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Particulate Air Pollutants, Brain Structure, and Neurocognitive Disorders in Older Women

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Appendix B. Additional Sensitivity Analyses

This Appendix was reviewed solely for spelling, grammar, and cross-references to the main text. It has not been formatted or fully edited by HEI. This document was reviewed by the HEI Review Committee.

Correspondence may be addressed to Dr. Jiu-Chiuan Chen, Department of Preventive Medicine, University of Southern California, Keck School of Medicine, 2001 N. Soto Street, MC 9237, Los Angeles, CA 90089; e-mail: jcchen@usc.edu.

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Table B.1. Multiple Linear Regression of Normal-Appearing White Matter Volume in Relation[†] to Fine PM Exposures in WHIMS MRI Study, 1999–2006 (Restricted to Non-Hispanic White Participants)

| Statistical Models | Total White Matter | Association Brain White Matter | Frontal White Matter | Parietal White Matter | Temporal White Matter | Corpus Callosum |
|---------------------------------|-------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------------------|---------------------------------|
| Crude (N=1276) | -6.52±1.33 (p<0.01) | -4.74±1.17 (p<0.01) | -2.22±0.61 (p<0.01) | -0.80±0.36 (p=0.02) | -1.72±0.35 (p<0.01) | -0.102±0.04 (p=0.01) |
| ^a Model I (N=1276) | -6.22±1.32 (p<0.01) | -4.52±1.17 (p<0.01) | -2.13±0.61 (p<0.01) | -0.71±0.35 (p=0.04) | -1.68±0.34 (p<0.01) | -0.111±0.04 (p<0.01) |
| ^b Model II (N=1272) | -6.16±1.32 (p<0.01) | -4.53±1.17 (p<0.01) | -2.12±0.61 (p<0.01) | -0.76±0.36 (p=0.03) | -1.65±0.35 (p<0.01) | -0.113±0.041 (p<0.01) |
| ^c Model III (N=1252) | -6.66±1.34 (p<0.01) | -4.93±1.17 (p<0.01) | -2.32±0.61 (p<0.01) | -0.84±0.36 (p=0.02) | -1.77±0.35 (p<0.01) | -0.124±0.041 (p<0.01) |
| ^d Model IV (N=1194) | -6.67±1.35 (p<0.01) | -4.92±1.19 (p<0.01) | -2.28±0.62 (p<0.01) | -0.90±0.36 (p=0.01) | -1.74±0.35 (p<0.01) | -0.111±0.042 (p<0.01) |
| ^e Model V (N=1165) | -6.85±1.38 (p<0.01) | -5.09±1.21 (p<0.01) | -2.39±0.63 (p<0.01) | -0.94±0.37 (p=0.01) | -1.76±0.36 (p<0.01) | -0.107±0.043 (p=0.01) |
| ^f Model VI (N=1159) | -7.2±1.39 (p<0.01) | -5.34±1.22 (p<0.01) | -2.53±0.64 (p<0.01) | -0.98±0.37 (p<0.01) | -1.83±0.36 (p<0.01) | -0.115±0.043 (p<0.01) |

[†] Expressed as the regression coefficients (±standard errors) per interquartile (3.49 µg/m³) increase in cumulative annual PM_{2.5} (1999–2006); all analyses adjusted for the intracranial volume (ICV). Boldfaced values are statistically significant.

^aModel I: adjusted for geographic region and age.

^bModel II: adjusted for Model I covariates + SES (education, income, and employment status).

^cModel III: adjusted for Model II covariates + lifestyle factors (smoking, alcohol use, physical activities).

^dModel IV: adjusted for Model III covariates + HT use + depressive symptoms + BMI.

^eModel V: adjusted for Model IV covariates + conventional CVD risk factors (hypertension, diabetes mellitus, hypercholesterolemia).

^fModel VI: adjusted for Model V covariates + CVD histories.

