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Short-Term Exposure to Wildfire Smoke and $PM_{2.5}$ and Cognitive Performance in a Brain-Training Game: A Longitudinal Study of U.S. Adults

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Background: There is increasing evidence that long-term exposure to fine particulate matter [PM ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$)] may adversely impact cognitive performance. Wildfire smoke is one of the biggest sources of $PM_{2.5}$ and concentrations are likely to increase under climate change. However, little is known about how short-term exposure impacts cognitive function.

Objectives: We aimed to evaluate the associations between daily and subdaily (hourly) $PM_{2.5}$ and wildfire smoke exposure and cognitive performance in adults.

Methods: Scores from 20 plays of an attention-oriented brain-training game were obtained for 10,228 adults in the United States (U.S.). We estimated daily and hourly $PM_{2.5}$ exposure through a data fusion of observations from multiple monitoring networks. Daily smoke exposure in the western U.S. was obtained from satellite-derived estimates of smoke plume density. We used a longitudinal repeated measures design with linear mixed effects models to test for associations between short-term exposure and attention score. Results were also stratified by age, gender, user behavior, and region.

Results: Daily and subdaily $PM_{2.5}$ were negatively associated with attention score. A $10\,\mu g/m^3$ increase in $PM_{2.5}$ in the 3 h prior to gameplay was associated with a 21.0 [95% confidence interval (CI): 3.3, 38.7]-point decrease in score. $PM_{2.5}$ exposure over 20 plays accounted for an estimated average 3.7% (95% CI: 0.7%, 6.7%) reduction in final score. Associations were more pronounced in the wildfire-impacted western U.S. Medium and heavy smoke density were also negatively associated with score. Heavy smoke density the day prior to gameplay was associated with a 117.0 (95% CI: 1.7, 232.3)-point decrease in score relative to no smoke. Although differences between subgroups were not statistically significant, associations were most pronounced for younger (18–29 y), older (≥70 y), habitual, and male users.

Discussion: Our results indicate that $PM_{2.5}$ and wildfire smoke were associated with reduced attention in adults within hours and days of exposure, but further research is needed to elucidate these relationships. https://doi.org/10.1289/EHP10498

Introduction

Wildfire smoke is a complex mixture of particulate matter (PM) and gases containing many chemical species.[1] Both wildfire smoke and many of its components have been previously associated with significant risks to human health (as reviewed by Reid et al.[2]). Of wildfire emissions, the primary pollutant of public health concern is fine PM [PM ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$)] (as reviewed by U.S. EPA[3]). In addition to the extensive body of epidemiologic evidence that daily and subdaily (hourly level)[4] exposure to $PM_{2.5}$ and smoke increases the risk of all-cause mortality and cardiovascular and respiratory morbidity (as reviewed by Atkinson et al.[5] and Jaffe et al.[1]), newer epidemiologic research has found that $PM_{2.5}$ exposure may also adversely impact cognitive function (as reviewed by Clifford et al.,[6] Delgado-Saborit et al.,[7] and Xu et al.[8]). The aim of this study was to further investigate the associations between exposure to $PM_{2.5}$ and wildfire smoke and cognitive performance. This is a pressing research question because exposure to $PM_{2.5}$ is ubiquitous, often elevated during wildfire events,[1] and likely to increase with the frequency and intensity of wildfires under climate change.[9–12]

Current epidemiologic research has identified $PM_{2.5}$ as a risk factor that can impair cognitive function, accelerate cognitive decline, and increase rates of dementia and Alzheimer's, especially in younger and older populations (as reviewed by Clifford et al.,[6] Delgado-Saborit et al.,[7] and Power et al.[13]). In addition to the epidemiologic literature, there is a growing body of research from animal and human studies that identifies the biological pathways and mechanisms by which air pollution likely impacts neurological health and cognitive function. It shows that $PM_{2.5}$ can cause systematic inflammation, reach the brain via the olfactory nerve, pass through the blood–brain barrier, or modulate the nervous system, leading to brain inflammation and oxidative stress (as reviewed by Delgado-Saborit et al.,[7] Schikowski and Altuğ,[14] and U.S. EPA[3]). Although epidemiologic evidence of the relationships between long-term exposure to $PM_{2.5}$ and cognitive function is mounting, evidence for short-term exposure is still scarce. The small number of studies that focused on short-term associations have found $PM_{2.5}$ exposure at the monthly, weekly, and daily level to be associated with increased risk of hospital admissions for neurological disorders[15–18] and poorer performance on cognitive tests measuring attention, memory, and fluid reasoning, as well as language, math, and reading skills.[19–25] However, there is limited epidemiologic evidence of the associations with subdaily exposure[26] and the associations in the working-age population,[23] and, to our knowledge, no evidence of the subdaily associations across multiple age groups or at lower level concentrations, which is largely due to limited availability of data on health outcomes and cognitive performance at the hourly timescale.

Although $PM_{2.5}$ is a main component of wildfire smoke, the particles have a different composition from typical ambient $PM_{2.5}$, and smoke also contains toxic chemicals and gases, which

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may lead to differential health effects compared with typical ambient $PM_{2.5}$.[27,28] Previous research has found agricultural fires and open fire usage indoors to be associated with reduced performance on neurocognitive tests.[29–31] Although these studies indicate a potentially important association with biomass smoke, to our knowledge, no study to date has investigated the relationship between wildfire smoke exposure and cognitive function. Because concentrations of $PM_{2.5}$ and smoke can change rapidly over days and hours during wildfire events and given that wildfires pose a growing threat to air quality and public health,[1] research is needed to assess how daily and subdaily exposure to $PM_{2.5}$ and smoke impact cognitive performance and the populations most at risk.

To address these knowledge gaps, we evaluated the associations between short-term $PM_{2.5}$ and wildfire smoke exposure and cognitive function in a large adult cohort across the contiguous U.S. We measured cognitive performance using data from the Lumosity brain-training platform, which consists of games aimed to measure and improve areas of cognitive function, including memory, attention, flexibility, processing speed, and problem solving. We used a longitudinal repeated measures study design to characterize associations between scores in an attention-oriented Lumosity game, and daily and subdaily $PM_{2.5}$ and wildfire smoke exposures. We evaluated these associations by age, gender, user behavior, and region to identify vulnerable populations. Although many research efforts have identified serious cardiopulmonary effects of short-term $PM_{2.5}$ and wildfire smoke exposure, neurological impacts can be more challenging to study because the time between exposure and outcome is often undefined. To our knowledge, this is one of the first epidemiologic studies to use Lumosity data to investigate the associations between short-term air pollution exposure and cognitive performance. It is also the first to investigate these relationships at both the daily and hourly timescale in a large, longitudinal cohort of adults ≥ 18 years of age.

