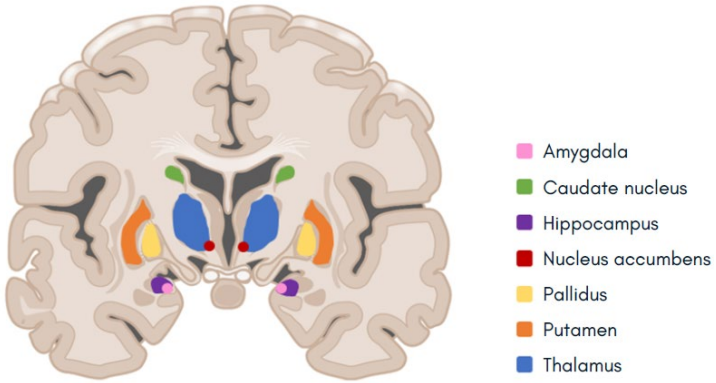
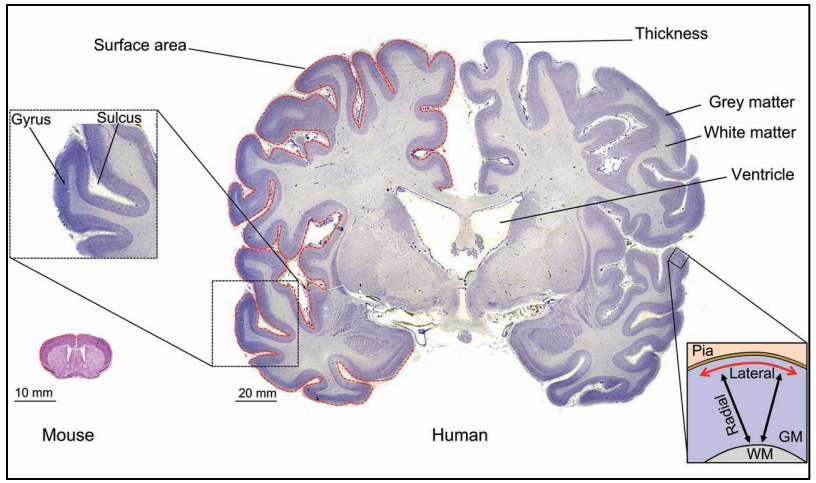
Brain morphology: what is it measured?



- Global brain volumes (e.g., cortical gray matter, cerebral white matter, ventricles, cerebellum, corpus callosum)

- Subcortical brain volumes





- Cortical thickness and surface area

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Air pollution and brain morphology

- 12 papers
- 7 epidemiological studies: 4 USA, 1 UK, 1 Spain, 1 Netherlands
- 6 pregnancy exposure; 7 childhood exposure (home or school)

