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Short-term NO_2 exposure and cognitive and mental health: A panel study based on a citizen science project in Barcelona, Spain

Florence Gignac [a,b,c], Valeria Righi [d], Raül Toran [a,b,c], Lucía Paz Errandonea [d], Rodney Ortiz [a,b,c], Bas Mijling [e], Aytor Naranjo [f], Mark Nieuwenhuijsen [a,b,c], Javier Creus [d], Xavier Basagaña [a,b,c,*]

[a] Barcelona Institute for Global Health (ISGlobal), Barcelona, Spain
[b] Universitat Pompeu Fabra (UPF), Barcelona, Spain
[c] CIBER Epidemiología y Salud Pública (CIBERESP), Spain
[d] Ideas For Change (IFC), Barcelona, Spain
[e] Royal Netherlands Meteorological Institute (KNMI), De Bilt, the Netherlands
[f] Lobelia Earth, Barcelona, Spain

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ABSTRACT

Background: The association between short-term exposure to air pollution and cognitive and mental health has not been thoroughly investigated so far.
Objectives: We conducted a panel study co-designed with citizens to assess whether air pollution can affect attention, perceived stress, mood and sleep quality.
Methods: From September 2020 to March 2021, we followed 288 adults (mean age = 37.9 years; standard deviation = 12.1 years) for 14 days in Barcelona, Spain. Two tasks were self-administered daily through a mobile application: the Stroop color-word test to assess attention performance and a set of 0-to-10 rating scale questions to evaluate perceived stress, well-being, energy and sleep quality. From the Stroop test, three outcomes related to selective attention were calculated and z-score-transformed: response time, cognitive throughput and inhibitory control. Air pollution was assessed using the mean nitrogen dioxide (NO_2) concentrations (mean of all Barcelona monitoring stations or using location data) 12 and 24 h before the tasks were completed. We applied linear regression with random effects by participant to estimate intra-individual associations, controlling for day of the week and time-varying factors such as alcohol consumption and physical activity.
Results: Based on 2,457 repeated attention test performances, an increase of 30 $\mu g/m^3$ exposure to NO_2 12 h was associated with lower cognitive throughput (beta = −0.08, 95% CI: −0.15, −0.01) and higher response time (beta = 0.07, 95% CI: 0.01, 0.14) (increase inattentiveness). Moreover, an increase of 30 $\mu g/m^3$ exposure to NO_2 12 h was associated with higher self-perceived stress (beta = 0.44, 95% CI: 0.13, 0.77). We did not find statistically significant associations with inhibitory control and subjective well-being.
Conclusions: Our findings suggest that short-term exposure to air pollution could have adverse effects on attention performance and perceived stress in adults.

1. Introduction

Whereas several adverse effects of air pollution on the heart and the lungs are well established (Chen and Hoek, 2020, Orellano et al., 2020), evidence on the relationships between poor air quality and the brain continues to emerge (Thurston et al., 2017). The brain is a complex organ that plays a fundamental role in the optimal development and the control of emotions, behaviors and cognitive functions (Wang et al., 2020) and is highly sensitive to environmental stressors like air pollution (Iqubal et al., 2020). Several air pollutants, in particular ultrafine particles (UFP, particles ≤ 0.1 μm in diameter) and others such as fine particulate matter ($PM_{2.5}$, particles ≤ 2.5 μm in diameter) and nitrogen dioxide (NO_2), are suspected of having harmful effects in the central nervous system (Schraufnagel, 2020, Salvi and Salim, 2019).

In urban areas, road traffic activities represent a major source of these air pollutants. For example, in Barcelona (Spain), road traffic accounts for around 70–80% of NO_2 concentration levels in the city (Perelló et al., 2021). Given that the percentage of the world population

* Corresponding author at: Barcelona Institute for Global Health (ISGlobal), Biomedical Research Park (PRBB), Doctor Aiguader, 88, 08003 Barcelona, Spain.
E-mail address: xavier.basagana@isglobal.org (X. Basagaña).

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living in urban settings is expected to rise to 68% in 2050 (United Nations, 2018) and that poor cognitive and mental health imposes important social and economic costs worldwide (The Lancet Global Health, 2020), it is important to improve knowledge on air pollution as a risk factor to brain health.

Epidemiological studies that are linking air pollution with brain health have explored the possible implication of air pollution in the development or worsening of a wide range of mental health and cognitive endpoints in people of all ages, including memory decline, attention-deficit/hyperactivity disorder, negative mood, depression, anxiety disorders and sleep disorders (Braithwaite et al., 2019, Borroni et al., 2021, Liu et al., 2020). Two biological mechanisms suspected to contribute to these adverse outcomes are the induction of oxidative stress and inflammation (Hahad et al., 2020, Salvi et al., 2020, Grases et al., 2014, Hovatta et al., 2010). For instance, high oxidative stress may lead to a reduction in the production of dopamine, a neurotransmitter essential in the regulation of cognition, attention, emotions and sleep (Levesque et al., 2013, Nieoullon, 2002).

The associations between short-term exposure to air pollution and cognitive and mental health have not been thoroughly investigated so far since most studies have focused on chronic exposures (Cedeño Laurent et al., 2021). As a result, specific short-time windows of exposures to air pollution that can trigger detrimental impacts on several mental and cognitive outcomes are not clearly established (Buoli et al., 2018). Furthermore, studies that have reported a correlation between acute exposure to air pollution and mental health tend to focus more on the aggravation of existing mental disorders (e.g. depression) and less on the changes of potential precursor symptoms of those disorders (e.g. lack of energy) (Bernardini et al., 2020, Buoli et al 2018). Accordingly, the aim of the present study was to assess the associations of short-term exposure to air pollution on different cognitive and mental health end-points in a panel of adults living in Barcelona, Spain. More specifically, we hypothesized that air pollution would have adverse effect on attention, perceived stress, mood and sleep quality.

2. Methods

2.1. Study design and participants

This panel study was part of the CitieS-Health project, a citizen science project on health and environment aiming to involve citizens in all phases of research (CitieS-Health, 2021). The study design was therefore developed in close collaboration with residents of Barcelona (Spain). Details on the co-creation activities conducted for the formulation of the research question and the design of the study are described in Gignac et al. (2022a). With specific regard to recruiting participants for data collection, the study was promoted by researchers from a health research institute and from an organization specializing in civic engagement practices and some citizens who were involved in previous co-creation activities, via their official websites, newsletters and/or social media platforms.