Methods

Study Population and Cognitive Outcome

To evaluate the associations between short-term exposure to $PM_{2.5}$ and wildfire smoke and cognitive performance, we conducted a retrospective analysis of scores in an attention-oriented game on the Lumosity brain-training platform. Specifically, we used user performance data from the game *Lost in Migration*, which is based on the Flanker Task and designed to target selective attention, the ability to focus on relevant information while ignoring distractions, and response inhibition, the ability to suppress response to distractions.[32]

In *Lost in Migration,* the user is shown a flock of five flying birds oriented left, right, up, or down. The goal of the game is for the user to use the arrow keys on a keyboard to correctly identify the orientation of the central bird, which is flanked by four birds oriented in the same or a different direction (Figure S1), as many times as possible. Each time the user selects the orientation of the central bird, correct or incorrect, the formation and orientation of the birds displayed updates. Each game of *Lost in Migration* lasts 45 s and the number of formations displayed depends on the user's response speed. Upon completion of the game, users are given an overall score based on their speed, accuracy, and bonus points.[33] Each correct answer is worth 50 points multiplied by the bonus at the time the answer was provided. The multiplier bonus is determined by the number of correct answers given in a row and changes over the course of the game. Although incorrect answers do not cause a user to lose points, they can decrease the multiplier bonus. At the end of the game, a user is given bonus points based on their current multiplier bonus. The cognitive focus and use of *Lost in Migration* as an attentional task has been characterized,[34] and the use of Lumosity games, including *Lost in Migration*, has been shown to improve attention in adults as measured by established neuropsychological tests.[35–38] In addition, *Lost in Migration* scores have been used in previous studies as a measure of attention.[23,39]

The cohort included all Lumosity users in the contiguous U.S. who were ≥ 18 years of age and who signed up for the platform and completed between 1 and 20 plays of *Lost in Migration* during 1 January 2017 to 31 December 2018. The cohort included both free users and paid subscribers. Although users can play *Lost in Migration* an unlimited number of times, we only had data on the first 20 plays, during which users experience a learning phase where their scores improve at first and then plateau (Figure 1). We restricted analysis to users who completed exactly 20 plays across unique dates (e.g., each play must have occurred on a different day from all other plays) to maximize the number of repeat measures per user and identify daily level associations. To ensure the same study population was used for all analyses, we applied this user inclusion criteria to both the daily and subdaily analyses. In addition, by limiting the analyses to users with 20 plays across unique dates, we were able to exclude users with gaps in play or abnormal playing patterns. We evaluated the robustness of the results with respect to the user inclusion criteria in sensitivity analyses.

For each Lumosity user, we had data on the first three digits of the user's ZIP code (ZIP3) location at sign-up, their self-reported age (≥ 18 y), gender, and education level at sign-up, as well as the device on which all games were played (iPhone, iPad, Android, or web). For each gameplay, data included the user's score at the end of the game (raw score) and their score relative to a normative population of Lumosity users sampled to match the 2010 U.S. Census for age, gender, and education level (percentile score). We used the raw score (hereafter referred to as the attention score) as the primary measure of cognitive performance and considered the percentile score in a sensitivity analysis. We interpreted the attention score as an indicator of users' ability to pay attention, given the game's design. The data set also included the timestamp of each gameplay and the play number, the number of times the user had played *Lost in Migration* up to and including the current gameplay.

$PM_{2.5}$ Exposure Data

To estimate ambient $PM_{2.5}$ for each ZIP3, we used measurements from the U.S. Environmental Protection Agency (EPA)'s Federal Reference Method/Federal Equivalent Method (FRM/FEM) monitors and the network of low-cost PurpleAir monitors. Hourly and daily average FRM/FEM observations were downloaded from the U.S. EPA's Air Quality System database.[40] We averaged nonzero FRM/FEM observations at duplicate space/time locations and only kept nonzero daily averages from stations that had more than 75% of hourly observations available for a given day. We used the PurpleAir application programming interface (API)[41] to download PurpleAir observations at 80-s or 2-min intervals and calculated daily and hourly averages, following a previously developed quality control and cleaning protocol to ensure quality and completeness.[42] PurpleAir sensors are known to overestimate $PM_{2.5}$ concentrations in both ambient and wildfire conditions.[42] To address this, we bias-corrected the PurpleAir data using a modified version of an existing U.S.-wide correction that uses a multiple linear regression with an additive relative humidity term to adjust the observations.[42]

We used the Bayesian Maximum Entropy (BME) framework to fuse the FRM/FEM and PurpleAir observations and generate daily and hourly estimates of average $PM_{2.5}$ concentrations at census tract population centers in the contiguous U.S. for 2017–2018. BME is a spatiotemporal modeling framework that can accurately estimate $PM_{2.5}$ at unmonitored locations by combining

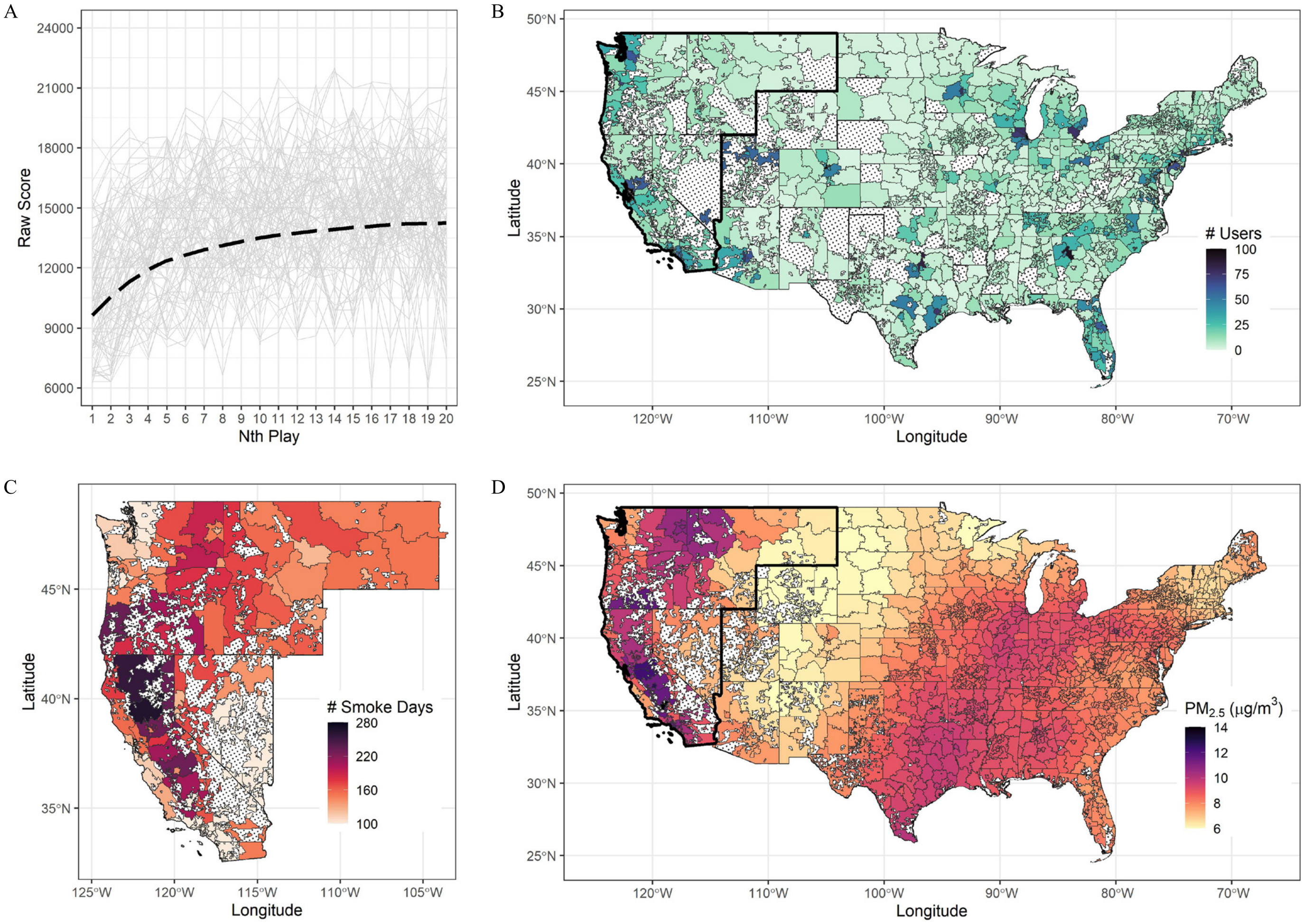

Figure 1. (A) Average learning curve for all contiguous U.S. Lumosity users (black, dashed line) and of 100 randomly selected users (gray, solid line); (B) location of the Lumosity users by ZIP3 (dotted areas indicate regions with no users); (C) total number of smoke days (light, medium or heavy) by ZIP3 in the western U.S., 2017–2018; and (D) average population-weighted daily $PM_{2.5}$ by ZIP3 in the contiguous U.S., 2017–2018. Note: $PM_{2.5}$, fine particulate matter; ZIP3, first three digits of a ZIP code.