Air pollution and brain morphology

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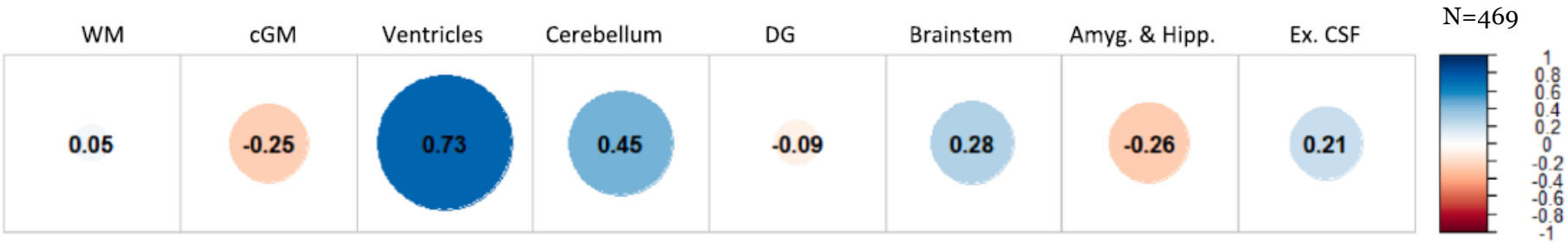
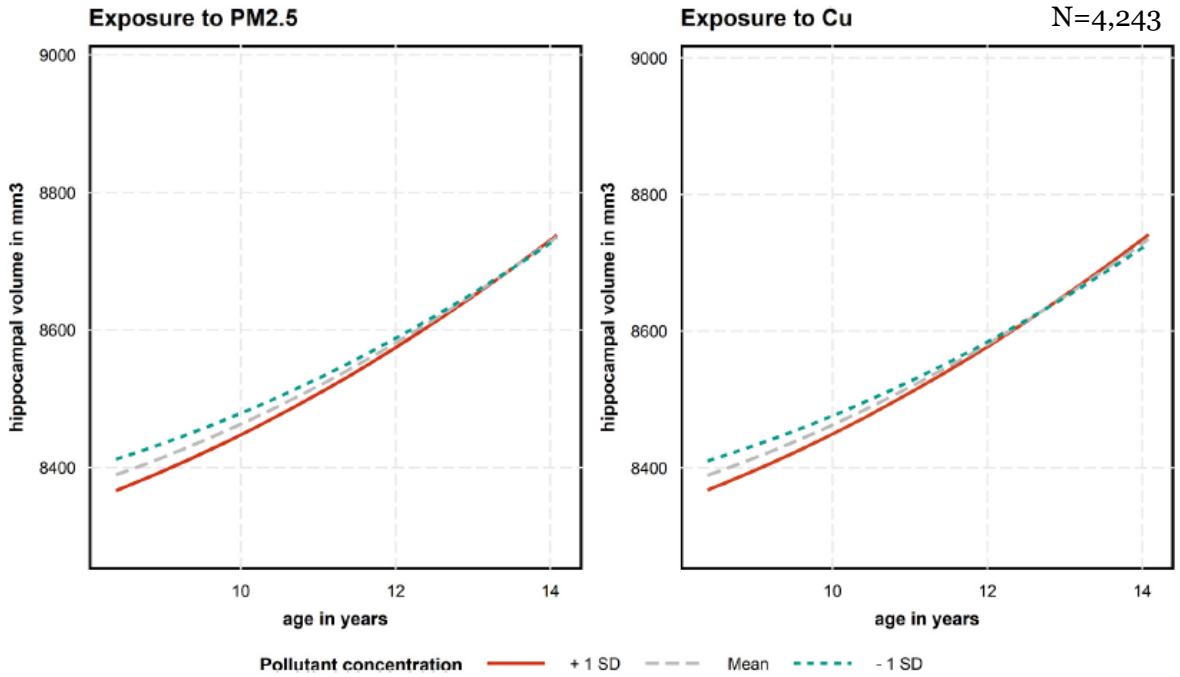
	Brain volumes	**Cortical thickness**
Pregnancy exposure	⇩/ ⇧ at birth and 8y *(Bos 2023, Peterson 2022)* ⇩ at 8y but no association at 14y *(Kusters 2025)*	⇩ at 8y and 10y *(Guxens 2018, Lubczynska 2020)*
Childhood exposure	⇩ / ⇧ at 9y and 10y *(Cserbik 2020, Lubczynska 2021)* ⇩ at 9y and 12y *(Mortamais 2017, Beckwith 2020)*	⇩ / ⇧ at 9y *(Cserbik 2020)* ⇩ at 10y and 12y *(Lubczynska 2020, Beckwith 2020)*

Pregnancy air pollution and brain volumes



Bos et al. Environ Int 2023;174:107921



Kusters et al. Environ Pollut 2025;373:126078

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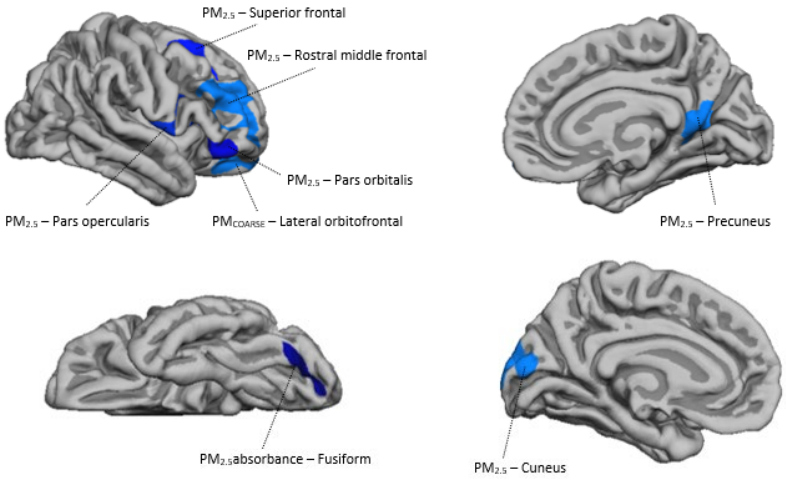
Pregnancy and childhood air pollution and cortical thickness

