RECENT DEVELOPMENTS IN THE TOXICOLOGY OF DIESEL COMBUSTION EMISSIONS

Renaud Vincent PhD

Inhalation Toxicology Laboratory
Hazard Identification Division
Environmental Health Science and Research Bureau
Radiation and Environmental Health Directorate

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Ontario Medical Association

2005-2006 Health and Economic Damage Estimates

Attributable to Air Pollution

	2005	2015	2026
Premature Deaths	5,829	7,436	10,061
Hospital Admissions	16,807	20,067	24,587
Emergency Room Visits	59,696	71,548	87,963
Minor illness•day	29 million	32 million	39 million

Health Direct Costs (2015)

Health care system	$571 million
Loss productivity	$402 million

Indirect Costs (2015)

Pain and suffering	$593 million
Loss of life	$8.3 billion

Annual Economic Loss

2005	$7.8 billion
2015	$9.8 billion
2026	$12.9 billion

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"Something's just not right—our air is clean, our water is pure, we all get plenty of exercise, everything we eat is organic and free-range, and yet nobody lives past thirty."
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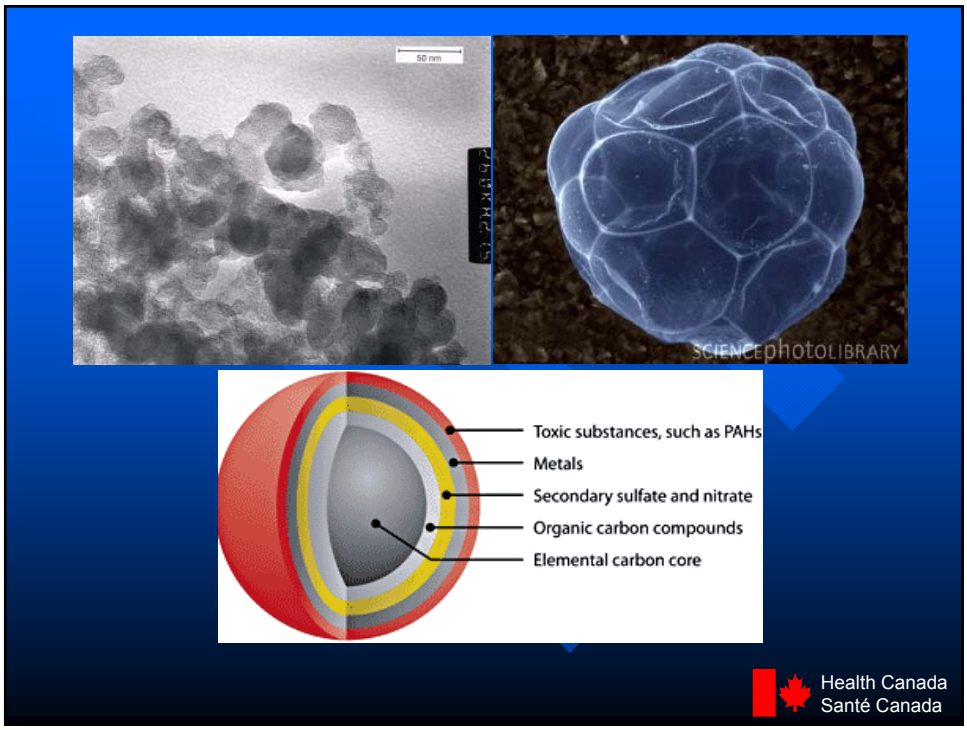
50 nm
SCIENCEphotoLIBRARY
Toxic substances, such as PAHs
Metals
Secondary sulfate and nitrate
Organic carbon compounds
Elemental carbon core
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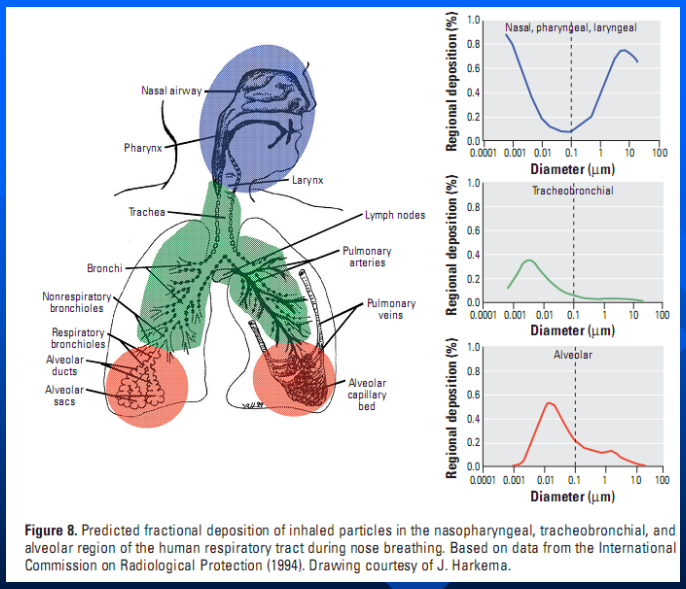

Figure 8. Predicted fractional deposition of inhaled particles in the nasopharyngeal, tracheobronchial, and alveolar region of the human respiratory tract during nose breathing. Based on data from the International Commission on Radiological Protection (1994). Drawing courtesy of J. Harkema.

Günter Oberdörster, Eva Oberdörster, Jan Oberdörster. Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles. Environ Health Perspect 113:823–839 (2005).

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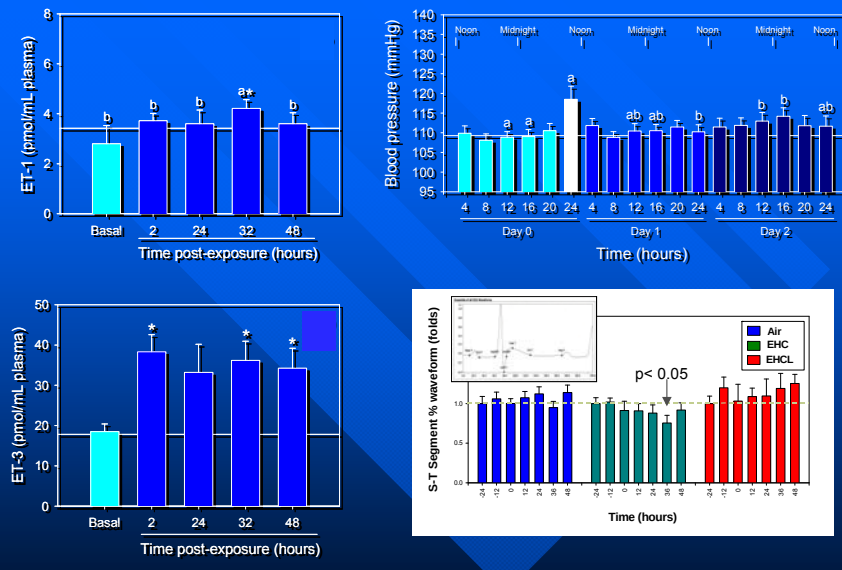

Vincent *et al*, Res Rep Health Effects Inst 104, 2001

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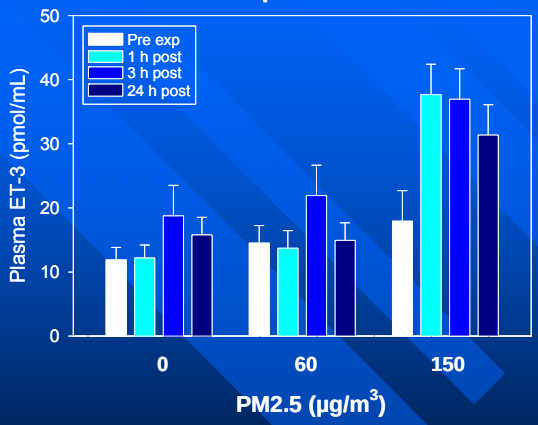
Human exposure to CAPs



CAPs: concentrated ambient particles
Vincent *et al. Am J Resp Crit Care Med* 163:A313 (2001)

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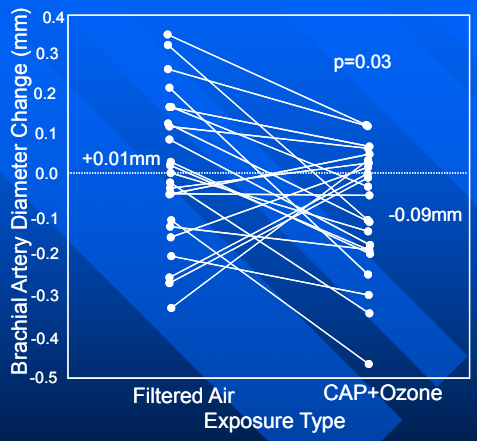
Brachial Artery Diameter Change (post – pre)