Between September 2020 and March 2021, we conducted a panel study in Barcelona with 288 residents aged 18–76 years in whom we measured different outcomes related to their cognitive and mental health. Persons living outside the Barcelona metropolitan area, younger than 18 years old, who were not understanding Catalan or Spanish, who had dyslexia, ADHD or clinical diagnostic of dementia, Alzheimer or other neurodegenerative diseases were not eligible for the study. Participants were involved for three weeks, more specifically consisting of two weeks of measurement and one week break in between. During the two weeks of measurements, participants had to complete every day one cognitive test, one mental health questionnaire and one questionnaire on daily lifestyle factors, all through the use of a custom-build mobile application (Ethica Data, 2021). Participants were required to install the app on their personal smartphone and one day prior to the start of their three-week follow-up they had to complete a socio-demographic background questionnaire. All participants received a daily reminder triggered on their smartphones at 18h00 and were allowed to complete the tasks from 18h00 to midnight. During these two weeks, we also collected location data using the Ethica Data application which acquired the phone's location record from global positioning system (GPS) satellites or cellular network. This information was collected only for participants who granted permission to access their location data. The study protocol was approved by Parc de Salut Mar Clinical Research Ethics Committee (approval number: 2020/9375), and informed consent was obtained from all participants.

2.2. Daily cognitive test and attention outcomes

The cognitive test used in this study was the Stroop color-word test (Stroop) and it aimed to evaluate the selective attention of the participants. This test has been used previously both in paper and electronic format in similar environmental epidemiology studies (Shehab and Pope, 2019, Cedeño Laurent et al., 2021, Cedeño Laurent et al., 2018). The task consisted of correctly identifying the font color of the words (Supplementary Figure S1). For instance, if the word "Blue" was written in red font, "Red" was the correct answer. The choice of answers (red, blue, black and green) were displayed below the word and participants had to tap on the correct button corresponding to the font color of the word. There were in total 24 trials appearing in random order: six congruent trials (trials in which the font of the color corresponded to the word), six incongruent trials (trials in which the font of the color did not correspond to the word) and six neutral trials (trials in which there was only a sequence of hash symbols written).

From the Stroop test, we obtained three cognitive performance metrics related to selective attention based on the works of Cedeño Laurent et al. (2021) and Cedeño Laurent et al. (2018): (1) Response time, which corresponded to the reaction time in milliseconds in the incongruent trials, (2) Cognitive throughput, which corresponded to number of correct responses per minute and (3) Inhibitory control, which was calculated as the difference between incongruent reaction time and mean congruent reaction time. An increase in response time and inhibitory control and a decrease in cognitive throughput indicated a deterioration in selective attention. Since participants were performing this test every day, the risk of a "learning effect" was considerable and thus, we z-score transformed each metric by subtracting the daily mean of all participants and dividing it by the daily standard deviation of all participants.

2.3. Socio-demographic, mental health and lifestyle factors questionnaires

One day prior to their three-week follow-up, participants had to complete a baseline questionnaire to provide information about socio-demographics, including age, gender, smoking status, residential address, district of the residence, education level and psychological status (if participants had or not a diagnosed psychiatric disorder). These variables were considered as the time-invariant variables of our study.

During a total of 14 days, participants had to complete two short questionnaires; one on different dimensions of mental health and the other about different lifestyle factors within the past 24 h (Supplementary Table S1). The questionnaire on mental health comprised four questions and all were on a Visual Analog Scale (VAS) using an unmarked ruler with labelled endpoints. The first item evaluated the perceived stress of the participant, ranging from Very low (0) to Very high (10). Previous studies demonstrated that using VAS has good validity to measure perceived stress in adults (Lesage et al., 2012, Lesage and Berjot, 2011, Mitchell et al., 2008). The second and the third items evaluated the perceived mood of the participants based on bipolar affective states: well-being (Unhappy (0) to Happy (10)) and energy or arousal (Sleepy (0) to Wide-awake (10)). For both items, we adopted similar features of the validated Affective Slider for the measurement of human emotions created by Betella et al. (2016). The fourth item evaluated was the perceived general sleep quality of the participant over the previous night, ranging from Very bad (0) to Very good (10). This item was not validated, but previous studies using similar single-item self-report measures of sleep quality provided evidence of their reliability and validity (Snyder et al., 2018, Atroszko et al., 2015, Cappelleri et al., 2009).

The last questionnaire was composed mainly of yes–no questions about different lifestyle factors in the past 24 h. The factors were the following: physical activity (30 mins or more), five hours or more of computer screen, hours outside home, healthy diet, alcohol, energetic drink and drug consumption, feeling sick and if other factors might have affected their performance in the Stroop test or affected their stress, mood or sleep quality. The list of questions to obtain information on these factors can be found in Supplementary Table S1. All these factors were considered as time-varying variables.

2.4. Air pollution exposure assessment

NO_2 was pre-specified as our main ambient air pollution exposure in the research protocol because it is known to be a good marker of traffic pollution in the city. Also, NO_2 was chosen since it was possible to estimate its exposure in three different ways due the availability of 1) hourly measurements from Barcelona monitoring stations, 2) hourly spatiotemporal models for NO_2 in the city and 3) personal NO_2 passive samplers. First, we calculated the mean NO_2 concentrations (in $\mu g/m^3$) of the nine air quality monitoring stations of the city of Barcelona 12 h (NO_2 12 h) and 24 h (NO_2 24 h) before the tasks were completed by the participants. Second, for participants who shared their location data, we calculated the mean NO_2 concentrations (in $\mu g/m^3$) 12 h and 24 h before the tasks were completed using validated hourly street-level NO_2 concentrations maps of Barcelona corresponding to the study period that were developed by Lobelia Earth (2021). Lobelia Air is an observation-based system providing hourly NO_2 concentrations at street-level resolution and uses a two-stage approach. In the first stage, to run an urban-air quality model, hourly variability in meteorological conditions and emission proxy data (traffic and residential) were taken into account, which was dynamically calibrated with recent measurements. In the second stage, current measurements were used in a data assimilation schema (optimal interpolation) (Mijling, 2020). For the period of time that participants were going outside Barcelona, we used air quality estimates from the Copernicus Atmosphere Monitoring Service (CAMS) to estimate NO_2 concentrations. In particular, we used the ENSEMBLE model hourly analysis of NO_2 concentration at the Surface on Europe, at a resolution of 0.1 degrees (METEO FRANCE et al., 2020).

