

Metabolic Dysfunction Modifies the Influence of Traffic-Related Air Pollution and Noise Exposure on Late-life Dementia and Cognitive Impairment

-A cohort study of older Mexican-Americans

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Table S1. Definition of metabolic dysfunction according to the recommendations of the Third Adult Treatment Panel of the National Cholesterol Education Program (NCEP ATP III).

| Metabolic Dysfunction | NCEP ATP III Criteria |
|------------------------------|---|
| Abdominal Obesity | Waist Circumference: ≥ 40 inches (Male), ≥ 35 inches (Female) |
| Hyperglycemia | Fasting glucose ≥ 100 mg/dl |
| Low HDL-cholesterol | HDL-Cholesterol: < 40 mg/dl (Male), < 50 mg/dl (Female) |

Note: HDL, high density lipoprotein;

Table S2. Air pollutions and noise exposure measure means, variances, and distributions.

| Exposure | N | Mean | Variance | Percentile | | | | | | | | |
|--|------|-------|----------|------------|----------|-----------|-----------|-----------|-----------|-----------|-----------|------------|
| | | | | <i>0</i> | <i>5</i> | <i>10</i> | <i>25</i> | <i>50</i> | <i>75</i> | <i>90</i> | <i>95</i> | <i>100</i> |
| Traffic-related NOx (ppb) ^a | 1612 | 2.59 | 4.69 | 0.01 | 0.43 | 0.67 | 1.15 | 1.90 | 3.34 | 5.22 | 6.93 | 13.20 |
| 24-hour noise (dB) ^a | 1612 | 68.46 | 78.78 | 39.4 | 55.1 | 57.5 | 62.4 | 67.6 | 74.2 | 81.3 | 84.4 | 100.0 |

Note: NOx, nitrogen oxides; dB, decibels; ppb, part per billion.

a. The Pearson correlation among the air pollution and noise exposures estimates is 0.43.

TableS3. Effect estimates (and 95% CI) of traffic-related NOx and 24-hour noise exposures (single exposure models) and each metabolic dysfunction on incident dementia/CIND from adjusted Cox proportional hazards regression models ^a.

| Parameter | Model 1 | Model 2 | Model 3 | Model 4 | Model 1 | Model 2 | Model 3 | Model 4 |
|---|----------------|-----------------|-----------------|-----------------|----------------|-----------------|----------------|-----------------|
| | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| Traffic-related NOx (per 2.29 ppb increase) | 1.2 (1.0, 1.4) | 1.2 (1.0, 1.4) | 1.2 (0.98, 1.4) | 1.2 (0.99, 1.4) | | | | |
| 24-hour noise (per 11.6 dB increase) | | | | | 1.2 (1.0, 1.5) | 1.2 (0.96, 1.5) | 1.2 (1.0, 1.5) | 1.2 (1.0, 1.5) |
| Obesity (Yes vs No) ^b | | 1.1 (0.78, 1.6) | | | | 1.1 (0.78, 1.6) | | |
| Hyperglycemia (Yes vs No) ^b | | | 1.5 (1.0, 2.1) | | | | 1.5 (1.1, 2.1) | |
| Low HDL-cholesterol (Yes vs No) ^b | | | | 1.3 (0.91, 1.8) | | | | 1.3 (0.91, 1.8) |

Note: CIND, cognitive impairment without dementia; HDL, high density lipoprotein; dB, decibels; ppb, part per billion.

- a. All the models were adjusted with baseline age, sex, education, occupation held during most of the life, neighborhood socio-economic status, smoking status, alcohol status, residential county, physical activity and household income, baseline cognition function.
- b. Definitions for metabolic dysfunction: (i) obesity: waist circumference of ≥ 40 in. in men; ≥ 35 in. in women; (ii) hyperglycemia: fasting glucose ≥ 100 mg/dl, or use of glucose-lowering medications; (iii) low HDL cholesterol: men: < 40 mg/dl; women: < 50 mg/dl, or use of statins.

Table S4. Superadditivity and multiplicativity for joint effect analyses ^a between traffic-related NO_x (<3.44 vs ≥ 3.44 ppb) or 24-hour noise exposure (<65 vs ≥ 65 dB) and metabolic dysfunction on incident dementia/CIND.

| Risk factor | Traffic-related NO _x (<3.44 vs ≥ 3.44 ppb) | | | 24-hour noise (<65 vs ≥ 65 dB) | | |
|---|--|--|-----------------------|---|--|-----------------------|
| | <i>Superadditivity</i> (<i>RERI</i>) | <i>Multiplicativity</i> (<i>Interaction term</i>) | | <i>Superadditivity</i> (<i>RERI</i>) | <i>Multiplicativity</i> (<i>Interaction term</i>) | |
| | RERI (95% CI) | HR (95% CI) | <i>p</i>-value | RERI (95% CI) | HR (95% CI) | <i>p</i>-value |
| <i>Obesity</i> ^b | 0.20 (-0.81, 1.2) | 1.2 (0.51, 2.7) | 0.72 | -0.11 (-1.1, 0.90) | 0.87 (0.39, 1.9) | 0.74 |
| <i>Hyperglycemia</i> ^b | 0.50 (-0.52, 1.5) | 1.4 (0.6, 3.3) | 0.40 | 0.32 (-0.54, 1.2) | 0.99 (0.46, 2.1) | 0.97 |
| <i>Low HDL-cholesterol</i> ^b | 1.1 (0.03, 2.1) | 2.2 (1.0, 4.8) | 0.05 | -0.01 (-0.93, 0.90) | 0.88 (0.42, 1.9) | 0.74 |