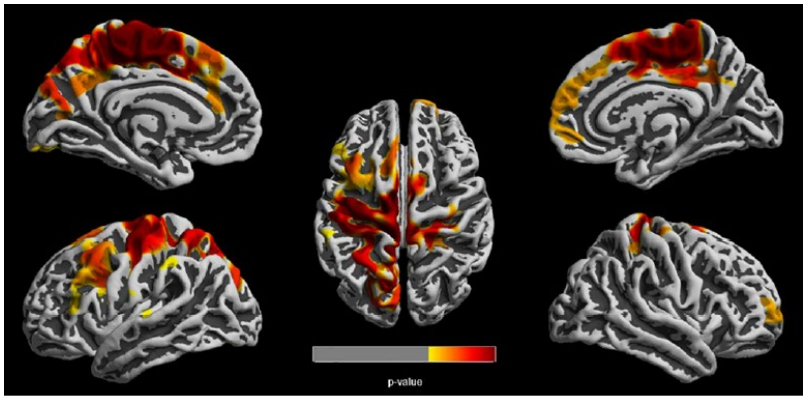
School-age children N=783

Pregnancy exposure



Guxens et al. Biol Psychiatr 2018;84(4):295-303

Preadolescent children N=135



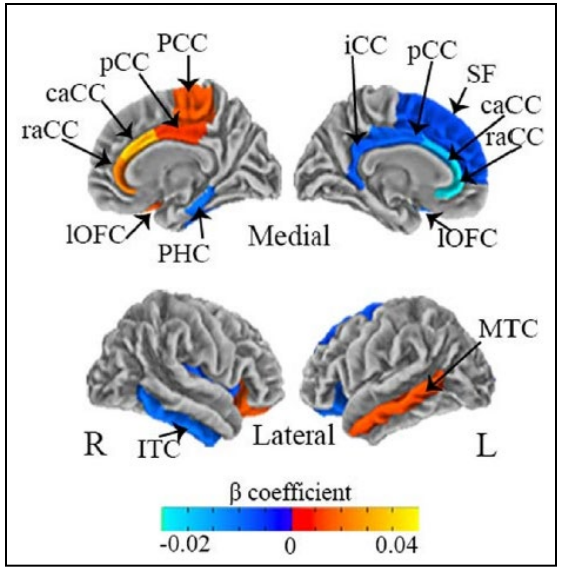
Beckwith et al. PLoS ONE 2020;15(1):e0228092

Preadolescent children N=3,133

Pregnancy exposure | Childhood exposure

Lubzynska et al. Environ Res. 2020;110446

Preadolescent children N=10,343



Cserbik et al. Environ Int 2020;143:105933

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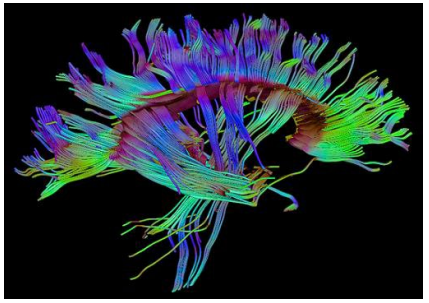
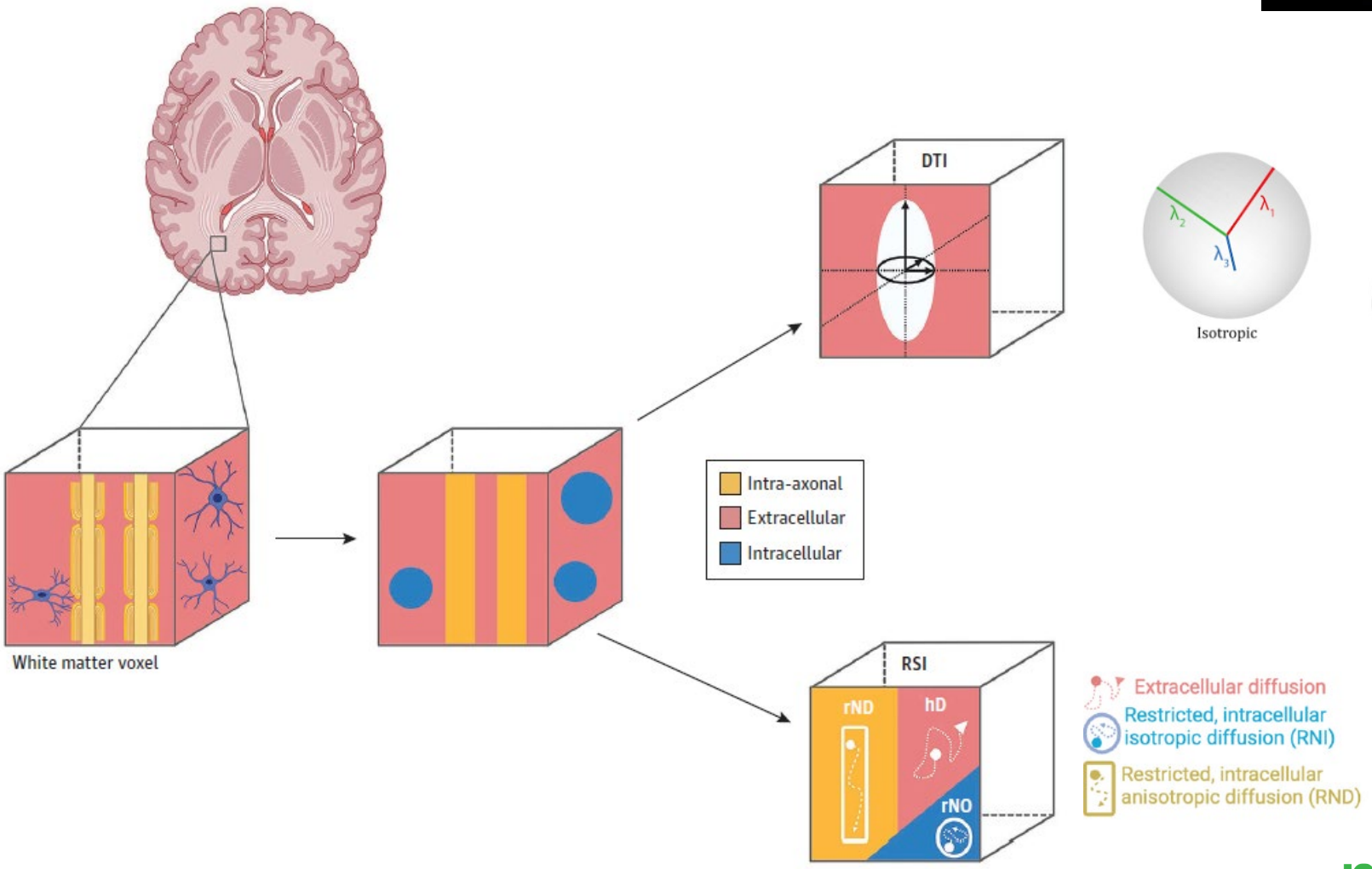
White matter microstructure: what is it measured?