Third, we measured personal exposure to NO_2 using Palmes-type passive diffusion tubes (Gradko International, England) (Yu et al., 2008). We asked participants to wear the tube for one week, equivalent to 168 h of exposure. Study participants were given a monitoring form to indicate the date and the time they started and ended wearing the tube as well as to report any incidences when wearing it. The analysis of the tubes was conducted at Gradko's laboratory. Personal exposure to NO_2 was expressed as the average concentration ($\mu g/m^3$) over the monitoring period (one week). This average was obtained by calculating the concentration of compounds on the tube with the uptake rate.

Furthermore, we estimated the concentrations (in $\mu g/m^3$) of two other air pollutants, $PM_{2.5}$ and black carbon for the day in which the tasks were completed. The mean $PM_{2.5}$ concentration was the average from six monitoring stations in Barcelona whereas the daily mean BC concentration came from one a single research urban background supersite (Palau Reial, IDAEA-CSIC) in the city.

2.5. Meteorological parameters

We obtained averages of temperature (°C),accumulated precipitation (mm), relative humidity (%) and atmospheric pressure (hPa) from the Catalan Service of Meteorology (http://www.meteo.cat, accessed on 4 August 2021). Due to very low quantity of precipitation during the days included in the study period, we treated accumulated precipitation as a binary variable, i.e. as "yes" or "no" event. When exploring our model adding meteorological parameters, we found that relative humidity and atmospheric pressure were not statistically significant and thus, only precipitation and mean temperature parameters were kept for the analysis.

2.6. Natural spaces indicator

Recent reviews of the literature have suggested that the residential proximity to natural spaces, including green and blue spaces, can affect positively mental health and well-being such as by reducing stress and improve cognitive functions such as by increasing attentional control (Gascon et al., 2017, Gianfredi et al., 2021, Stevenson et al., 2018). Natural spaces may affect mental health indirectly as they have been also associated with lower levels of air pollutants and thus, they could potentially modify the NO_2 effect on mental health (Son et al., 2021).

We assessed the exposure to natural spaces as the presence or not of green and blue spaces within 300 m from the residential address of the participant at time of enrolment. This distance represents around five minutes' walk of participants' homes and is a common indicator to study the effect of natural spaces on health (World Health Organization, 2016). Following previous studies (O'Callaghan-Gordo et al., 2020, Triguero-Mas et al., 2017), we used the Urban Atlas categories of land use and land cover to consider green space as "public green areas for predominantly recreational use such as gardens, zoos, parks of at least 0.25 Ha and/or forest (i.e. forests with ground coverage of tree canopy $>$ 30%, tree height $>$ 5 m, including bushes and shrubs at the fringe of the forest of at least one Ha)". Blue spaces included water bodies of at least one Ha including sea, lakes, rivers and canals. To create this binary indicator, we generated a Euclidean (straight-line) distance buffers by drawing a circle around the geocoded address of residence of the study participants, at a radius of 300 m. This buffer was then spatially intersected with the green and blue spaces land cover from the Urban Atlas map of Barcelona (European Environment Agency, 2018). We performed these spatial queries using geographic information systems (QGIS Desktop, version 3.10.2).

2.7. Residential noise exposure assessment

Another environmental exposure that is suspected to have an adverse effect on cognitive and mental health is noise (Hegewald et al., 2020). Air pollution and noise are highly correlated exposures since one of the main sources of noise is transportation (Tzivian et al., 2015).

To estimate noise exposure in our study, we used the Strategic Noise Map of Barcelona (Generalitat de Catalunya, 2016). We characterized noise exposure as the total environmental noise including all sources (road traffic, railway, industry, etc.). An average day–evening–night noise level (L_{den}) above 55 dB was defined by the European Environment Agency (2019) as the threshold for excess exposure that can be potentially harmful for human health. To attribute the L_{den} value to each participant's residence (residential noise exposure), we identified the street that was the closest to the geocoded residential address (nearest neighbor spatial joins using QGIS) and we created a binary indicator of whether the street was higher than 55 dB L_{den}.

2.8. Statistical analyses

We examined the histogram of model residuals to assess the normality assumption distribution of the outcome variables. We applied linear regression with random effects by participant to estimate intra-individual associations, controlling for day of the week, mean temperature, precipitation, sociodemographic characteristics (age, gender, education, smoking status and psychological status), residential availability to natural spaces, residential noise exposure and time-varying factors. Time-varying factors were included in the model if they showed a statistically significant (p-value < 0.05) crude association with one of the attention outcomes. The same process to select the time-varying factors for adjustment was done for the model with mental health outcomes. We used linear splines with two knots to test for potential non-linear effects. We reported the p-value for a test of the resulting three fitted slopes being equal, and visually inspected the fitted predictive function to assess whether assuming linearity was reasonable.

Participants may experience what is called an "emotional inertia", which is a concept that refers to the correlation of an emotion with itself over a time-lagged period (Kuppens et al., 2010). To control for that, our models accounted for the possible temporal dependence of certain mental health outcomes (perceived stress, well-being and energy/arousal) between consecutive days by including a first-order autocorrelation component.

The estimated effects were reported as follow. For exposure to NO_2, the estimated effects were reported for a 30 μg/m^3 increase in NO_2 and this value was determined according to the difference between the 90th percentile and the 10th percentile of the observed distribution of NO_2 concentrations across all participants. In other words, the estimated effect represented a comparison between a clean day (taken as a day with values in the 10th percentile) and a polluted day (taken as a day with values in the 90th percentile) in our study setting. For exposure to daily $PM_{2.5}$ and BC, the estimated effects were reported for a 10 μg/m^3 and 1.4 μg/m^3 increase, respectively and these values were also determined according to the difference between the 90th percentile and the 10th percentile of the observed distribution of concentrations across all participants.