information from a site-specific knowledge base (S-KB), which contains information on the observed concentrations at monitoring sites, and a general knowledge base (G-KB), which contains information on the trends and variability in the data.[43–45] In our implementation of BME, the S-KB included the $PM_{2.5}$ observations from both the FRM/FEM and PurpleAir stations and the G-KB included the mean and covariance of the observations from the FRM/FEM stations. The PurpleAir data was not used to derive the G-KB given the potential bias of these observations. The S-KB differentiates data with no associated uncertainty (hard data) from data with associated uncertainty (soft data). Hard data have the greatest influence on the BME estimate and the influence of a given hard data observation decreases with increased distance based on the covariance in the G-KB. The influence of the soft data depends on the uncertainty of a given observation, where observations with lower associated uncertainty have greater influence. In our data fusion, we treated the FRM/FEM observations as hard and the PurpleAir observations as soft, using the 95% confidence interval (CI) produced during the PurpleAir bias correction to determine the associated uncertainty. The leave-one-out and 10-fold cross-validation R^2 values for the data fusion estimates were 0.815 and 0.795, respectively. The data fusion estimates were generated using MATLAB (version R2017b; MathWorks). BME has previously been used to estimate $PM_{2.5}$ concentrations across the U.S.[46–50] and to generate exposure estimates for epidemiologic studies.[51,52] Additional details on the theory and mathematical implementation of the BME framework can be found in previously published literature.[43–50,53]

To match the spatial resolution of the Lumosity data, we calculated ZIP3-level population-weighted daily and hourly average $PM_{2.5}$ concentrations from the census tract-level estimates using the following equation:

$$PM_{ZIP3_j,t} = \sum_{s \in ZIP3_j} PM_{s,t} \times \frac{Pop_s}{\sum_{s \in ZIP3_j} Pop_s}, \tag{1}$$

where $PM_{ZIP3_j,t}$ is the population-weighted $PM_{2.5}$ concentration in ZIP3 j on day or hour t; s is a census tract within ZIP3 j; $PM_{s,t}$ is the average $PM_{2.5}$ data fusion estimate at the population center of census tract s on day or hour t; and Pop_s is the total population of census tract s, obtained from the 2010 U.S. Census.

Smoke Exposure Data

Wildfire smoke exposure in each ZIP3 in the western U.S. was estimated using smoke density data from the National Oceanic and Atmospheric Administration (NOAA)'s Hazard Mapping System (HMS) Fire and Smoke Product.[54] The HMS Smoke Product is based on a visual classification of plumes, relying on Advanced Baseline Imager true-color imagery from Geostationary

Operational Environmental Satellites (GOES) satellites to identify smoke plumes and a deterministic air quality dispersion model to classify smoke plume density. The density of a plume can be classified as light ($PM_{2.5}$ concentrations 0–10 $\mu g/m^3$), medium ($PM_{2.5}$ concentrations 10–21 $\mu g/m^3$), or heavy ($PM_{2.5}$ concentrations $>21\ \mu g/m^3$). HMS smoke plume densities have been used in previous epidemiologic studies to inform exposure[55,56] and have been shown to correlate well with surface concentrations.[57,58] To match the spatial resolution of the Lumosity data, we calculated the daily maximum smoke density (none, light, medium, or heavy) in each ZIP3, based on all plumes observed over a ZIP3 on a given day. We considered only smoke density data in the western U.S.—defined as Oregon, Washington, California, Montana, Idaho, and Nevada—because that region experiences the largest and most direct wildfire smoke impacts[1,59] and we wanted to reduce the potential for visual misclassification of plumes. During 2017 and 2018, there were nearly 33,000 wildfires in these western states, burning close to 11 million acres and accounting for almost 60% of the total acreage burnt by wildfires in the U.S. over these 2 y.[60]

Statistical Analyses

The primary aim of our analyses was to estimate the associations between the $PM_{2.5}$ and smoke exposure metrics and the attention scores. To do so, we used a longitudinal repeated measures study design with linear mixed effects models. For daily $PM_{2.5}$ exposure, we used an unconstrained distributed lag model with 7 lags of population-weighted daily average $PM_{2.5}$, where lag 0 is the concentration on the day of gameplay, lag 1 is concentration the day prior, and so on. We selected 7 lags to capture associations with same-day exposure[24,25] and exposure in the days leading up to play.[21] For subdaily $PM_{2.5}$ exposure, we used the maximum population-weighted hourly average $PM_{2.5}$ concentration in the 3, 6, and 12 h prior to gameplay. For smoke exposure, we evaluated how daily maximum smoke density on the day of gameplay (lag 0), the day prior to play (lag 1), and in the 1 wk prior to play were associated with attention score. We could not evaluate subdaily exposure to smoke because the HMS data are limited by satellite overpass times. For the $PM_{2.5}$ analyses, we evaluated the associations between daily and subdaily concentrations and attention scores across the contiguous U.S. To characterize the exposure–outcome relationship in regions directly impacted by wildfire smoke, we also restricted analysis to the western U.S. We conducted the smoke analyses solely in the western U.S., as discussed above.

The secondary aim of our analyses was to explore differences in associations with respect to gender, age group, and user's habitual behavior to identify particularly vulnerable populations. Users were stratified into six different age groups: 18–29, 30–39, 40–49, 50–59, 60–69, and ≥70 y. Habitual players were defined as users whose median time between plays was ≤7 d and whose standard deviation (SD) for the time-of-day played was ≤2 h. Subgroup analyses were conducted in both the western and contiguous U.S. for $PM_{2.5}$ and solely in the western U.S. for smoke density.

All linear mixed effects models included a $\log(n)$ term to control for learning, where n corresponds to the play number. This controls for the learning curve over 20 plays, which followed a logarithmic shape (Figure 1). To further account for improvements in score over time, all models also included a third-order autoregressive process. In addition, the models included an interaction term between $\log(n)$, the device type, and the user's age group to account for the age and device-variable learning curves (Figure S2). Finally, the models included a random intercept by user. The linear mixed effects model used for all analyses can be described using the following equation:

$$\begin{aligned} Score_{n,i,s,t} = {} & \beta_0 + u_{0,i} + \beta_1 \log(n) + \beta_2 Score_{i,n-1} + \beta_3 Score_{i,n-2} \\ & + \beta_4 Score_{i,n-3} + \beta_5 Exposure_{s,t} + \beta_6 Device_i \\ & + \beta_7 AgeGroup_i + \beta_8 \log(n) Device_i + \beta_9 \log(n) AgeGroup_i \\ & + \beta_{10} \log(n) AgeGroup_i Device_i + \beta_x covariate_{n,i,s,t} + \varepsilon_{n,i,s,t} \end{aligned} \tag{2}$$

where $Score_{n,i,s,t}$ is user i's attention score on play n in ZIP3 s at time t. β_0 is the intercept; $u_{0,i}$ is the user-specific intercept; and $Score_{i,n-1,2,3}$ is the third-order autoregression. $Exposure_{s,t}$ is the ZIP3-level exposure metric, either $PM_{2.5}$ concentration or wildfire smoke density, described in detail above; $\log(n)$, $Device_i$, and $AgeGroup_i$ are the log of the play number, device, and user age group, respectively. The other covariate terms ($covariate_{n,i,s,t}$) in the models included: *a*) categorical variables for the time-of-day (0–23), day-of-week (0–6), and month of the gameplay (1–12), *b*) the number of days since the user last played, *c*) user gender and education level, *d*) ZIP3-level population-weighted daily average relative humidity and temperature, *e*) ZIP3-level population-weighted annual average $PM_{2.5}$, and *f*) the ZIP3's poverty rate, high school graduation rate, and rural–urban continuum code (RUCC). Temperature and relative humidity data were obtained from NOAA[61] and the poverty rate, high school graduation rate, and RUCC were obtained from the U.S. Census Bureau's 2015–2019 5-y American Community Survey.[62] Finally, $\varepsilon_{n,i,s,t}$ is the error term. By controlling for individual-level characteristics and including a third-order autoregressive process and random intercept by user, we controlled for differences in performance across users and focused the analyses on within-individual differences in responses. Results are reported as a change in attention score associated with a $10\ \mu g/m^3$ increase in daily or subdaily $PM_{2.5}$ or a change in score associated with light, medium, or heavy density smoke at the daily or weekly level, relative to no smoke. Results were considered statistically significant if the 95% CI of the estimates did not contain 0. Differences between subgroups were considered statistically significant if the 95% CIs of two estimates did not overlap.

