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Physical Activity-Induced Modification of the Association of Long-Term Air Pollution Exposure with the Risk of Depression in Older Adults

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Purpose: Evidence suggests that long-term air pollution exposures may induce depression; however, the influence of physical activity on this effect is unclear. We investigated modification of the associations between air pollution exposures and depression by the intensity of physical activity.

Materials and Methods: This cross-sectional study included 1454 Korean adults. Depression was defined as a Geriatric Depression Scale score ≥8. Concentrations of particulate matter (PM_{10} and $PM_{2.5}$: diameter ≤10 μm and ≤2.5 μm, respectively) and nitrogen dioxide (NO_2) level at each participant's residential address were estimated. Based on metabolic equivalents, physical activity intensity was categorized as inactive, minimally active, or health-enhancing physical activity (HEPA).

Results: Each 1-part per billion (ppb) NO_2 concentration increase was significantly associated with a 6% [95% confidence interval (CI), 4%–8%] increase in depression risk. In older adults (≥65 years), a 1-ppb NO_2 increase was associated (95% CI) with a 4% (1%–7%), 9% (5%–13%), and 21% (9%–33%) increase in depression risk in the inactive, minimally active, and HEPA groups, respectively. Compared with the inactive group, the minimally active (p=0.039) and HEPA groups (p=0.004) had higher NO_2 exposure-associated depression risk. Associations of PM_{10} and $PM_{2.5}$ with depression did not significantly differ by the intensity of physical activity.

Conclusion: We suggest that older adults who vigorously exercise outdoors may be susceptible to air pollution-related depression.

Key Words: Air pollution, depression, physical activity, particulate matter, nitrogen dioxide, exercise intensity

INTRODUCTION

Major depressive disorder is an emerging major public health threat worldwide and has resulted in more than 60% increase in disability-adjusted life years between 1990 and 2019.[1] Depression is projected to become the second leading cause of

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disease burden and disability worldwide by 2030.[2] Air pollution is a major risk factor for depression. A meta-analysis reported that a 10-unit increase in particulate matter with aerodynamic diameters of ≤2.5 μm ($PM_{2.5}$) was associated with a 10% increased risk of depression,[3] and epidemiological studies have demonstrated that exposure to nitrogen dioxide (NO_2) increases the risk of depression.[4] Recently obtained evidence suggests that physical activity decreases the risk of depression and mitigates depressive symptoms.[5] However, there is limited or contradictory evidence regarding the association of physical activity with the risk of air pollution-related depression. An analysis of approximately 40000 participants from the UK Biobank exhibited that in older adults with low physical activity intensities, $PM_{2.5}$ levels were associated with an increased risk of major depressive disorder; this suggest that regular physical activity may protect against the effect of long-term $PM_{2.5}$ exposure.[6] In contrast, a neuroimaging study reported a positive association between $PM_{2.5}$ levels and the volume of white matter hyperintensities (an indicator of small-vessel disease) in individuals who exercised vigorously.[7] Therefore, intense physical activity may exacerbate the adverse effects of long-term $PM_{2.5}$ exposure on cerebrovascular health.

Given the conflicting research findings, the present study aimed to investigate whether the association of air pollution exposure with depression in older adults differs based on their physical activity intensities in order to facilitate the development of physical activity guidelines for the prevention of depression in older adults who are exposed to high levels of air pollution.

MATERIALS AND METHODS

Study participants

In this cross-sectional study, we analyzed baseline data obtained from the Environmental-Pollution-Induced Neurologic Effects study, a prospective cohort study of the Korean communities from two large and two small cities (Seoul and Incheon, and Wonju and Pyeongchang, respectively). During the baseline survey period from August 2014 to March 2017, adults aged ≥50 years, without diagnosis of neurological disease (dementia, stroke, and Parkinson's disease), were recruited for the study by advertising in the local communities. The participants completed questionnaires as part of a standardized survey protocol including the Mini-Mental State Examination and the Korean version of the Geriatric Depression Scale-Short Form (SGDS-K) and underwent anthropometry and blood pressure measurements; blood and urine samples were collected for other relevant tests. Fasting (≥12 hours) blood samples were analyzed in the central laboratory (Seoul Clinical Laboratory Co., Ltd., Seoul, Republic of Korea). Among the individuals who were enrolled for the baseline survey, only those who completed the SGDS-K (556 men and 898 women) were included in the present study. Informed consent was obtained from all of the participants. This study was approved by the Yonsei University Health System Institutional Review Board (IRB approval no. 4-2022-0418).

