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Fine Particulate Matter Is Associated With Lower Executive Functioning in Middle-aged and Older Adults: Cardiometabolic Disease as a Mediator

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Abstract

Background: $PM_{2.5}$ pollution is expected to worsen in many places due to climate change, as a result of hotter temperatures, less precipitation, and increases in wind speed. $PM_{2.5}$ exposure has adverse effects on humans that may accelerate the aging process. Less is known about whether physical and mental health conditions mediate the relationship between $PM_{2.5}$ exposure and aging-related cognitive and functional limitations.

Methods: Longitudinal data from the Midlife in the United States study (MIDUS 2: 2004–05; MIDUS 3: 2013–14) were used, with a sample of approximately 5 000 individuals aged 32–84. Based on individuals' residential addresses at each wave, we identified census tract-level $PM_{2.5}$ exposure as defined by 5-year annual averages. Missing data were handled using multiple imputation by chained equations. We examined cross-sectional and longitudinal associations between $PM_{2.5}$ exposure and aging-related limitations (ie, executive functioning and functional limitations), and tested cardiometabolic disease and depressive symptoms as mediators.

Results: Higher $PM_{2.5}$ exposure was associated with lower executive functioning cross-sectionally and longitudinally, but not with functional limitations. The cross-sectional association between $PM_{2.5}$ and executive functioning was partially mediated by cardiometabolic disease, accounting for 8.1% of the estimate. Depressive symptoms were not a significant mediator.

Conclusions: Findings suggest the importance of considering the indirect ways in which climate change may affect health of middle-aged and older adults.

Keywords: Aging, Air pollution, Cardiovascular and metabolic disease, Cognition, Functional limitations

Climate change is expected to increase the concentration of fine particulate matter (particles ≤2.5 μg in diameter or $PM_{2.5}$) in the ambient air in many places. This increase is the result of hotter temperatures, less precipitation, and increases in windspeed (1,2). $PM_{2.5}$ exposure is associated with many adverse health effects, including those affecting the respiratory, cardiovascular, and neurological systems (3). Older adults are a population that is vulnerable to the effects of air pollution and climate change (4) due to changes that occur with aging, for example, deterioration of the immune system, increased permeability of the blood–brain barrier, reduced lung function, increased prevalence of chronic diseases, and mobility limitations (4–6). Notably, demographic shifts are resulting in growing numbers of older adults. In 2020, 1 billion people were aged 60 years or older, a number that is expected to rise to 1.4 billion by 2030 (7).

As people age, many individuals experience changes in both cognitive and physical functioning. Declines in cognitive functioning are especially observed in the domain of executive functioning (EF) which involves cognitive control processes (eg, working memory, processing speed, flexibility) that relate to planning, inhibition, and shifting (redirecting the focus of attention) (8). Advancing age also increases the risk of physical limitations that can prevent engagement in daily activities and cause loss of independence, especially among adults with underlying health conditions (9).

Prior evidence indicates that fine particulate matter air pollution has negative impacts on the cognitive functioning of middle-aged and older adults including in 2 recent meta-analyses (10,11). Those analyses have demonstrated with moderate certainty that greater $PM_{2.5}$ exposure is associated with lower general cognition in adults over 40 years old (10), and that general cognition is more tightly linked to $PM_{2.5}$ than to other air pollutants (ie, NO_x, O_3, and PM_{10}) (11). Several papers have reported associations between $PM_{2.5}$ and EF specifically (12,13). This association was positive but not statistically significant in

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a meta-analysis that included estimates from 6 studies (11). A meta-analysis including 14 studies reported a nonsignificant and negative association between $PM_{2.5}$ and attention and/or EF, but with low certainty due to inconsistencies across studies (10). Thompson et al. (10) suggested that the mixed findings between studies of EF may be due to variability in the skills included in EF scales. Given prior work, we hypothesize that greater $PM_{2.5}$ exposure is associated with reduced EF and with a greater decline in EF over time (H1).

While numerous studies have examined $PM_{2.5}$ and cognitive functioning, few have considered how functional limitations may be worsened by $PM_{2.5}$. $PM_{2.5}$ could increase functional limitations by discouraging individuals from engaging in outdoor exercise (9,14) or worsening chronic health conditions (14–16). The results of studies on $PM_{2.5}$ and functional limitations have been mixed (9,14–16). As with EF, additional high-quality analyses are needed. Nonetheless, we hypothesize that greater $PM_{2.5}$ exposure is associated with reduced functional limitations and with a greater decline in functional limitations over time (H2).

There is limited research on sex or age-based differences in how air pollution exposure influences the aging process. Studies have identified sex differences in sensitivity to the effects of air pollution on a variety of health conditions throughout the life course, but findings have been mixed with both males and females being identified as at-risk (17–19). Age moderation is less often examined than sex moderation. One study found that air pollution had a larger negative effect on the physical health of older adults compared to middle-aged individuals (20).

