Neurotoxic effects of air pollution in early life

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Philadelphia
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Minamata 1956
Effects of prenatal exposure to mercury

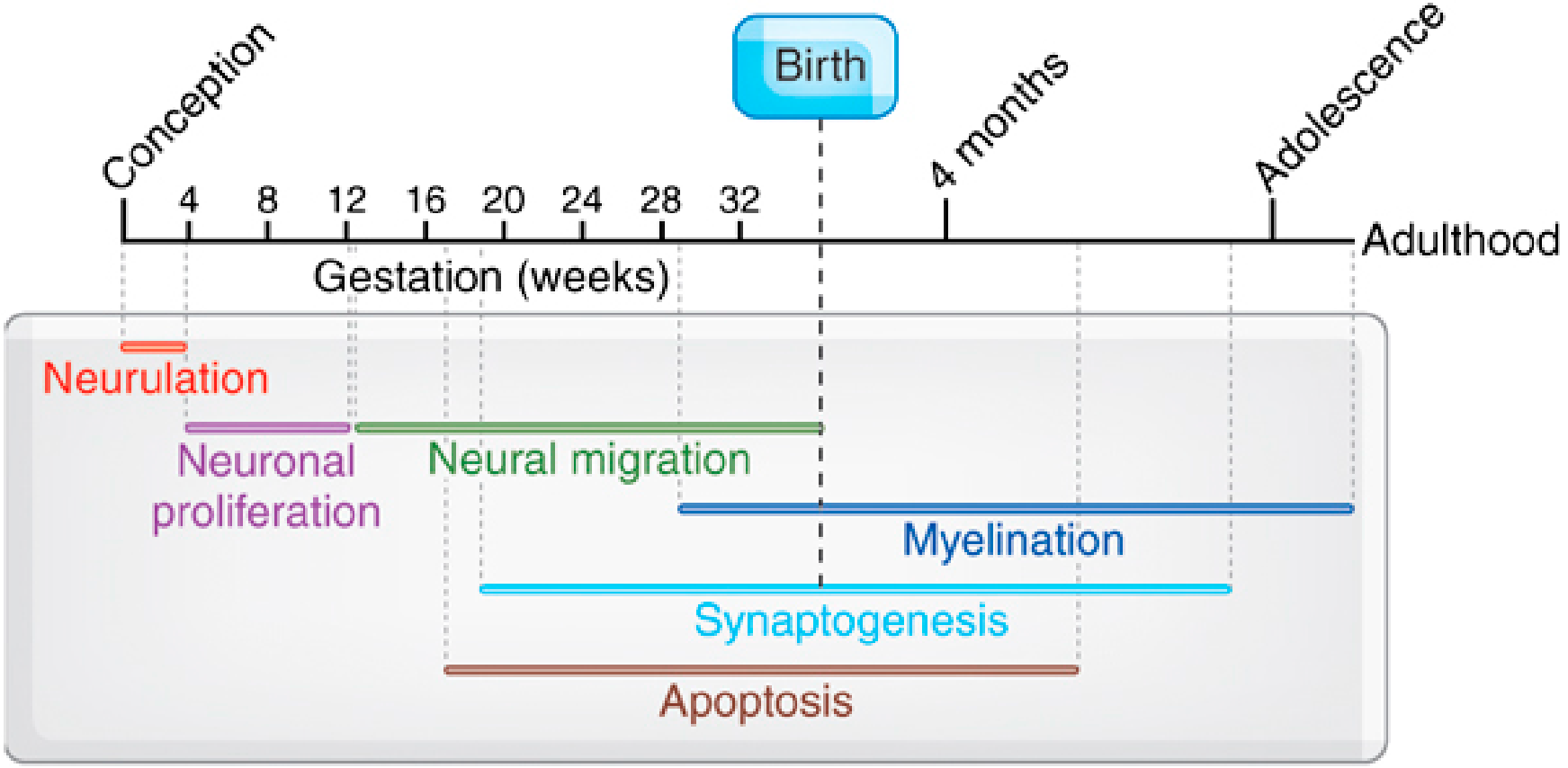
- Outbreak of an unknown disease of the central nervous system
- Symptoms include ataxia, general muscle weakness, and damage of vision, hearing and speech
- In extreme cases, paralysis, coma, and death follow within weeks of the onset of symptoms

Lesson from Minamata

…in every case the mother was healthy, and it was not until more than three months after birth that the symptoms were recognized

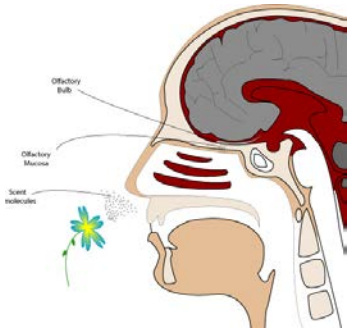
Shoji Kitamura (1959)

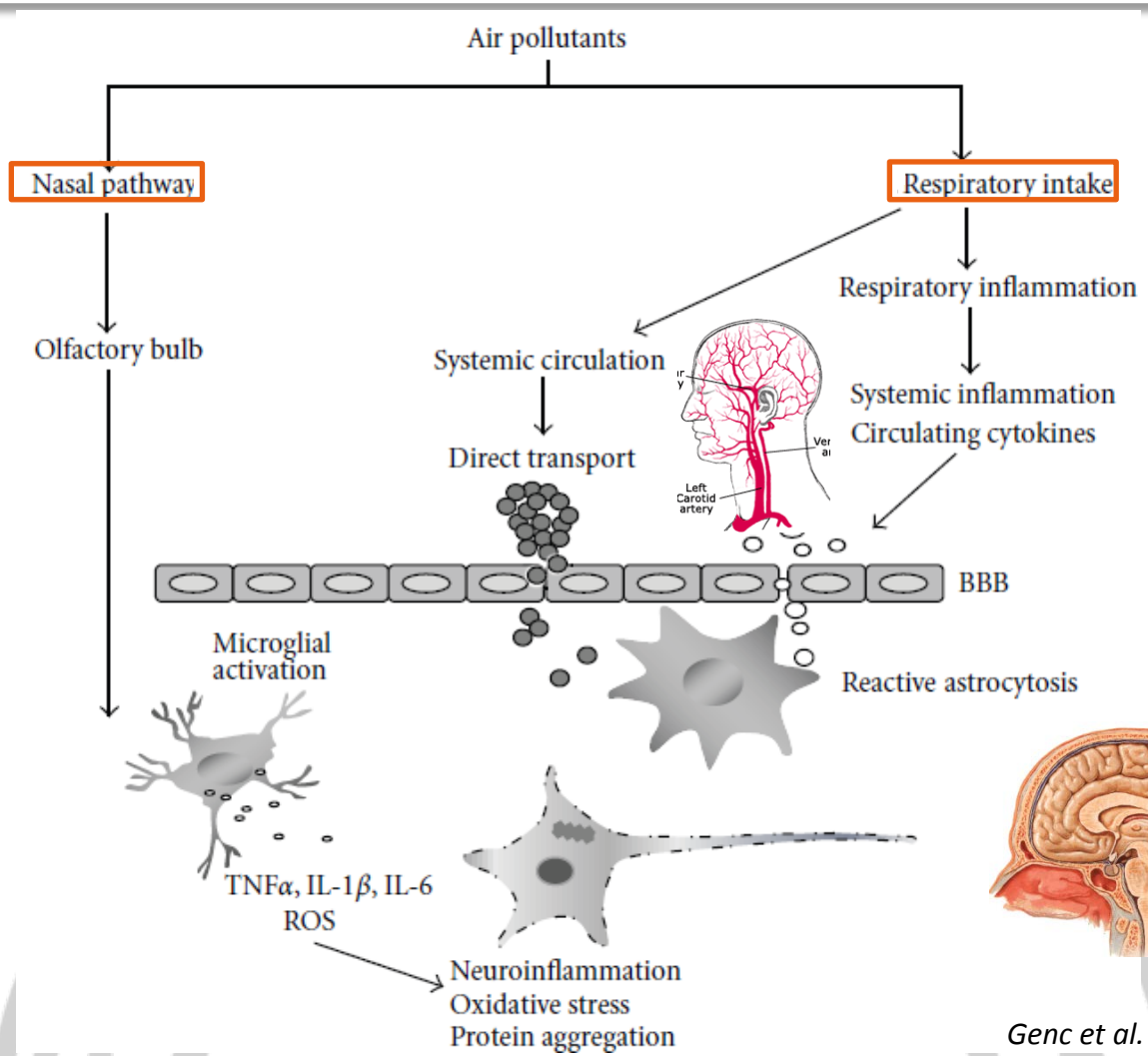
“You have only one chance to develop a brain” – Prof. Philippe Grandjean