Burnor et al. JAMA Net Open 2021;4(12):e2138300

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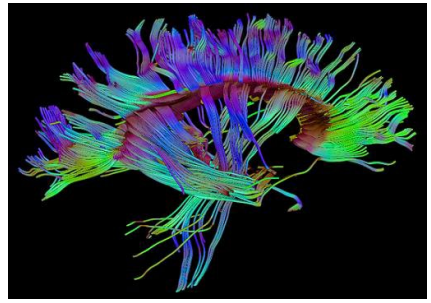
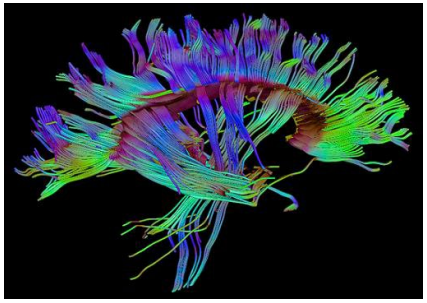
Air pollution and white matter microstructure



- 7 papers
- 4 epidemiological studies: 2 USA, 1 Spain, 1 Netherlands
- 3 pregnancy exposure; 10 childhood exposure (home or school)

Air pollution and white matter microstructure

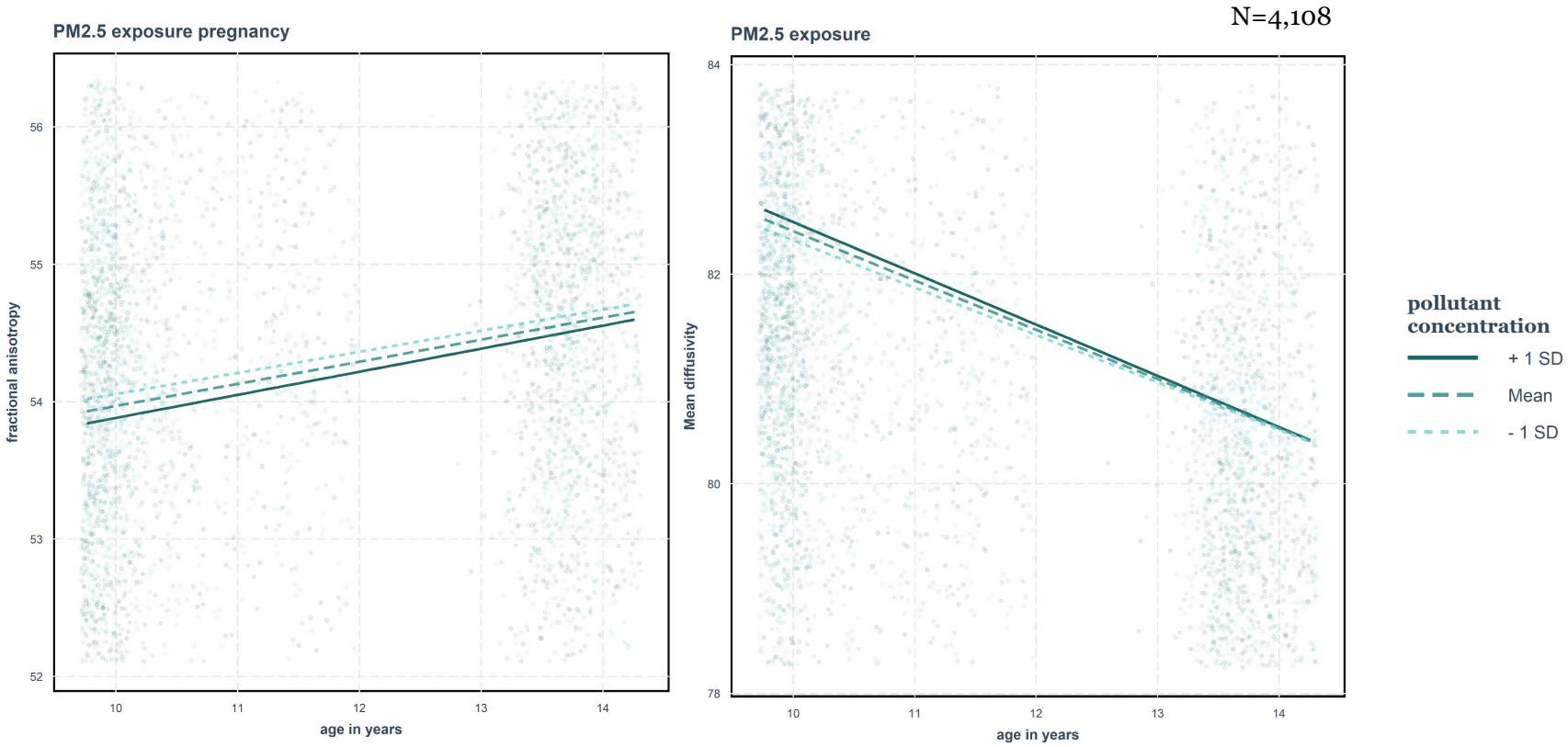


- 7 papers
- 4 epidemiological studies: 2 USA, 1 Spain, 1 Netherlands
- 3 pregnancy exposure; 10 childhood exposure (home or school)

	Whole-brain effects	**Regional effects**
Pregnancy exposure	⇩ FA at 10y and 14y ⇧ MD only at 10y *(Kusters 2024, Lubczynska 2020)*	⇧ FA at 10y ⇧ / ⇩ MD at 10y *(Peterson 2022)*