Note: CIND, cognitive impairment without dementia; HDL, high density lipoprotein; NO_x, nitrogen oxides; dB, decibels; ppb, part per billion; HR, hazard ratio; 95% CI, 95% confidence interval, RERI, relative excess risk due to interaction.

- a. All the models were adjusted with baseline age, sex, education, occupation held during most of the life, neighborhood socio-economic status, smoking status, alcohol status, residential county, physical activity and household income, baseline cognition function.
- b. Definitions for metabolic dysfunction: (i) obesity: waist circumference of ≥40 in. in men; ≥35 in. in women; (ii) hyperglycemia: fasting glucose ≥100 mg/dl, or use of glucose-lowering medications; (iii) low HDL cholesterol: men:<40 mg/dl; women:<50 mg/dl, or use of statins.

Table S5. Joint effects ^a for traffic-related NOx (<2.68 vs ≥ 2.68 ppb) or 24-hour noise exposure (<75 dB vs ≥ 75dB) and metabolic dysfunction on incident dementia/CIND.

| Risk Factor | Traffic-related NOx | | | | | | 24-hour noise | | | | | |
|--|---------------------|------|--------------|----------------|-------------------|--------------|----------------------|------|--------------|----------------------|-------------------|--------------|
| | NOx <2.68 ppb | | | NOx ≥ 2.68 ppb | | | 24-hour noise < 75dB | | | 24-hour noise ≥ 75dB | | |
| | Case/Total | HR | 95% CI | Case/Total | HR | 95% CI | Case/Total | HR | 95% CI | Case/Total | HR | 95% CI |
| <i>Obesity ^b</i> | | | | | | | | | | | | |
| No | 33/400 | 1.00 | - | 18/207 | 1.25 | (0.67, 2.32) | 40/466 | 1.00 | - | 11/141 | 1.07 | (0.52, 2.18) |
| Yes | 62/589 | 1.15 | (0.70, 1.88) | 32/312 | 1.59 ^c | (0.92, 2.73) | 65/696 | 1.05 | (0.67, 1.64) | 29/205 | 1.79 ^c | (1.05, 3.06) |
| <i>Hyperglycemia ^b</i> | | | | | | | | | | | | |
| No | 52/581 | 1.00 | - | 21/259 | 1.01 | (0.55, 1.87) | 48/648 | 1.00 | - | 25/192 | 1.72 | (0.95, 3.12) |
| Yes | 51/481 | 1.41 | (0.89, 2.23) | 35/291 | 2.09 ^c | (1.29, 3.40) | 66/594 | 1.79 | (1.16, 2.76) | 20/178 | 2.35 ^c | (1.34, 4.13) |
| <i>Low HDL-Cholesterol ^b</i> | | | | | | | | | | | | |
| No | 62/671 | 1.00 | - | 32/355 | 1.29 | (0.78, 2.11) | 64/788 | 1.00 | - | 30/238 | 1.79 | (1.07, 3.00) |
| Yes | 41/391 | 1.31 | (0.83, 2.07) | 24/195 | 1.85 ^c | (1.08, 3.18) | 50/454 | 1.53 | (0.99, 2.34) | 15/132 | 1.76 ^c | (0.96, 3.23) |

Note: CIND, cognitive impairment without dementia; HDL, high density lipoprotein; NOx, nitrogen oxides; dB, decibels; ppb, part per billion; HR, hazard ratio; 95% CI, 95% confidence interval.

- a. All the models were adjusted with baseline age, sex, education, occupation held during most of the life, neighborhood socio-economic status, smoking status, alcohol status, residential county, physical activity and household income, baseline cognition function.
- b. Definitions for metabolic dysfunction: (i) obesity: waist circumference of ≥40 in. in men; ≥35 in. in women; (ii) hyperglycemia: fasting glucose ≥100 mg/dl, or use of glucose-lowering medications; (iii) low HDL cholesterol: men:<40 mg/dl; women:<50 mg/dl, or use of statins.