Human Subjects Exposed to Toronto $PM_{2.5}$
(0.12 ppm ozone + 153 ug/m³ CAP, 2 hours at rest)



Note: no change of blood pressure, no change of flow mediated dilation
Brook *et al. Circulation* 105:1534-1536 (2002)

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Research | Children's Health

Elevated Plasma Endothelin-1 and Pulmonary Arterial Pressure in Children Exposed to Air Pollution

Lilian Calderón-Garcidueñas,[1,2] Renaud Vincent,[3] Antonieta Mora-Tiscareño,[1] Maricela Franco-Lira,[4] Carlos Henríquez-Roldán,[5] Gerardo Barragán-Mejía,[1] Luis Garrido-García,[1] Laura Camacho-Reyes,[1] Gildardo Valencia-Salazar,[1] Rogelio Paredes,[1] Lina Romero,[1] Hector Osnaya,[1] Rafael Villarreal-Calderón,[2] Ricardo Torres-Jardón,[6] Milan J. Hazucha,[7,8] and William Reed[8,9]

[1]Instituto Nacional de Pediatría, Mexico City, Mexico; [2]The Center for Structural and Functional Neurosciences, University of Montana, Missoula, Montanta, USA; [3]Inhalation Toxicology and Aerobiology Section, Safe Environments Programme, Health Canada, Ottawa, Ontario, Canada; [4]Escuela Médico Militar, Universidad del Ejército y Fuerza Aérea, México; [5]Departamento de Estadística, Universidad de Valparaíso, Valparaíso, Chile; [6]Centro de Ciencias de la Atmósfera, Universidad Nacional Autónoma de México, Mexico City, Mexico; [7]Department of Medicine, [8]Center for Environmental Medicine, Asthma and Lung Biology, and [9]Department of Pediatrics, University of North Carolina, Chapel Hill, North Carolina, USA

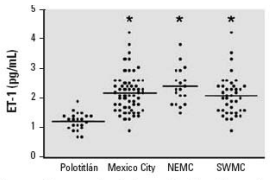


Figure 1. A scatterplot of plasma ET-1 levels by region. Mean plasma ET-1 levels for Mexico City children as a whole ($n = 59$), as well as for northeast (NEMC, $n = 19$) and southwest (SWMC, $n = 40$) Mexico City children analyzed separately were significantly greater than the mean for control (Polotitlán) children ($n = 22$). Horizontal bar indicates group means.
*$p < 0.001$.

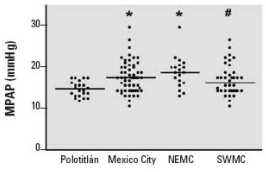


Figure 2. A scatterplot of MPAP by region. The average MPAP for Mexico City children as a whole ($n = 59$), as well as for northeast (NEMC, $n = 19$) and southwest (SWMC, $n = 40$) Mexico City children analyzed separately were significantly greater than the mean for control (Polotitlán) children ($n = 22$). Horizontal bar indicates group means.
*$p < 0.01$; #$p < 0.05$.

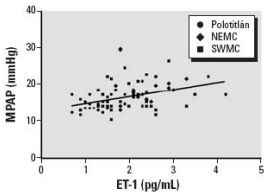


Figure 3. A plot of MPAP versus ET-1 levels for Polotitlán, northeast (NEMC), and southwest (SWMC) Mexico City children. MPAPs were significantly correlated with ET-1 levels ($r = 0.43$, $p = 0.0001$). A linear regression fit to the data is shown.

Research

Diesel Exhaust Inhalation Elicits Acute Vasoconstriction *in Vivo*

Alon Peretz,[1] Jeffrey H. Sullivan,[1] Daniel F. Leotta,[2] Carol A. Trenga,[1] Fiona N. Sands,[1] Jason Allen,[1] Chris Carlsten,[1,3] Charles W. Wilkinson,[4] Edward A. Gill,[3] and Joel D. Kaufman[1,3]

BACKGROUND: Traffic-related air pollution is consistently associated with cardiovascular morbidity and mortality. Recent human and animal studies suggest that exposure to air pollutants affects vascular function. Diesel exhaust (DE) is a major source of traffic-related air pollution.

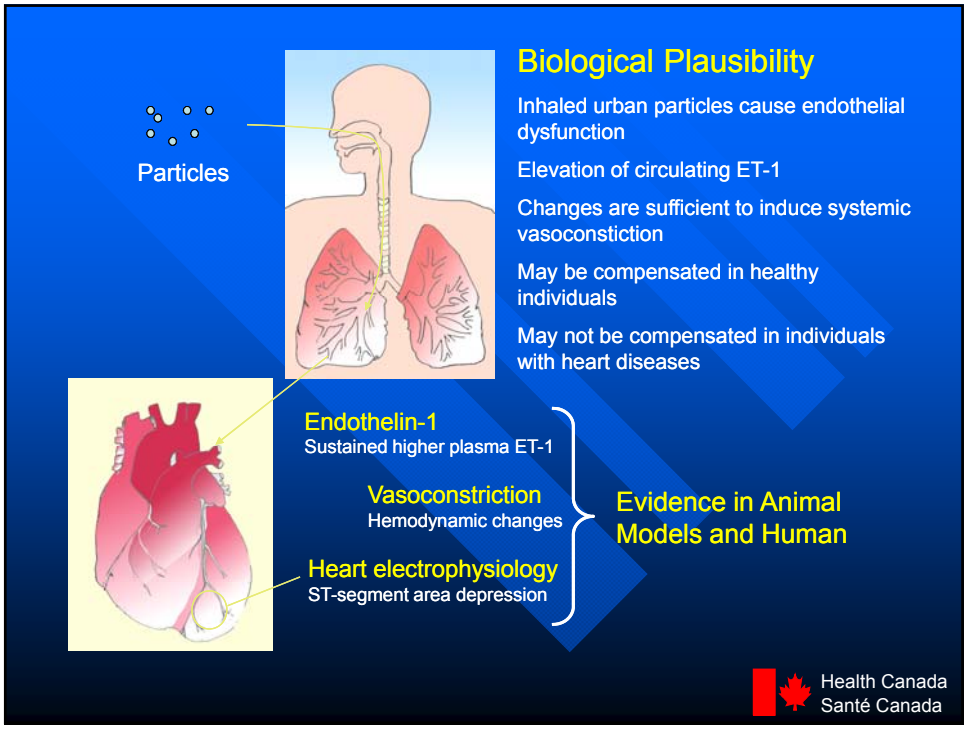
OBJECTIVES: Our goal was to study the effects of short-term exposure to DE on vascular reactivity and on mediators of vascular tone.

METHODS: In a double-blind, crossover, controlled exposure study, 27 adult volunteers (10 healthy and 17 with metabolic syndrome) were exposed in randomized order to filtered air (FA) and each of two levels of diluted DE (100 or 200 μg/m^3 of fine particulate matter) in 2-hr sessions. Before and after each exposure, we assessed the brachial artery diameter (BAd) by B-mode ultrasound and collected blood samples for endothelin-1 (ET-1) and catecholamines. Postexposure we also assessed endothelium-dependent flow-mediated dilation (FMD).

RESULTS: Compared with FA, DE at 200 μg/m^3 elicited a decrease in BAd (0.11 mm; 95% confidence interval, 0.02–0.18), and the effect appeared linearly dose related with a smaller effect at 100 μg/m^3. Plasma levels of ET-1 increased after 200 μg/m^3 DE but not after FA ($p = 0.01$). There was no consistent impact of DE on plasma catecholamines or FMD.

CONCLUSIONS: These results demonstrate that short-term exposure to DE is associated with acute endothelial response and vasoconstriction of a conductance artery. Elucidation of the signaling pathways controlling vascular tone that underlie this observation requires further study.