Air pollution is related to other health conditions that, in turn, may contribute to aging-related cognitive and physical limitations. Existing evidence points to the possibility that chronic health conditions, like cardiometabolic (CMB) disease and depression, could lie on the casual pathway between $PM_{2.5}$ and cognitive and functional limitations. However, limited research to date has examined these as mediators of associations between pollution exposure and cognitive functioning, with mixed findings (21–24). Separate studies find that air pollution is associated with CMB disease (25) and that CMB risk factors (eg, blood pressure) are associated with EF decline (26). These studies lead us to hypothesize that CMB disease will mediate cross-sectional and longitudinal associations between greater $PM_{2.5}$ exposure and EF (H3). Air pollution is also associated with depression (27) and major depression is associated with impaired EF (28). Oxidative stress and neuroinflammation could be driving these associations (21). As such, we hypothesize that depression will mediate cross-sectional and longitudinal associations between greater $PM_{2.5}$ exposure and EF (H4). No studies have examined depression or CMB as mediators of associations between $PM_{2.5}$ and functional limitations. The limited prior evidence for such mediation leads us to not pose hypotheses for functional limitations.

Given the limitations in existing work (eg, inclusion of 1 sex or narrow age group, cross-sectional analyses, not looking at executive function or functional limitations, and lack of moderation tests by age or sex or consideration of chronic health conditions as mediators), we examined cross-sectional and longitudinal associations between $PM_{2.5}$ exposure and EF and functional limitations, including testing for moderation by sex and age. We then tested depression and CMB disease as mediators.

Method

Study Design and Participants

Our analyses relied on a cohort study of middle-aged and older adults in the United States. Data came from waves 2 and 3 of the Midlife in the United States (MIDUS) study, one of the first national surveys to investigate factors related to the midlife aging process among U.S. adults. Participants were initially recruited in 1995–96, with follow-up data collection occurring in 2004–05 (wave 2; M2) and 2013–14 (wave 3; M3). Around one-half of the original MIDUS sample was a national probability sample obtained via random digit dialing, with the remaining portion coming from oversamples in selected metropolitan areas, siblings of the probability sample, and a sample of twin pairs. The response rate for the phone interview at M2 was approximately 75% among living participants (29). MIDUS added a sample of Black/African Americans from Milwaukee (MKE) in 2005–06 corresponding to M2 and a follow-up in 2016 that aligns with M3.

Study variables were assessed during distinct components of the MIDUS study (eg, a self-administered questionnaire and telephone-administered cognitive battery), resulting in differences in data availability across measures. Of the 5 555 participants (including MKE) completing the phone interview at M2, functional limitations were assessed for 4 612, with missing data largely due to noncompletion of the self-administered questionnaire. Executive functioning was assessed as part of the MIDUS Cognitive Project, conducted at approximately the same time as M2 and M3. Valid EF assessments were available at M2 for 3 909 individuals, with missing data due to nonparticipation (the participation rate was 81%) or because cognitive data were judged invalid based on established criteria (30). Sample sizes for M3 measures are smaller due to nonparticipation in individual components or study attrition, including death between M2 and M3 (n = 635). In total, 3 298 participants had data on functional limitations and 3 291 had valid EF assessments at M3. Missing data were handled using multiple imputation by chained equations (MICE), as described in the Statistical Analysis.

Participant residential addresses at M2 and M3 were obtained by the MIDUS study team and geocoded to the census tract using 2010 boundaries. For the present study, area-level variables were linked to participant records by the MIDUS administrative staff, with geographic identifiers removed prior to returning linked data to the study team (for information on MIDUS procedures for linking contextual variables, see https://midus.wisc.edu/data/MIDUS_Geocoding_README_20220329.pdf).

Outcome Assessment

Executive functioning was assessed as part of the Brief Test of Adult Cognition by Telephone (BTACT), a battery of validated cognitive tests administered by telephone (30). There are seven cognitive tests forming the BTACT. When conducting exploratory factor analysis, researchers determined that 5 of the tests loaded onto a construct representing EF and the other 2 onto an episodic memory construct (31). We used those 5 tests to assess EF. They are described in detail elsewhere (30) and included backward digit span; category-specific verbal fluency; pattern completion using sets of number series; counting backward from 100; and the Stop & Go Switch Task. These tests are intended to assess working memory, processing speed, inductive reasoning, reaction

time, attention, task switching, and inhibitory control. The BTACT has been shown to be a reliable and valid assessment for monitoring EF. In particular, scores from telephone and in-person administration are strongly correlated (r = 0.74 for the EF composite between modalities), individual tests showed moderate to strong factor loadings on the EF construct (β = 0.45–0.73), and the test-retest reliability was satisfactory over a 6-month interval (30,31). The BTACT is strongly correlated with other in-person instruments for EF (31). The EF scale at both timepoints was standardized to our sample at M2 to facilitate interpretation while allowing for longitudinal comparison.

As a measure of functional limitations, MIDUS includes 7 self-reported limitations. MIDUS modified these items from the Functional Status Questionnaire and they have been used in prior research (32). These self-reported measures were compared favorably with measures of objectively assessed physical capacity in middle-aged adults (33). Participants were asked about the extent to which their health limited them doing the following activities (1 = not at all, 4 = a lot): lifting/carrying groceries; climbing several flights of stairs; bending, kneeling, or stooping; walking more than one mile; walking several blocks; vigorous activities such as running and lifting heavy objects; and moderate activities such as bowling and vacuuming. The responses to each item were averaged to create a summary score, with high internal consistency (α = 0.94); higher scores indicate more functional limitations.