Childhood exposure	⇩ FA at 10y and 14y ⇧ MD only at 10y *(Kusters 2024, Lubczynska 2020)* no association FA at 10y *(Pujol 2016b, Burnor 2021)* ⇩ MD and at 10y *(Burnor 2021)*	⇧ FA near/within caudate nucleus at 9y (Pujol 2016a) ⇧ / ⇩ RNI and RND at 9y and from 9y to 11y *(Burnor 2021; Cotter 2024)*

Whole-brain effects: pregnancy and childhood air pollution and longitudinal white matter microstructure at 10-14y

N=4,108



Kuster et al. Environ Res 2024; 262(Pt 2):119828

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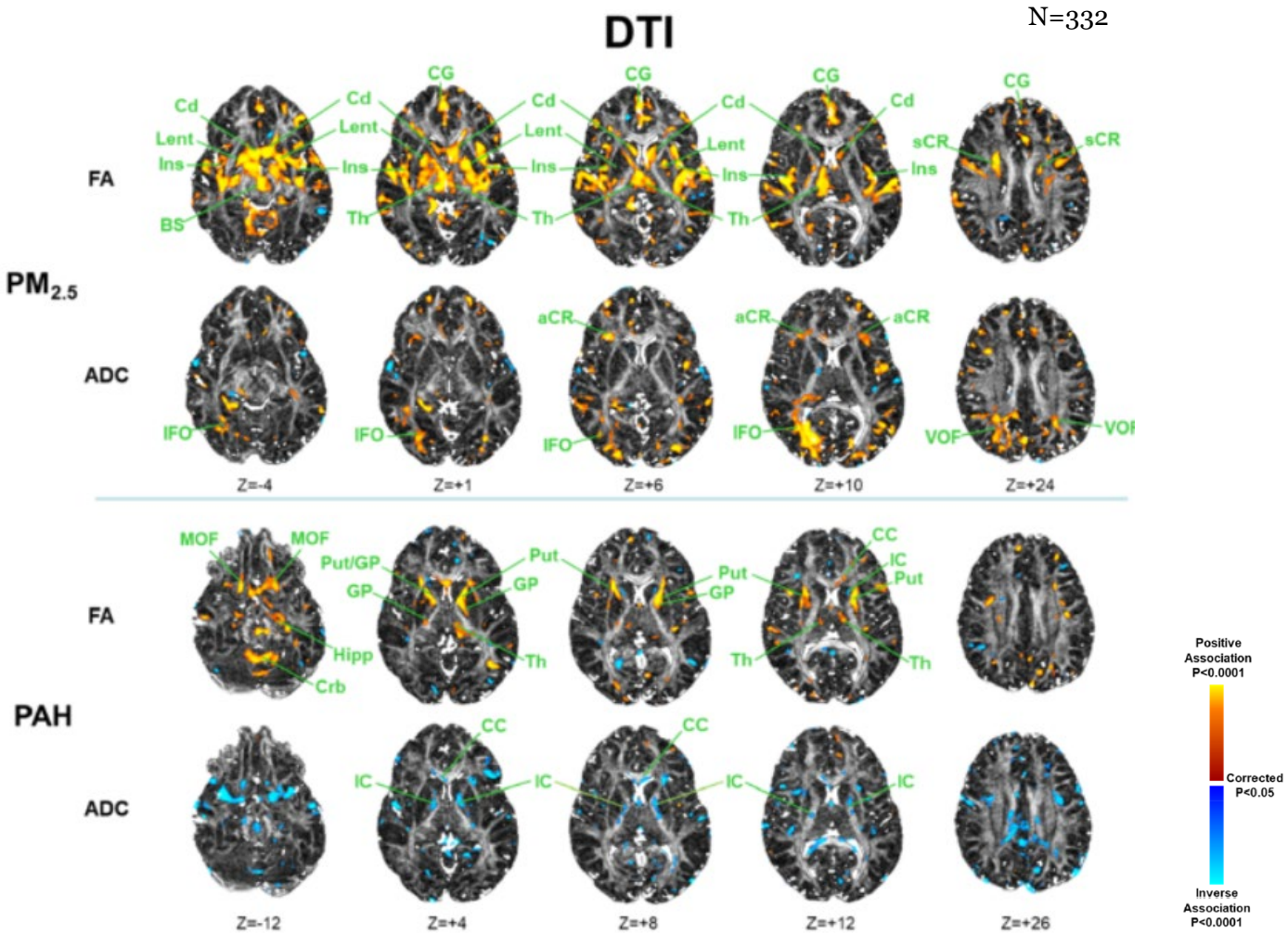
Regional effects: pregnancy air pollution and white matter microstructure at 10y