Table S6. Effect estimates (and 95% CI) for traffic-related NOx and 24-hour noise exposures (single exposure models) and each metabolic dysfunction (defined without considering medication information) on incident dementia/CIND from adjusted Cox proportional hazards regression models ^a.

| Parameter | Model 1 | Model 2 | Model 3 | Model 4 | Model 1 | Model 2 | Model 3 | Model 4 |
|---|----------------|-----------------|-----------------|-----------------|----------------|-----------------|-----------------|-----------------|
| | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| Traffic-related NOx (per 2.29 ppb increase) | 1.2 (1.0, 1.4) | 1.2 (1.0, 1.4) | 1.2 (0.98, 1.4) | 1.2 (0.99, 1.4) | | | | |
| 24-hour noise (per 11.6 dB increase) | | | | | 1.2 (1.0, 1.5) | 1.2 (0.96, 1.5) | 1.2 (0.97, 1.5) | 1.2 (0.96, 1.5) |
| Obesity (Yes vs No) ^b | | 1.1 (0.78, 1.6) | | | | 1.1 (0.78, 1.6) | | |
| Hyperglycemia (Yes vs No) ^b | | | 1.6 (1.1, 2.2) | | | | 1.6 (1.1, 2.2) | |
| Low HDL-cholesterol (Yes vs No) ^b | | | | 1.4 (0.97, 2.0) | | | | 1.4 (0.96, 2.0) |

Note: CIND, cognitive impairment without dementia; HDL, high density lipoprotein; NOx, nitrogen oxides; dB, decibels; ppb, part per billion; HR, hazard ratio; 95% CI, 95% confidence interval.

- a. All the models were adjusted with baseline age, sex, education, occupation held during most of the life, neighborhood socio-economic status, smoking status, alcohol status, residential county, physical activity and household income, baseline cognition function.
- b. Definitions for metabolic dysfunction: (i) obesity: waist circumference of ≥ 40 in. in men; ≥ 35 in. in women; (ii) hyperglycemia: fasting glucose ≥ 100 mg/dl; (iii) low HDL cholesterol: men: < 40 mg/dl; women: < 50 mg/dl.

Table S7. Joint effects ^a between traffic-related NO_x (<3.44 vs ≥ 3.44 ppb) or 24-hour noise (<65 vs ≥ 65 dB) exposure and metabolic dysfunction (defined without considering medication information) on incident dementia/CIND.

| Risk Factor | Traffic-related NO _x | | | | | | 24-hour noise | | | | | |
|--|---------------------------------|------|--------------|----------------------------|-------------------|--------------|-------------------|------|--------------|-------------------|-------------------|--------------|
| | NO _x <3.44 ppb | | | NO _x ≥ 3.44 ppb | | | 24hr noise < 65dB | | | 24hr noise ≥ 65dB | | |
| | Case/Total | HR | 95% CI | Case/Total | HR | 95% CI | Case/Total | HR | 95% CI | Case/Total | HR | 95% CI |
| <i>Obesity ^b</i> | | | | | | | | | | | | |
| No | 38/463 | 1.00 | - | 13/144 | 1.31 | (0.67, 2.58) | 16/226 | 1.00 | - | 35/381 | 1.45 | (0.76, 2.78) |
| Yes | 69/678 | 1.14 | (0.72, 1.80) | 25/223 | 1.73 ^c | (0.99, 3.03) | 31/339 | 1.31 | (0.67, 2.53) | 63/562 | 1.65 ^c | (0.89, 3.07) |
| <i>Hyperglycemia ^b</i> | | | | | | | | | | | | |
| No | 51/614 | 1.00 | - | 12/168 | 1.07 | (0.54, 2.09) | 19/303 | 1.00 | - | 44/479 | 1.29 | (0.73, 2.29) |
| Yes | 54/519 | 1.45 | (0.95, 2.22) | 27/200 | 2.42 ^c | (1.44, 4.04) | 26/256 | 1.60 | (0.87, 2.95) | 55/463 | 2.21 ^c | (1.27, 3.85) |
| <i>Low HDL-Cholesterol ^b</i> | | | | | | | | | | | | |
| No | 69/756 | 1.00 | - | 18/256 | 0.97 | (0.55, 1.69) | 29/383 | 1.00 | - | 58/629 | 1.31 | (0.80, 2.14) |
| Yes | 37/379 | 1.13 | (0.73, 1.77) | 21/112 | 2.85 ^c | (1.65, 4.91) | 17/178 | 1.48 | (0.79, 2.75) | 41/313 | 1.89 ^c | (1.12, 3.20) |

Note: CIND, cognitive impairment without dementia; HDL, high density lipoprotein; NO_x, nitrogen oxides; dB, decibels; ppb, part per billion; HR, hazard ratio; 95% CI, 95% confidence interval.

- a. All the models were adjusted with baseline age, sex, education, occupation held during most of the life, neighborhood socio-economic status, smoking status, alcohol status, residential county, physical activity and household income, baseline cognition function.
- b. Definitions for metabolic dysfunction: (i) obesity: waist circumference of ≥40 in. in men; ≥35 in. in women; (ii) hyperglycemia: fasting glucose ≥100 mg/dl; (iii) low HDL cholesterol: men:<40 mg/dl; women:<50 mg/dl.