Mediator Assessment

Depressive symptoms were assessed using the World Health Organization Composite International Diagnostic Interview Short Form (34). First, participants were asked if they had felt "sad, blue, or depressed" for 2 weeks or more in the past 12 months. If responding affirmatively, participants were asked if they experienced any of the following depressive symptoms: losing interest in most things; losing/increasing appetite; feeling more tired than usual; having trouble falling asleep; having more trouble concentrating than usual; feeling down on yourself/no good/worthless; and thinking a lot about death. The number of symptoms was summed, with a range from 0 to 7 depressive symptoms (35).

Cardiometabolic disease was measured as a summary score consisting of 4 conditions: hypertension; diabetes; heart trouble; and abdominal obesity. Participants reported if they received a medical diagnosis or treatment in the past 12 months for "high blood pressure/hypertension" and "diabetes/high blood sugar," and whether "heart trouble" was ever suspected or confirmed by a doctor. Although self-reported conditions are subject to reporting bias—particularly from conditions being undiagnosed—prior research has shown that self-reports of hypertension, diabetes, and myocardial infarction (an example of heart trouble) show substantial agreement with medical records (kappa from 0.75 to 0.80) while heart failure (another example of heart trouble) had moderate agreement (36). One study of MIDUS participants showed elevated levels of objectively assessed cardiovascular risk factors for participants self-reporting heart trouble (37). For abdominal obesity, participants were provided a tape measure, instructed on how to measure waist circumference at the navel, and asked to report to the nearest quarter inch. We applied thresholds of ≥102 cm for males and ≥88 cm for females to determine if participants had abdominal obesity. Abdominal obesity was selected as it more strongly predicts CMB disease and mortality as compared to general obesity (38) and is preferred for longitudinal analysis as compared to waist-to-height ratio (given stable and even slight declines in height in adulthood) (39). Clinical assessments of waist circumference were available for select individuals participating in a substudy for whom we found substantial agreement for abdominal obesity between the self-report and technician measurements (n = 1 201, kappa = 0.66). Given differences in prevalence across conditions, the 4 indicators were standardized and averaged to create the summary measure which was then restandardized to the sample at M2 to facilitate longitudinal comparison.

As a robustness check, we created an alternative CMB measure that leverages self-reports of specific diagnoses for participants who reported "heart trouble." MIDUS staff categorized participant responses into 9 conditions or other. Although these conditions allow for selection of specific cardiovascular diseases, self-reports undercount prevalence of individual conditions due to being asked in an open-ended format. In the alternative CMB measure, we substituted "heart trouble" for the count of select cardiovascular diseases (ie, heart attack, angina, valve disease, coronary artery disease, arrhythmia, congestive heart failure, and stroke [assessed separately using 2 items]). We summed affirmative responses to these diagnoses and coded the alternative CVD variable as 0, 1, or ≥ 2. We used this variable in the CMB composite alongside hypertension, diabetes, and abdominal obesity; the 4 indicators were standardized and averaged to create a summary measure.

Exposure Assessment

Ambient air pollution was assessed using $PM_{2.5}$ concentration. Annual $PM_{2.5}$ concentration estimates came from the Center for Air, Climate, and Energy Solutions v1 empirical models and were derived using data from US EPA monitoring sites and other air quality monitoring networks, with modeled values informed by land use variables and satellite-derived estimates of $PM_{2.5}$ (40). We computed tract-level 5-year averages of $PM_{2.5}$ concentration for 2001–2005 and 2006–2010, with 2001–2005 corresponding to the period leading up to M2 and 2006–2010 corresponding to the years between M2 and M3. We linked 2001–2005 tract-$PM_{2.5}$ values to respondents using their residential address at M2. For M3, we linked 2006–2010 $PM_{2.5}$ to respondents' address by weighting the $PM_{2.5}$ concentration based on the proportion of time spent at the M2 versus M3 address between 2004–2005 and 2013–2014.

In the cross-sectional models, we use $PM_{2.5}$ (2001–2005) to predict the outcomes at M2 (2004–2005). In the longitudinal models, we use $PM_{2.5}$ (2006–2010) when predicting residualized change in the outcomes from M2 (2004–2005) to M3 (2013–2014). We do not include $PM_{2.5}$ in 2001–2005 when predicting M3 outcomes because we aim to model the change in outcomes that corresponds with the intervening exposure, not the lagged effects.

Covariates

We included multiple sociodemographic characteristics that are known correlates of aging-related limitations: age (in years), biological sex (male, female), race/ethnicity (non-Hispanic [NH] White, NH Black/African American, Hispanic any race, NH Native American, NH Asian, NH other race), marital status (married/cohabiting, separated/divorced, widowed, never married), education (less than high school,

completed high school, some college, 4-year college degree or more), household total income (natural log [total of wages, pension, social security, and other sources + 1]), nativity status (U.S. born, foreign-born), and employment status (working now/self-employed, unemployed/temporarily laid off, retired, homemakers, others). Additionally, we adjusted for differences between MIDUS samples (ie, national probability sample, sibling, twin, city-oversample, Milwaukee sample), as there is differential attrition and small differences in data collection protocols between samples.