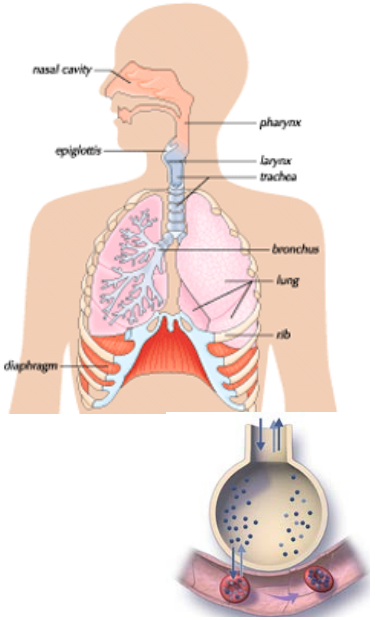


Tau and Peterson. Neuropsychopharmacology. 2010;35:147–168

How do air pollutants reach the brain?
- based on animal studies -

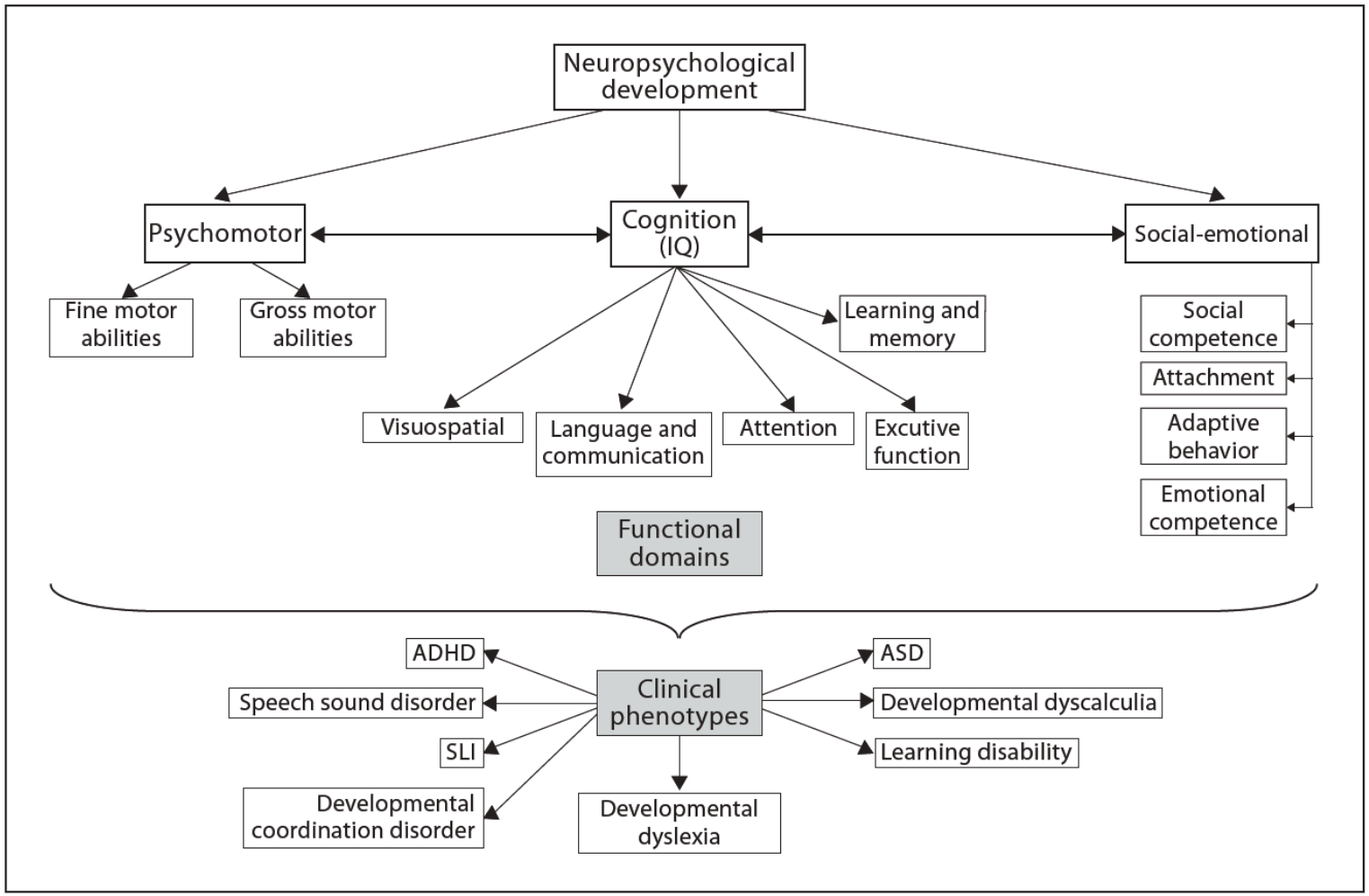






Genc et al. J Toxicol. 2012;2012:782462

Conceptual framework of the neuropsychological developmental process



Forns et al. Neuroepidemiology. 2012;38:203-8

How do we assess children's neuropsychological development?

- Psychologist

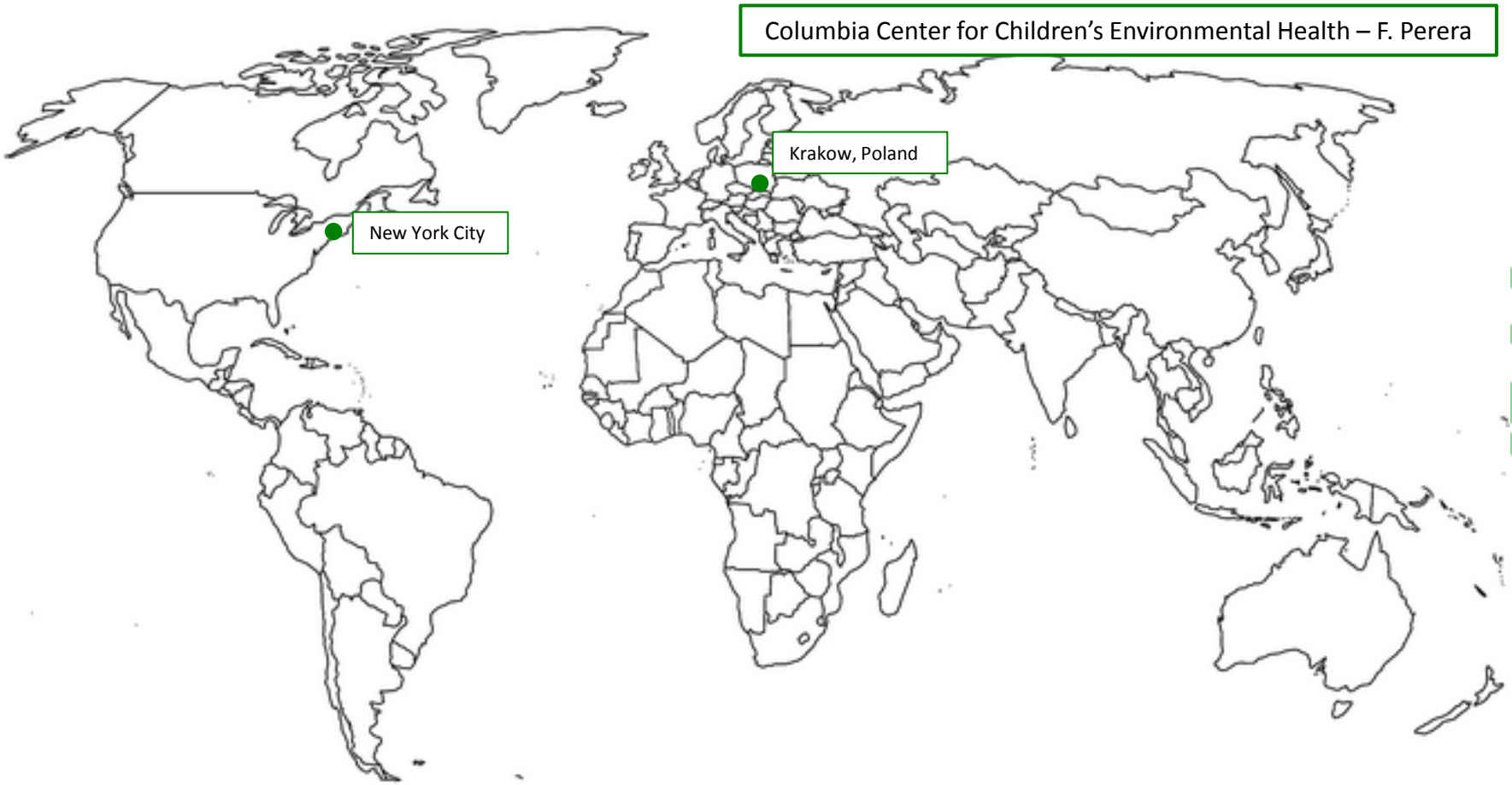
- Computer-based tests

- Reported by mother, father, teacher, child himself

Hyperactivity Scale	Not True	Somewhat True	Certainly True
Restless, overactive, cannot stay still for long	0	1	2
Constantly fidgeting or squirming	0	1	2