Exposure assessment

This study used particulate matter with aerodynamic diameters of ≤10 μm (PM_{10}) and NO_2 data from spatiotemporal modeling that was based on approximately 300 nationwide air-quality-regulatory monitoring sites from 2001 to 2016.[8] This model comprising the mean and variance components was constructed using the universal kriging method, wherein more than 300 geographical factors that correlated with spatial and non-spatial variability in air-pollutant concentrations (such as physical geography and transportation) were considered. The 5-year average concentrations of PM_{10} and NO_2 prior to the baseline survey (i.e., 2010–2014, 2011–2015, and 2012–2016 for the first, second, and third years of the survey, respectively) were estimated for each participant's residential address. In addition, as the national regulatory monitoring data were available from 2015, the concentration of $PM_{2.5}$ in 2015 was estimated at each participant's residential address.

Outcome assessment

Depressive symptoms were evaluated using the SGDS-K.[9] Trained nurses conducted face-to-face interviews with all participants. SGDS-K, one of the most common tests for screening depression in older adults in the inpatient and outpatient settings, consists of 15 items that best correspond to depressive symptoms in older adults,[10] on a scale of 0 to 15.[9] We defined participants with depression by using the cutoff of SGDS-K (no depression or depression if SGDS-K <8 or ≥8, respectively).[9]

Physical activity assessment

Physical activity was assessed through a self-reported questionnaire by standards of the Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire 2005. The questions were "during the last week, how many days did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling," "during the last week, how many days did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis, except walking," and "during the last week, how many days did you walk for at least 10 minutes at a time?" The intensity of physical activity was evaluated using metabolic equivalents (MET) and classified into three categories: the health-enhancing physical activity (HEPA), minimally active, and inactive categories.[11] The HEPA group was defined as follows: 1) vigorous physical activity equivalent to 1500 MET-min/week for at least 3 days or 2) walking or moderate-to-vigorous activity equivalent to 3000 MET-min/week for at least 7 days. The minimally active group was defined as follows: 1) at least 20-minute vigorous activity per day for 3 or more days; 2) at least 30-minute moderately intense activity or walking per day for 5 or more days; or 3) walking or moderate-to-vigorous activity equivalent to at least 600 MET-min/week for 5 or more days. The remaining participants were categorized as the inactive group.

Covariates

We considered age (years), gender (men and women), educational level (years), marital status (living with a spouse or partner), and several cardiovascular risk factors as covariates. The cardiovascular risk factors included history of cardiovascular diseases (hypertension, diabetes, and angina or myocardial infarction), smoking status (current smoker, former smoker, and never smoker), alcohol consumption (current drinking), body mass index, fasting blood glucose, and total cholesterol levels.

Statistical analysis

Categorical and continuous variables are presented as frequency (percentage) and mean±SD, respectively. A logistic regression model was used to estimate the risk of depression associated with exposure to PM_{10}, $PM_{2.5}$, and NO_2. Model 1 was adjusted for age, gender, and educational level. Model 2 was adjusted for age, gender, educational level, marital status, hypertension, diabetes, angina, myocardial infarction, smoking status, alcohol consumption, body mass index, fasting blood glucose, and total cholesterol levels. To investigate whether physical activity modified the association between air pollution exposure and the risk of depression, we conducted logistic regression analyses (adjusted for Model 2 variables) after stratification by the intensity of physical activity. Significance of intergroup differences in the association was tested using the method described by Altman and Bland,[12] and *p*-values for interactions were calculated. Additionally, the same analyses were performed after further stratification by gender and age groups (<65 years and ≥65 years). The risk of depression associated with air pollution was expressed as odds ratios (OR) and corresponding 95% confidence intervals (CI). All statistical analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA).