The effect estimates for the three outcomes (response time, cognitive throughput and inhibitory control) derived from the Stroop test were expressed as changes in z-scores. To understand those z-score changes in a meaningful scale, we additionally reported the changes due to air pollution as a percentage of the individual maximum variation. To do so, we divided the regression coefficient by the average difference between the maximum and the minimum values of the outcome variable over all days. As the four items related to mental health were based on a 0 to 10 point scale, the effects estimates were presented as change in points for an increase in the air pollutants concentrations. An increase in points for stress indicated higher perceived stress level, while a decrease in points in the two mood states (well-being and energy) and sleep quality indicated detrimental effects on these variables.

When specifically analyzing NO_2 exposure using GPS data (for 12 h and 24 h), we excluded observations (person-days) for which the total time of recorded GPS data was<10 h. This threshold was based on a common valid daily minimum temporal GPS wear time used by other public health studies (Harada et al., 2018, Loebach and Gilliland, 2016) and the fact that the median total time recorded of GPS data in our observations was 9.3 h. The method of handling missing data in days with>10 h of recorded GPS data was by using the last known location data (coordinates) available. All data were imputed with no limit with regard to time or distance of lapse.

Moreover, we conducted a stratified analysis by the presence of natural spaces around the residence and by residential noise exposure and tested the interactions of both. Sensitivity analysis comprised the same methodology but using participant ID as fixed effect or further adjusting the model with sleep quality, since the latter is considered an important contributing factor to the worsening of cognitive performance and mental disorders (Tahmasian et al., 2020). Another sensitivity analysis was to further adjust the model that assessed the estimated effect of air pollution on cognitive outcomes for sleep quality, perceived stress and well-being.

Finally, we conducted a cross-sectional analysis with the average NO_2 concentration measured from the passive tube and the results of the Stroop test and mental health questionnaire on the day the participants finished wearing the tube. In this analysis, we only included participants who used the tube for six days (greater than or equal to 144 h of exposition) and no more than eight days (lower than or equal to 192 h). We fitted a linear regression model adjusting for day of the week, age, gender, education, smoking status, psychological status, presence of natural spaces, residential noise exposure as well as all time-variant variables retrieved in the daily questionnaire. We also further adjusted this model for sleep quality and the month of the year. We considered statistical significance at $p < 0.05$. All analyses were conducted using Stata 16.1 (StataCorp, College Station, TX, USA). Power calculations about the sample size are provided in Supplementary Material. The dataset used for this study is available for download and free use through the file repository Zenodo (Gignac et al., 2022b).

3. Results

The study population characteristics at baseline and during the study period are summarized in Table 1. The majority of the participants were women (70.7%) and had a university degree (82.4%). The mean (standard deviation [SD]) age was 37.9 (12.1) years. Around 62.4% of the participants did not reside close to a natural space and 83.3% were residing close to a street with noise level higher than 55 dB. Only a minority of participants reported being an active smoker or exposed to secondhand smoke. During the study period, the majority of the observations (person-day) reported having done physical activity (65.8%), had a healthy diet (76.1%) and consumed energetic drinks (63.8%) (Table 1). The average number of Stroop tests completed per participant was 11.

Table 2 shows descriptive statistics on air pollution concentrations and mean temperature during the study period. The mean NO_2 at 12 h and at 24 h from the nine air quality monitoring stations of the city of Barcelona were 31.0 (SD = 13.4) μg/m^3 and 30.9 (SD = 12.0) μg/m^3, respectively. Similarly, on average, the mean NO_2 concentrations using GPS data of the participants coupled with spatiotemporal modelled concentrations was 31.2 (SD = 14.5) at 12 h and 30.4 (SD = 12.4) at 24 h. Correlations between NO_2, $PM_{2.5}$ and BC were high (r values between 0.51 and 0.85), and specifically between the NO_2 using monitoring stations and GPS data as well (r values between0.71 and 0.88) (Supplementary Table S3). Descriptive statistics on results of variables from the Stroop test (before z-transformation) and mental health questionnaire during the study period can be found in Supplementary Table S4.

Table 3 shows the associations between cognitive and mental health outcomes and recent air pollution (NO_2 exposure after 12 h and 24 h) based on repeated attention test performances (n = 2,457). Generally, the changes induced by mean NO_2 concentrations estimated at 12 h and 24 h were similar, except for the changes induced to perceived stress. Also, we found more statistically significant changes using the 12 h period. When using NO_2 concentrations estimated from all monitoring stations in the previous 24 h, we only found statistically significant changes in response time (β 0.08 95% CI: 0.01, 0.14) for a 30 μg/m^3 increase in NO_2 concentrations. Put differently, the change in response time associated with a 30 μg/m^3 increase in NO_2 was equivalent to around 5% of the observed individual daily variation in response time (Fig. 1). When using NO_2 concentrations in the previous 12 h (from monitoring stations), we observed a higher response time (β 0.07, 95% CI: 0.01, 0.14) and a lower cognitive throughput (β −0.08, 95% CI: −0.15, −0.01) (increase inattentiveness) associated with an increase of 30 μg/m^3 exposure to NO_2. When using mean NO_2 concentrations based on location data, we found no statistically significant changes in cognitive outcomes for both lag periods.

Regarding mental health outcomes, for each increase of 30 μg/m^3 in mean NO_2 concentrations from all monitoring stations at a lag of 12 h, perceived stress increased by 0.25 points (CI 95%: 0.04 to 0.45), energy decreased by 0.20 (CI 95%: −0.36 to −0.03) and sleep quality decreased by 0.37 (CI 95%:−0.56 to −0.18). Using location data to estimate exposure to NO_2, we found only statistically significant changes in perceived stress at lag of 12 h and 24 h with an increase of 0.44 (CI 95%: 0.13 to 0.77) and 0.47 (CI 95%: 0.14 to 0.79) points, respectively.

Table 1
Characteristics of the study participants at baseline (n = 288) and of time-varying factors during the study period.