- Clinical diagnosis by a doctor

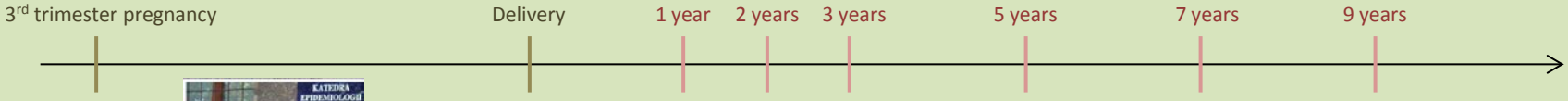
Personal prenatal exposure to air pollution



Personal prenatal exposure to air pollution

Columbia Center for Children's Environmental Health – F. Perera

Birth cohort studies



Personal monitor PAH - 48h

Maternal / Cord blood PAH-DNA adduct

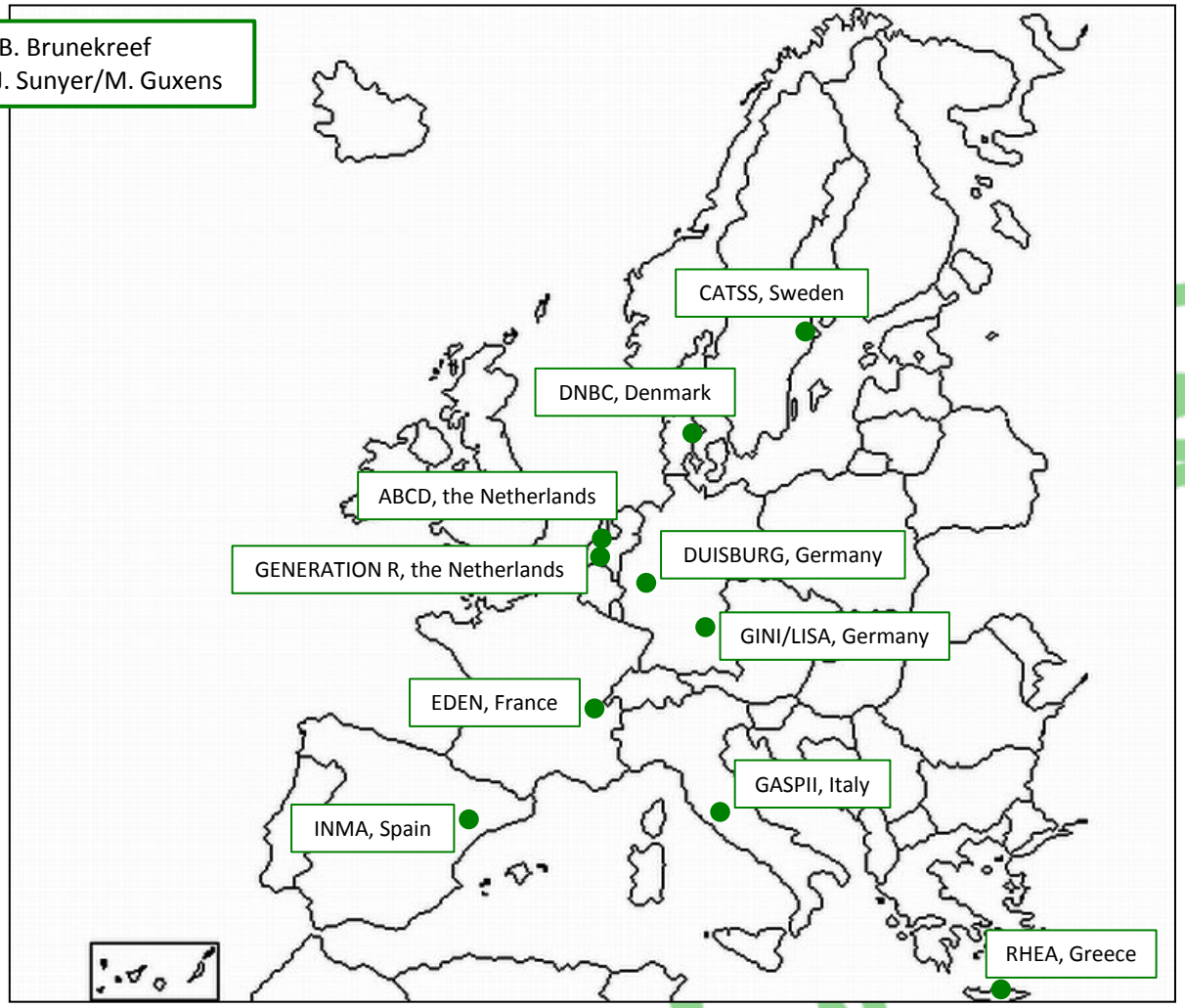
Cognition (IQ), Psychomotor, Behaviour problems, Brain structural and functional MRI

Personal prenatal exposure to air pollution

	1y	2y	3y	5y			7y			9y	
	NYC PAH air (n=181)	NYC PAH air (n=181)	NYC PAH air (n=181)	NYC PAH air (n=240)	Poland PAH air (n=214)	NYC PAH-DNA cord blood (n=96)	NYC PAH air (n=253)	Poland PAH air (n=170)	NYC PAH-DNA cord blood (n=205)	NYC PAH-DNA cord blood (n=162)	NYC PAH-DNA mother (n=233)
General cognition (IQ)	—	—	✓	✓				—			
Verbal				✓				✓			
Non-verbal				—	✓			—			
Psychomotor	—	—	—								
Total behaviour problems			—								
Anxious/depressed			—			✓	✓		—		
DSM-Anxiety problems			—			✓	✓		—		
Attention problems			—			✓	✓		✓		
DSM-ADHD problems			—				—			—	✓
Aggressive behaviour			—								
Other subscales			—								

Residential prenatal exposure to air pollution

ESCAPE Project – B. Brunekreef
Neuro working group – J. Sunyer/M. Guxens



Residential prenatal exposure to air pollution

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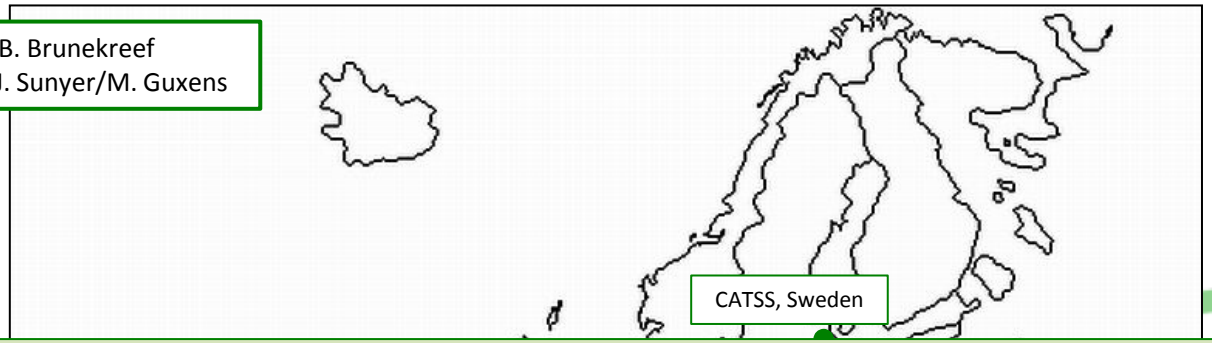
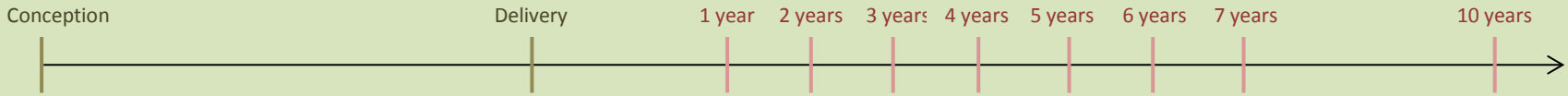
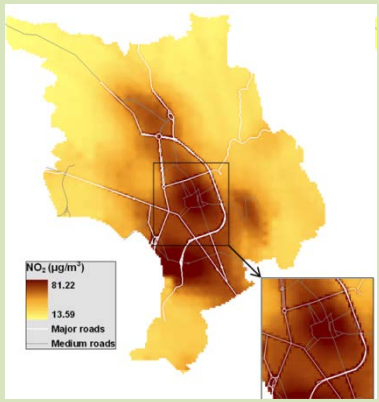


Birth cohort studies



Land use regression models –
Air pollution levels at participant's address

Cognition (IQ), Psychomotor, Behaviour problems



Air Pollution During Pregnancy and Childhood Cognitive and Psychomotor Development