RESULTS

Participant characteristics

Of the 1454 participants, 236 (16.3%) had depression (Table 1). The mean±SD concentrations of PM_{10}, $PM_{2.5}$, and NO_2 were 49.9±5.2 μg/m^3, 25.9±0.7 μg/m^3, and 27.7±10.7 ppb, respectively. The numbers of the inactive, minimally active, and HEPA groups were 98 (41.5%), 111 (47.0%), and 27 (11.4%), respectively.

Associations of air pollution and physical activity with depression

PM_{10} and $PM_{2.5}$ did not exhibit significant associations with the risk of depression (Table 2). A 1-ppb increase in NO_2 was significantly associated with the risk of depression in both Model 1 (OR, 1.05; 95% CI, 1.03–1.07) and Model 2 (OR, 1.06; 95% CI, 1.04–1.08). None of the associations of levels of physical activity with depression were statistically significant.

Modification of effects of air pollution on the risk of depression by physical activity

After stratification of the participants according to the intensity of physical activity, a 1-ppb increase in NO_2 was significantly associated with the risk of depression in all the physical activity groups (Table 3). The risk of depression associated with NO_2 was significantly higher in the minimally active group (OR, 1.09; 95% CI, 1.05–1.13) than in the inactive group (OR, 1.03; 95% CI, 1.00–1.05) (*p* for interaction=0.006). The difference in the risk of depression associated with NO_2 between the inactive and HEPA groups showed borderline significance (*p* for interaction=0.055). The risks of depression associated with PM_{10} and $PM_{2.5}$ did not significantly differ among the physical activity groups.

Effect modification by physical activity in men and women

In men, a 1-ppb increase in NO_2 was significantly associated with an increased risk of depression in the minimally active (OR, 1.10; 95% CI, 1.05–1.15) and HEPA groups (OR, 1.09; 95% CI, 1.01–1.18), with this risk being significantly higher in the minimally active group than in the inactive group (*p*=0.047) (Table 4). In women, a 1-ppb increase in NO_2 was significantly associated with an increased risk of depression in the inactive (OR, 1.03; 95% CI, 1.00–1.06) and minimally active groups (OR, 1.08; 95% CI, 1.03–1.13). This difference between the two groups was not statistically significant (*p* for interaction=0.106). In both men and women, the associations of PM_{10} and $PM_{2.5}$ with the risk of depression did not significantly differ by the intensity of physical activity.

Effect modification by physical activity in the older and younger participants

Among the older participants (≥65 years of age), PM_{10} and $PM_{2.5}$ did not exhibit significant associations with the risk of depression in any of the physical activity groups (Table 5). An increase in NO_2 was significantly associated with an increased risk of depression in all the physical activity groups. The risk of depression associated with NO_2 was significantly higher in the minimally active group (OR, 1.09; 95% CI, 1.05–1.13) than in the inactive group (OR, 1.04; 95% CI, 1.01–1.07) (*p* for interaction=0.039). A similar finding was observed between the HEPA (OR, 1.21; 95% CI, 1.09–1.33) and inactive groups (*p* for interaction=0.004). In the younger participants (<65 years of age), the risk of depression associated with NO_2 was higher in the minimally active group (OR, 1.10; 95% CI, 1.00–1.21) than in the inactive group (OR, 1.02; 95% CI, 0.97–1.06), though the difference was not statistically significant (*p* for interaction=0.144).