Multiple sensitivity analyses were run to assess the robustness of our findings. Specifically, we evaluated the sensitivity of the results to *a*) using the percentile score as the outcome of interest instead of the raw score, *b*) including <7 lags in the daily $PM_{2.5}$ distributed lag model, *c*) different definitions of habitual users (e.g., different cutoffs for the median time between plays or the SD for time-of-day played), *d*) less strict inclusion criteria for users (e.g., including users with <20 plays or users who completed 20 plays across <20 unique dates), and *e*) covariate model specification (e.g., models with less covariate or interaction terms). We also considered the possibility of a nonlinear relationship between daily $PM_{2.5}$ and attention score by fitting cubic splines to the $PM_{2.5}$ lags. All statistical analyses were conducted in R (version 4.0.3; R Development Core Team). All data included in the Lumosity data set were deidentified and analyzed in accordance with Lumos Lab, Inc.'s Privacy Policy.[63] This study was determined by the Office of Human Research Ethics at the University of North Carolina at Chapel Hill to not constitute human subjects research as defined under federal regulations and did not require Institutional Review Board approval (reference no. 273020).

Results

Characteristics of Lumosity Users

The study population included 10,228 contiguous U.S. users and 1,809 western U.S. users (Table 1 and Figure 1). The western and contiguous U.S. users had very similar characteristics. Most

Table 1. Characteristics of western and contiguous U.S. Lumosity users and exposure data.

Characteristic	Western U.S. ($n = 1{,}809$)	Contiguous U.S. ($n = 10{,}228$)
Gender [n (%)]		
Female	1,250 (69.1)	7,214 (70.5)
Male	559 (30.9)	3,014 (29.5)
Age group (y), [n (%)]		
18–29	147 (8.1)	859 (8.4)
30–39	254 (12.0)	1,238 (12.1)
40–49	276 (15.3)	1,530 (15.0)
50–59	457 (25.3)	2,752 (26.9)
60–69	427 (23.6)	2,614 (25.6)
≥70	248 (13.7)	1,235 (12.1)
Education [n (%)]		
Some high school	34 (1.9)	152 (1.5)
High school diploma	203 (11.2)	1,447 (14.1)
Some college	375 (20.7)	1,959 (19.2)
Associate degree	178 (9.8)	937 (9.2)
Professional degree	91 (5.0)	419 (4.1)
Bachelor's degree	576 (31.8)	3,115 (30.5)
Master's degree	278 (15.4)	1,820 (17.8)
Doctoral degree	29 (1.6)	190 (1.9)
Other	45 (2.5)	189 (1.8)
Device [n (%)]		
Android	606 (33.5)	3,462 (33.8)
iPad	264 (14.6)	1,638 (16.0)
iPhone	668 (36.9)	3,858 (37.7)
Web	271 (15.0)	1,270 (12.4)
Habitual behavior [n (%)]		
Habitual	146 (8.1)	873 (8.5)
Nonhabitual	1,663 (91.9)	9,355 (91.5)
Attention score [mean (SD)]		
All 20 plays	13,161.8 (4,202.5)	13,075.5 (4,108.7)
1st play	9,721.5 (4,189.3)	9,645.7 (4,093.6)
20th play	14,317.2 (3,928.0)	14,250.7 (3,795.7)
Days between plays [mean (SD)]	8.4 (15.1)	8.3 (14.0)
Hour of day played [mean (SD)]	13.8 (5.6)	13.7 (5.6)
Daily $PM_{2.5}$ ($\mu g/m^3$), [mean (IQR)][a]	10.0 (6.2)	8.7 (5.0)
Hourly $PM_{2.5}$ ($\mu g/m^3$), [mean (IQR)][a]	10.2 (6.2)	9.3 (5.2)
Smoke Density [n (%)][b]		
None	29,512 (81.6)	—
Light	3,859 (10.7)	—
Medium	1,318 (3.6)	—
Heavy	1,491 (4.1)	—

Note: There were no missing values in the Lumosity and exposure data sets. —, not applicable; IQR, interquartile range; $PM_{2.5}$, fine particulate matter; SD, standard deviation; ZIP3, first three digits of a ZIP code.
[a]Average of daily and hourly ZIP3-level population-weighted $PM_{2.5}$ concentrations on the day or hour of gameplay across 36,180 western U.S. observations (1,809 users with 20 plays) and 204,560 contiguous U.S. observations (10,228 users with 20 plays).
[b]Total number and percentage of the 36,180 western U.S. observations (1,809 users with 20 plays) with smoke present on the day of gameplay.

users were female and ≥50 years of age. Approximately two-thirds of users had some college education or higher and most played on mobile devices. More than 90% of users lived in metropolitan areas across the U.S. Older users were more likely to be habitual players and use an iPad or the web to play, whereas younger users were less habitual and more likely to use a mobile device. Although there was notable variety in each user's individual learning curve, the learning curves generally followed a logarithmic curve, with a steeper improvement in attention score during earlier plays and less steep improvement during later plays. On average, users played a game of *Lost in Migration* every 1–2 wk and improved their score by more than 4,500 points (47.7%) from the 1st to the 20th play. In addition, users completed their plays most frequently in the morning between 0700 and 1200 hours or in the evening between 2000 and 2200 hours (Figure S3). Younger users tended to perform better than older users, with higher attention scores across all 20 plays and steeper learning curves during earlier plays (Figure S4). Web and iPhone users had higher scores in comparison with Android and iPad users, especially among younger players (Figure S2). There were no notable differences in scores or learning curve by gender or habitual behavior (Figure S4). The attention scores across all 20 plays followed a relatively normal distribution (Figure S5). Additional information on the characteristics, learning curves, and attention score distributions of the western and contiguous U.S. study populations, overall and by different user subgroups, can be viewed online at https://ehs-bccdc.shinyapps.io/PMSmoke_Attention_Dashboard/.

Characteristics of Exposure Data

When compared with all users, western U.S. users were exposed to higher levels (mean ± SD) of $PM_{2.5}$ on the day (10.0 ± 6.2 vs. $8.7 \pm 5.0\ \mu g/m^3$) or hour (10.2 ± 6.2 vs. $9.3 \pm 5.2\ \mu g/m^3$) of gameplay, as well as a wider range of concentrations during the 2017–2018 study period (Table 1). The western states, especially central California and southern Oregon, also had the highest estimated concentrations (Figure 1) and spatial and temporal variability (Figure S6) of $PM_{2.5}$, in part due to the air quality impacts of wildfires in these regions. In addition, every ZIP3 in the western U.S. had multiple days affected by wildfire smoke during the study period. Southern Oregon and central and northern California were the most smoke impacted during 2017–2018, with smoke plumes identified on nearly 40% of days. Of the 36,180 western U.S. observations included in this study (20 plays for 1,809 users), 18.4% of observations had light, medium, or heavy smoke density present at the ZIP3-level on the day of gameplay, with light smoke density occurring most frequently. Maps of the ZIP3-level population-weighted daily average $PM_{2.5}$ and daily maximum smoke density, along with maps of the BME data fusion estimates, monitoring station locations, and daily smoke plume shapes, can be viewed online at https://ehs-bccdc.shinyapps.io/PMSmoke_Attention_Dashboard/.