Characteristics at baseline (% missing)	Category	N (%) or N (mean, SD)
Gender (0.3%)	Female	203 (70.7%)
	Male	83 (28.9%)
	Other	1 (0.4%)
Age, in years (5.2%)	–	273 (37.9, 12.1)
Education level (9.4%)	Primary school or less	7 (2.7%)
	Secondary school	39 (14.9%)
	University	215 (82.4%)
Residential district (4.9%)	Sant Martí	59 (21.5%)
	Eixample	51 (18.6%)
	Gràcia	45 (16.4%)
	Sants-Monjuïc	23 (8.4%)
	Ciutat Vella	21 (7.7%)
	Sant Andreu	21 (7.7%)
	Horta-Guinardo	18 (6.6%)
	Sarria Sant-Gervasi	16 (5.8%)
	Nou Barris	9 (3.3%)
	Les Corts	5 (1.8%)
	Other	6 (2.2%)
Active or passive smoking (10.4%)	Yes	57 (22.1%)
	No	201 (77.9%)
Diagnosed with a psychiatric disorder (11.5%)	Yes	57 (22.1%)
	No	238 (77.9%)
Presence of natural space around the residence [a] (10.4%)	Yes	97 (37.6%)
	No	161 (62.4%)
Residential proximity to high ambient noise level street[b] (10.4%)		
	Yes	215 (83.3%)
	No	43 (16.7%)
Time-varying variables [c]		
Physical activity (30 mins or more) (3.5%)	Yes	2,126 (65.8%)
	No	1,106 (34.2%)
Computer screen time (5 h or more) (3.6%)	Yes	1,615 (50.51%)
	No	1,612 (49.95%)
Healthy diet (3.6%)	Yes	2,455 (76.1%)
	No	771 (23.9%)
Alcohol consumption (3.8%)	Yes	822 (25.5%)
	No	2,400 (74.5%)
Energetic drink (3.7%)	Yes	2,056 (63.8%)
	No	1,169 (36.3%)
Drug consumption (3.6%)	Yes	60 (1.9%)
	No	3,167 (98.1%)
Feeling sick (3.8%)	Yes	538 (16.7%)
	No	2,683 (83.3%)
Other factors (4.1%)	Yes	1,022 (31.8%)
	No	2,188 (68.2%)
Time outside home, in hours (3.5%)	–	3,231 (5.2, 4.2)

[a] We assessed the exposure to natural spaces as the presence or not of green and blue spaces within 300 m from the residential address of the participant at time of enrolment.
[b] High ambient noise level street was considered if the closest street from the residence had a L_{den} value above 55 dB.
[c] N denotes the number of observations (person-day).

The outcome variables were reasonably normally distributed and the model results did not change after excluding the outliers of attention outcomes (Supplementary Figure S2 and Table S2). When testing non-linearity of our models, we found significant results between NO2 concentrations from all monitoring stations and using GPS data at a lag of 12 h and 24 h with perceived stress and well-being outcomes, but a visual inspection of the plots suggested a that a linear approximation was reasonable (Supplementary Figure S3).When using other pollutants as exposures in the analyses for cognitive and mental health outcomes, we only found decreases in energy or sleep quality associated with increases in BC concentrations, and no associations with $PM_{2.5}$ (Supplementary Table S5).

Table 2
Average levels of air pollution and mean temperature prior to the starting time of the test completed among study participants on the 160 participation days during the study period (September 2020 to March 2021).

Variable	N [a]	Mean (SD)	Min	P25	Median	P75	Max
Air pollution, μg/m^3							
NO_2 12 h – Monitoring stations	3,348	31.0 (13.4)	5.2	21.3	29.5	39.8	85.0
NO_2 24 h – Monitoring stations	3,348	30.9 (12.0)	5.8	21.7	30.2	38.4	68.3
NO_2 12 h – Using GPS data	3,146	31.2 (14.5)	0.5	20.0	30.1	41.0	91.4
NO_2 24 h – Using GPS data	3,151	30.4 (12.4)	0.7	21.3	30.2	37.9	75.1
NO_2 – Passive tube (168 h)	251	26.4 (9.6)	1.8	20.7	25.7	31.0	64.2
Daily $PM_{2.5}$	3,348	13.2 (3.6)	8.0	10.2	12.5	15.7	40.0
Daily BC	3,068	0.9 (0.6)	0.6	0.5	0.8	1.2	4.1
Mean temperature, (°C)							
12 h	3,348	16.2 (3.7)	8.4	13.5	15.3	18.5	27.2
24 h	3,348	15.3 (3.6)	7.7	13.0	14.2	17.5	26.0

[a] N denotes the number of observations (person-day) or number of participants for the passive tube.

Additional adjustment for sleep quality changed only a few results, where changes in perceived stress and energy using mean NO_2 concentrations based on the monitoring stations data at lag 12 h were no longer statistically significant (Supplementary Table S6). Associations persisted after further controlling for sleep quality, perceived stress and well-being in our model with response time and cognitive throughput (Supplementary Table S7). After changing participant's ID as fixed effect, the results for NO_2 did not change in cognitive outcomes nor with BC in mental health outcomes (energy/arousal and sleep quality) (Supplementary Table S8 and S9). However, we observed inconsistencies in the association between well-being and NO_2, with a change of direction of the estimates compared to the main analysis.

We detected statistically significant interactions by the presence of natural spaces (Supplementary Table S10 and S11), but none were found with the residential noise exposure. At a lag of 24 h, NO_2 was associated with a higher response time z-score (i.e. worse attention performance) in adults residing not close to a natural space (β = 0.15; 95% CI: 0.07, 0.24) and with somewhat lower response time z-score for those residing close to a natural space (β = -0.04; 95% CI: −0.15, 0.07) (p-interaction < 0.01). At a lag 12 h, NO_2 was associated with a lower cognitive throughput z-score (i.e. worse attention performance) in adults residing not close to a natural space (β = -0.14; 95% CI: −0.23, −0.05) while cognitive throughput z-score was not affected for those residing close to a natural space (β = 0.01; 95% CI: −0.10, 0.13) (p-interaction < 0.01). There was no evidence of modification by the presence of natural spaces between air pollution (NO_2 and BC) and mental health outcomes.

Finally, a total of 190 participants wore the passive tube for an average time of 165 h. Average NO_2 concentration during the week was of 25.9 μg/m^3. Similar to what we found in the main analysis, in this cross-sectional analysis we observed statistically significant changes in response time (β 0.02; 95% CI: 0.00, 0.04) and cognitive throughput (β − 0.02; 95% CI: −0.05, −0.00) using NO_2 exposure measured with passive tubes (Table 4). However, we found no statistically significant

Table 3
Changes in cognitive and mental health outcomes and CI 95% for each 30 µg/m^3 of air pollution (NO_2) levels.