KEY WORDS: air pollution, brachial artery, catecholamines, endothelin-1, vasoconstriction. *Environ Health Perspect* 116:937–942 (2008). doi:10.1289/ehp.11027 available via *http://dx.doi.org/* [Online 18 March 2008]


Biological Plausibility
Inhaled urban particles cause endothelial dysfunction
Elevation of circulating ET-1
Changes are sufficient to induce systemic vasoconstiction
May be compensated in healthy individuals
May not be compensated in individuals with heart diseases
Particles
Endothelin-1
Sustained higher plasma ET-1
Vasoconstriction
Hemodynamic changes
Heart electrophysiology
ST-segment area depression
Evidence in Animal Models and Human
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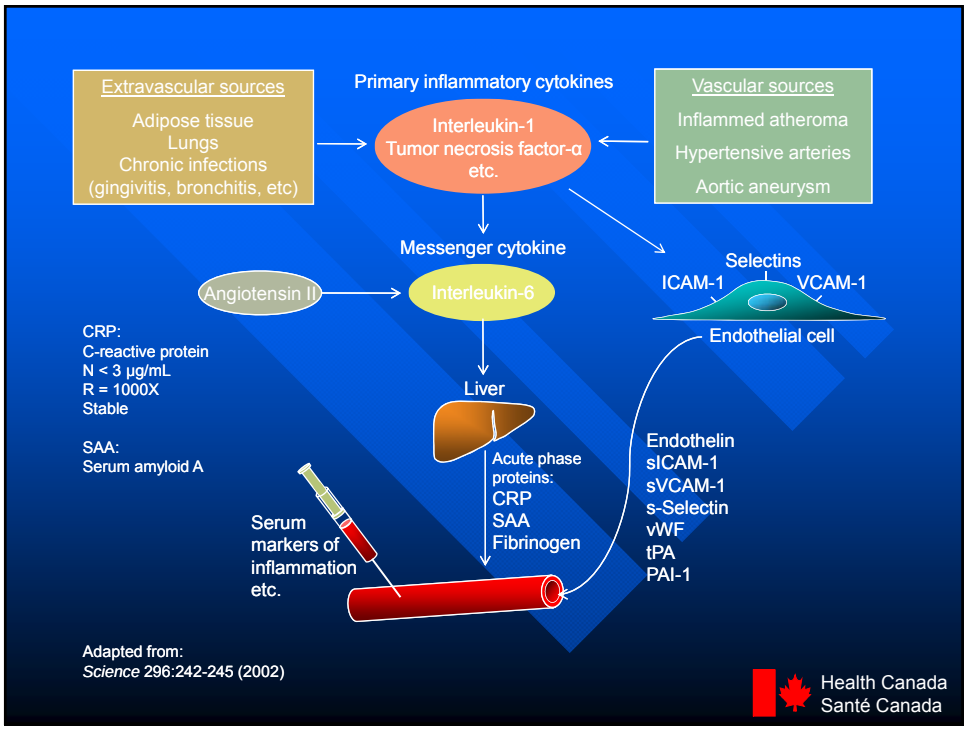
Extravascular sources
Adipose tissue
Lungs
Chronic infections
(gingivitis, bronchitis, etc)
Primary inflammatory cytokines
Interleukin-1
Tumor necrosis factor-α
etc.
Vascular sources
Inflammed atheroma
Hypertensive arteries
Aortic aneurysm
Messenger cytokine
Angiotensin II
Interleukin-6
Selectins
ICAM-1
VCAM-1
Endothelial cell
CRP:
C-reactive protein
N < 3 µg/mL
R = 1000X
Stable
SAA:
Serum amyloid A
Liver
Acute phase proteins:
CRP
SAA
Fibrinogen
Endothelin
sICAM-1
sVCAM-1
s-Selectin
vWF
tPA
PAI-1
Serum markers of inflammation etc.
Adapted from:
Science 296:242-245 (2002)
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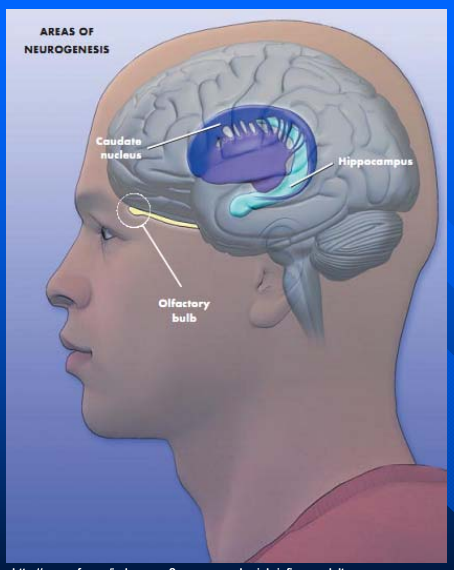
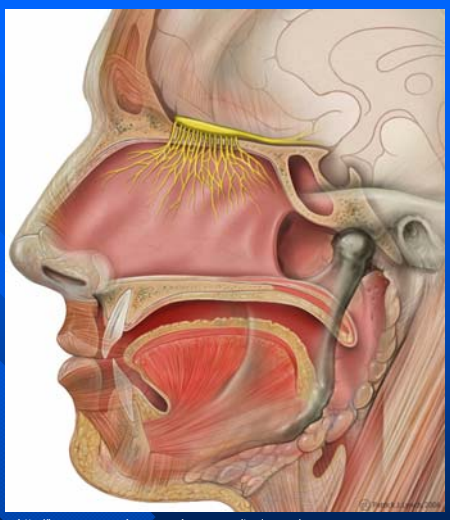


http://www.sfn.org/index.aspx?pagename=brainbriefings_adult_neurogenesis#fullsize



http://beersensoryscience.wordpress.com/tag/aroma/

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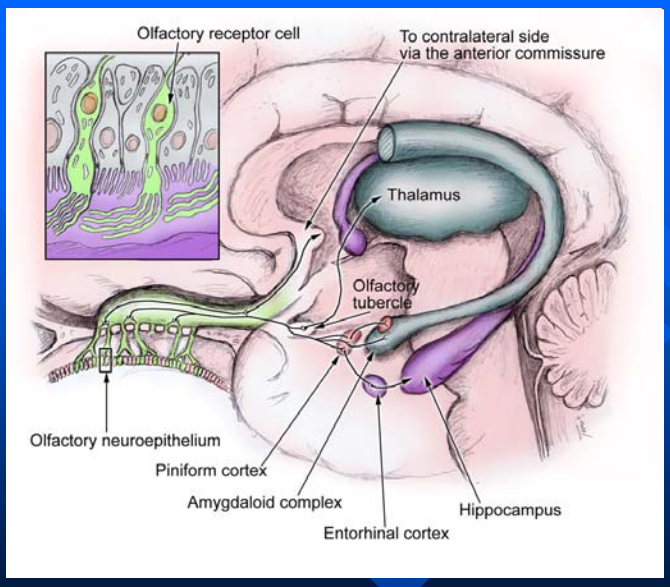

http://www.yalescientific.org/2011/05/the-neural-basis-of-olfaction/

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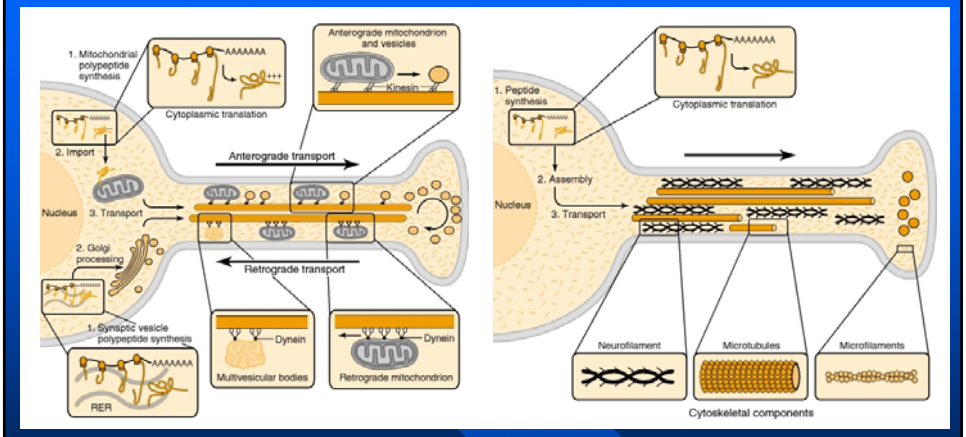

From: Discovery and Conceptual Development of Fast and Slow Axonal Transport. Basic Neurochemistry: Molecular, Cellular and Medical Aspects. 6th edition. Siegel GJ, Agranoff BW, Albers RW, et al., editors. Philadelphia: Lippincott-Raven; 1999. Copyright © 1999, American Society for Neurochemistry.