Table B.2. MAR Sensitivity Analyses Using Multiple Linear Regression of Normal-Appearing White Matter Volume in Relation[†] to Fine PM Exposures in the WHIMS-MRI Study, 1999–2006

| Statistical Models | Total White Matter | Association Brain White Matter | Frontal White Matter | Parietal White Matter | Temporal White Matter | Corpus Callosum |
|------------------------------------|-------------------------------|--------------------------------|-------------------------------|------------------------|-------------------------------|---------------------------------|
| Crude (N=1369) | -4.84±1.24 (P<0.01) | -3.26±1.09 (P<0.01) | -1.31±0.57 (P=0.02) | -0.46±0.33 (P=0.17) | -1.49±0.32 (P<0.01) | -0.099±0.037 (P<0.01) |
| ^a Model I (N=1369) | -4.40±1.23 (P<0.01) | -2.92±1.08 (P<0.01) | -1.17±0.57 (P=0.04) | -0.35±0.33 (P=0.29) | -1.4±0.32 (P<0.01) | -0.106±0.037 (P<0.01) |
| ^b Model II (N=1365) | -4.35±1.23 (P<0.01) | -2.90±1.08 (P<0.01) | -1.15±0.57 (P=0.04) | -0.38±0.33 (P=0.24) | -1.37±0.32 (P<0.01) | -0.109±0.038 (P<0.01) |
| ^c Model III (N=1343) | -4.76±1.24 (P<0.01) | -3.22±1.09 (P<0.01) | -1.3±0.57 (P=0.02) | -0.46±0.33 (P=0.17) | -1.46±0.32 (P<0.01) | -0.114±0.038 (P<0.01) |
| ^d Model IV (N=1282) | -4.47±1.25 (P<0.01) | -2.96±1.1 (P<0.01) | -1.16±0.57 (P=0.04) | -0.42±0.34 (P=0.21) | -1.37±0.33 (P<0.01) | -0.108±0.039 (P<0.01) |
| ^e Model V (N=1252) | -4.57±1.27 (P<0.01) | -3.04±1.12 (P<0.01) | -1.22±0.58 (P=0.04) | -0.44±0.34 (P=0.20) | -1.38±0.33 (P<0.01) | -0.103±0.039 (P<0.01) |
| ^f Model VI (N=1245) | -4.86±1.28 (P<0.01) | -3.25±1.12 (P<0.01) | -1.34±0.59 (P=0.02) | -0.47±0.34 (P=0.17) | -1.45±0.33 (P<0.01) | -0.111±0.04 (P<0.01) |

[†] Expressed as the regression coefficients (±standard errors) per interquartile (3.49 µg/m³) increase in cumulative annual PM_{2.5} (1999-2006).

Sensitivity analyses restricted to subjects with at least 60% of yearly DPM estimates in 1996-2005 were conducted to evaluate the assumed exposure data missing at random (MAR). All analyses were adjusted for the intracranial volume. Boldfaced values are statistically significant.

^aModel I: adjusted for geographic region, age and race.

^bModel II: adjusted for Model I covariates + SES (education, income, and employment status).

^cModel III: adjusted for Model II covariates + lifestyle factors (smoking, alcohol use, physical activities).

^dModel IV: adjusted for Model III covariates + HT use + depressive symptoms + BMI.

^eModel V: adjusted for Model IV covariates + conventional CVD risk factors (hypertension, diabetes mellitus, hypercholesterolemia).

^fModel VI: adjusted for Model V covariates + CVD histories.

Table B.3. Multiple Linear Regression of Ventricular and Gray Matter Volumes[†] with Cumulative Exposures to On-Road Diesel PM (1996–2005) in the WHIMS-MRI Study (Restricted to Non-Hispanic White Participants)