As tract-level covariates, we included urban–rural classification, walkability, and median household income, which are correlates of aging-related cognitive and physical limitations (41,42). Tract features were assessed in approximately 2010, and we assumed that measurements are relatively stable over the period of our study. Urban–rural classifications come from the National Center for Education Statistics where U.S. territory is divided into city, suburb, town, and rural classifications (43). Next, tracts were classified into these same types when 90% of the 2010 tract population falls within a single classification for the locale and are otherwise coded as mixed (44). For tract walkability, we utilized an established compactness composite index that incorporates: gross population density, gross employment density, job-population balance, degree of job mixing, weighted average Walk Score, percentage of small urban blocks, average block size, intersection density, and percentage of 4-or-more-way intersections (45). Tract median household income, assessed using 2006–2010 American Community Survey 5-year estimates (46), was included as a direct measure of area financial resources that correlates with a broad set of area socioeconomic conditions (47).

Statistical Analysis

We first presented univariate descriptive statistics for the sample and quantified raw changes in the outcome and mediating variables from M2 to M3. To reduce bias due to attrition and minimize sample size differences between outcomes, we used MICE to handle missing data. Multiple imputation by chained equations uses fully conditional specifications where each variable is imputed sequentially using custom prediction equations that allow for different outcome variable types and to specify the variables included as predictors. The imputation procedure is done iteratively so models can be simultaneously estimated. We conducted 20 imputations, with 10 iterations per chain to achieve convergence (ie, burn-in period). Values were imputed only for individuals who participated at M2, reported race/ethnicity (age and sex had no missingness), and had linked tract-level data. Variable-specific exclusion criteria were applied: EF was imputed only for participants raised in a household where English was spoken regularly as the validity of imputed values may be weak for non-English speakers (30), and M3 outcomes and mediators were imputed only among participants alive at the time of the study wave. All variables were included in prediction equations, with the exception of M3 measures not being used to impute M2 measures. To better meet the assumption of data missing at random, we included self-rated health as an auxiliary variable as it predicts longitudinal participation (29). Missingness was minimal for most demographic variables (<0.5%) except nativity status (5.5%) and household income (20.0%). For CMB, functional limitations, and EF measures, missingness ranged from 16.7% to 28.6% at M2 and 32.6% to 41.1% at M3. Although we have a moderate level of missing data, multiple imputation has been shown to adequately handle missingness of 50% or more (although less so for the exposure) (48). Multiple imputation by chained equations was implemented using the *mi impute chained* command in Stata 18.0.

Using the 20 multiply imputed datasets, we fit linear regression models to estimate associations between tract-level $PM_{2.5}$ concentration and both EF and functional limitations, with each outcome modeled at M2 (cross-sectional) and M3 adjusting for M2 levels of the outcome (longitudinal). We combined the model results from each imputed dataset using Rubin's rules (49), which adjust coefficients and standard errors to account for variability between imputations. After modeling the association between $PM_{2.5}$ and each outcome, we separately tested whether associations were moderated by age and sex. When examining moderation by age, we tested a linear age term and then three age groupings to allow for nonlinear moderation (ie, less than 50 years, 50–64 years, and 65 years and older at M2). Moderation was tested by interacting age terms with $PM_{2.5}$, and mean-centering continuous variables to simplify interpretation of the estimates. To test moderation by sex, we interacted with the binary sex variable with $PM_{2.5}$. All models included individual and area-level covariates.

Next, we used path modeling techniques to examine mediation by depressive symptoms and CMB disease. We fit path models only for outcome variables where $PM_{2.5}$ was a significant predictor in regression models. Mediation was formally tested by estimating indirect effects using the product-of-coefficient method, and we quantified the extent of mediation by reporting the total effect explained by the mediator (50). Models were fit using *regression* and *gsem* commands preceded by *mi estimate:* in Stata 18.0. Cluster-robust standard errors were estimated to account for clustering of observations within census tracts. Spatial analysis that incorporates the spatial relationships between tracts was not possible, as MIDUS protocols for linking area-level variables do not allow for the release of geographic identifiers. We conducted 2 sensitivity analyses related to the path models. The first substitutes the alternative CMB measure for the original. The second excludes the autoregressive terms for the outcome and mediator (ie, M2 measurement does not predict the same measurement at M3). This addresses potential bias from including baseline measures of outcomes when studying temporal changes (51).

Results

Table 1 presents the sample characteristics, first for only the observed data and then when adding imputed data. Mean values were generally comparable across the observed and imputed data, although EF appears to be lower across waves when missing data are imputed. With the exception of depressive symptoms, outcome and mediator variables appear to show age-related changes from M2 to M3. However, mean levels for sample participants at M2 are not directly comparable to M3 due to sample attrition. When restricted to the sample participating at both waves, results from paired sample t-tests confirm age-related declines in EF (difference = –0.42 *SD* [standard deviation] units, $p < .001$); increased functional limitations (difference = 0.29, $p < .001$); increased CMB disease (difference = 0.34 *SD* units, $p < .001$); and no difference in depressive symptoms ($p = .67$).