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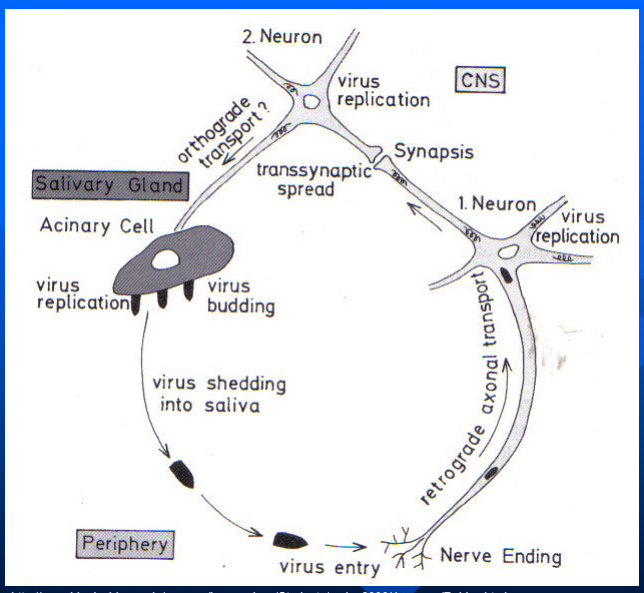

http://www.bio.davidson.edu/courses/immunology/Students/spring2006/Jameson/Rabies.html

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Table 5. Translocation of NSPs in the blood circulation to bone marrow in mice.

Particle size	Type	Finding	Reference
~10 nm	PEG quantum dots	Fast appearance of quantum dots in liver, spleen, lymph nodes, and bone marrow (mouse)	Ballou et al. 2004
< 220 nm	Metallo-fullerene	Highest accumulation in bone marrow after liver; continued increase in bone marrow but decrease in liver (mouse)	Cagle et al. 1999
90–250 nm	HSA-coated polylactic acid nanoparticles	Significant accumulation in bone marrow, second to liver (rat)	Bazile et al. 1992
240 nm	Polystyrene (nonbiodegradable) polylisohexylcyonacrylate (biodegradable)	Rapid passage through endothelium in bone marrow, uptake by phagocytizing cells in tissue (mouse)	Gibaud et al. 1996, 1998, 1994

HSA, human serum albumin.

Table 6. Studies of neuronal translocation of UFPs from respiratory tract.

Reference	Study
Bodian and Howe 1941	Olfactory axonal transport of polio virus (30 nm) after intranasal instillation in chimpanzee; transport velocity, 2.4 mm/hr
de Lorenzo 1970	Olfactory axonal transport of 50 nm silver-coated gold after intranasal instillation in squirrel monkey; transport velocity, 2.5 mm/hr
Hunter and Dey 1998	Retrograde tracing of trigeminal neurons from nasal epithelium with microspheres
Hunter and Undem 1999	Rhodamine-labeled microspheres (20–200 nm) translocation via sensory nerves of TB region to ganglion nodosum in hamster after intratracheal instillation
Oberdörster et al. 2004	^{13}C particles (CMD ~ 36 nm) in olfactory bulb after whole-body inhalation exposure in rats

TB, tracheobronchial.

Günter Oberdörster, Eva Oberdörster, Jan Oberdörster. Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles. Environ Health Perspect 113:823–839 (2005).

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Toxicologic Pathology, 32:1–9, 2004

Brain Inflammation and Alzheimer's-Like Pathology in Individuals Exposed to Severe Air Pollution

LILIAN CALDERÓN-GARCIDUEÑAS,[1,2] WILLIAM REED,[3] ROBERT R. MARONPOT,[4] CARLOS HENRÍQUEZ-ROLDÁN,[5] RICARDO DELGADO-CHAVEZ,[6] ANA CALDERÓN-GARCIDUEÑAS,[7] IRMA DRAGUSTINOVIS,[8] MARICELA FRANCO-LIRA,[9] MARIANA ARAGÓN-FLORES,[10] ANNA C. SOLT,[11] MICHAEL ALTENBURG,[2] RICARDO TORRES-JARDÓN,[12] AND JAMES A. SWENBERG,[2,13]

ABSTRACT

Air pollution is a complex mixture of gases (e.g., ozone), particulate matter, and organic compounds present in outdoor and indoor air. Dogs exposed to severe air pollution exhibit chronic inflammation and acceleration of Alzheimer's-like pathology, suggesting that the is adversely affected by pollutants. We investigated whether residency in cities with high levels of air pollution is associated with human brain inflammation. Expression of cyclooxygenase-2 (COX2), an inflammatory mediator, and accumulation of the 42-amino acid form of β-amyloid (Aβ42), a cause of neuronal dysfunction, were measured in autopsy brain tissues of cognitively and neurologically intact lifelong residents of cities having low (n:9) or high (n:10) levels of air pollution. Genomic DNA apurinic/apyrimidinic sites, nuclear factor-κB activation and apolipoprotein E genotype were also evaluated. Residents of cities with severe air pollution had significantly higher COX2 expression in frontal cortex and hippocampus and greater neuronal and astrocytic accumulation of Aβ42 compared to residents in low air pollution cities. Increased COX2 expression and Aβ42 accumulation were also observed in the olfactory bulb. These findings suggest that exposure to severe air pollution is associated with brain inflammation and Aβ42 accumulation, 2 causes of neuronal dysfunction that precede the appearance of neuritic plaques and neurofibrillary tangles, hallmarks of Alzheimer's disease.

Keywords. Brain; β-amyloid; cyclooxygenase 2; inflammation; neuropathology; air pollution; Mexico City.

TABLE 1.—

Group	Age (years)	Gender, occupation, and years of schooling	Clinical diagnosis	ApoE genotyping $\varepsilon 2, \varepsilon 3, \varepsilon 4$
Low pollution	34	F, housewife, 14	Undifferen Ca	3/4
Low pollution	46	F, housewife, 10	Lung embolism	3/3
Low pollution	49	F, housewife, 10	Cervical Ca	3/3
Low pollution	53	M, carpenter, 12	MI	3/3
Low pollution	58	M, farmer, 6	Renal Ca	3/3
Low pollution	66	M, farmer, 7	Gastric Ca	3/4
Low pollution	68	M, laborer, 6	MI	3/3
Low pollution	73	F, housewife, 6	MI	3/3
Low pollution	76	F, fruit seller, 9	Cervical Ca	3/3
High pollution	32	M, policeman, 13	DOA accident	3/3*
High pollution	38	F, secretary, 15	DOA accident	ND*
High pollution	39	M, office worker, 12	DOA accident	3/3
High pollution	42	M, electrician, 12	Lung Ca	4/4
High pollution	43	M, policeman, 13	MI	3/3*
High pollution	52	F, housewife, 6	Breast Ca	3/3
High pollution	55	M, outdoor vendor, 6	DOA accident	2/2
High pollution	61	M, laborer, 6	Colon Ca	3/3
High pollution	67	F, housewife, 7	Cervical Ca	2/3
High pollution	83	F, housewife, 7	Arrhythmia	3/3

*Diffuse Aβ42 plaques in frontal cortex.
ND, not determined.

Study Cities

We conducted a study using autopsy brain samples from Mexican subjects, lifelong residents of 2 large cities with severe air pollution, Mexico City and Monterrey, and 5 small cities with low levels of air pollution, Abasolo, Iguala, El Mante, Tlaxcala, and Veracruz. Mexico City (MC) is a megacity with 20 million inhabitants, 3.5 million vehicles and extensive industrial activity (Bravo and Torres, 2002). Monterrey is the second largest industrial city in the country with 3.5 million residents and thousands of industries (Junco-Munoz et al., 1996). Ozone (O_3) and PM are the major air pollutants for both MC and Monterrey. Bacterial lipopolysaccharides (LPS) and metals are important components of PM (Junco-Munoz et al., 1996; Bravo and Torres, 2002; Osornio-Vargas et al., 2003). The climatic conditions are remarkably stable in both cities, so pollutant concentrations are consistent from year-to-year, while ozone and PM levels exceed the U.S. standards most of the year (Junco-Munoz et al., 1996; Bravo and Torres, 2002). In the cities with low levels of air pollution, the combination of relatively few emission sources from industry and cars, and good ventilation conditions by regional winds, keep criteria pollutant concentrations below the current U.S. standards. Three additional factors considered in the selection of the control cities included: (1) an altitude above sea level similar to Mexico City, (2) studies in dogs from these cities showing minimal pathology in lungs and hearts (Calderón-Garcidueñas et al., 2001), and (3) knowledge that children residing in control cities show no evidence of upper or lower respiratory pathology and no systemic involvement (Calderón-Garcidueñas et al., 2003b).