Table 1. Characteristics of the Study Population

	Total (n=1454)	Depression		*p* value
		Yes (n=236)	No (n=1218)	
Gender				0.401
Men	556 (38.2)	84 (35.6)	472 (38.8)	
Women	898 (61.8)	152 (64.4)	746 (61.3)	
Age (yr)	67.5±6.5	71.2±6.5	66.8±6.3	<0.001
Education level (yr)	9.6±4.3	8.7±4.3	9.8±4.2	<0.001
Marital status (living with a spouse or partner)	1194 (82.1)	171 (72.5)	1023 (84.0)	<0.001
Smoking status				0.352
Current smokers	77 (5.3)	17 (7.2)	60 (4.9)	
Former smokers	341 (23.6)	53 (22.5)	288 (23.7)	
Never smokers	1036 (71.3)	166 (70.3)	870 (71.4)	
Alcohol drinking	583 (40.1)	86 (36.4)	497 (40.8)	0.238
History of disease				
Angina or myocardial infraction	120 (8.3)	21 (8.9)	99 (8.1)	0.792
Hypertension	452 (31.1)	57 (24.2)	395 (32.4)	0.015
Diabetes	228 (15.7)	32 (13.6)	196 (16.1)	0.378
BMI (kg/m^2)	24.5±3.02	24.3±3.1	24.6±3.0	0.239
Fasting blood glucose (mg/dL)	98.0±21.3	99.4±21.7	97.8±21.2	0.265
Total cholesterol (mg/dL)	185.5±36.7	179.6±34.9	186.7±36.9	0.007
PM_{10} (μg/m^3)	49.9±5.2	50.3±4.2	49.8±5.4	0.183
$PM_{2.5}$ (μg/m^3)	25.9±0.7	25.9±0.8	25.9±0.6	0.325
NO_2 (ppb)	27.7±10.7	31.6±8.9	26.9±10.9	<0.001
Physical activity (MET-min/week)				0.917
Inactive	601 (41.3)	98 (41.5)	503 (41.3)	
Minimally active	675 (46.4)	111 (47.0)	564 (46.3)	
HEPA	178 (12.2)	27 (11.4)	151 (12.4)	

BMI, body mass index; PM, particulate matter; PM_{10}, PM ≤10 μm in aerodynamic diameter; $PM_{2.5}$, PM ≤2.5 μm in aerodynamic diameter; NO_2, nitrogen dioxide; HEPA, health-enhancing physical activity.
Data are presented as mean±standard deviation or n (%). *p*-value was the significance of difference in characteristics between individuals with and without depression, calculated from chi-squared test (for categorical variables) and t-test (for continuous variables). Presence of depression was defined based on the Korean version of the Short Geriatric Depression Scale (SGDS-K) (i.e., Yes if 8≤SGDS-K≤15; No if 0≤SGDS-K<8). Physical activity was divided into three categories. The 'minimally active' was 1) 3 or more days of vigorous activity of at least 20 minutes per day; 2) 5 or more days of moderate-intensity activity or walking of at least 30 minutes per day; or 3) 5 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 600 MET-min/week. The HEPA category was 1) vigorous-intensity activity on at least 3 days achieving a minimum of at least 1500 MET-minutes/week or 2) 7 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 3000 MET-minutes/week. Individuals who did not meet the above criteria were treated as the 'inactive' category.

DISCUSSION

In this study, we used cross-sectional data to investigate whether the air pollution-exposure-related risk of depression differed according to the intensity of physical activity. We found that the risk of depression associated with long-term exposure to NO_2 was higher in participants who vigorously exercised than in those who were inactive. This modification was particularly evident in men and older adults (≥65 years of age). In contrast, the associations of PM_{10} and $PM_{2.5}$ exposures with depression did not significantly differ by the intensity of physical activity.

There is scarce evidence of the effect of physical activity on the air pollution-exposure-associated risk of depression. Wu, et al.[6] analyzed samples from the UK Biobank and found that an increase in $PM_{2.5}$ was associated with an increased risk of major depressive disorder in older adults with low physical activity, suggesting that physical activity has a protective influence against the effects of $PM_{2.5}$ exposure on depression. However, our study found that the air pollution-exposure-associated risk of depression was higher in the vigorous physical activity group than in the inactive group. The contradictory findings of the present and the earlier study may be attributed to differences in populations, methodologies, and geographical regions. Wu, et al.[6] examined lifetime experiences of depression (combining items on help-seeking for mental health and items from the Patient Health Questionnaire), whereas we assessed the point prevalence of depression by using a validated test that was specifically developed for older adults.[9] Moreover, regional differences in air pollution concentrations may also have contributed to this discrepancy. Although the study by Wu, et al.[6] did