Peterson et al. J Child Psychol Psychiatry 2022;63(11):1316-31

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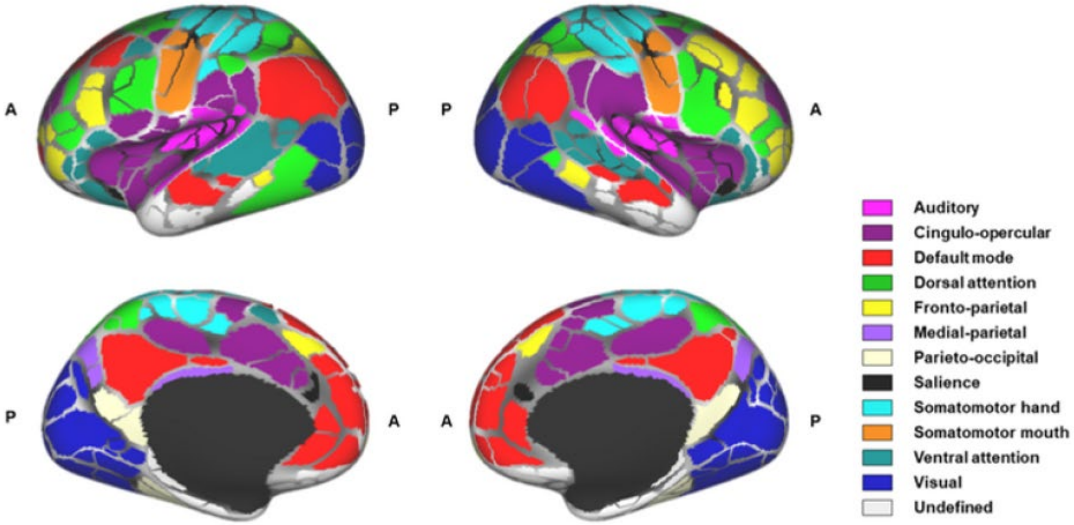
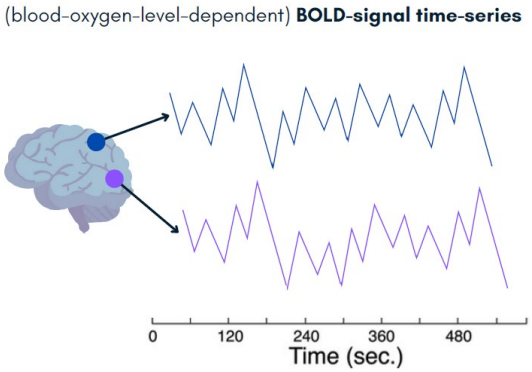
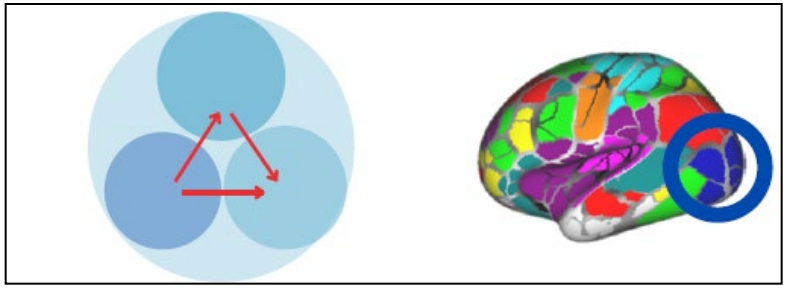
Brain network connectivity: what is it measured?