Calderon-Garciduenas et al. Toxicologic Pathology 32 1 2004

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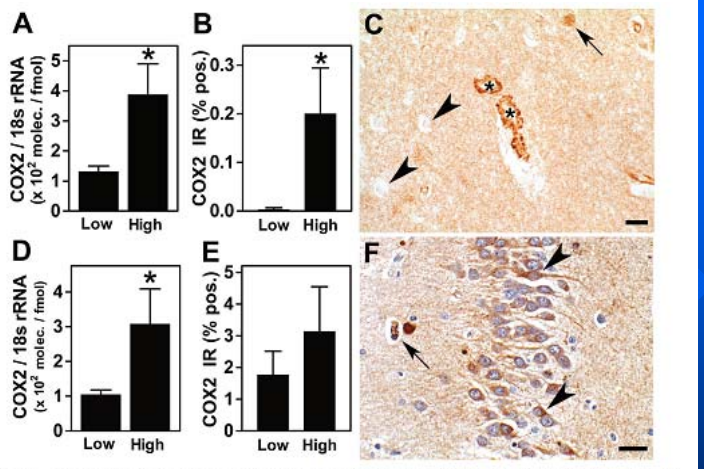

FIGURE 1.—COX2 expression in frontal cortex and hippocampus. (A and D) COX2 mRNA abundance was measured by RT-PCR and normalized for 18s rRNA levels. Means ± SEMs are shown. COX2 mRNA was significantly elevated in the high-exposure group in both frontal cortex (A, * $p = 0.009$) and hippocampus (D, * $p = 0.04$) from the high-exposure group. (B and E) COX2 protein expression in sections of paraffin-embedded tissues was localized by COX2 immunohistochemistry (IHC) and the percent of tissue area that was immunoreactive (COX2 IR) was measured by quantitative image analysis. Means ± SEMs are shown. COX2 IR was significantly elevated in frontal cortex (B, * $p = 0.01$), but not in hippocampus (E) from the high-exposure group. (C) Representative COX IHC in frontal cortex from a subject in the high-exposure group showing strong staining of endothelial cells in the capillaries (*), and pyramidal neurons (arrow), while other neurons were negative (arrowheads). Scale = 20 μm. (F) Representative COX IHC in dentate gyrus from a subject in the high-exposure group showing COX2 positive neurons (arrowheads) and capillaries (short arrow). Scale = 15 μm.

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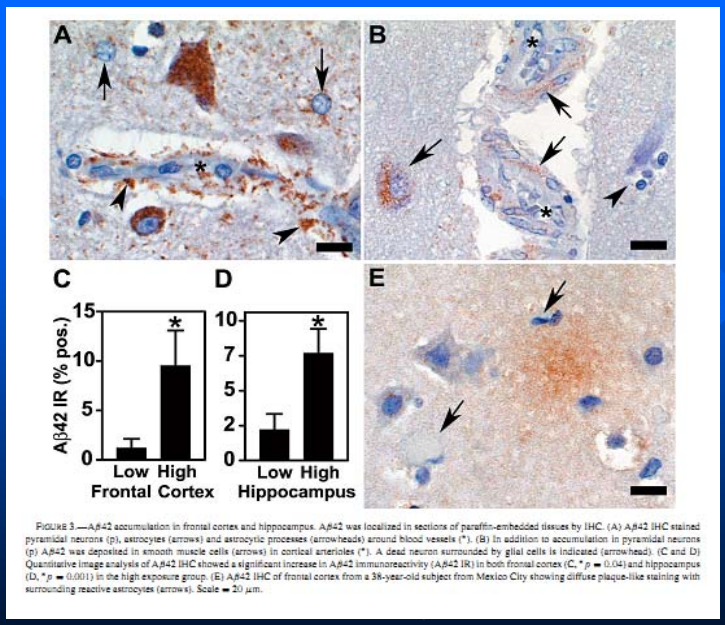

FIGURE 3.—Aβ42 accumulation in frontal cortex and hippocampus. Aβ42 was localized in sections of paraffin-embedded tissues by IHC. (A) Aβ42 IHC stained pyramidal neurons (p), astrocytes (arrows) and astrocytic processes (arrowheads) around blood vessels (*). (B) In addition to accumulation in pyramidal neurons (p) Aβ42 was deposited in smooth muscle cells (arrows) in cortical arterioles (*). A dead neuron surrounded by glial cells is indicated (arrowhead). (C and D) Quantitative image analysis of Aβ42 IHC showed a significant increase in Aβ42 immunoreactivity (Aβ42 IR) in both frontal cortex (C, * $p = 0.04$) and hippocampus (D, * $p = 0.001$) in the high exposure group. (E) Aβ42 IHC of frontal cortex from a 38-year-old subject from Mexico City showing diffuse plaque-like staining with surrounding reactive astrocytes (arrows). Scale = 20 μm.

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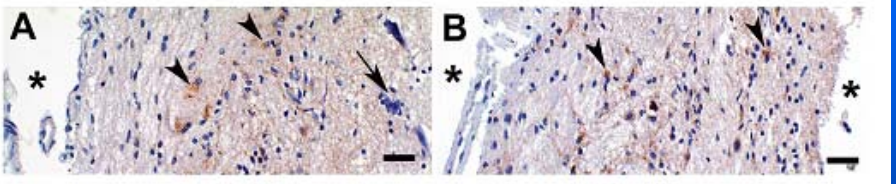

FIGURE 4.—Aβ42 accumulation in olfactory bulb and nerve in a subject from the high-exposure group. Aβ42 was localized by IHC in sections of paraffin-embedded olfactory bulb and nerve from the same subject whose frontal cortex is shown in Figure 3B. Aβ42 accumulation was seen in ensheathing cells and astrocytes both in the bulb (A, arrowheads) and the nerve (B, arrowheads). There was no Aβ42 accumulation in blood vessels in the subarachnoid space (*). In the olfactory bulb (A) a mitral neuron is indicated by an arrow. Scale = 25 μm.

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Environmental Research

Air pollution alters brain and pituitary endothelin-1 and inducible nitric oxide synthase gene expression ☆

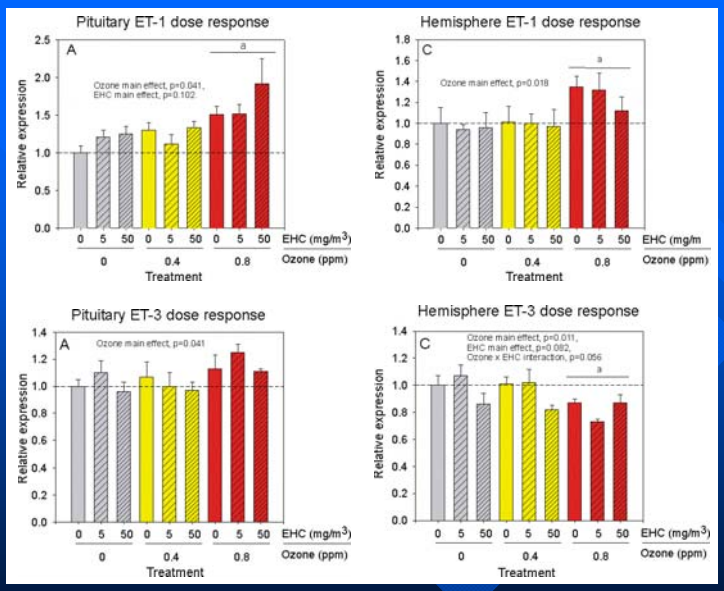
Errol M. Thomson[a,b], Prem Kumarathasan[a], Lilian Calderón-Garcidueñas[c,d], Renaud Vincent[a,b,*]

Abstract

Recent work suggests that air pollution is a risk factor for cerebrovascular and neurodegenerative disease. Effects of inhaled pollutants on the production of vasoactive factors such as endothelin (ET) and nitric oxide (NO) in the brain may be relevant to disease pathogenesis. Inhaled pollutants increase circulating levels of ET-1 and ET-3, and the pituitary is a potential source of plasma ET, but the effects of pollutants on the expression of ET and NO synthase genes in the brain and pituitary are not known. In the present study, Fischer-344 rats were exposed by nose-only inhalation to particles (0, 5, 50 mg/m^3 EHC-93), ozone (0, 0.4, 0.8 ppm), or combinations of particles and ozone for 4 h. Real-time reverse transcription polymerase chain reaction was used to measure mRNA levels in the cerebral hemisphere and pituitary 0 and 24 h post-exposure. Ozone inhalation significantly increased preproET-1 but decreased preproET-3 mRNAs in the cerebral hemisphere, while increasing mRNA levels of preproET-1, preproET-3, and the ET-converting enzyme (ECE)-1 in the pituitary. Inducible NO synthase (iNOS) was initially decreased in the cerebral hemisphere after ozone inhalation, but increased 24 h post-exposure. Particles decreased tumour necrosis factor (TNF)-α mRNA in the cerebral hemisphere, and both particles and ozone decreased TNF-α mRNA in the pituitary. Our results show that ozone and particulate matter rapidly modulate the expression of genes involved in key vasoregulatory pathways in the brain and pituitary, substantiating the notion that inhaled pollutants induce cerebrovascular effects.