Table 1. Sample Characteristics

Variables	Mean ± *SD*	%	*n*	Pooled Mean or (%)
M2 age, in years	55.03 ± 12.45		5 481	
Biological sex (1 = female)		54.2	5 481	
Race/ethnicity			5 481	
Non-Hispanic (NH) White		80.1	4 391	
NH Black/African Americans		13.9	760	
Hispanic, any race		2.9	160	
NH Native American		1.4	76	
NH Asian		0.4	21	
NH other race		1.3	73	
M2 marital status			5 475	
Married/cohabiting		66.4	3 635	(66.4)
Separated/divorced		16.2	889	(16.2)
Widowed		7.3	402	(7.3)
Never married		10.0	549	(10.0)
Education			5 473	
Less than high school		7.6	413	(7.6)
Completed high school		27.9	1 525	(27.9)
Some college		30.2	1 650	(30.1)
4-Year college degree or more		34.4	1 885	(34.4)
Nativity, (1 = U.S. born)		96.4	5 176	(96.3)
Employment status			5 455	
Working now or self-employed		63.2	3 445	(63.0)
Unemployed or temporarily laid off		3.2	172	(3.2)
Retired		23.5	1 279	(23.6)
Homemaker		5.2	282	(5.2)
Other		5.1	277	(5.1)
$PM_{2.5}$ concentration (μg/m^3; 2001–05)	11.57 ± 2.63		5 481	
$PM_{2.5}$ concentration (μg/m^3; 2006–10)	10.16 ± 2.23		4 837	
M2 Executive functioning	0.00 ± 1.00		3 877	−0.08
M3 executive functioning	−0.27 ± 0.76		2 831	−0.35
M2 functional limitations	0.82 ± 0.90		4 563	0.81
M3 functional limitations	1.01 ± 0.96		3 271	1.00
M2 cardiometabolic diseases	0.00 ± 1.00		4 583	−0.01
M3 cardiometabolic diseases	0.26 ± 1.06		3 222	0.25
M2 depressive symptoms	0.64 ± 1.76		5 481	
M3 depressive symptoms	0.60 ± 1.71		3 650	0.63

Notes: M2 = wave 2, M3 = wave 3. Mean and standard deviation, percentage of participants within categories, and sample size are presented for observed data in columns 2–4. In column 5, the pooled mean or percentages of participants (noted with parentheses) per category are presented from the imputed datasets.

Table 2 presents the regression results for $PM_{2.5}$ concentration as a predictor of EF. Estimates for $PM_{2.5}$ were statistically significant and indicated that 10 μg/m^3 higher $PM_{2.5}$ concentration corresponded to 0.11 *SD* lower EF at M2 and 0.13 *SD* lower EF at M3 controlling for EF at M2. Age (continuous variable) did not significantly moderate the association between $PM_{2.5}$ and EF in either the cross-sectional or longitudinal model. Age group moderation was also not significant (model not shown in Table 2). As shown in the final column of Table 2, biological sex was not a significant moderator, although both estimates indicate that $PM_{2.5}$ was more closely related to EF at M2 and residualized change from M2 to M3 for male relative to female participants.

Table 3 presents the regression results for $PM_{2.5}$ concentration as a predictor of functional limitations. $PM_{2.5}$ concentration was not associated with functional limitations at M2 nor residualized change in functional limitations from M2 to M3. The association between $PM_{2.5}$ and functional limitations at M2 did not vary by age (shown in Table 3) or age group (not shown), and estimates were in opposite directions for the cross-sectional and longitudinal models. Sex was not a significant moderator in either model.

Based on our findings that $PM_{2.5}$ concentration significantly predicted EF, we used path analysis to separately test the extent to which (a) CMB disease and (b) depressive symptoms acted as mediators. We simultaneously modeled one mediator and EF at both waves (M2 and M3), adjusting each for the

Table 2. Pooled Cross-sectional and Longitudinal Model Results for Ambient $PM_{2.5}$ Concentration as a Predictor of Executive Functioning

Predictor Variables	*B* (robust *SE*)	*B* (robust *SE*)	*B* (robust *SE*)
Cross-sectional (*n* = 5 429)			
$PM_{2.5}$ concentration, 10 μg/m³ in 2001–2005	−0.11‡ (0.05)	−0.11‡ (0.05)	−0.17‡ (0.07)
Age, 10 years	−0.27* (0.02)	−0.27* (0.02)	−0.27* (0.02)
Female (reference = male)	−0.08† (0.03)	−0.08† (0.03)	−0.08† (0.03)
$PM_{2.5}$ concentration * age		0.02 (0.04)	
$PM_{2.5}$ concentration * female			0.12 (0.09)
Longitudinal (*n* = 4 806)			
$PM_{2.5}$ concentration, 10 μg/m³ in 2006–2010	−0.13‡ (0.05)	−0.13‡ (0.05)	−0.15‡ (0.07)
Age, 10 years	−0.14* (0.01)	−0.14* (0.01)	−0.14* (0.01)
Female (reference = male)	0.00 (0.02)	0.00 (0.02)	0.00 (0.02)
$PM_{2.5}$ concentration * age		0.00 (0.04)	
$PM_{2.5}$ concentration * female			0.05 (0.08)

Notes: *B* = unstandardized regression coefficient, *SE* = standard error. Estimates are pooled across 20 models from imputed datasets. All models controlled for M2 covariates: age, biological sex, race/ethnicity, marital status, education, household income, MIDUS sample, nativity status, employment status, tract urbanicity, tract walkability, and tract median income. The longitudinal models included adjustment for M2 executive functioning.
*$p < .001$
†$p < .01$.
‡$p < .05$.