| Statistical Models | Ventricle* | Association Brain Gray Matter [†] | Frontal Gray Matter [†] | Parietal Gray Matter [†] | Temporal Gray Matter [†] |
|------------------------------------|------------------------------|--|----------------------------------|-----------------------------------|-----------------------------------|
| Crude (N=1276) | 1.80±0.46 (P<0.01) | -13.12±1.96 (P<0.01) | -6.88±0.93 (P<0.01) | -3.73±0.57 (P<0.01) | -2.52±0.66 (P<0.01) |
| ^a Model I (N=1276) | 1.38±0.46 (P<0.01) | -14.84±1.92 (P<0.01) | -7.67±0.92 (P<0.01) | -4.39±0.55 (P<0.01) | -2.78±0.64 (P<0.01) |
| ^b Model II (N=1272) | 1.36±0.46 (P<0.01) | -14.42±1.93 (P<0.01) | -7.46±0.92 (P<0.01) | -4.26±0.55 (P<0.01) | -2.70±0.64 (P<0.01) |
| ^c Model III (N=1252) | 1.40±0.47 (P<0.01) | -13.94±1.94 (P<0.01) | -7.15±0.93 (P<0.01) | -4.24±0.56 (P<0.01) | -2.54±0.65 (P<0.01) |
| ^d Model IV (N=1194) | 0.99±0.49 (P=0.04) | -12.58±1.98 (P<0.01) | -6.43±0.96 (P<0.01) | -4±0.57 (P<0.01) | -2.15±0.66 (P<0.01) |
| ^e Model V (N=1165) | 0.93±0.50 (P=0.06) | -12±2.02 (P<0.01) | -6.11±0.98 (P<0.01) | -3.85±0.58 (P<0.01) | -2.04±0.67 (P<0.01) |
| ^f Model VI (N=1159) | 0.92±0.50 (P=0.07) | -11.88±2.03 (P<0.01) | -6.07±0.98 (P<0.01) | -3.79±0.59 (P<0.01) | -2.02±0.68 (P<0.01) |

* Difference in ventricular volume per interquartile change of DPM (0.31 µg/m³).

† Difference in brain volume comparing 4th quartile (median=0.78 µg/m³) vs. 1st-3rd quartiles of diesel PM (median=0.29 µg/m³).

All analyses were adjusted for the intracranial volume. Boldfaced values are statistically significant.

^aModel I: adjusted for geographic region and age.

^bModel II: adjusted for Model I covariates + SES (education, income, and employment status).

^cModel III: adjusted for Model II covariates + lifestyle factors (smoking, alcohol use, physical activities).

^dModel IV: adjusted for Model III covariates + HT use + depressive symptoms + BMI.

^eModel V: adjusted for Model IV covariates + conventional CVD risk factors (hypertension, diabetes mellitus, hypercholesterolemia).

^fModel VI: adjusted for Model V covariates + CVD histories.

Table B.4. MAR Sensitivity Analyses Using Multiple Linear Regression of Ventricular and Gray Matter[†] with Cumulative Exposures to On-Road Diesel PM (1996–2005) in the WHIMS-MRI Study

| Statistical Models | Ventricle* | Association Brain Gray Matter [†] | Frontal Gray Matter [†] | Parietal Gray Matter [†] | Temporal Gray Matter [†] |
|------------------------------------|------------------------------|--|----------------------------------|-----------------------------------|-----------------------------------|
| Crude (N=1369) | 1.74±0.39 (P<0.01) | -15.29±1.83 (P<0.01) | -7.93±0.86 (P<0.01) | -4.21±0.53 (P<0.01) | -3.15±0.61 (P<0.01) |
| ^a Model I (N=1369) | 1.36±0.40 (P<0.01) | -15.51±1.81 (P<0.01) | -8.08±0.87 (P<0.01) | -4.49±0.52 (P<0.01) | -2.93±0.61 (P<0.01) |
| ^b Model II (N=1365) | 1.35±0.41 (P<0.01) | -15.09±1.82 (P<0.01) | -7.87±0.87 (P<0.01) | -4.37±0.52 (P<0.01) | -2.85±0.61 (P<0.01) |
| ^c Model III (N=1343) | 1.40±0.42 (P<0.01) | -14.74±1.83 (P<0.01) | -7.65±0.88 (P<0.01) | -4.34±0.53 (P<0.01) | -2.75±0.61 (P<0.01) |
| ^d Model IV (N=1280) | 1.10±0.43 (P=0.01) | -13.59±1.87 (P<0.01) | -7.05±0.91 (P<0.01) | -4.13±0.54 (P<0.01) | -2.41±0.63 (P<0.01) |
| ^e Model V (N=1251) | 1.07±0.44 P=0.02 | -13.07±1.91 (P<0.01) | -6.78±0.92 (P<0.01) | -3.99±0.55 (P<0.01) | -2.3±0.64 (P<0.01) |
| ^f Model VI (N=1244) | 1.03±0.44 (P=0.02) | -12.81±1.92 (P<0.01) | -6.68±0.93 (P<0.01) | -3.9±0.56 (P<0.01) | -2.22±0.64 (P<0.01) |

* Difference in ventricular volume per interquartile change of DPM (0.31 µg/m³).