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not measure NO_2, the concentrations of PM_{10} and $PM_{2.5}$ were much lower in the UK Biobank sample than in our study (16 μg/m^3 vs. 50 μg/m^3 for PM_{10} and 10 μg/m^3 vs. 26 μg/m^3 for $PM_{2.5}$). The average $PM_{2.5}$ concentration in our study (similar to that from the national average concentration of 25 μg/m^3) was higher than the level recommended by the Korean Ministry of Environment, the World Health Organization, and United State Environmental Protection Agency (15 μg/m^3). Hence, it is reasonable to assume that the risk of depression associated with air pollution exposure among individuals who vigorously exercised is already high in geographical areas with high levels of air pollution.

It is well-known that NO_2 exposure increases the risk of depression via systemic inflammation and oxidative stress mechanisms.[13] Exposure to air pollution may increase the concentration of inflammatory molecules, such as tumor necrosis factor-α or interleukin-6, and this can cause depression-related structural and functional changes in the brain.[14-16] An animal study demonstrated that NO_2 exposure damaged myelin and contributed to anxiety and depressive behaviors in mice.[17] In contrast, exercise may decrease the risk of depression via neurofibrillary tangle mechanisms[18] and upregulation of neurogenesis.[19] However, the present study did not show significantly reduced risks of depression associated with the minimally active and vigorous physical activity groups, when compared with the inactive group. This might be due to the fact that the inactive group included individuals who exercised below the minimally active level. Furthermore, we found that the NO_2-exposure-associated risk of depression was rather higher in the minimally active and vigorous physical activity groups compared to the inactive group. Although the mechanism is not clearly understood, we speculate that an increased respiratory rate following vigorous physical activity may, even at the same air pollutant concentrations, increase inhalational exposure to air pollutants. This speculation is in line with a neuroimaging study that reported that the adverse effect of $PM_{2.5}$ on cerebral small-vessel disease was higher in individuals with vigorous physical activity than that in those who were inactive.[7] Taken together, air pollution exposure may deteriorate cerebrovascular health in people who vigorously exercise, leading to an increased risk of depression.

This study had some limitations. First, in this cross-sectional study, there is a possibility of reverse associations between air pollution exposures and the risk of depression. However, this study examined the effects of long-term air pollution exposure over 5 years, and 84.0% of participants lived at the same address during this 5-year period. Second, the number of individuals with depression that was defined using the SGDS-K screening tool may have been overestimated, though the test has high performance (sensitivity: 0.94; specificity: 0.73, using an 8-point criterion)[9] and has been widely used in previous studies.[20] Third, although the adverse effects of $PM_{2.5}$ are well-known, we could not find any significant association between exposure to $PM_{2.5}$ and the risk of depression. In this study, $PM_{2.5}$ concentrations were estimated based on air quality monitoring data of 2015 only; hence, the range of the data was narrow, with a standard deviation of 0.7 μg/m^3. Therefore, the variability in the $PM_{2.5}$

Table 2. Associations of Air Pollution and Physical Activity with Depression

	Model 1	Model 2
	OR (95% CI)	OR (95% CI)
Air pollutants (per 1 unit increase)		
PM_{10} (μg/m^3)	1.01 (0.98–1.04)	1.02 (0.99–1.05)
$PM_{2.5}$ (μg/m^3)	0.88 (0.70–1.10)	0.91 (0.73–1.14)
NO_2 (ppb)	1.05 (1.03–1.07)	1.06 (1.04–1.08)
Physical activity		
Inactive	Reference	Reference
Minimally active	1.02 (0.75–1.39)	1.01 (0.74–1.38)
HEPA	1.15 (0.71–1.87)	1.11 (0.67–1.83)