Table 3. Pooled Cross-sectional and Longitudinal Model Results for Ambient $PM_{2.5}$ Concentration as a Predictor of Functional Limitations

Predictor Variables	*B* (robust *SE*)	*B* (robust *SE*)	*B* (robust *SE*)
Cross-sectional (*n* = 5 481)			
$PM_{2.5}$ concentration, 10 μg/m³ in 2001–2005	0.03 (0.05)	0.03 (0.05)	0.03 (0.06)
Age, 10 years	0.17* (0.01)	0.17* (0.01)	0.17* (0.01)
Female (reference = male)	0.19* (0.02)	0.19* (0.02)	0.19* (0.02)
$PM_{2.5}$ concentration * age		0.04 (0.04)	
$PM_{2.5}$ concentration * female			0.00 (0.09)
Longitudinal (*n* = 4 837)			
$PM_{2.5}$ concentration, 10 μg/m³ in 2006–2010	−0.03 (0.06)	−0.03 (0.06)	−0.02 (0.08)
Age, 10 years	0.14* (0.02)	0.14* (0.02)	0.14* (0.02)
Female (reference = male)	0.05 (0.03)	0.05 (0.03)	0.05 (0.03)
$PM_{2.5}$ concentration * age		−0.06 (0.05)	
$PM_{2.5}$ concentration * female			0.00 (0.11)

Notes: *B* = unstandardized regression coefficient, *SE* = standard error, Estimates are pooled across 20 models from imputed datasets. All models controlled for M2 covariates: age, biological sex, race/ethnicity, marital status, education, household income, MIDUS sample, nativity status, employment status, tract urbanicity, tract walkability, and tract median income. The longitudinal models included adjustment for M2 functional limitations.
*$p < .001$.
†$p < .01$.
‡$p < .05$.

full set of controls. The model testing CMB disease as a mediator is presented in Figure 1. Estimates indicate that $PM_{2.5}$ in 2001–2005 is associated with higher CMB disease at M2, but $PM_{2.5}$ in 2006–2010 was not a significant predictor of CMB disease at M3 controlling for M2 levels of EF; however, these cross-sectional and longitudinal estimates are of comparable magnitude (0.13 and 0.11 *SD* units per 10 μg/m³). The indirect effect of $PM_{2.5}$ on EF at M2 through CMB disease was significant ($B = -0.009$, $SE = 0.004$, $p = .048$), and CMB disease accounted for 8.1% of the total effect of $PM_{2.5}$ on EF at M2 ($B = -0.106$, $SE = 0.049$, $p = .030$). The indirect effect of $PM_{2.5}$ on residualized change from M2 to M3 through CMB disease at M3 was nonsignificant ($B = -0.004$, $SE = 0.003$, $p = .22$) and accounted for only 2.9% of the total effect. These results indicate that CMB disease partially mediated the cross-sectional association between $PM_{2.5}$ and EF, albeit to a relatively weak degree.

The model testing depressive symptoms as a mediator is shown in Figure 2. Indirect effects of $PM_{2.5}$ on EF through depression were nonsignificant for the cross-sectional and longitudinal models. $PM_{2.5}$ was not associated with depression at either wave nor was depression associated with EF.

Sensitivity Analyses

Figure S1 provides the results when using the alternative CMB measure, after reimplementing the multiple imputation procedure with this CMB measure. Estimates for the mediation were comparable to those reported in Figure 1. The cross-sectional indirect effect ($PM_{2.5}$ →CMB →EF) was statistically significant, explaining 11.5% of the association

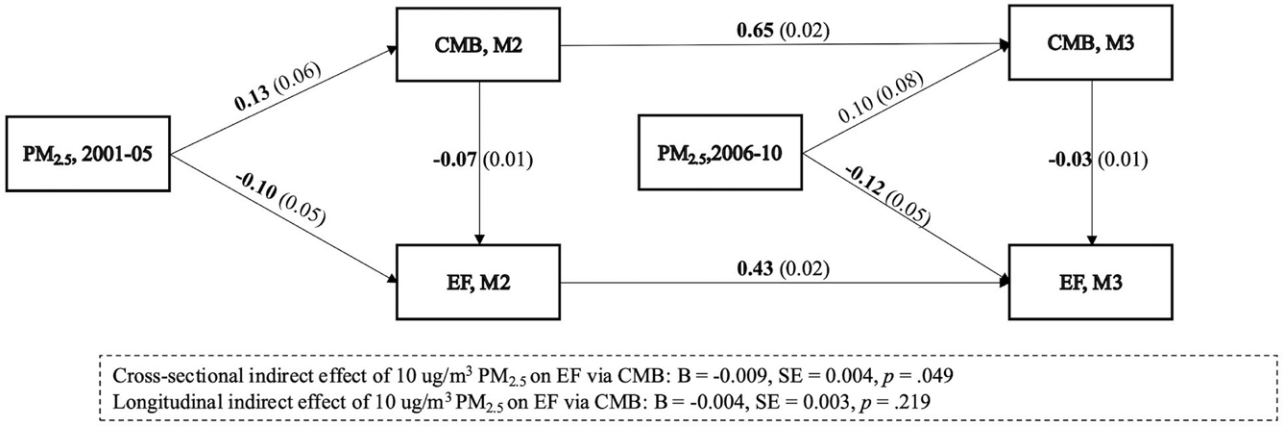

Figure 1. Pooled path model testing cardiometabolic disease (CMB) as mediator of the association between $PM_{2.5}$ concentration and executive functioning (EF). *Notes:* Bold font for the estimates indicates $p < .05$. Estimates are unstandardized regression coefficients and (standard errors) but mediator and outcome variables are standardized, such that estimates involving $PM_{2.5}$ refer to standardized units per 10 μg/m³ increase. Estimates are pooled across 20 models from imputed datasets.