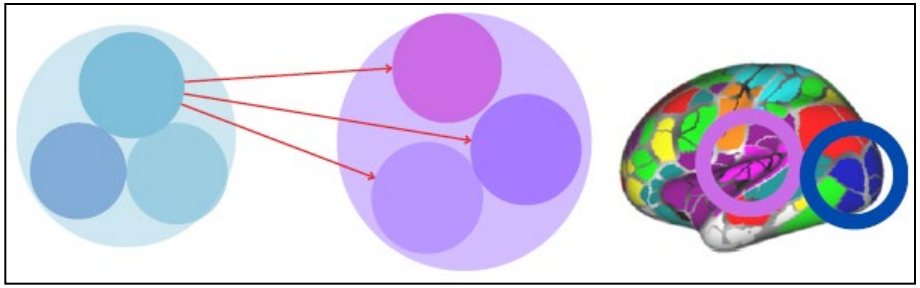




Within-network connectivity



Between-network connectivity



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Air pollution and brain network connectivity

- 5 papers
- 3 epidemiological studies: 1 USA, 1 Spain, 1 Netherlands
- 1 pregnancy exposure; 5 childhood exposure (home or school)

Within-network connectivity	**Between-network connectivity**	**Subcortical-network connectivity**
⇩ connectivity at 10y *(Pujol 2016b)* ⇩ / ⇧ connectivity from 9y to 11y *(Cotter 2023, Zundel 2024)*	⇩ connectivity at 10y and 14y *(Pujol 2016b, Kusters 2025)* ⇩ / ⇧ connectivity from 9y to 11y *(Cotter 2023, Zundel 2024)*	⇩ connectivity at 10y and 14y *(Pujol 2016a, Kusters 2025)* ⇩ / ⇧ connectivity from 9y to 11y *(Cotter 2023)*

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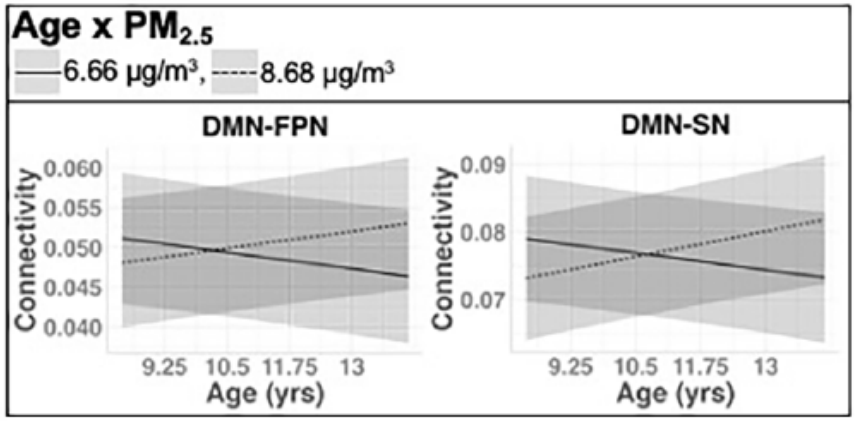
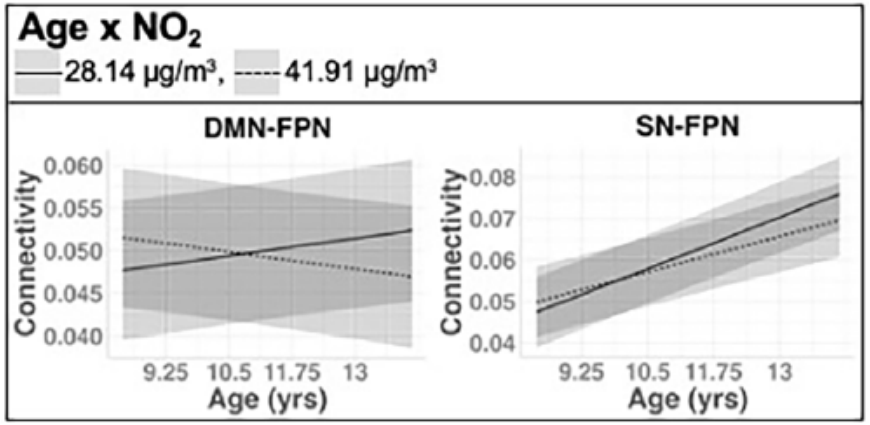
Air pollution and between-network connectivity

N=9,497





Cotter et al. Environ Int 2023;177:108001

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Which are the functional/clinical implication of all these brain imaging findings?