$PM_{2.5}$ and Cognitive Performance

Daily and subdaily $PM_{2.5}$ exposure were associated with significant decreases in attention score for both western and contiguous U.S. users, with more pronounced associations in the western states (Figure 2; Table S1). Of the $PM_{2.5}$ exposure metrics considered, the 7-d cumulative exposure had the strongest association with score. A $10\ \mu g/m^3$ increase in $PM_{2.5}$ was associated with a 47.6 (95% CI: 7.2, 88.1)- and 33.0 (95% CI: 3.4, 62.5)-point reduction in score in the western and contiguous U.S., respectively. The observed 7-d cumulative associations were driven by the associations with $PM_{2.5}$ on the day of gameplay (lag 0), which was –44.3 (95% CI: –84.3, –4.3) in the western U.S. and –26.4 (95% CI: –47.9, –4.9) in the contiguous U.S. The associations at lags 1–6 were largely null. Subdaily exposure was also significantly associated with decreases in attention score. A $10\ \mu g/m^3$ increase in the maximum hourly $PM_{2.5}$ concentration in the 3 and 12 h prior to gameplay were associated with a 41.7 (95% CI: 13.6, 69.7)- and 40.7 (95% CI: 15.0, 66.4)-point decrease in score, respectively, for western U.S. users. For contiguous U.S. users, the 3- and 12-h maximum exposure metrics were associated with a 21.0 (95% CI: 3.3, 38.7)- and 24.5 (95% CI: 8.3, 40.7)-point decrease in score, respectively.

Consistent with the results for all users, associations between $PM_{2.5}$ and attention score were generally more pronounced among western U.S. users in the models stratified by age group, gender, and habitual behavior (Figure 3; Table S2). In both the western and contiguous U.S., the youngest (18–29) and older age

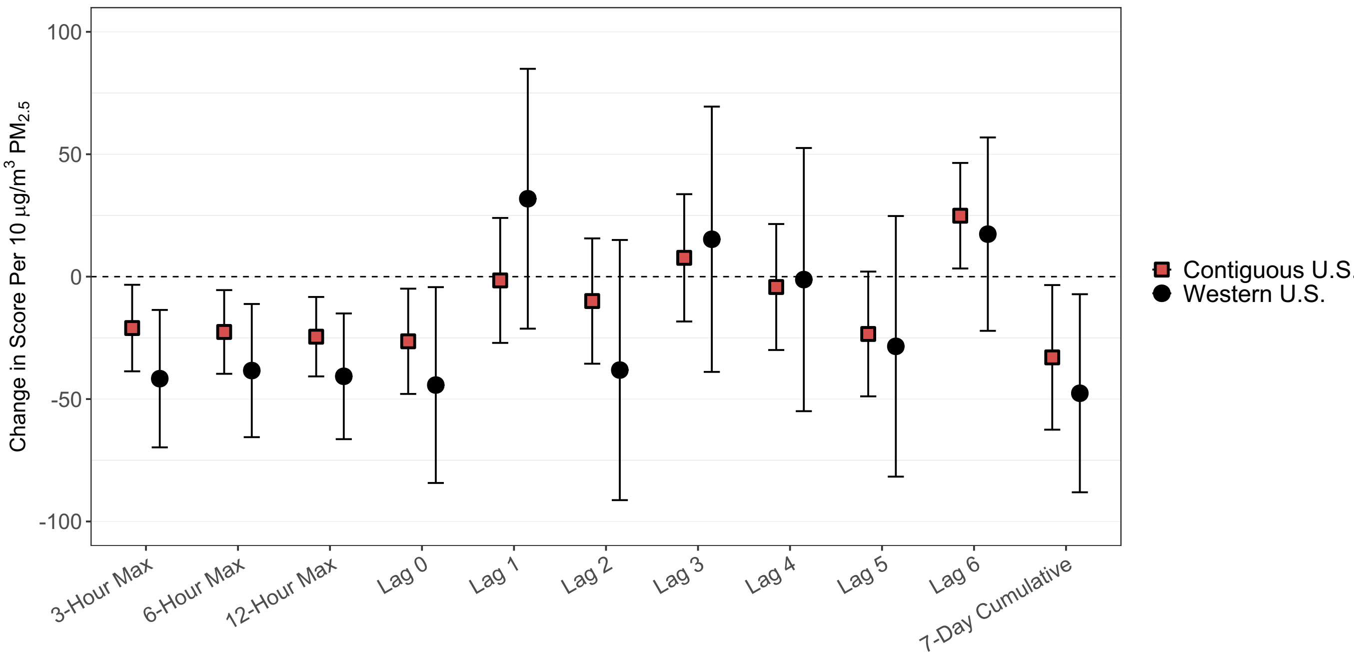

Figure 2. Change in attention score associated with a $10\ \mu g/m^3$ increase in daily and subdaily $PM_{2.5}$ for all users in the western and contiguous U.S. Exposure metrics include the maximum population-weighted hourly average $PM_{2.5}$ in the 3, 6, and 12 h prior to gameplay (3-, 6-, and 12-Hour Max) and the population-weighted daily average $PM_{2.5}$ in the 7 d prior to gameplay (lags 0–6 and 7-Day Cumulative). The numeric results can be found in Table S1. Note: Hour Max, hour maximum; $PM_{2.5}$, fine particulate matter.

groups (50–59 and ≥70 y) had the strongest associations with daily and subdaily $PM_{2.5}$ exposure. The most pronounced associations were observed for those ≥70 years of age in the western U.S., who had an 89.7 (95% CI: 1.0, 178.4)-point reduction in score per $10\ \mu g/m^3$ of $PM_{2.5}$ at lag 0. Although the $PM_{2.5}$-score associations did not vary notably by gender, the associations were generally more pronounced in habitual users, with the magnitude of association two to three times greater than in nonhabitual players across daily and subdaily exposures in the western U.S. For example, in the western U.S., a $10\ \mu g/m^3$ increase in the maximum hourly $PM_{2.5}$ concentration in the 12 h prior to play was associated with a 122.5 (95% CI: 38.0, 207.0)-point decrease in score for habitual users and only a 34.2 (95% CI: 7.3, 61.10)-point decrease for nonhabitual users. Although the observed differences between age groups and habitual and nonhabitual players are noteworthy, they were not statistically significant. Differences in the precision of the estimates between the western and contiguous U.S. and within subgroups were largely due to differences in the number of users included in each population. Results for all daily (lags 0–6) and subdaily (3-, 6-, and 12-h maximum) exposure metrics for western and contiguous U.S. users, overall and by age, gender, and habitual behavior, can be viewed online at https://ehs-bccdc.shinyapps.io/PMSmoke_Attention_Dashboard/.

Wildfire Smoke and Cognitive Performance

Wildfire smoke density was negatively associated with attention score at both the daily and weekly level among western U.S. users (Figure 4; Table S3). There were significant decreases in attention score when medium density smoke was present the day of gameplay (lag 0) and when heavy density smoke was present the day prior to play (lag 1) and in the 1 wk prior to play. The presence of light density smoke prior to play was not associated with score. The strongest associations were observed for heavy smoke density at lag 1 and in the 1 wk prior to play, with 117.0 (95% CI: 1.7, 232.3)- and 119.3 (95% CI: 26.4, 212.2)-point decreases in score relative to no smoke, respectively. Aligning with the $PM_{2.5}$ results, the observed associations with heavy smoke density in the 1 wk prior to play were driven by the associations at lag 1.