	N	NO_2 – 24 h			NO_2 – 12 h		
		β	95% CI	*p*-value	β	95% CI	*p*-value
Stroop test [a]							
z-response time	2,457	0.08	(0.01, 0.14)	0.03 *	0.07	(0.01, 0.14)	0.03*
z-cognitive throughput	2,457	−0.07	(−0.14, −0.00)	0.05	−0.08	(−0.15, −0.01)	0.02*
z-inhibitory control	2,457	0.04	(−0.07, 0.15)	0.51	0.07	(−0.04, 0.18)	0.20
		NO_2–24h GPS			**NO_2–12h GPS**		
	N	**β**	**95% CI**	***p*-value**	**β**	**95% CI**	***p*-value**
z-response time	1,147	0.02	(−0.09, 0.12)	0.75	0.03	(−0.07, 0.13)	0.52
z-cognitive throughput	1,147	−0.04	(−0.15, 0.07)	0.44	−0.06	(−0.17, 0.05)	0.30
z-inhibitory control	1,147	0.01	(−0.14, 0.17)	0.86	0.03	(−0.12, 0.18)	0.70
		NO_2–24h			**NO_2–12h**		
	N	**β**	**95% CI**	***p*-value**	**β**	**95% CI**	***p*-value**
Mental health questionnaire [b]							
Perceived stress	2.621	0.13	(−0.09, 0.34)	0.24	0.25	(0.04, 0.45)	0.02 *
Well-being	2,657	−0.03	(−0.19, 0.13)	0.72	−0.10	(−0.25, 0.05)	0.20
Energy	2,640	−0.20	(−0.37, −0.03)	0.02 *	−0.20	(−0.36, −0.03)	0.02 *
Sleep quality	2,630	−0.24	(−0.43, −0.04)	0.02 *	−0.37	(−0.56, −0.18)	< 0.01 *
		NO_2–24h GPS			**NO_2–12h GPS**		
	N	**β**	**95% CI**	***p*-value**	**β**	**95% CI**	***p*-value**
Perceived stress	1,232	0.47	(0.14, 0.79)	0.01 *	0.44	(0.13, 0.77)	0.01 *
Well-being	1,250	−0.07	(−0.32, 0.17)	0.55	−0.06	(−0.30, 0.18)	0.60
Energy	1,238	−0.13	(−0.40, 0.14)	0.33	−0.13	(−0.39, 0.14)	0.36
Sleep quality	1,234	−0.20	(−0.49, 0.10)	0.19	−0.21	(−0.50, 0.08)	0.16

Statistically significant changes (p-value < 0.05) are indicated with a (*).
[a]Analyses were adjusted for day of the week, mean temperature, precipitation, age, gender, education, smoking status, psychological status, drugs, energetic drinks, feeling sick, presence of natural spaces and residential noise exposure.
[b]Analyses were adjusted for day of the week, mean temperature, precipitation, age, gender, education, smoking status, psychological status, drugs, energetic drinks, feeling sick, hours outside, physical activity, hours of computer screen, healthy diet, alcohol, other factor, presence of natural spaces and residential noise exposure. Analyses were corrected for autocorrelation, except for sleep quality.

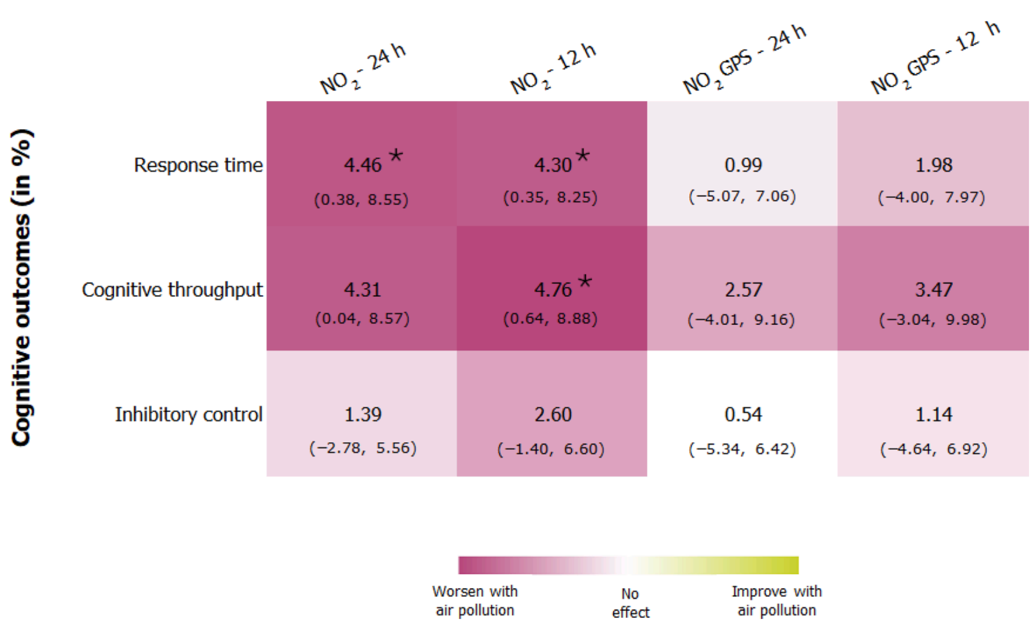

Fig. 1. Changes in cognitive outcomes due to short-term air pollution exposure and CI 95% expressed as percentages of the individual variability in z-score. Statistically significant changes (p-value < 0.05) are indicated with a (*).

changes for stress, well-being, energy and sleep quality.

4. Discussion

In this panel study, we found evidence for an association between short-term exposure to air pollution and attention, perceived stress and sleep quality after controlling for several factors such as physical activity, alcohol consumption and time spent in front of the computer. We did not observe any statistically significant associations with inhibitory control (selective attention) nor with well-being. Also, statistically significant associations were found with energy/arousal and sleep quality when looking at daily BC but none were found with daily $PM_{2.5}$.

Table 4
Association between cognitive and mental health outcomes and short-term air pollution exposures using personal passive tubes (n = 190).