† Difference in brain volume comparing 4th quartile (median=0.78 µg/m³) vs. 1st-3rd quartiles of diesel PM (median=0.29 µg/m³).

Sensitivity analyses restricted to 1369 subjects with at least 60% of yearly DPM estimates in 1996-2005 were conducted to evaluate the assumed exposure data missing at random (MAR).

All analyses were adjusted for the intracranial volume. Boldfaced values are statistically significant.

^aModel I: adjusted for geographic region, age, and race.

^bModel II: adjusted for Model I covariates + SES (education, income, and employment status).

^cModel III: adjusted for Model II covariates + lifestyle factors (smoking, alcohol use, physical activities) .

^dModel IV: adjusted for Model III covariates + HT use + depressive symptoms + BMI.

^eModel V: adjusted for Model IV covariates + conventional CVD risk factors (hypertension, diabetes mellitus, hypercholesterolemia).

^fModel VI: adjusted for Model V covariates + CVD histories.

Table B.5. Sensitivity Analyses Using Multivariable-Adjusted Cox Models for the Effects* of Time-Varying Cumulative On-Road Diesel PM on Mild Cognitive Impairment/Dementia Risks in WHIMS (1996–2007)

| Sensitivity Analyses [†] | Models | Mild Cognitive Impairment (MCI) | Dementia | MCI/Dementia |
|-----------------------------------|------------------------|---|---|---|
| Part A | Crude | <i>N</i> =6351, <i>n</i> =243, 0.88 (0.74, 1.04) <i>P</i> =0.14 | <i>N</i> =6472, <i>n</i> =182, 0.95 (0.78, 1.14) <i>P</i> =0.57 | <i>N</i> =6467, <i>n</i> =359, 0.92 (0.80, 1.05) <i>P</i> =0.22 |
| | ^a Model I | <i>N</i> =6351, <i>n</i> =243, 0.83 (0.69, 0.99) <i>P</i> =0.04 | <i>N</i> =6472, <i>n</i> =182, 0.91 (0.74, 1.11) <i>P</i> =0.35 | <i>N</i> =6467, <i>n</i> =359, 0.87 (0.76, 1.01) <i>P</i> =0.07 |
| | ^b Model II | <i>N</i> =6315, <i>n</i> =240, 0.87 (0.72, 1.04) <i>P</i> =0.12 | <i>N</i> =6435, <i>n</i> =180, 0.93 (0.76, 1.13) <i>P</i> =0.45 | <i>N</i> =6430, <i>n</i> =355, 0.91 (0.78, 1.05) <i>P</i> =0.18 |
| | ^c Model III | <i>N</i> =6187, <i>n</i> =233, 0.86 (0.72, 1.04) <i>P</i> =0.12 | <i>N</i> =6301, <i>n</i> =171, 0.95 (0.77, 1.16) <i>P</i> =0.61 | <i>N</i> =6296, <i>n</i> =342, 0.91 (0.79, 1.06) <i>P</i> =0.23 |
| | ^d Model IV | <i>N</i> =5853, <i>n</i> =211, 0.89 (0.74, 1.08) <i>P</i> =0.25 | <i>N</i> =5954, <i>n</i> =148, 1 (0.80, 1.24) <i>P</i> =0.97 | <i>N</i> =5950, <i>n</i> =308, 0.95 (0.81, 1.10) <i>P</i> =0.48 |
| | ^e Model V | <i>N</i> =5748, <i>n</i> =207, 0.89 (0.73, 1.09) <i>P</i> =0.26 | <i>N</i> =5844, <i>n</i> =143, 1.03 (0.83, 1.28) <i>P</i> =0.77 | <i>N</i> =5840, <i>n</i> =299, 0.96 (0.82, 1.13) <i>P</i> =0.62 |