Keywords: Air pollution; Endothelin; Inducible nitric oxide synthase (iNOS); Brain; Pituitary; Particulate matter; Ozone

Environmental Research 105 (2007) 224–233



Thomson et al Environ Res 105 224 2007

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Particle and Fibre Toxicology

BioMed Central

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Short report

Open Access

Exposure to diesel exhaust induces changes in EEG in human volunteers

Björn Crüts[1], Ludo van Etten[1], Håkan Törnqvist[2], Anders Blomberg[2], Thomas Sandström[2], Nicholas L Mills[3] and Paul JA Borm*[1]

Abstract

Background: Ambient particulate matter and nanoparticles have been shown to translocate to the brain, and potentially influence the central nervous system. No data are available whether this may lead to functional changes in the brain.

Methods: We exposed 10 human volunteers to dilute diesel exhaust (DE, 300 μg/m³) as a model for ambient PM exposure and filtered air for one hour using a double blind randomized crossover design. Brain activity was monitored during and for one hour following each exposure using quantitative electroencephalography (QEEG) at 8 different sites on the scalp. The frequency spectrum of the EEG signals was used to calculate the median power frequency (MPF) and specific frequency bands of the QEEG.

Results: Our data demonstrate a significant increase in MPF in response to DE in the frontal cortex within 30 min into exposure. The increase in MPF is primarily caused by an increase in fast wave activity (β2) and continues to rise during the 1 hour post-exposure interval.

Conclusion: This study is the first to show a functional effect of DE exposure in the human brain, indicating a general cortical stress response. Further studies are required to determine whether this effect is mediated by the nanoparticles in DE and to define the precise pathways involved.

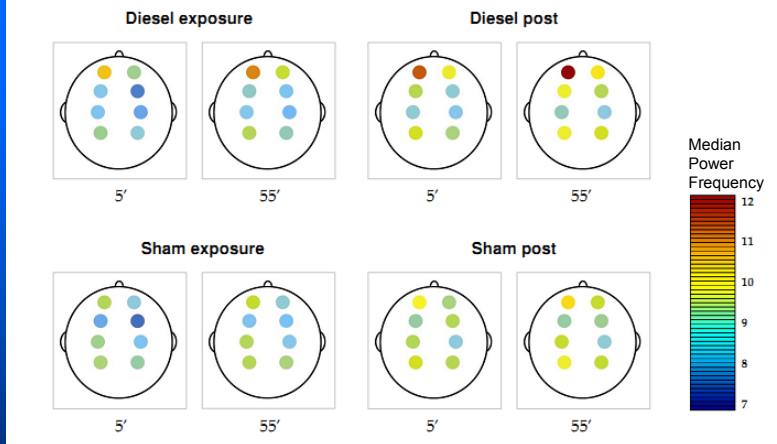

Figure 2
MPF values per electrode localisation. The figures represent the 8 electrode localizations, from the frontal areas at the top (Fp1, Fp2) to the parietal areas at the bottom (P3, P4). Amplitudes of MPF are indicated by colors, ranging from deep blue (7 Hz) to red (12 Hz). MPF amplitudes are presented as mean values of the first and last 5 minutes of the exposure hour and post exposure hour. The highest values for MPF during diesel exposure are observed at the frontal polar electrode sites (Fp1, Fp2). At these sites MPF increases significantly during diesel exposure compared to sham exposure. Following the diesel exposure MPF continued to increase resulting in significant differences at the frontal polar and the frontal sites (Fp1, Fp2, F3, F4) compared to the post-sham exposure period.

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Research | Children's Health

Association of Traffic-Related Air Pollution with Children's Neurobehavioral Functions in Quanzhou, China

Shunqin Wang,[1,2] Jinliang Zhang,[1,3] Xiaodong Zeng,[4] Yimin Zeng,[5] Shengchun Wang,[1] and Shuyun Chen[6]

[1]Department of Occupational and Environmental Health Science, School of Public Health, Peking University, Beijing, People's Republic of China; [2]Xiamen Municipal Health Bureau, Xiamen, Fujian Province, People's Republic of China; [3]Division of Environmental Pollution and Health, Chinese Research Academy of Environmental Sciences, Beijing, People's Republic of China; [4]Quanzhou Municipal Health Inspection Station, [5]Quanzhou Municipal Health Bureau, and [6]Licheng District Center for Disease Control and Prevention, Quanzhou, Fujian Province, People's Republic of China

BACKGROUND: With the increase of motor vehicles, ambient air pollution related to traffic exhaust has become an important environmental issue in China. Because of their fast growth and development, children are more susceptible to ambient air pollution exposure. Many chemicals from traffic exhaust, such as carbon monoxide, nitrogen dioxide, and lead, have been reported to show adverse effects on neurobehavioral functions. Several studies in China have suggested that traffic exhaust might affect neurobehavioral functions of adults who have occupational traffic exhaust exposure. However, few data have been reported on the effects on neurobehavioral function in children.

RESULTS: Media concentrations of NO_2 in school A and school B campus were 7 μg/m^3 and 36 μg/m^3, respectively ($p < 0.05$). The ordinal logistic regression analyses showed that, after controlling the potential confounding factors, participants living in the polluted area showed poor performance on all testing; differences in results for six of nine tests (66.7%) achieved statistical significance: Visual Simple Reaction Time with preferred hand and with nonpreferred hand, Continuous Performance, Digit Symbol, Pursuit Aiming, and Sign Register.

CONCLUSION: We found a significant relationship between chronic low-level traffic-related air pollution exposure and neurobehavioral function in exposed children. More studies are needed to explore the effects of traffic exhaust on neurobehavioral function and development.

KEY WORDS: air pollution, children, health effects, neurobehavioral functions, traffic-related air pollution *Environ Health Perspect* 117:1612–1618 (2009). doi:10.1289/ehp.0800023 available via *http://dx.doi.org/* [Online 11 May 2009]

Research

Traffic-Related Air Pollution and Cognitive Function in a Cohort of Older Men

Melinda C. Power,[1,2] Marc G. Weisskopf,[1,2] Stacey E. Alexeeff,[1] Brent A. Coull,[3] Avron Spiro III,[4,5] and Joel Schwartz[1,2]

BACKGROUND: Traffic-related particles induce oxidative stress and may exert adverse effects on central nervous system function, which could manifest as cognitive impairment.

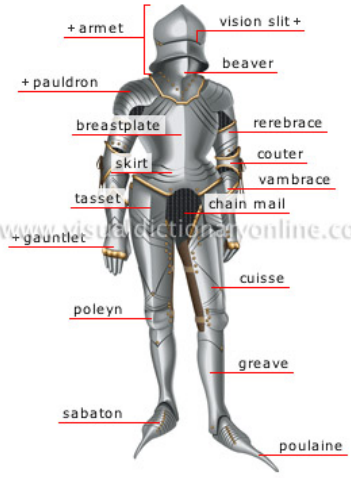
OBJECTIVE: We assessed the association between black carbon (BC), a marker of traffic-related air pollution, and cognition in older men.

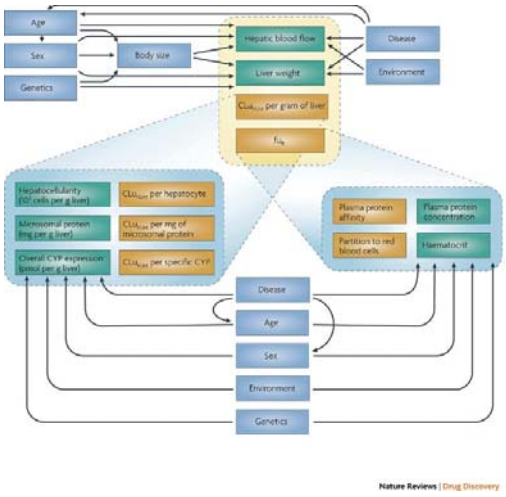
METHODS: A total of 680 men (mean ± SD, 71 ± 7 years of age) from the U.S. Department of Veterans Affairs Normative Aging Study completed a battery of seven cognitive tests at least once between 1996 and 2007. We assessed long-term exposure to traffic-related air pollution using a validated spatiotemporal land-use regression model for BC.

RESULTS: The association between BC and cognition was nonlinear, and we log-transformed BC estimates for all analyses [ln(BC)]. In a multivariable-adjusted model, for each doubling in BC on the natural scale, the odds of having a Mini-Mental State Examination (MMSE) score ≤ 25 was 1.3 times higher [95% confidence interval (CI), 1.1 to 1.6]. In a multivariable-adjusted model for global cognitive function, which combined scores from the remaining six tests, a doubling of BC was associated with a 0.054 SD lower test score (95% CI, –0.103 to –0.006), an effect size similar to that observed with a difference in age of 1.9 years in our data. We found no evidence of heterogeneity by cognitive test. In sensitivity analyses adjusting for past lead exposure, the association with MMSE scores was similar (odds ratio = 1.3; 95% CI, 1.1 to 1.7), but the association with global cognition was somewhat attenuated (–0.038 per doubling in BC; 95% CI, –0.089 to 0.012).