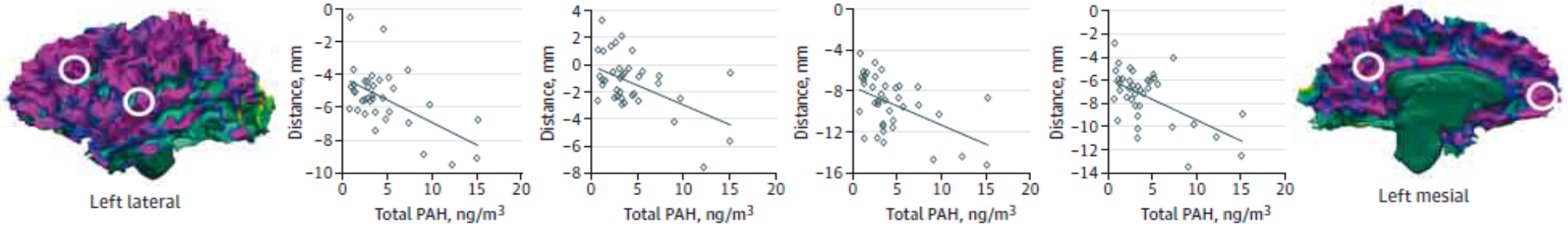
Effects of Prenatal Exposure to Air Pollutants (Polycyclic Aromatic Hydrocarbons) on the Development of Brain White Matter, Cognition, and Behavior in Later Childhood

Bradley S. Peterson, MD; Virginia A. Rauh, ScD; Ravi Bansal, PhD; Xuejun Hao, PhD; Zachary Toth, BA; Giancarlo Nati, BA; Kirwan Walsh, BA; Rachel L. Miller, MD; David Semanek, BA; Frederica Perera, DrPH, PhD

JAMA Psychiatry. 2015

N=40

A Correlations with prenatal PAH levels



B Co

Prenatal PAH exposure → Reduced white matter surface → Slower information processing speed in childhood

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Archival Report

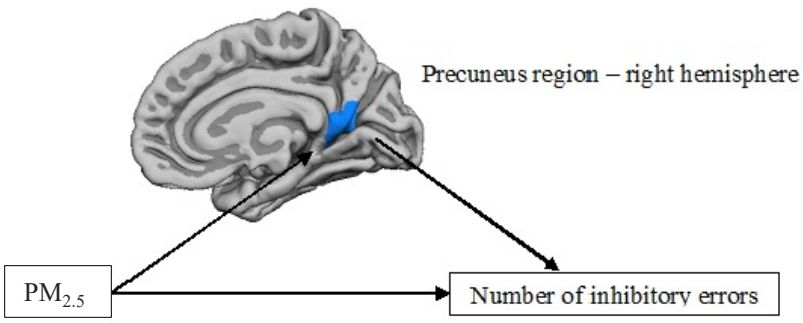
Biological Psychiatry

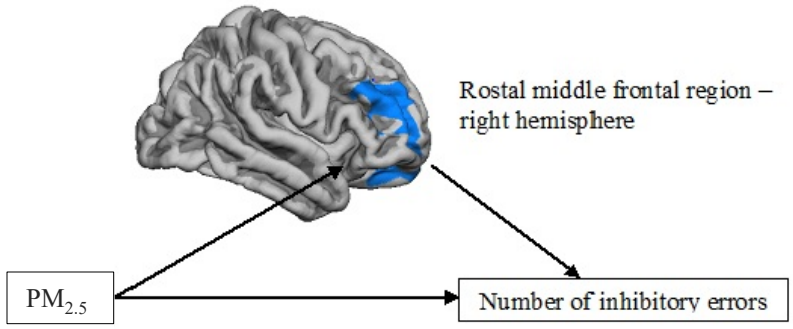
Air Pollution Exposure During Fetal Life, Brain Morphology, and Cognitive Function in School-Age Children

Mònica Guxens, Małgorzata J. Lubczyńska, Ryan L. Muetzel, Albert Dalmau-Bueno, Vincent W.V. Jaddoe, Gerard Hoek, Aad van der Lugt, Frank C. Verhulst, Tonya White, Bert Brunekreef, Henning Tiemeier, and Hanan El Marroun

Biol Psychiatry 2018;84(4):295-303

N=783





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Overall conclusion

- Air pollution has been associated with several brain structural and functional changes from infancy to adolescence
- Different results were observed depending on the study (or within the same study depending on the air pollutant)
- Little is known on the functional/clinical implication of the brain imaging findings

Challenges

- Most findings based on very few epidemiological studies, with varying sample sizes → publication bias?
- Outcome measures or analytical approach not harmonized between (or within) studies which limits comparability
- Very complex outcome measure, not well understood
- All studies in countries from the Global North with “relatively” low levels of air pollution

Opportunities and future directions

- Research of biological mecanisms in the brain in general healthy population – important besides cognitive function and mental health
- Longitudinal brain neuroimaging to identify susceptibility periods of exposure
- Harmonize outcomes measures from different studies
- Consider other urban environmental exposure
- Which implications have these findings at older ages?

Thank you!

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