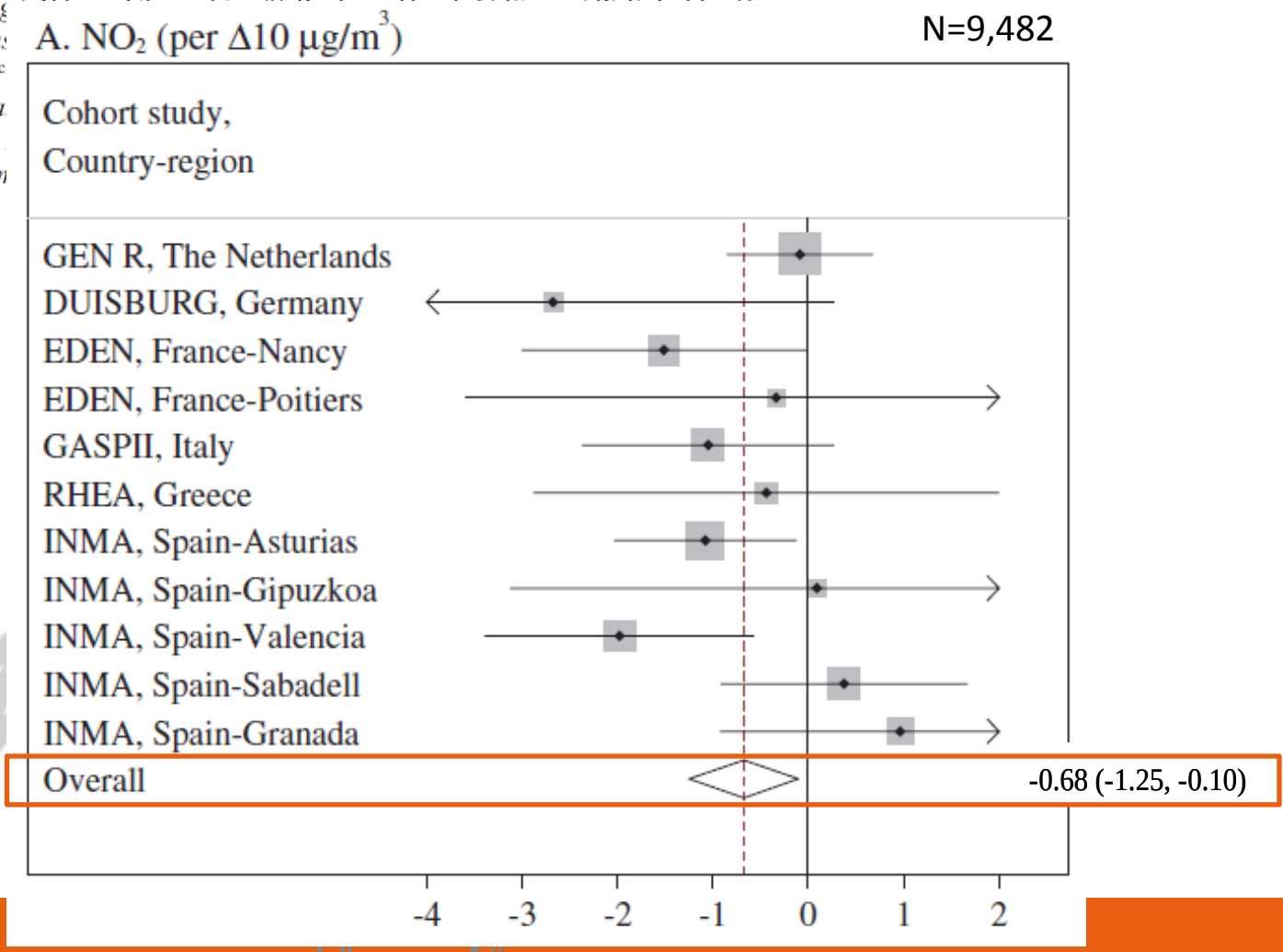
Six European Birth Cohorts

Mònica Guxens,[a,b,c] Raquel Garcia-Esteban,[a,b,c] Lise Giorgis-Allemand,[d,e] Joan Forns,[a,b,c] Chiara Badaloni,[f] Ferran Ballester,[c,g,h] Rob Beelen,[i] Giulia Cesaroni,[f] Leda Chatzi,[j] Maria de Agostini,[k,l] Audrey de Nazelle,[a,b,c,m] Marloes Eeftens,[i] Mariana F. Fernandez,[c,n,o] Ana Fernández-Somoano,[c,p] Francesco Forastiere,[f] Ulrike Gehring[ ] Claudia Klümper,[t] Manolis Kogevinas[ ] Nerea Lertxuni,[y,z] Mario Murcia,[c] Rosa Ramos,[c,o] Theano Roumeliota[ ] Dorothea Sugiri,[t] Adonina Tardón,[c,p] Tanja Vrijkotte,[gg,hh] Michael Wilhelm

Epidemiology. 2014;25:636-47

Psychomotor development

N=9,482



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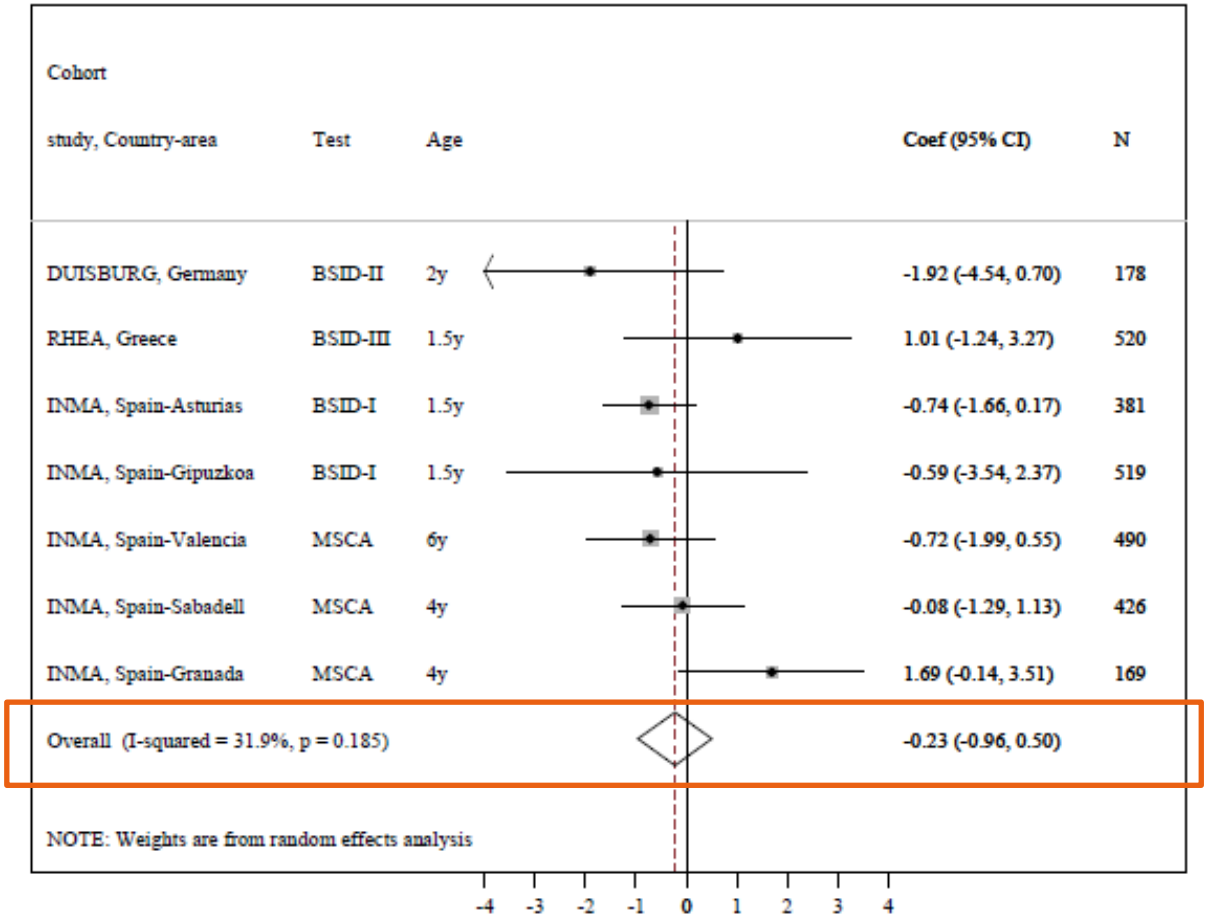
Epidemiology. 2014;25:636-47