OR, odds ratio; CI, confidence interval; PM, particulate matter; PM_{10}, PM ≤10 μm in aerodynamic diameter; $PM_{2.5}$, PM ≤2.5 μm in aerodynamic diameter; NO_2, nitrogen dioxide, HEPA: health-enhancing physical activity.
Model 1 was adjusted for age, gender, and education level; Model 2 was adjusted for age, gender, hypertension, body mass index, alcohol, smoking, education level, diabetes, fasting blood glucose, marital status, total cholesterol, and angina or myocardial infraction; Presence of depression was defined based on the Korean version of the Short Geriatric Depression Scale (SGDS-K) (i.e., Yes if 8≤SGDS-K≤15; No if 0≤SGDS-K<8). Physical activity was divided into three categories. The 'minimally active' was 1) 3 or more days of vigorous activity of at least 20 minutes per day; 2) 5 or more days of moderate-intensity activity or walking of at least 30 minutes per day; or 3) 5 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 600 MET-min/week. The HEPA category was 1) vigorous-intensity activity on at least 3 days achieving a minimum of at least 1500 MET-minutes/week or 2) 7 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 3000 MET-minutes/week. Individuals who did not meet the above criteria were treated as the 'inactive' category.

Table 3. Modification of Effects of Air Pollutants on Depression by Physical Activity

Physical activity	PM_{10} (per 1 μg/m^3 increase)		$PM_{2.5}$ (per 1 μg/m^3 increase)		NO_2 (per 1 ppb increase)	
	OR (95% CI)	*p* for interaction	OR (95% CI)	*p* for interaction	OR (95% CI)	*p* for interaction
Inactive	1.00 (0.95–1.04)	Reference	0.88 (0.61–1.25)	Reference	1.03 (1.00–1.05)	Reference
Minimally active	1.03 (0.98–1.08)	0.398	0.89 (0.61–1.20)	0.926	1.09 (1.05–1.13)	0.006
HEPA	1.09 (0.99–1.19)	0.118	1.59 (0.77–3.29)	0.149	1.09 (1.03–1.15)	0.055

PM, particulate matter; PM_{10}, PM ≤10 μm in aerodynamic diameter; $PM_{2.5}$, PM ≤2.5 μm in aerodynamic diameter; NO_2, nitrogen dioxide; OR, odds ratio; CI, confidence interval; HEPA, health-enhancing physical activity.
p for interaction was the significance of difference in the association between air pollution and depression.

Table 4. Modification of Effects of Air Pollutants on Depression by Physical Activity in Men and Women

	PM_{10} (per 1 μg/m^3 increase)		$PM_{2.5}$ (per 1 μg/m^3 increase)		NO_2 (per 1 ppb increase)	
	OR (95% CI)	*p* for interaction	OR (95% CI)	*p* for interaction	OR (95% CI)	*p* for interaction
Men (n=556)						
Physical activity						
Inactive	0.96 (0.87–1.07)	Reference	0.83 (0.39–1.77)	Reference	1.03 (0.98–1.07)	Reference
Minimally active	1.01 (0.93–1.10)	0.461	0.97 (0.55–1.72)	0.737	1.10 (1.05–1.15)	0.047
HEPA	1.08 (0.94–1.24)	0.209	1.07 (0.37–3.06)	0.702	1.09 (1.01–1.18)	0.161
Women (n=898)						
Physical activity						
Inactive	1.00 (0.96–1.06)	Reference	0.85 (0.55–1.30)	Reference	1.03 (1.00–1.06)	Reference
Minimally active	1.03 (0.97–1.09)	0.539	0.76 (0.49–1.17)	0.727	1.08 (1.03–1.13)	0.106
HEPA	1.09 (0.92–1.29)	0.364	3.63 (0.78–16.98)	0.074	1.06 (0.97–1.16)	0.564

PM, particulate matter; PM_{10}, PM ≤10 μm in aerodynamic diameter; $PM_{2.5}$, PM ≤2.5 μm in aerodynamic diameter; NO_2, nitrogen dioxide; OR, odds ratio; CI, confidence interval; HEPA, health-enhancing physical activity.
p for interaction was the significance of difference in the association between air pollution and depression. Presence of depression was defined based on the Korean version of the Short Geriatric Depression Scale (SGDS-K) (i.e., Yes if 8≤SGDS-K≤15; No if 0≤SGDS-K<8).