| | ^f Model VI | <i>N</i> =5700, <i>n</i> =202, 0.90 (0.74, 1.10) <i>P</i> =0.30 | <i>N</i> =5796, <i>n</i> =142, 1.04 (0.84, 1.29) <i>P</i> =0.71 | <i>N</i> =5792, <i>n</i> =294, 0.97 (0.82, 1.13) <i>P</i> =0.67 |
| Part B | Crude | <i>N</i> =7295, <i>n</i> =355, 1.09 (0.98, 1.2) <i>P</i> =0.12 | <i>N</i> =7447, <i>n</i> =229, 1.03 (0.89, 1.19) <i>P</i> =0.69 | <i>N</i> =7437, <i>n</i> =497, 1.07 (0.98, 1.17) <i>P</i> =0.12 |
| | ^a Model I | <i>N</i> =7295, <i>n</i> =355, 0.93 (0.82, 1.05) <i>P</i> =0.23 | <i>N</i> =7447, <i>n</i> =229, 0.94 (0.80, 1.10) <i>P</i> =0.42 | <i>N</i> =7437, <i>n</i> =497, 0.94 (0.85, 1.04) <i>P</i> =0.24 |
| | ^b Model II | <i>N</i> =7253, <i>n</i> =350, 0.94 (0.83, 1.06) <i>P</i> =0.29 | <i>N</i> =7404, <i>n</i> =226, 0.94 (0.81, 1.11) <i>P</i> =0.47 | <i>N</i> =7394, <i>n</i> =491, 0.95 (0.86, 1.05) <i>P</i> =0.31 |
| | ^c Model III | <i>N</i> =7096, <i>n</i> =339, 0.94 (0.83, 1.07) <i>P</i> =0.37 | <i>N</i> =7239, <i>n</i> =215, 0.96 (0.81, 1.13) <i>P</i> =0.60 | <i>N</i> =7229, <i>n</i> =472, 0.96 (0.86, 1.06) <i>P</i> =0.42 |
| | ^d Model IV | <i>N</i> =6680, <i>n</i> =298, 0.97 (0.85, 1.1) <i>P</i> =0.61 | <i>N</i> =6803, <i>n</i> =183, 0.96 (0.81, 1.15) <i>P</i> =0.68 | <i>N</i> =6795, <i>n</i> =413, 0.97 (0.87, 1.09) <i>P</i> =0.65 |
| | ^e Model V | <i>N</i> =6546, <i>n</i> =289, 0.95 (0.83, 1.09) <i>P</i> =0.46 | <i>N</i> =6663, <i>n</i> =178, 0.98 (0.82, 1.18) <i>P</i> =0.86 | <i>N</i> =6656, <i>n</i> =399, 0.97 (0.86, 1.09) <i>P</i> =0.62 |
| | ^f Model VI | <i>N</i> =6485, <i>n</i> =284, 0.95 (0.83, 1.09) <i>P</i> =0.48 | <i>N</i> =6602, <i>n</i> =177, 0.99 (0.83, 1.18) <i>P</i> =0.91 | <i>N</i> =6595, <i>n</i> =394, 0.97 (0.87, 1.09) <i>P</i> =0.65 |

* Expressed as the hazard ratios (95% confidence interval) associated with each interquartile increment of time-varying cumulative annual exposures (per 0.35 µg/m³) to on-road DPM.

† Part A: all models restricted to non-Hispanic white participants; Part B: all models not including geographic region in the listed covariates.

^aModel I: adjusted for geographic region, age and race/ethnicity.

^bModel II: adjusted for Model I covariates + SES (education, income, and employment status).

^cModel III: adjusted for Model II covariates + lifestyle factors (smoking, alcohol use, physical activities).

^dModel IV: adjusted for Model III covariates + HT use + depressive symptoms + BMI.

^eModel V: adjusted for Model IV covariates + conventional CVD risk factors (hypertension; diabetes mellitus; hypercholesterolemia).

^fModel VI: adjusted for Model V covariates + CVD histories.