Cognitive development

N=2,683

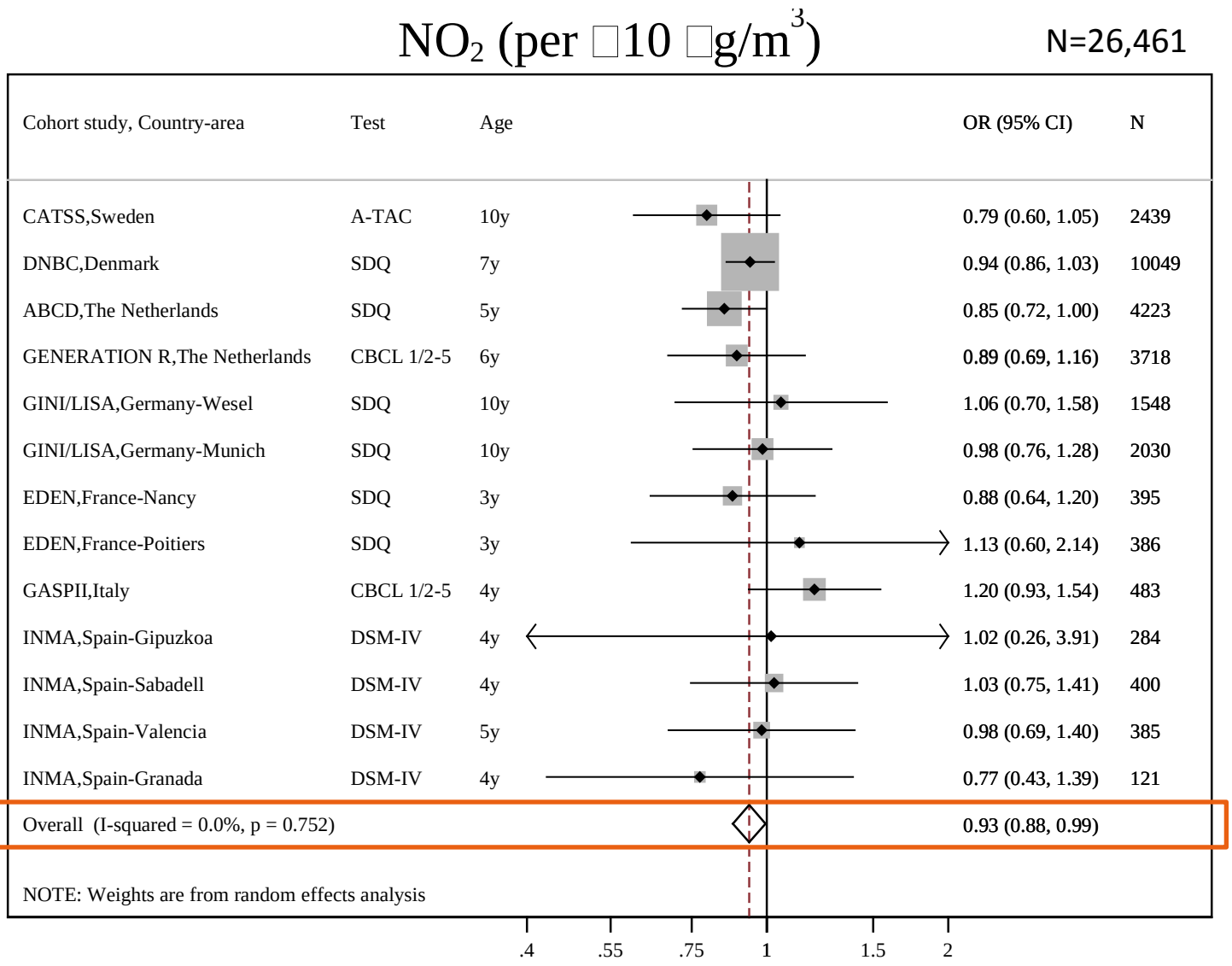
NO_2 (per $\Delta 10\ \mu g/m^3$)



Air pollution exposure during pregnancy and childhood ADHD symptomatology in eight European cohort studies

Joan Forns, Raquel Garcia-Esteban, …, Jordi Sunyer, Mònica Guxens

In preparation



Residential postnatal exposure to air pollution

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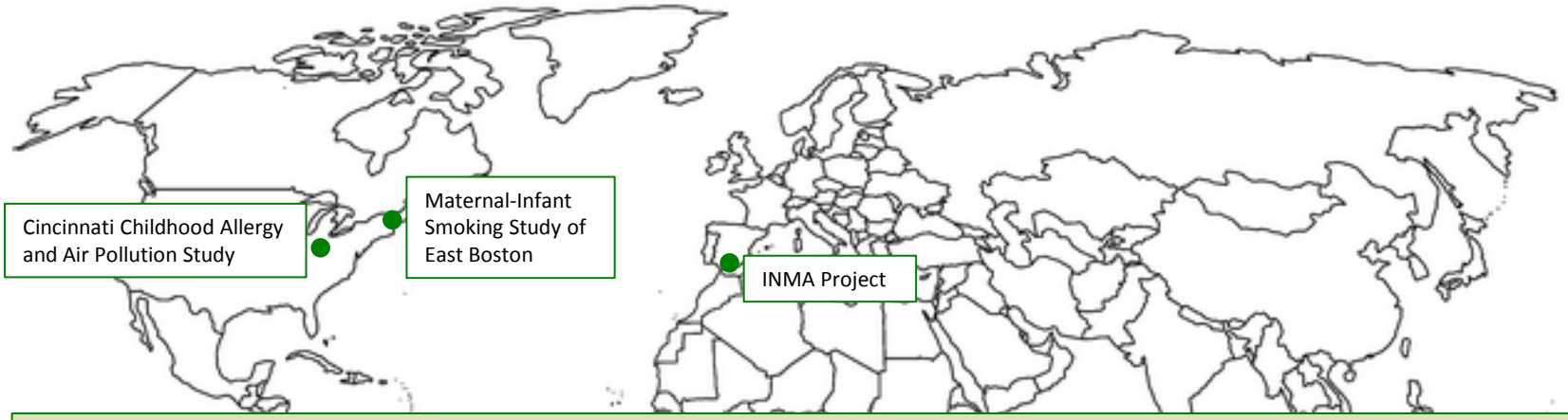
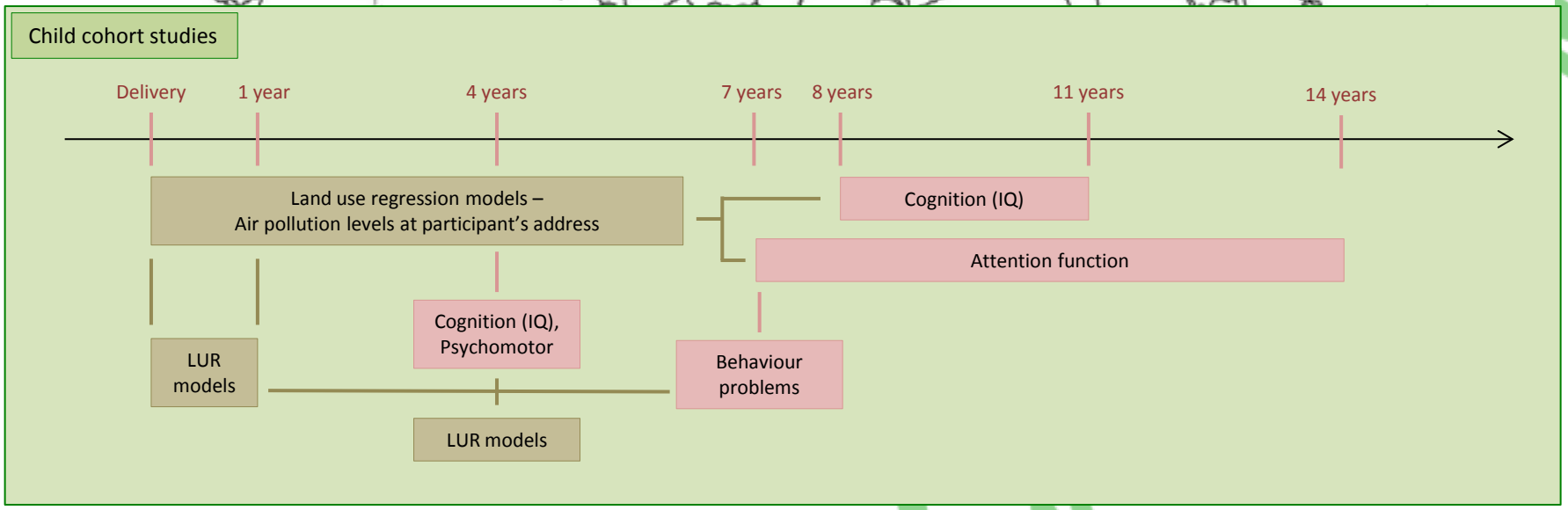
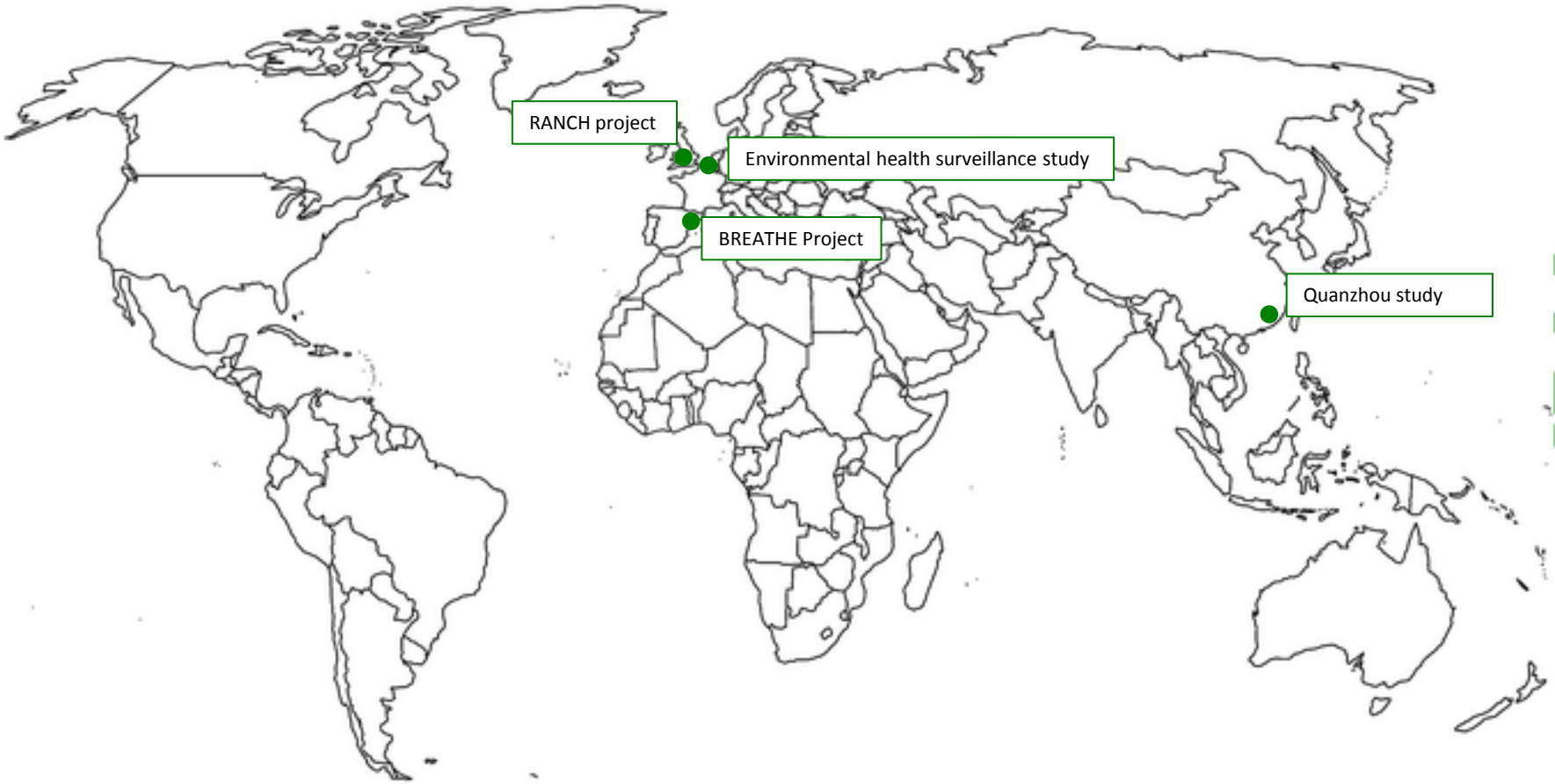