Table 5. Modification of Effects of Air Pollutants on Depression by Physical Activity in the Elderly and Middle-Aged Participants

	PM_{10} (per 1 μg/m^3 increase)		$PM_{2.5}$ (per 1 μg/m^3 increase)		NO_2 (per 1 ppb increase)	
	OR (95% CI)	*p* for interaction	OR (95% CI)	*p* for interaction	OR (95% CI)	*p* for interaction
Age <65 years (n=500)						
Physical activity						
Inactive	0.97 (0.89–1.06)	Reference	0.47 (0.17–1.27)	Reference	1.02 (0.97–1.06)	Reference
Minimally active	1.10 (0.96–1.27)	0.115	1.93 (0.77–4.85)	0.041	1.10 (1.00–1.21)	0.144
HEPA	0.80 (0.51–1.23)	0.387	2.18 (0.17–27.97)	0.272	N/E	N/E
Age ≥65 years (n=954)						
Physical activity						
Inactive	1.00 (0.95–1.06)	Reference	0.96 (0.66–1.42)	Reference	1.04 (1.01–1.07)	Reference
Minimally active	1.00 (0.96–1.06)	0.982	0.72 (0.50–1.03)	0.274	1.09 (1.05–1.13)	0.039
HEPA	1.10 (1.00–1.22)	0.101	1.20 (0.57–2.51)	0.607	1.21 (1.09–1.33)	0.004

PM, particulate matter; PM_{10}, PM ≤10 μm in aerodynamic diameter; $PM_{2.5}$, PM ≤2.5 μm in aerodynamic diameter; NO_2, nitrogen dioxide; OR, odds ratio; CI, confidence interval; HEPA, health-enhancing physical activity; N/E, non-estimable.
p for interaction was the significance of difference in the association between air pollution and depression. Presence of depression was defined based on the Korean version of the Short Geriatric Depression Scale (SGDS-K) (i.e., Yes if 8≤SGDS-K≤15; No if 0≤SGDS-K<8).

data may not have been sufficient to detect a significant association with the risk of depression. Future research using long-term monitoring data are required to increase the predictability. Fourth, information on depression medication history was not available. Theoretically, depression medication history may not fulfill the definition of confounding (i.e., a bidirectional relationship with air pollution exposures). Hence, the approach that did not control for depression medication history may not have distorted our results. Last, we did not consider the day-to-day variations in the intensity of physical activity. We acknowledge that there is a possibility of behavioral modification (e.g., avoiding outdoor activities) on days with poor air quality. However, this study investigated the long-term effects of air pollution exposures on depression while focusing on the usual intensity of physical activity. Although there was some discrepancy between the period of exercise evaluation (during the past week) and that of air pollution exposure (for 5 years prior to the survey), we assumed that the intensity of physical activity during the past week may reflect the usual intensity of physical activity. Future studies are required to collect individual-level time-activity data for investigating the effect of physical activity on the association between air pollution and depression.

In conclusion, NO_2 exposure had more pronounced effect on the risk of depression in individuals who vigorously exercised than in those who were inactive, especially in men and older adults (≥65 years of age). The results of this study suggest that older adults who vigorously exercise outdoors might be susceptible to depression due to exposure to air pollution. Our findings may contribute to establishment of specific guidelines for individual avoidance behaviors and physical activity to improve mental health in older adults.

AVAILABILITY OF DATA AND MATERIAL

The datasets generated and/or analyzed during the current study are not publicly available to ensure privacy protection

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of the participants, but are available from the corresponding author upon reasonable request.

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Conceptualization: Changsoo Kim and Jaelim Cho. Data curation: Heeseon Jang. Formal analysis: Woongbi Park. Funding acquisition: Changsoo Kim and Jaelim Cho. Investigation: Jungwoo Sohn, Young Noh, and Sang-Baek Koh. Methodology: Jaelim Cho. Project administration: Heeseon Jang and Jungwoo Sohn. Resources: Sun-Young Kim. Software: Sun-Young Kim. Supervision: Jaelim Cho. Validation: Changsoo Kim and Jaelim Cho. Visualization: Woongbi Park. Writing—original draft: Woongbi Park. Writing—review & editing: Juyeon Ko, Changsoo Kim, and Jaelim Cho. Approval of final manuscript: all authors.

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