The age, gender, and habitual behavior-specific associations were consistent with the results for all western U.S. users, where the presence of medium or heavy smoke density had significant negative associations with attention score (Figure 4; Table S3). Although the results by age group were inconsistent across densities and exposure metrics, the associations with heavy smoke were most pronounced for users 18–29 and 40–49 years of age. For example, for users 40–49 years of age, the presence of heavy smoke density in the 1 wk prior to play was associated with a 261.3 (95% CI: 3.1, 519.6)-point reduction in score. In addition, the scores of male users had stronger associations with smoke density than female users, with the most notable differences observed for heavy smoke. For male users, heavy smoke density at lag 1 was associated with a 258.6 (95% CI: 43.0, 474.3)-point decrease in score relative to no smoke, whereas for female users it was associated with only a 52.2 (95% CI: –84.3, 188.8)-point decrease. Further, aligning with the $PM_{2.5}$ results, the associations with smoke density were generally more pronounced in habitual users than nonhabitual users. The presence of medium smoke density the day of gameplay was associated with a 269.7 (95% CI: 69.8, 609.2)-point decrease for habitual users compared with a 98.8 (95% CI: 15.7, 213.3)-point decrease for nonhabitual users. Although younger, male, and habitual user attention scores appeared to have stronger associations with wildfire smoke, the differences between user subgroups were not statistically significant. Results for all smoke analyses can also be viewed online at https://ehs-bccdc.shinyapps.io/PMSmoke_Attention_Dashboard/.

Sensitivity Analyses

Multiple sensitivity analyses were run to assess the robustness of the methods and findings (Tables S4 and S5). When the percentile score was used as the outcome of interest instead of the raw

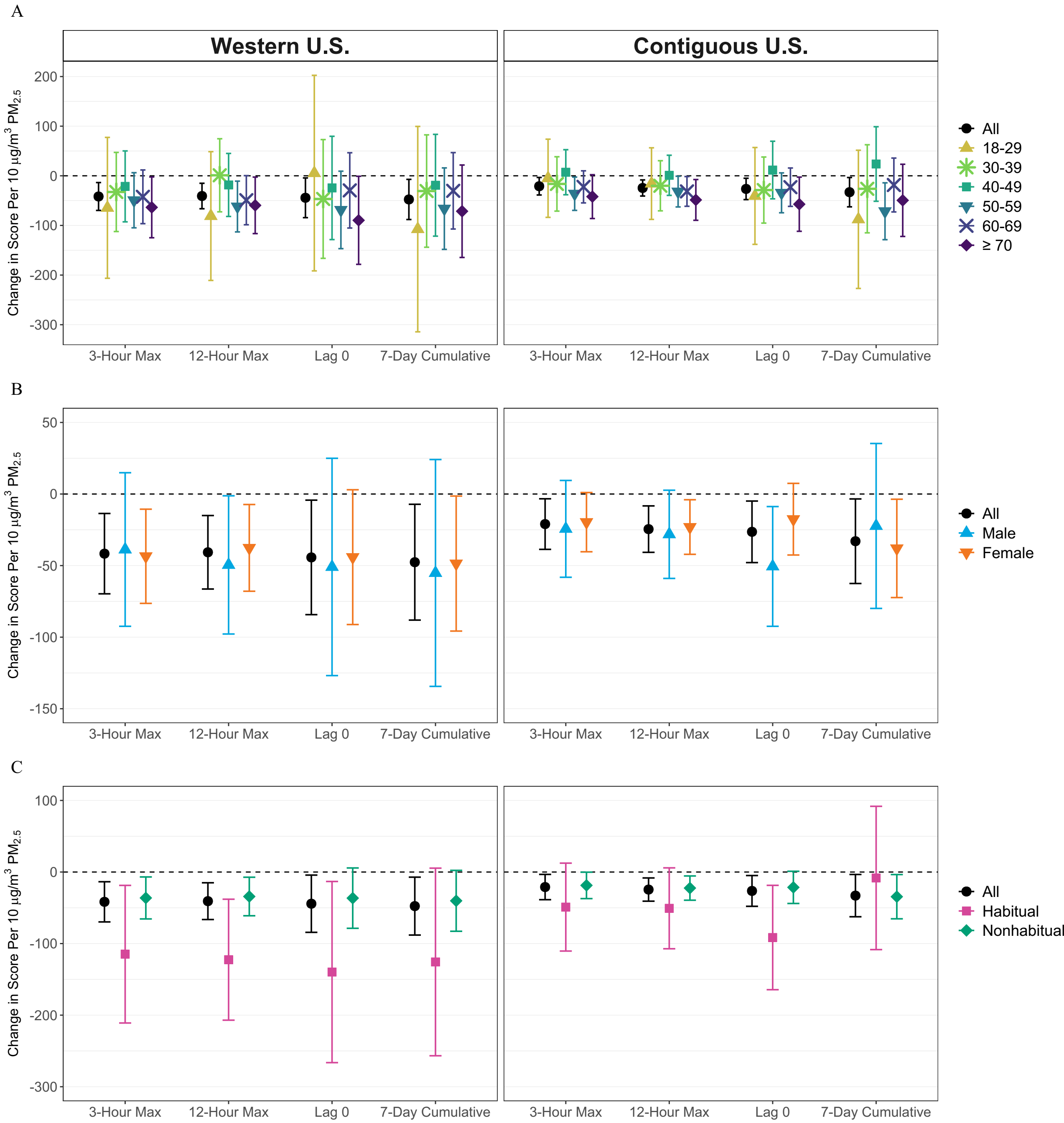

Figure 3. Change in attention score associated with a $10\,\mu g/m^3$ increase in daily and subdaily $PM_{2.5}$ for western and contiguous U.S. users by (A) age group, (B) gender, and (C) habitual behavior. Exposure metrics include the maximum population-weighted hourly average $PM_{2.5}$ in the 3 and 12 h prior to gameplay (3- and 12-Hour Max), the population-weighted daily average $PM_{2.5}$ the day of gameplay (Lag 0), and the cumulative population-weighted daily average $PM_{2.5}$ in the 7 d prior to gameplay (7-Day Cumulative). The numeric results can be found in Table S2. Note: Hour Max, hourly maximum; $PM_{2.5}$, fine particulate matter.

score, the results were largely consistent with the primary findings, albeit slightly attenuated in the contiguous U.S. (Figure S7). The daily $PM_{2.5}$ distributed lag model was not sensitive to the number of lags included, with both the lag 0 and *n*-day cumulative associations remaining consistent regardless of how many lags were used (Figure S8). Further, the results were generally insensitive to the definition of habitual users. When less strict definitions were considered, habitual users still had stronger associations with $PM_{2.5}$ and smoke density than nonhabitual users, although the differences between the two groups were less pronounced (Figure S9). The results were also robust to covariate model specification, with consistent results when less adjusted models were used (e.g., models with less covariate or interaction terms) (Figure S10). We also investigated the possibility of a nonlinear relationship between $PM_{2.5}$ and attention score. For both the western and contiguous U.S., the nonlinear relationships had wide CIs and the associations across all concentrations were null (Figure S11).