CONCLUSIONS: Ambient traffic-related air pollution was associated with decreased cognitive function in older men.

KEY WORDS: aging, black carbon, cognitive dysfunction, epidemiology, particulate matter. *Environ Health Perspect* 119:682–687 (2011). doi:10.1289/ehp.1002767 [Online 20 December 2010]





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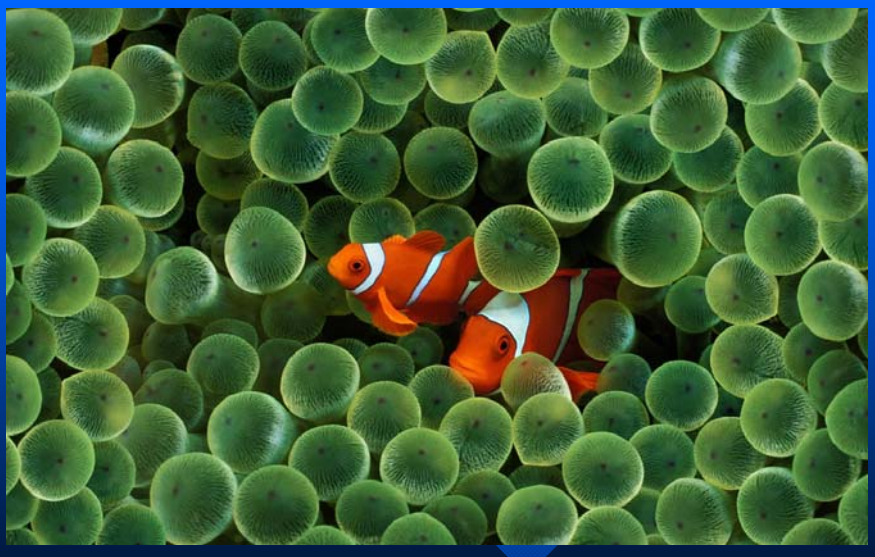

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HYPOTHESIS

Cardiovascular status is affected by the presence of ambient air contaminants

The cardiovasacular system is at homeostatic baseline when breathing clean air

Detection of a difference in the cardiovascular status (ambient air vs clean air) will reveal physiological effects attributable to inhaled contaminants

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EXPERIMENTAL APPROACH

Blind, randomized, crossover, placebo-controlled trials

Controlled exposure of mobile subjects to air pollutants (ambient and indoor)

Positive air pressure respiratory protection system (3M Breathe Easy Turbo PAPR Assembly)

Selective removal of pollutants using specific filters (dummy, HEPA, OVC, OVC/HEPA, etc)

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Positive Air Pressure Respiratory Protection Systems
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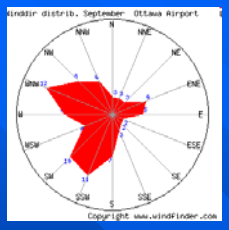
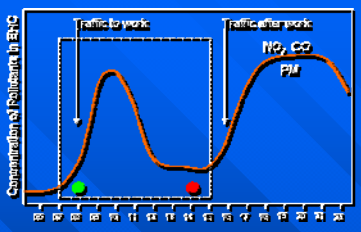
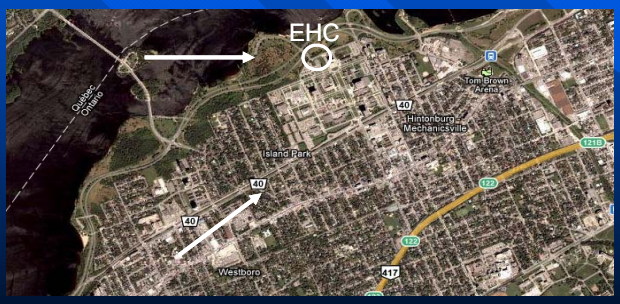
Positive Air Pressure Respiratory System and Physiological Equipment
10 lbs – 4.6 kg

STUDY SITE

ENVIRONMENTAL HEALTH CENTRE







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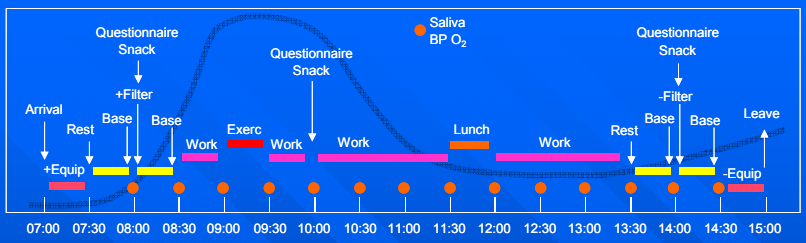

STUDY DESIGN

Ten (10) subjects
Total of 4 days: 2 days dummy filter and 2 days full filter (blind)
Not necessarily consecutive days or on same week
Work station to volunteers at EHC
Lunch and snack provided during the study

DATA ACQUISITION

Air pollutants: continuous data acquisition
Holter monitor: continuous acquisition of ECG data
BP monitor: automatic measure every 30 minutes
Saliva: sample recovery every 30 minutes
Oxygen saturation: reading every 30 minutes

SCHEDULE

07:00	Fitting of equipment
07:30	Rest
08:00	Baseline physiology
08:01	Installation of filters
08:30	Baseline physiology
09:00	Activity routine
09:30	Daily work
11:30	Lunch
12:00	Daily work
13:30	Rest
14:00	Baseline physiology
14:01	Removal of filters
14:30	Baseline physiology
14:31	Removal of equipment

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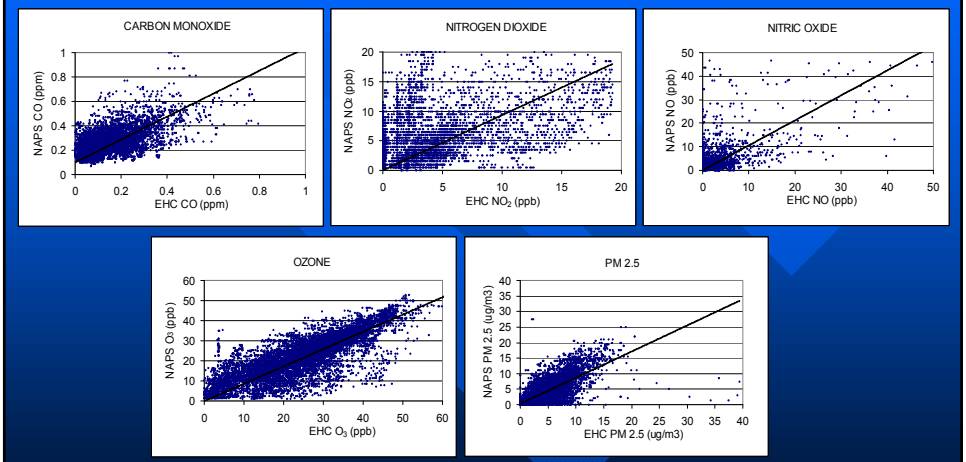
AIR POLLUTANTS IN EHC BUILDING

Ambient air pollutants penetrate indoors (1:1)