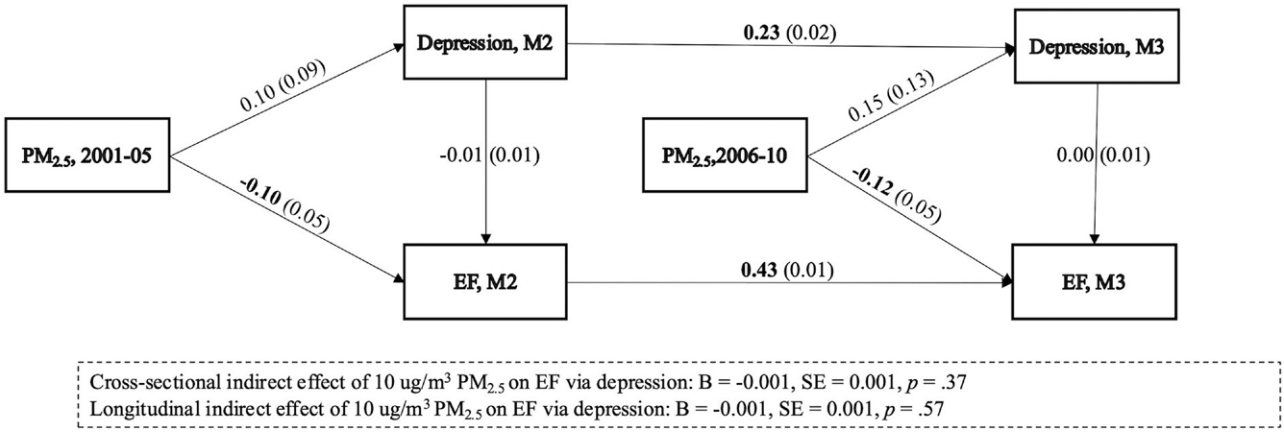

Figure 2. Pooled path model testing depression as a mediator of the association between $PM_{2.5}$ concentration and executive functioning (EF). *Notes*: Bold font for the estimates indicates $p < .05$. Estimates are unstandardized regression coefficients and (standard errors) but mediator and outcome variables are standardized, such that estimates involving $PM_{2.5}$ refer to standardized units per 10 μg/m³ increase. Estimates are pooled across 20 models from imputed datasets.

between $PM_{2.5}$ and EF at M2. The estimate for the longitudinal indirect effect remained nonsignificant.

Figure S2 provides results when removing the autoregressive terms. As compared to results in Figure 1, the association between $PM_{2.5}$ and EF at M3 appeared to increase in magnitude (from –0.12 to –0.17 *SD* units per 10 μg/m³), as was the case for $PM_{2.5}$ and CMB at M3 (from 0.10 to 0.18 *SD* units, now $p < .05$). The standardized association between CMB and EF at M3 also appeared to increase from –0.03 to –0.06.

Discussion

Among a middle-aged and older sample, we found that ambient $PM_{2.5}$ concentration was associated with lower EF initially as well as EF approximately 9 years later controlling for the initial assessment, supporting H1. Point estimates from cross-sectional and longitudinal models were comparable, strengthening the credibility of the findings. The significant association between $PM_{2.5}$ and EF also aligns with other studies (12,13), although findings from two meta-analyses have been inconclusive due to limitations in prior studies (10,11). Another review highlighted that 5 of 9 studies reviewed on air pollution (not exclusively $PM_{2.5}$) and EF found an association, but that associations with air pollution were stronger for dementia than for EF (6). In our sample, we observed that EF decreased by an average of 0.42 *SD* over approximately 9 years, which translates to an annual decline of nearly 0.05 *SD*. This annual decrease aligns with existing literature, which indicates an approximate reduction of 0.04 *SD* per year in age-related changes in cognitive performance (52,53). We estimated a residualized change of 0.13 *SD* greater decline from M2 to M3 that would be expected from 10 μg/m³ higher $PM_{2.5}$ exposure, equal to nearly one-third of the expected age-related decline during this period (equivalent to just under three additional years of aging). Thus, our findings underscore the substantial association between fine particulate matter exposure and changes in executive function. Identifying modifiable risk factors related to age-related declines in EF, like air pollution, is important given the personal, societal, and economic costs of premature cognitive aging (6).

We find that $PM_{2.5}$ was not associated with functional limitations, which does not support H2. When looking at age

moderation, the association varies by age in nonsignificant and contrasting ways when comparing the cross-sectional and longitudinal estimates. While there are few studies on the topic to date, our null finding matches one from the Netherlands that also finds no association between $PM_{2.5}$ and self-reported functional limitations in a longitudinal study (16). However, several other studies report significant associations. Exposure to $PM_{2.5}$ was associated with reduced physical mobility among adults in six low- and middle-income countries (15). In China, higher long-term $PM_{2.5}$ exposure was associated with worse physical functioning (9) and higher incidence of disability among adults at least 80 years old (14). While it is plausible that $PM_{2.5}$ could negatively affect physical functioning (eg, by aggravating chronic diseases, which then causes physical limitations), we did not find evidence for this association in the MIDUS sample.