Residential postnatal exposure to air pollution

	INMA Project NO_2	Cincinnati study EC	Boston study BC	
	4y (n=210)	7y (n=576)	7-14y (n=174)	8-11y (n=202)
General cognition (IQ)	—			✓
Verbal	—			—
Non-verbal	—			✓
Memory	—			✓
Learning				✓
Executive function	—			
Working memory	—			
Attention function			✓	
Gross motor	✓			
Fine motor	—			
Hyperactivity		✓		
Inattention		—		
Agression		—		
Conduct problems		—		
Atypicality		—		

Exposure to air pollution at school



Exposure to air pollution at school

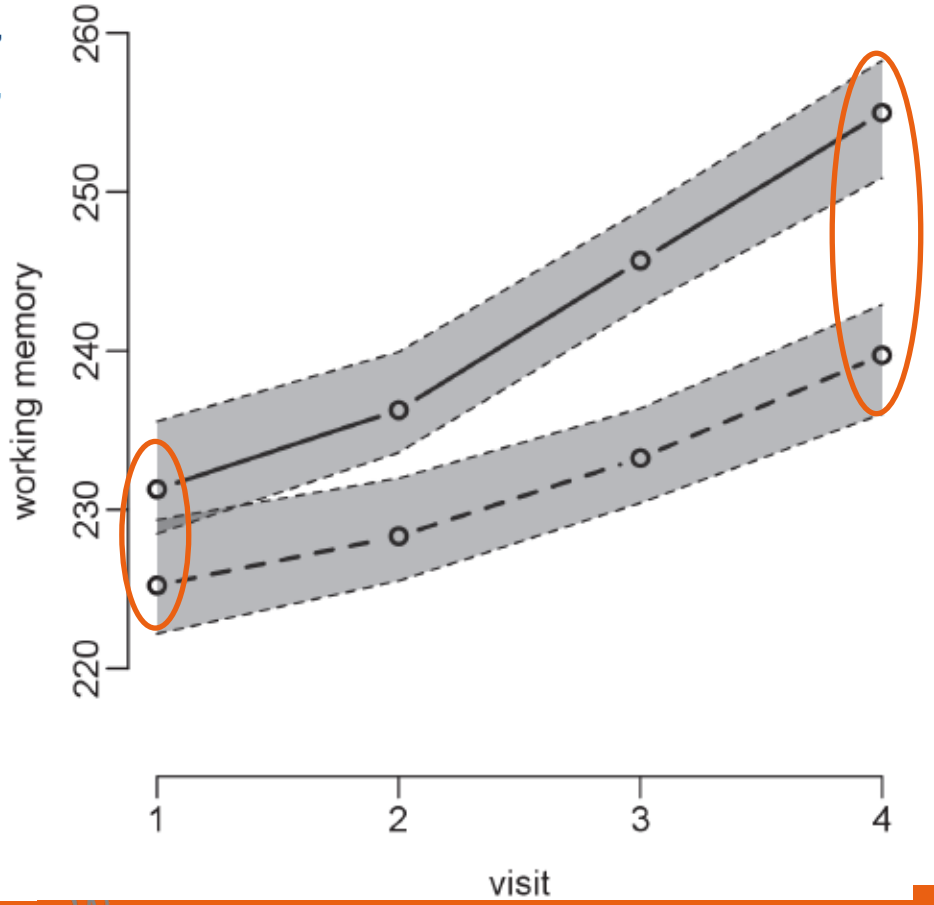
	Breathe study EC, NO_2, UFP	Quanzhou NO_2, PM_{10}	Ranch study NO_2		Belgium study Combined traffic factor
	7-10y (n=2,715) 39 schools	8-10y (n=861) 2 schools	9-10y (n=719) 22 schools	9-11y (n=553) 24 schools	15y (n=606) ---
Working memory	✓		—		
Attention function	✓	✓		—	✓
Memory		✓	—	✓	—
Visuo-motor coordination		✓			
Psychomotor				—	—
Non-verbal				—	
Reading comprehension			—		

Exposure to air pollution at school

Association between Traffic-Related Air Pollution in Schools and Cognitive Development in Primary School Children: A Prospective Cohort Study

Jordi Sunyer*[1,2,3,4], Mikel Esnaola[1,2,3], Mar Alvarez-Pedrerol[1,2,3], Joan Forns[1,2,3], Ioar Rivas[1,2,3,5], Mònica López-Vicente[1,2,3], Elisabet Suades-González[1,2,3,6], Maria Foraster[1,2,3], Raquel Garcia-Esteban[1,2,3], Xavier Basagaña[1,2,3], Mar Viana[5], Marta Cirach[1,2,3], Teresa Moreno[5], Andrés Alastuey[5], Núria Sebastian-Galles[2], Mark Nieuwenhuijsen[1,2,3], Xavier Querol[5]

PLoS Med. 2015;12(3):e1001792



Dashed line = high traffic air pollution
Continuous line = low traffic air pollution
Gray shading = 95% CIs

Air pollution and autism spectrum disorders

Traffic-Related Air Pollution, Particulate Matter, and Autism

Heather E. Volk, PhD, MPH; Fred Lurmann; Bryan Penfold; Irva Hertz-Picciotto, PhD; Rob McConnell, MD

JAMA Psychiatry. 2013;70(1):71-7

Ambient Air Pollution and Autism in Los Angeles County, California

Tracy Ann Becerra,[1] Michelle Wilhelm,[1] Jørn Olsen,[1] Myles Cockburn,[2] and Beate Ritz[1]

Environ Health Perspect. 2013;121:380–6

Autism Spectrum Disorder and Particulate Matter Air Pollution before, during, and after Pregnancy: A Nested Case–Control Analysis within the Nurses' Health Study II Cohort

Raanan Raz,[1] Andrea L. Roberts,[2] Kristen Lyall,[3,4] Jaime E. Hart,[1,5] Allan C. Just,[1] Francine Laden,[1,5,6] and Marc G. Weisskopf[1,6]

Environ Health Perspect. 2015;123:264-70

Particulate Matter Exposure, Prenatal and Postnatal Windows of Susceptibility, and Autism Spectrum Disorders