Additional sensitivity analyses examined how relaxing the inclusion criteria for users affected the observed associations. When the inclusion criteria were relaxed to include users who completed 20 plays across <20 unique dates, the associations

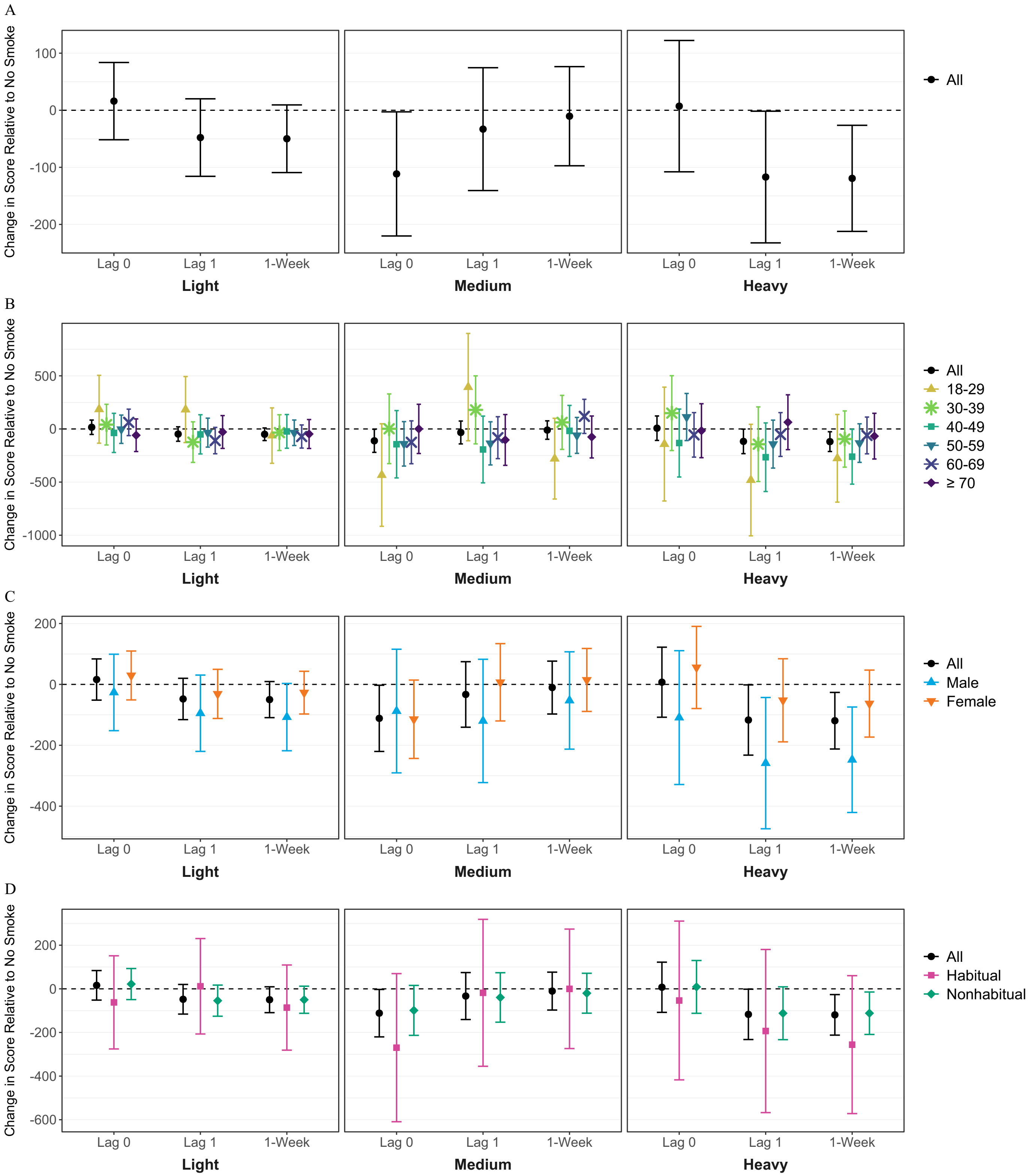

Figure 4. Change in attention score associated with light, medium, or heavy density smoke, relative to no smoke, for (A) all western U.S. users and by (B) age group, (C) gender, and (D) habitual behavior. Exposure metrics include the daily maximum smoke density the day of and day prior to gameplay (Lag 0 and Lag 1) and in the 1 wk prior to gameplay (1-Week). The numeric results can be found in Table S3.

between $PM_{2.5}$ and smoke density and score were slightly attenuated (Figure S12). Similarly, when we relaxed the inclusion criteria to include users who completed <20 plays, the associations across all exposure metrics were attenuated (Figure S13), indicating that the results were somewhat sensitive to user longevity on the platform. Results for all sensitivity analyses can also be viewed online at https://ehs-bccdc.shinyapps.io/PMSmoke_Attention_Dashboard/.

Discussion

We found evidence of significant associations between short-term exposure to $PM_{2.5}$ and wildfire smoke and decreased attention in adults, as measured by Lumosity's *Lost in Migration* game. Exposure to $PM_{2.5}$ at the daily and hourly level were associated with a reduction of more than 20 points in attention score per $10\,\mu g/m^3$ of $PM_{2.5}$. Likewise, exposure to heavy or medium smoke density at the daily and weekly level were associated with a reduction of >100 points in attention score relative to no smoke.

Using the estimated association at lag 0, we can compare users' predicted scores at the observed $PM_{2.5}$ concentrations with their predicted scores in the absence of $PM_{2.5}$, concentrations of $0\,\mu g/m^3$. By doing so, we estimate that western U.S. users lost on average a total of 887 (95% CI: 86, 1,688) points over 20 plays, with an average 40- to 50-point loss for each play, due to same-day $PM_{2.5}$ exposure. The estimated loss of 887 points from the average 20th play score of 14,317 points corresponds to a 6.2% (95% CI: 0.6%, 11.8%) reduction in final score associated with $PM_{2.5}$. Further, assuming no multiplier bonus is applied, an 887-point loss is equivalent to ~ 18 fewer correct answers over 20 plays. In comparison, we estimate contiguous U.S. users lost on average 529 (95% CI: 98, 960) points [3.7% (95% CI: 0.7%, 6.7%) reduction in 20th play score and ~ 11 fewer correct answers] over 20 plays due to $PM_{2.5}$.

The strongest associations with $PM_{2.5}$ were observed within a short exposure window, showing that $PM_{2.5}$ is associated with reduced attention within 3 h of exposure. Although we were unable to evaluate the impacts of subdaily exposure to wildfire smoke, the strongest associations were also observed within a short exposure window of ≤ 2 d. Because the $PM_{2.5}$ associations were driven by hourly and same-day exposure, we hypothesize that the relationships between short-term variations in $PM_{2.5}$ and cognitive performance, such as those experienced during wildfire smoke episodes, may be transient. However, given that we observed associations at ambient concentrations typically experienced in U.S. communities in the absence of extreme air pollution events, it is likely that long-term exposure also has implications for cognitive function. Such associations have been observed in recent epidemiologic studies identifying the chronic cognitive impacts of sustained exposure,[64–67] but further research into the links between extended $PM_{2.5}$ and wildfire smoke exposure and cognitive performance is needed.

In addition to varying by exposure duration, the associations of $PM_{2.5}$ with attention were also more pronounced in the western U.S., with the magnitude of association nearly double that of the contiguous U.S. This may be due in part to geographic differences in the sources and chemical composition of $PM_{2.5}$.[68] Wildfires are a significant source of $PM_{2.5}$ in the western U.S., which can affect the toxicity of the particles and may modify their associated health effects.[27,28,69] The other physical and mental health effects of wildfire events may also play a role. For example, eye irritation[70,71] could impact the ability of users to effectively interact with mobile devices, and increased anxiety[72,73] could affect the ability to focus. The observed associations with both $PM_{2.5}$ and smoke density in the western U.S. provide evidence that individuals living in wildfire-impacted regions may be more vulnerable to the cognitive impacts of air pollution. This vulnerability may be further exacerbated as $PM_{2.5}$ concentrations in areas affected by wildfires increase under climate change.[9,10,74]

Further, although the differences were not statistically significant, habitual users had stronger associations with both smoke and $PM_{2.5}$ exposure than nonhabitual users. This is potentially due to behavioral differences between the groups. Because habitual users train more frequently, their decision to play may be less dependent on environmental conditions and their short-term variations in exposure may be better represented with areal averages when compared with more sporadic users. In addition, the moderate sensitivity of the results to the user inclusion criteria could also be due to differences in user behavior. Prior research has found that Lumosity users who drop out early tend to exhibit poorer performance and shallower learning trajectories, potentially due to lower motivation or less desire to continue playing.[75] Although it is not fully clear how lower motivation to play impacts the associations between $PM_{2.5}$ and smoke and Lumosity performance, the observed attenuation may be due to stronger exposure misclassification in users with less predictable patterns of behavior or the suppression of scores in users with less desire to play. However, all possibilities for the cause of any user behavior-related differences will be unknown until Lumosity data is used more broadly in a research context.

