



Nitrogen Dioxide Exposure May Be Associated with Poststroke Emotional Symptoms

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Dear Editor,

We tested the hypothesis that exposure to certain air pollutants and weather conditions is associated with poststroke depression (PSD) and poststroke emotional incontinence (PSEI) using data from the Efficacy of Early Administration of Escitalopram on Depressive and Emotional Symptoms and Neurologic Dysfunction After Stroke (EMOTION), a multicenter, double-blind, placebo-controlled, randomized study.¹ Details of the EMOTION study are available elsewhere.¹

This study obtained data on the levels of particulate matter with a diameter of <10 µm (PM₁₀), sulfur dioxide, nitrogen dioxide (NO₂), ozone, and carbon monoxide (CO) from the Korea Ministry of Environment. Data from each city where patients were hospitalized were recorded. The average values of air pollutants during the 7 days before assessing PSD and PSEI were used. The study was approved by the ethics committee at each participating center.

PSD and PSEI were assessed the Montgomery-Åsberg Depression Rating Scale (MADRS), and modified Kim's criteria, respectively.¹ The cutoff score of 8 was used for the presence of PSD.² Exhibiting excessive or inappropriate laughing, crying, or both relative to the premorbid state was considered to indicate the presence of PSEI. Pearson's chi-square test, Student's *t* test, and the Mann-Whitney U test were used to evaluate differences between groups. Multivariate logistic regression analysis was applied to age, sex, and factors that were significant in the univariate analyses. A two-sided probability value of *p*<0.05 was considered significant.

The study enrolled 478 patients (aged from 30 years to 92 years) between 2011 and 2014. PSD and PSEI were present in 275 (57.5%) and 32 (6.7%) patients, respectively. PSD was related to female sex, older age, higher National Institutes of Health Stroke Scale (NIHSS) score, not smoking, and cognitive dysfunction, while PSEI was associated with a higher NIHSS score. PSD was associated with a lower level of NO₂ and higher humidity, whereas PSEI was associated with higher levels of NO₂ and CO and lower humidity (Supplementary Table 1 in the online-only Data Supplement). The multivariate analysis showed that high NO₂ was independently associated with PSEI (*p*=0.003), whereas only a high NIHSS score was associated with PSD (*p*=0.001) (Table 1).

Ambient exposure to NO₂ is known to increase airway inflammation and cardiac arrhythmia.³ Since physical illness can be related to the mood or emotional status, we assumed that NO₂ exposure might be associated with emotional disturbances. However, after adjusting for covariates, only NO₂ was related to PSEI in the acute stage, and it was not related to PSD. Although the reason for this difference remains unclear, it may be due to the different impacts of brain serotonin metabolism in the two conditions. NO₂ is a potent oxidant that can efficiently permeate the thoracic airways, resulting in oxidative stress and decreased respiratory function. The resultant hypoxemia might increase the level of brain tyrosine hydroxylase and decrease the serotonin level.⁴

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Received September 15, 2020

Revised November 30, 2020

Accepted December 1, 2020

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Table 1. Factors associated with PSD and PSEI in multivariate logistic regression analysis

Factor	B	SE	p	Exp(B)
PSD				
Age, years	0.002	0.009	0.814	1.002
Sex (female)	0.330	0.272	0.224	1.391
Baseline NIHSS score	0.133	0.037	0.001	1.142
Smoking	0.163	0.259	0.529	1.177
Montreal Cognitive Assessment score	-0.027	0.017	0.114	0.973
NO ₂ , ppb	-0.018	0.011	0.099	0.982
Humidity, %	0.011	0.009	0.194	1.011
Constant	-0.838	1.123	0.455	0.432
PSEI				
Age, years	0.004	0.016	0.813	1.004
Sex (female)	-0.415	0.412	0.314	0.660
Baseline NIHSS score	0.083	0.061	0.172	1.087
NO ₂ , ppb	0.083	0.018	0.003	1.087
CO, 0.1 ppm	-0.081	0.136	0.551	0.922
Humidity, %	-0.004	0.018	0.827	0.996
Constant	-4.572	1.725	0.008	0.010

CO: carbon monoxide, NIHSS: National Institutes of Health Stroke Scale, NO₂: nitrogen dioxide, PSD: poststroke depression, PSEI: poststroke emotional incontinence, SE: standard error.

While both PSD and PSEI are related to alterations in the neurotransmitter system, PSEI appears to be more closely associated with changes in brain serotonin, whereas PSD is more closely associated with psychologic reactions secondary to neurologic dysfunction, especially in the acute stage of stroke.^{5,6} These differences might explain why exposure to NO₂ was more closely associated with PSEI than PSD. Most admitted patients stay indoors and indoor NO₂ levels are strongly correlated with outdoor levels, which may explain why only NO₂ was associated with PSEI.⁷

Our study had some limitations. First, the number of patients was relatively small, and none of them had a severe medical condition or strong suicidal thoughts. Second, we were not able to investigate biomarkers that might explain the relationship between NO₂ and PSEI. Third, data on fine PM_{2.5} were not available because their levels were not measured before 2015 in Korea. Further studies are required to confirm the present findings.

Supplementary Materials

The online-only Data Supplement is available with this article at <https://doi.org/10.3988/jcn.2021.17.2.317>.

Author Contributions

Conceptualization: Hyuk Sung Kwon, Dongwhane Lee, Jong S. Kim. Data curation: Hyuk Sung Kwon, Eun-Jae Lee, Dongwhane Lee, Ji Sung Lee. Formal analysis: Hyuk Sung Kwon, Ji Sung Lee. Supervision: Eun-Jae Lee, Jong S. Kim. Writing—original draft: Hyuk Sung Kwon. Writing—review & editing: Jong S. Kim.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Acknowledgements

None

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