Cognitive and mental health outcomes	Model 1[a]				Model 2[b]			
	N	β	95% CI	*p*-value	N	β	95% CI	*p*-value
Stroop test								
z-response time	129	0.02	(0.00, 0.03)	0.03 *	127	0.02	(0.00, 0.04)	0.03 *
z-cognitive throughput	129	−0.02	(−0.04, −0.00)	0.02 *	127	−0.02	(−0.05, −0.00)	0.03 *
z-inhibitory control	129	0.00	(−0.01, 0.02)	0.64	127	0.01	(−0.01, 0.02)	0.47
Mental health questionnaire								
Perceived stress	151	−0.03	(−0.08, 0.01)	0.16	150	−0.04	(−0.09, 0.01)	0.13
Well-being	153	0.01	(−0.02, 0.04)	0.57	151	0.01	(−0.02, 0.05)	0.48
Energy	152	0.00	(−0.03, 0.04)	0.88	151	−0.00	(−0.03, 0.03)	0.99
Sleep quality	151	0.02	(−0.03, 0.06)	0.45	Not applicable			

Statistically significant changes (p-value < 0.05) are indicated with a (*).
[a] Model 1 adjusting for day of the week, age, gender, education, smoking status, psychological status, presence of natural spaces, residential noise level as well as all time-variant variables retrieved in the daily questionnaire.
[b] Model 2 is Model 1 additionally adjusted for month of the year and sleep quality.

Moreover, we detected statistically significant interactions by residential proximity to natural spaces, showing that the adverse effect of NO_2 on attention performance was only present among participants not residing close to natural spaces.

We found that selective attention, measured as response time and cognitive throughput, was associated with short-term exposure to air pollution. There are only a few studies that investigated the alterations induced by a short-term exposure to air pollution on attention functions in healthy adults (Shehab and Pope, 2019, Gao et al., 2021). Shehab and Pope (2019) conducted an experimental study in which 30 healthy adults had to perform a battery of cognitive tests including the Stroop test after approximately 30 min of commuting next to a major road either by walking, cycling, taking the bus or train (the levels of NO_2 were not estimated). Contrary to our results, the authors reported no statistically significant differences in the Stroop scores following the commuting exposure. However, they found that the intervention had an adverse effect on the selective attention (measured using the Ruff 2 and 7 test) and on general cognitive performance (measured using the Mini-Mental State Examination) of the participants. A possible explanation for these different results may be that this study used a different version of the Stroop test in which subjects were asked to read out loud the color of the word, which thus involved a different sub-domain of cognition that is motor speech/reading. The timing of exposure was also different (30 min in their study and 12 or 24 h in our study). In Gao et al. (2021) study, they identified a short-term ($\leq$28 days) association between $PM_{2.5}$ and general cognitive function (including attention) among older men (mean age of 69.2 years). We did not find significant associations with $PM_{2.5}$ and a possible explanation is that older adults are more susceptible to cognitive effects of air pollution. It is worth pointing out that, in healthy children, which is also a more susceptible population group, one can find inconsistent results on the relationship between short-term exposure air pollution and attention processes (Gignac et al. 2021, Saenen et al., 2016).

Our results showed that short-term exposure to NO_2 was associated with higher perceived stress rating. This finding is similar to that of Mehta et al. (2015), who observed that, in a sample of 987 older men (mean age of 69 years), weekly levels of NO_2, $PM_{2.5}$ and BC were associated with higher levels of perceived stress. In contrast, however, Nuyts et al (2019) found that, in a panel of 20 healthy volunteers of between 58 and 76 years of age, an increment of 10 $\mu g/m^3$ of personal NO_2 exposure in the previous five days was not associated with higher perceived stress rating. It should be noted, that both Mehta et al. (2015) and Nuyts et al. (2019) used a different validated measurement for evaluating stress (the Perceived Stress Scale) in comparison to our measurement. Nonetheless, if we consider that high perceived stress plays a role in the development and exacerbation of other mental disorders such as anxiety or depression (Cohen et al., 1983), our findings are in line with several epidemiological studies investigating the estimated effect of short-term increase in NO_2 with mental disorders (Lu et al., 2020, Borroni et al., 2021). For instance, Lu et al. (2020) reported that a short-term increase in NO_2 (per 10 $\mu g/m^3$) was associated with increased hospital outpatient visits for mental disorders.

In our study, we measured two outcomes related to mood, which were subjective well-being and energy. To the best of our knowledge, no previous studies have investigated the association between air pollution and those same outcomes. Therefore, the comparison of our findings with the literature on air quality and mood is difficult. Nonetheless, since mood is a concept that generally refers to a positive or negative affective state, we could consider here that a lower subjective energy or well-being rating suggest a negative affect and higher rating, a positive effect (Feldman Barrett and Russell, 1999). We found that short-term exposure to NO_2 was associated with a lower subjective energy rating but not with a lower well-being rating. In Nuyts et al. (2019) study, using the Positive and Negative Affect Schedule to measure mood, they found that air pollution was associated with decreases of momentary feelings of positive affect and increases of momentary feelings of negative affect. Furthermore, the lack of consistency between our analyses with fixed or random effects may indicate that the results for mood (well-being and energy) could be affected by residual confounding by unobserved time-varying characteristics and therefore these results should be interpreted with caution. Our contradicting findings for an association between air pollution and mood reflects the current inconsistent evidence also found in four European general population cohorts (Zijlema et al., 2016).

In our study, we also found that poor sleep quality was associated with recent exposure to NO_2. Although there is a limited number of studies on air pollution and sleep health that have been conducted so far, the current literature generally shows a negative relationship between exposures to air pollution and different sleep outcomes (Liu et al., 2020). For example, a study of 395,651 older Chinese found that short exposure to NO_2 (lag days 2 and 3) was associated with an increased risk of a hospital visit for sleep disorders (Tang et al., 2020).