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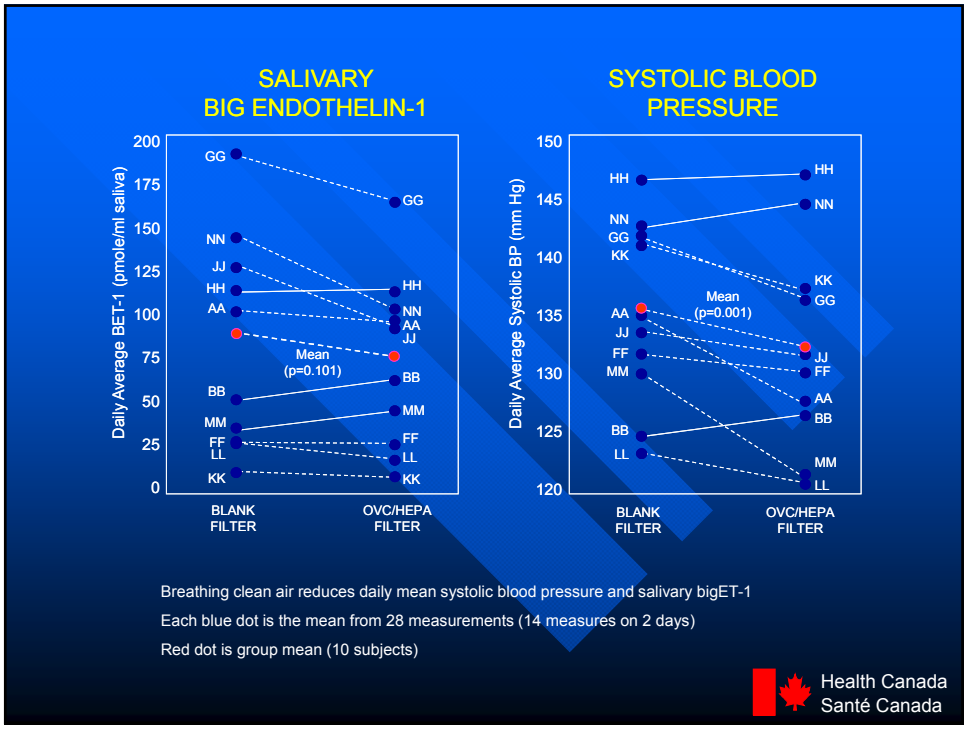
SALIVARY
BIG ENDOTHELIN-1
Daily Average BET-1 (pmole/ml saliva)
200
175
150
125
100
75
50
25
0
GG
NN
JJ
HH
AA
Mean
(p=0.101)
BB
MM
FF
LL
KK
BLANK
FILTER
OVC/HEPA
FILTER
SYSTOLIC BLOOD
PRESSURE
Daily Average Systolic BP (mm Hg)
150
145
140
135
130
125
120
HH
NN
GG
KK
Mean
(p=0.001)
AA
JJ
FF
MM
BB
LL
BLANK
FILTER
OVC/HEPA
FILTER
Breathing clean air reduces daily mean systolic blood pressure and salivary bigET-1
Each blue dot is the mean from 28 measurements (14 measures on 2 days)
Red dot is group mean (10 subjects)
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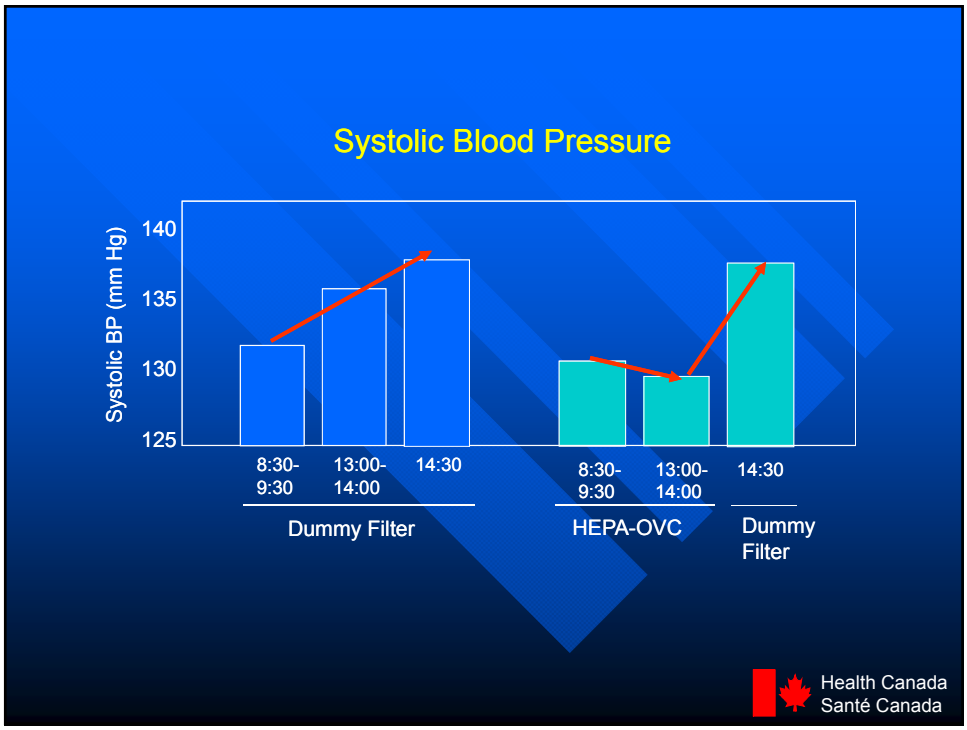
Systolic Blood Pressure
Systolic BP (mm Hg)
140
135
130
125
8:30-
9:30
13:00-
14:00
14:30
Dummy Filter
8:30-
9:30
13:00-
14:00
14:30
HEPA-OVC
Dummy
Filter
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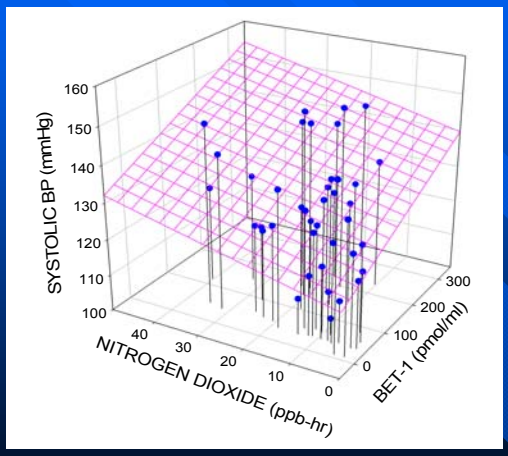
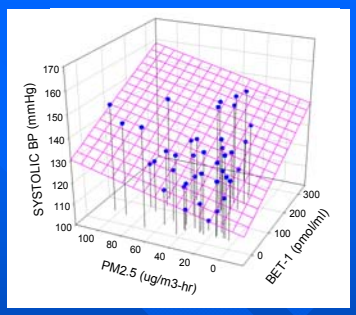
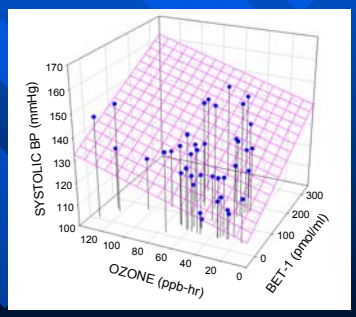
DOSE-RESPONSE

Dose-dependent increases of systolic blood pressure and salivary bigET-1 as a function of cumulative pollutant exposures (subjects without masks)







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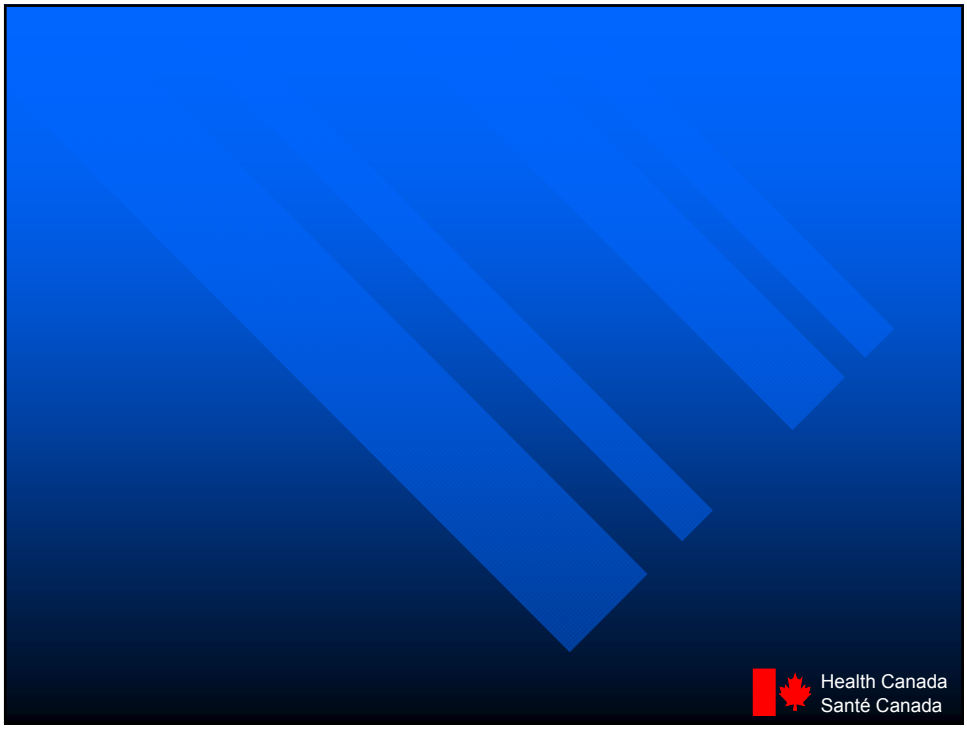
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