Amy E. Kalkbrenner,[a] Gayle C. Windham,[b] Marc L. Serre,[c] Yasuyuki Akita,[c] Xuexia Wang,[a] Kate Hoffman,[d] Brian P. Thayer,[a] and Julie L. Daniels[c]

Epidemiology. 2015;26:30-42

Air Pollution and Newly Diagnostic Autism Spectrum Disorders: A Population-Based Cohort Study in Taiwan

Chau-Ren Jung, Yu-Ting Lin, Bing-Fang Hwang*

PLoS One. 2013;8(9):e75510

Air pollution and autism spectrum disorders

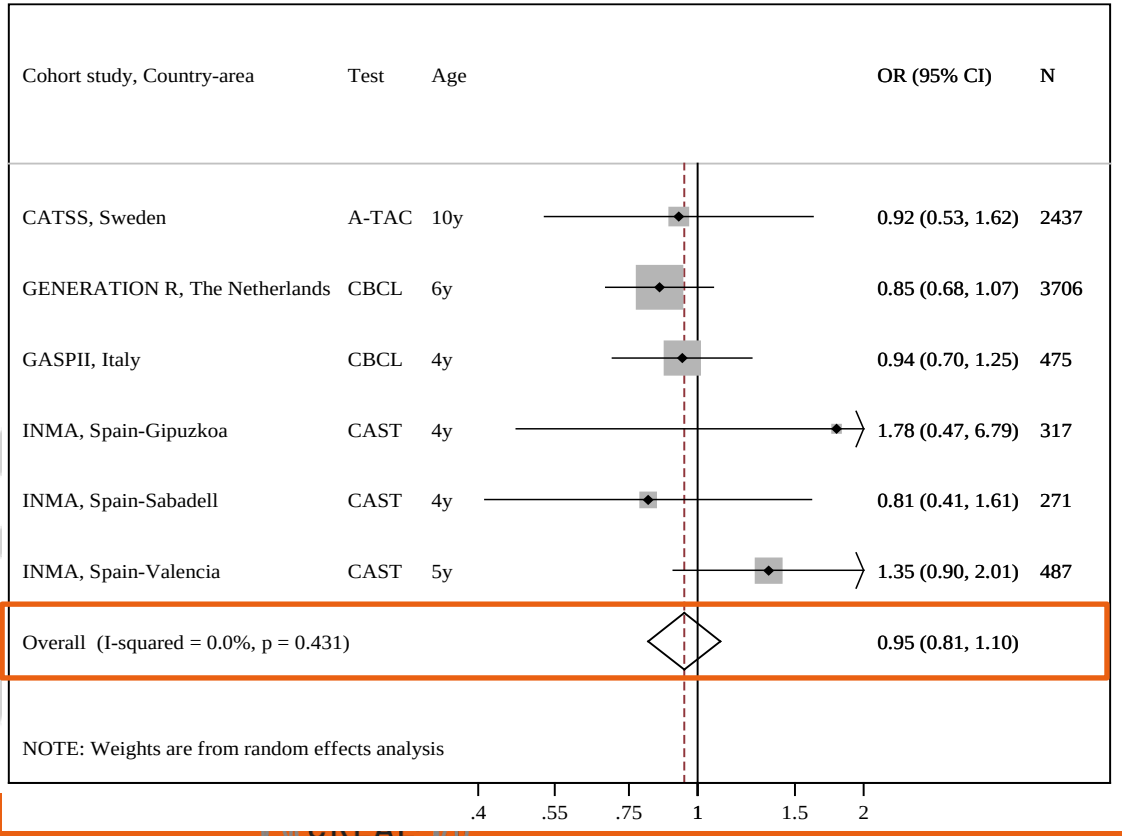
Air pollution exposure during pregnancy and childhood autistic traits in four European population-based cohort studies

Mònica Guxens,[1,2,3,4] Akhgar Ghassabian,[4,5] Tong Gong,[6] Raquel Garcia-Esteban,[1,2,3] Daniela Porta,[7] Lise Giorgis-Allemand,[8,9] Catarina Almqvist,[6] Aritz Aranbarri,[10,11] Rob Beelen,[12] Chiara Badaloni,[7] Giulia Cesaroni,[7] Audrey de Nazelle,[1,2,3,13] Marisa Estarlich,[3,14] Francesco Forastiere,[7] Joan Forns,[1,2,3,12] Ulrike Gehring,[13] Jesús Ibarluzea,[3,11,16] Vincent W.V. Jaddoe,[5,17,18] Michal Korek,[19] Paul Lichtenstein,[6] Mark J. Nieuwenhuijsen,[1,2,3] Marisa Rebagliato,[3,20] Rémy Slama,[8,9] Henning Tiemeier,[4,18,21] Frank C. Verhulst,[4] Heather E. Volk,[22] Göran Pershagen,[19] Bert Brunekreef,[12,23] Jordi Sunyer[1,2,3,24]

Environ Health Perspect 2015
(provisionally accepted)

NO_2 (per $\Delta 10\ \mu g/m^3$)

N=8,079

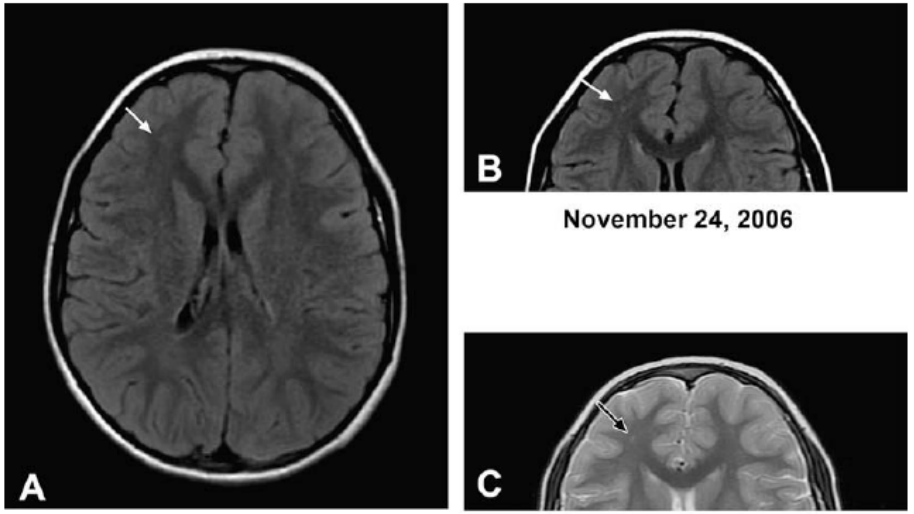


Air pollution and brain MRI

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

Lilian Calderón-Garcidueñas [a,b,*], Antonieta Mora-Tiscareño
Gilberto Gómez-Garza [a], Gerardo Barragán-Mejía [a], James B
Gildardo Valencia-Salazar [a], Valerie Jewells [e], Robert R. Mar
Beatriz Pérez-Guillé [a], Ricardo Torres-Jardón [h], Lou Herrit [b],
Maria E. Monroy [a], Angelica González-Maciel [a], Rafael Reyn
Anna C Solt [j], Randall W. Engle [c,1]

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



Exposure to severe urban air pollution influences cognitive outcomes, brain volume and systemic inflammation in clinically healthy children

Lilian Calderón-Garcidueñas [a,b], Randall Engle [c], Antonieta Mora-Tiscareño [a], Martin Styner [d],
Gilberto Gómez-Garza [a], Hongtu Zhu [e], Valerie Jewells [f], Ricardo Torres-Jardón [g], Lina Romero [a],
Maria E. Monroy-Acosta [a], Christopher Bryant [e], Luis Oscar González-González [a],
Humberto Medina-Cortina [a], Amedeo D'Angiulli [h,*]

Brain Cogn. 2011;77(3):345-355

White Matter Hyperintensities, Systemic Inflammation, Brain Growth, and Cognitive Functions in Children Exposed to Air Pollution

Lilian Calderón-Garcidueñas[a,b,*], Antonieta Mora-Tiscareño[a], Martin Styner[c], Gilberto Gómez-garza[a],
Hongtu Zhu[d], Ricardo Torres-Jardón[e], Esperanza Carlos[a], Edelmira Solorio-López[a],
Humberto Medina-Cortina[a], Michael Kavanaugh[b] and Amedeo D'Angiulli[f]

J Alzheimers Dis. 2012;31:183-91

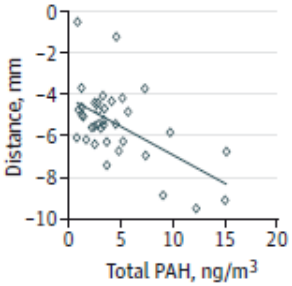
Effects of Prenatal Exposure to Air Pollutants (Polycyclic Aromatic Hydrocarbons) on the Development of Brain White Matter, Cognition, and Behavior in Later Childhood