In terms of mediation, we found that the cross-sectional association between $PM_{2.5}$ and EF was partially mediated by CMB disease, though only to a modest extent with the association reduced by 8.1%. For the longitudinal association, the indirect effect was not significant. Thus, we found only partial support for H3. However, the longitudinal analysis may underestimate the true direct effect of $PM_{2.5}$ on CMB and EF as well as the indirect effect if: $PM_{2.5}$ exposure during 2001–2005 influenced CMB or EF at M2, and these early changes influence subsequent rates of change from M2 to M3 (51). Although both of these conditions are plausible, omitting the earlier levels for each variable could alternatively result in an overestimate of the associations. Indeed, the sensitivity analyses revealed that removing the autoregressive terms resulted in associations of greater magnitude (Figure S2). To address this challenge, we simultaneously modeled the cross-sectional and longitudinal associations to provide information on both temporal relationships.

Several other studies, looking at $PM_{2.5}$ and different aging-related outcomes, have also demonstrated mediation by CMB disease or related risk factors. In Australia, a cross-sectional study found a negative indirect effect of $PM_{2.5}$ on cognitive function via CMB disease risk factors (23). CMB disease was also a mediator of associations between $PM_{2.5}$ and dementia in Sweden (24). Using longitudinal data, Ilango et al. (21) reported that 21% of the effect of $PM_{2.5}$ on dementia in Ontario (Canada) was due to CMB disease (assessed based on health care visits for heart disease, heart failure, or stroke). Herein, we add evidence of CMB disease being a mediator of the link between $PM_{2.5}$ and EF, an important cognitive endpoint that could be targeted with interventions among aging individuals.

Counter to H4, we found that depressive symptoms were not a mediator. This aligns with another related study that predicted episodic memory among women in the United States (22). In that study, depression did not mediate associations between $PM_{2.5}$ and memory. Instead, $PM_{2.5}$ indirectly increased depression symptoms via declines in memory. This suggests the possibility of multidirectional associations and signals that more research is needed on the role of air pollution, depression, and aging processes, especially as evidence mounts linking air pollution to depression (27).

Findings from sex moderation tests for EF were nonsignificant but were in a consistent direction across cross-sectional and longitudinal models showing that men may be more sensitive in terms of the direct association of $PM_{2.5}$ with EF. Larger cognitive risks following air pollution exposure for men relative to women have emerged in some studies. For example, Chinese men's scores on a verbal cognitive performance test were more affected than women's by air pollution (19). Sex differences in responses to air pollution may be due to biological differences, for example, differences in the size of airways, lung volume and smooth muscle, vascular function, and hormones (54), as well as social factors related to gender roles. Given the seemingly larger associations for males, our results suggest the importance of including both sexes (and persons of differing gender identities) in studies of air pollution and aging. In a meta-analysis of air pollution and cognitive functioning, 8 of the 26 publications did not include males (11). There were no substantive findings for age moderation suggesting that the effect of $PM_{2.5}$ on EF is consistent across ages.

Limitations

There are several limitations associated with our use of MIDUS data. MIDUS does not include measures of indoor air quality. Having this measurement would have enabled more accurate estimates of air pollution exposure. While MIDUS well-represents non-Hispanic White and Black people, the sample lacks representation of Hispanic/Latinx or Asian populations in the United States. MIDUS also does not ask people about their gender identity, meaning we had to rely only on biological sex in our analyses. An additional weakness is that functional limitations influenced participation in the study, which could have biased findings. The use of self-reports for CMB disease is another limitation as prevalence may have been underestimated, although prior research has shown substantial-to-moderate agreement between self-reports and medical records (36). While the longitudinal aspect is a strength, this study would be more rigorous with longer follow-up (> 10 years) and more measurements (> 2). Finally, the relationship between the mediators and outcome variables may be bidirectional whereas our models assumed unidirectional effects from the mediator to the outcome. Further research is needed to identify the temporal ordering of physical and mental health conditions and aging-related cognitive limitations.

Implications

This study demonstrates the complex and indirect ways in which air pollution affects the health of middle-aged and older adults. This type of research is increasingly important as the population ages and the climate changes. With better understanding of these complex dynamics, we can anticipate potential challenges that may emerge and work to address them in advance to improve the health and quality of life of adults. In the regulatory arena, enforcing and lowering fine particulate matter standards can protect human health. Enforcing fuel efficiency standards, enacting clean energy policies, reducing fossil fuel use, and targeting a select number of superemitters of $PM_{2.5}$ for emissions reductions are potentially viable pathways toward reducing $PM_{2.5}$ (55).

Healthcare providers can provide their patients with strategies for limiting air pollution exposure including wearing face masks, in-home particle removal and ventilation methods, and making behavioral changes (eg, exercising in the morning, avoiding travel to high pollution regions if one suffers from chronic conditions exacerbated by pollution) (56). Reducing exposure to fine particulate matter is one potential pathway to successful aging. Reducing population-level exposure will require societal- and individual-level interventions.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

None.

Data Availability

MIDUS data can be obtained via https://www.icpsr.umich.edu/web/ICPSR/series/203. The air pollution data can be downloaded at https://www.caces.us/. Walkability data and urban/rural classifications can be downloaded at https://gis.cancer.gov/research/adopt.html. Tract median household income can be accessed at https://data.census.gov/.

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