Our findings are largely consistent with existing epidemiologic research. Prior studies have identified associations between daily $PM_{2.5}$ concentrations and poorer cognitive performance, as measured by Lumosity performance[23] and Mini-Mental State Examination (MMSE),[21] global cognitive function,[21] fluid reasoning,[24] and standardized test scores.[19,20,22,25] However, this analysis did not have the power to detect a nonlinear association as was reported by some prior studies.[21,23,24] Although there is very limited research on the relationships between cognitive function and subdaily exposure, one study with 63 participants identified an association between hourly exposure to PM via outdoor commuting and candle burning and reduced MMSE performance.[26] In addition, although differences between age groups were not statistically significant, younger and older users having stronger associations with exposure aligns with existing research linking $PM_{2.5}$ to reduced academic and cognitive performance in youth and accelerated cognitive decline in older adults (as reviewed by Clifford et al.[6]). The only other study that has used Lumosity data to investigate how daily $PM_{2.5}$ varies with cognitive performance did not report significant associations among older users, but they did find younger users to be more impacted.[23] Finally, although no prior epidemiologic study has examined the association between wildfire smoke density and cognitive performance, our results are generally consistent with other studies that identified associations between agricultural fires and open fire usage and decreased cognitive function, as measured by MMSE,[29] word recall,[29–31] and mental intactness[30,31] tests.

Our study has many strengths, the first of which is the repeated measures study design. The Lumosity data set provided detailed, longitudinal measurements for a large adult population, enabling us to conduct one of the first large-scale studies of the links between short-term $PM_{2.5}$ and wildfire smoke exposure and cognitive function. This allowed us to overcome some of the limitations associated with clinical or laboratory studies, which can be time and cost intensive with a limited number of participants. In addition, because the data set provided repeat measures for over 10,000 diverse users across the contiguous U.S., we were able to identify significant associations in the larger working-age population. Another notable strength is our use of BME data fusion to estimate $PM_{2.5}$ concentrations. Most such studies rely solely on data from the closest monitoring station to inform exposure.[19–25] By fusing observations from both FRM/FEM and PurpleAir monitors, we were able to increase the spatial coverage of observations and get more information on $PM_{2.5}$ exposure at the hourly and daily level while still accounting for the uncertainty in the PurpleAir measurements. Further, by population-weighting the $PM_{2.5}$ estimates to the ZIP3 level, we were able to account for the spatial distribution of the population and give proportionally greater weight to the $PM_{2.5}$ experienced in the most densely populated regions. This approach likely generated estimates that were more representative of exposure than taking a simple spatial average. Finally, an important strength of this study was the ability to investigate associations with subdaily $PM_{2.5}$ exposure. Most epidemiologic studies on the health effects of $PM_{2.5}$ and wildfire smoke have focused on 24-h average exposure (as reviewed by Reid et al.[2] and Atkinson et al.[5]), often because data on health outcomes are only available at the daily timescale.[4] By identifying how quickly changes in hourly $PM_{2.5}$ concentrations are linked to decreased cognitive performance, our findings may be useful for time-sensitive public health decision-making processes during extreme air pollution events, such as wildfires.

This study is not without limitations. First, performance on the Lumosity platform is not a clinical measure of cognitive function. Use of Lumosity has been associated with improved performance in other neuropsychological tests,[35,36,76–78] and brain-training games can improve performance on tasks involving similar cognitive domains (as reviewed by Simons et al.[79] and Smid et al.[80]). In addition, *Lost in Migration* scores have been used in other studies as a measure of attention,[23,39] and the cognitive focus of Lumosity games has been characterized.[34] However, it is unclear whether changes Lumosity scores have generalizable impacts on everyday learning and cognitive tasks. Second, there is the possibility of exposure misclassification. The analyses were conducted at the ZIP3 level, which is a relatively coarse resolution for studying the impacts of $PM_{2.5}$ and smoke given that concentrations and density can change rapidly over short distances. In addition, we assumed that users did not move and completed all plays at their sign-up ZIP3 location. It is very possible that users, especially those using mobile devices, played *Lost in Migration* in different ZIP3s during their 20 plays, which would lead to nondifferential exposure misclassification and attenuation of the true associations toward the null. This is especially true in regions with higher variability in $PM_{2.5}$ concentrations within a ZIP3, such as in the western U.S. (Figure S5). In addition, the visibility on smoke days may influence a user's movement and in turn their performance or decision to play. Although this is difficult to verify with the current data, we confirmed that 6,668 plays occurred on 409 smoke days in 96 ZIP3s. In comparison, 6,716 plays occurred on the 508 nonsmoke days in the week prior to a smoke day in same ZIP3s. This leads us to believe that a user's decision to play is likely not influenced by the presence or visibility of smoke. Third, the inclusion of paid subscribers in the cohort did not constitute a random sample. The Lumosity brain-training games are promoted as tools aimed to improve cognitive abilities and it is unclear how the willingness to pay and motivation to play affects the direction and magnitude of the observed associations. This should be considered in future investigations. Fourth, we were unable to control for all individual-level factors, such as socioeconomic status, leaving the possibility of residual confounding. However, we were able to control for related confounders, such as education at the individual level and socioeconomic status at the ZIP3 level. In addition, given the relatively coarse spatial resolution of the Lumosity data set, we may have been unable to account for all spatial correlation present in the data. Further, although the results of the subgroup analyses are informative, showing more pronounced associations in younger (18–29 y), older ($\geq$70 y), and male users, the differences between groups were not statistically significant. There was also a lack of precision for some of the subgroup estimates due to small sample sizes. Additional research using a larger study population is needed to clearly identify vulnerable subpopulations. Finally, the generalizability of our findings may be limited to adults with similar demographics to our study population who use brain-training games, such as Lumosity.

Despite these limitations, our findings help expand the knowledge base on the cognitive function risks posed by poor air quality. This is one of the first epidemiologic studies to identify the link between daily and subdaily $PM_{2.5}$ exposure and cognitive performance in the working-age population and to show that $PM_{2.5}$ is associated with reduced attention within hours of exposure. It is also the first to identify an association between wildfire smoke density and decreased cognitive performance. Further, we show that Lumosity data can be a useful tool for investigating the associations between environmental exposures and cognitive function. The platform provides cognitive performance data for a large population using controlled and repeated games that can be combined with appropriate statistics to conduct robust epidemiologic research. Future work could include expanding analyses to Lumosity games beyond *Lost in Migration* that target cognitive domains other than attention. In addition, research using Lumosity data over a longer duration could enable the investigation of the short- and longer-term impacts of exposure in tandem. Research considering the interaction between wildfire smoke and $PM_{2.5}$ could also be informative given that $PM_{2.5}$ is likely on the causal pathway between smoke exposure and cognitive performance and that prior studies have found PM-health associations to be more pronounced on smoky days,[81] possibly because of very high concentrations, PM composition, or coexposure with gaseous pollutants. Finally, additional research into the associations between short-term $PM_{2.5}$ and wildfire smoke exposure and cognitive function using different measures of cognitive performance and in other wildfire-impacted regions would be valuable to validate our findings and further elucidate these relationships.

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