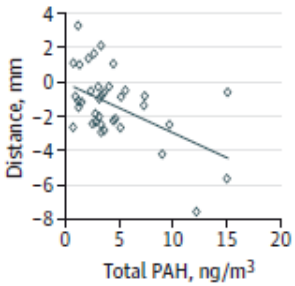
JAMA Psychiatry. 2015

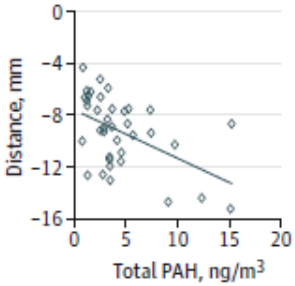
Bradley S. Peterson, MD; Virginia A. Rauh, ScD; Ravi Bansal, PhD; Xuejun Hao, PhD; Zachary Toth, BA; Giancarlo Nati, BA; Kirwan Walsh, BA; Rachel L. Miller, MD; David Semanek, BA; Frederica Perera, DrPH, PhD

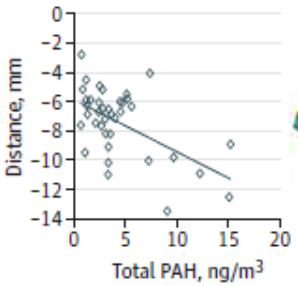
A Correlations with prenatal PAH levels

Left lateral



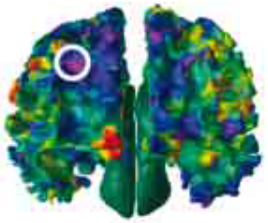




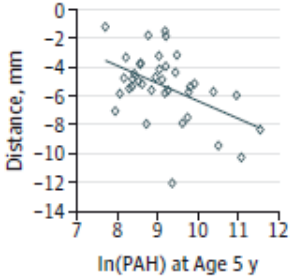


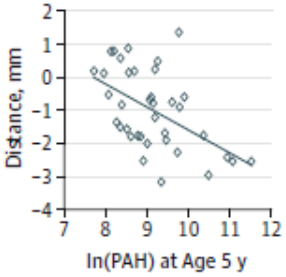
Left mesial

B Correlations with postnatal PAH levels



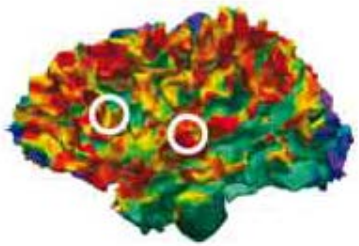
Anterior

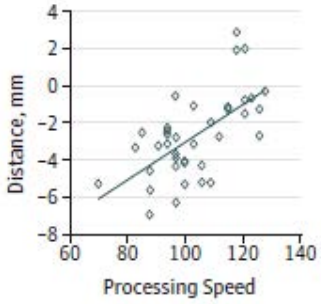




Left mesial

Correlations With WISC-IV Processing Speed





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

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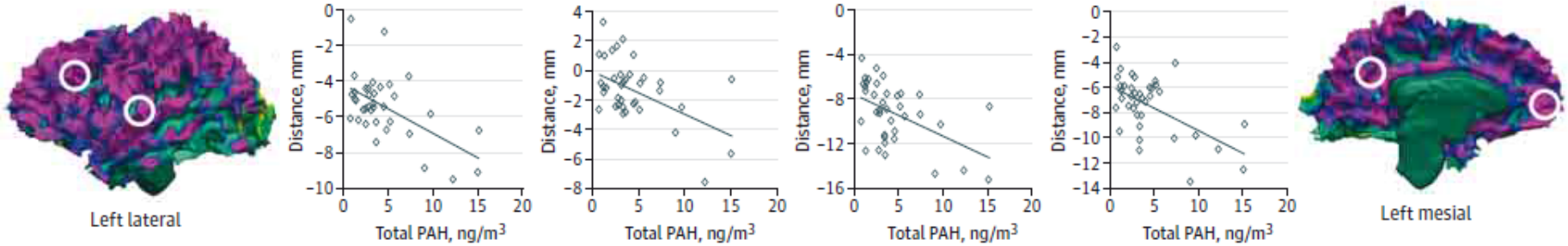
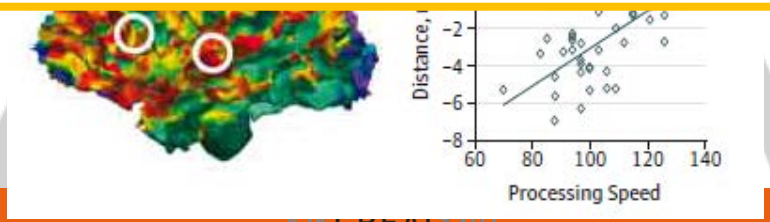
A Correlations with prenatal PAH levels



B Correlations with postnatal PAH levels

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



Challenges

- Assess the appropriate brain function at the appropriate age and using the appropriate tool
- Which specific air pollutant is behind this association?
- Which is the role of noise exposure?
- Which is the most critical period of neurotoxicity?
- Why air pollution was associated to autism spectrum disorders in US studies but was not associated with autistic traits in European studies?

Future directions

- Brain structural and functional MRI will help to understand better which brain areas and brain functions are affected
- Studies including a more detailed exposure assessment (PM composition, UFP, source apportionment, multi-pollutant models, etc)
- Studies including noise exposure
- Studies including a more comprehensive exposure assessment along children's lifetime
- Replicate US studies on autism spectrum disorder in Europe following a similar study design

Conclusions

- Air pollution exposure during pregnancy and in the first years of life seems to be associated to a decreased children's brain development

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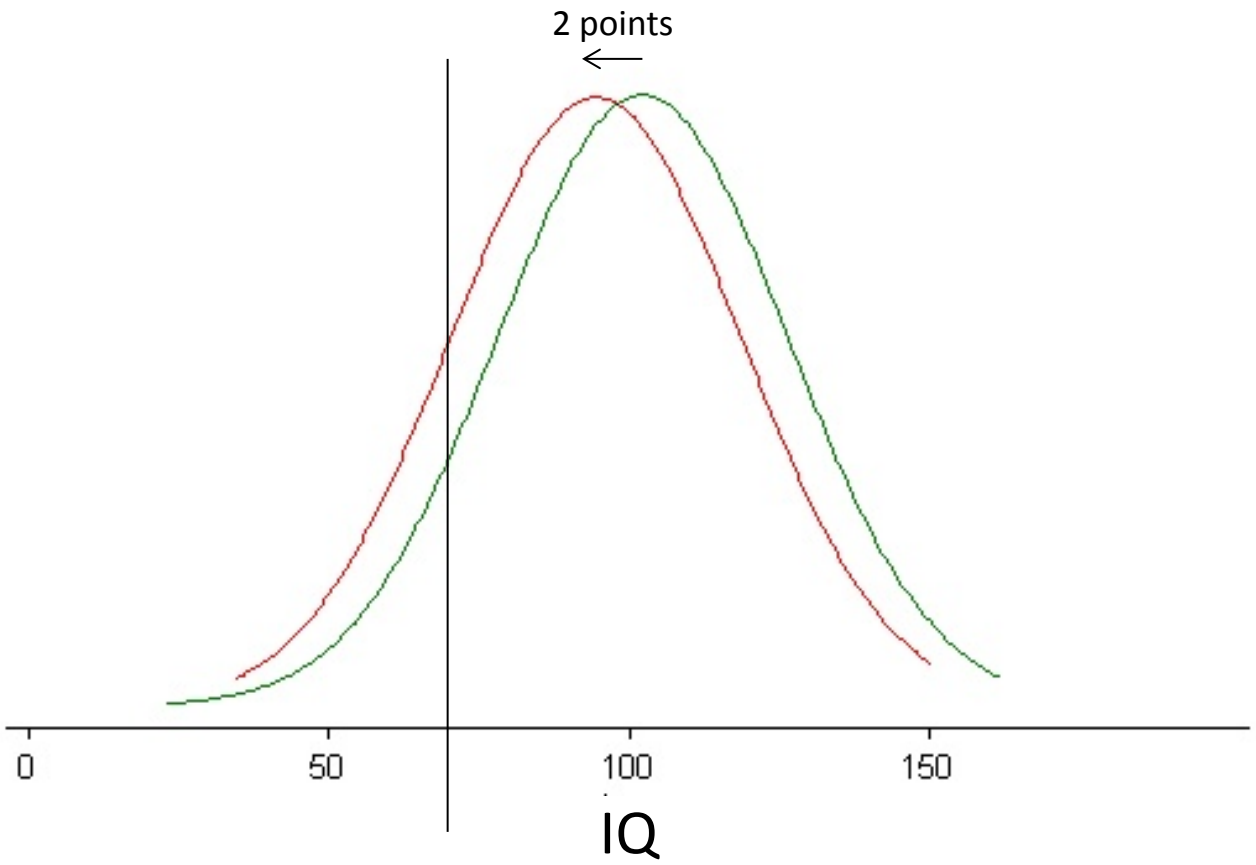
Sick Individuals and Sick Populations

GEOFFREY ROSE



Thank you very much!

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