Based on our findings and those of the previously mentioned studies, what becomes an apparent source of heterogeneity in the results is the different timing of effects investigated, which can range from less than hour (Shehab and Pope, 2019) to a few days or weeks (Nuyts et al., 2019, Gao et al. 2021, Mehta et al., 2015). This question of timing goes hand in hand with the issue of understanding the possible biological mechanisms as well as identifying the dose where the effects are observed. The biological mechanisms of how an acute exposure to air pollution, such as NO_2 or $PM_{2.5}$, can affect attention, stress and sleep quality in adults remain unclear. The role of oxidative stress and inflammation is a plausible explanation of our findings and are shared mechanisms among the cognitive and mental health endpoints examined in our study. For instance, in a double blind randomized crossover design with ten male adults, Crüts et al. (2008) found that higher median power frequency in the frontal cortex was induced only after 30 min exposure to diesel exhaust, but with a very higher dose. The increase in median power frequency continued to rise one hour after the exposure. The frontal cortex is especially important for humans to perform cognitive task, to control emotional responses such as stress and to regulate mood. Some experimental and animal studies led us to believe that the changes observed in our cognitive and mental health endpoints would have been expressed in a greater way after assessing other short-term timescales of exposure. For example, Salvi et al. (2017) observed that both a high brief dose (30 min/day) and a low dose prolonged (5 h/day) for two weeks to vehicle exhaust were leading to an increase in anxiety and depression-like behaviors and impaired learning-memory function in rats. The authors suggested that NO_2 might have increased the levels of oxidative stress and create a buildup of free radicals in the pre-frontal cortex, hippocampus and amygdala (Salvi et al., 2020). These two former regions of the brain are known to play a role in regulating cognitive functions and the latter region in regulating mood and emotions (Broersen, 2000, Davis and Whalen, 2001). Moreover, in an intervention study including 53 healthy adults aged 22–52, it was observed that short-term (12 h and 24 h) NO_2 exposures were significantly associated with increase in different inflammatory cytokines (Hu et al., 2020). The latter are known for their potential impact on the central nervous system (Block et al., 2012).

In our study, we observed a potential alleviating effect of natural spaces for negative effects of air pollution on cognition. We defined the exposure to natural spaces as the presence or not of green and blue spaces within 300 m from the residential address of the participant. This indicator does not give information about the use nor the quality of those natural spaces, but notwithstanding this issue, this finding is worth consideration for future research to investigate green and blue spaces as potential effect modifier to the impacts of air pollution on the brain (Son et al., 2021). To better understand the impact of air pollution and cognitive health, there is a need to take into account for multiple built and natural environmental influences such as street network, density, mixed land use and determine how individuals interact with those features (Cerin, 2019).

Whilst our results with NO_2 were robust to the sensitivity analyses conducted, particularly for the attention outcomes, it should be stressed there are some inconsistencies between the three different measures of NO_2 exposure. More specifically, we observed similar directions of estimates between NO_2 from monitoring stations and from mobility data, but the latter produced estimates that are lower and with wider confidence intervals, indicating more uncertainty. Also, NO_2 measured from monitoring stations and from passive diffusion tubes are consistent with attention outcomes, but not with mental health outcomes. In this regard, this study helped to reflect some of the advantages and disadvantages in relying on ambient air pollution exposure versus personal air pollution exposure measures (Weisskopf and Webster, 2017). Exposure estimated by monitoring stations from Barcelona may lead to exposure misclassification, but there it has less potential for residual confounding in comparison to using data from NO_2 personal passive tube (Weisskopf and Webster, 2017). Moreover, although personal passive tube could reduce measurement error by increasing the precision of our estimates, personal behaviors could have influenced the exposure and increased a bias in our estimates from reverse causation (e.g. a participant feeling stressed or has a bad mood, thus unwilling to go out, which in turns made him or her less exposed to NO_2) (Weisskopf and Webster, 2017). In this study, however, we were able to take into account many potential variables to decrease uncertainty regarding real exposure such as the amount of time spent away from home. We were also able to estimate another personal NO_2 exposure measurement by using participants' daily mobility data. Daily mobility data was useful to overcome the reduced temporal resolution of the exposure from the passive tube (cumulative exposure for one week). However, missing location data and the uncertainty of predicted concentrations of spatiotemporal models affect the validity of the exposure estimate. With these advantages and disadvantages in mind, the estimates of exposure derived from the fixed monitoring stations are likely to be less affected by potential confounding by personal factors. Besides, the results with monitoring stations were very similar to those obtained when using GPS data of the participants coupled with spatiotemporal modelled concentrations. Regardless of all these issues, it is still of concern to observe that both the average daily and weekly levels of NO_2 concentrations found in our study were higher than the newly recommended short-term (24-hour) air quality guideline level for NO_2 set at 25 $\mu g/m^3$ by the WHO (2021).

This study has several strengths. We used three different estimates for measuring short-term NO_2 exposure and covered different recent time windows of exposure (effects up to 12 h and 24 h, and effects after one week). We also examined mental health symptoms that are related to mental or cognitive disorders instead of the disorders directly (which take more time to develop). This gave us the opportunity to observe changes on cognitive and mental health functions that translates more realistically the biological effect of a short-term air pollution exposure on the brain. Moreover, our repeated measurement study design enabled us to have a high number of measurements and to compare each participant with itself on different days, eliminating possible biases for not having a representative sample of the population. Indeed, even though it does not impact the interpretation of our results, it is important to point out that despite having made considerable efforts to recruit diverse population groups, a majority of our participants were women, highly educated and from districts of moderate to high socioeconomic status.

However, our study had several limitations. First, participants were aged 18–76 and therefore, our findings may not be generalizable to younger children and elderly people for which cognitive, emotional and behavioral development is more vulnerable to air pollution. Second, although our sample size (N = 288) was close to the one determined by a-priori power calculations (N = 300), and the total number of observations (between 1,147 and 2,647, depending on the analysis) is higher than previous panel studies using cognitive tests (Cedeño Laurent et al., 2018, Saenen et al., 2016), a higher sample size may be needed to conduct the secondary analyses (e.g., stratified analyses) and to bring more confidence in the results. Another aspect that could affect the generalizability of the results is the study period, which was ran from September 2020 to March 2021. Thus, this period was a few months after the COVID-19 lockdown in Barcelona where the NO_2 levels had not returned to pre-pandemic levels (annual averages [in $\mu g/m^3$] in 2019: 35.8; in 2020: 26.3; in 2021: 24.6) and mobility patterns had changed. Hence, in this study, it is expected that the population was exposed to lower levels of NO_2 compared to the 'normal' or pre-pandemic days. Third, the lack of an accurate measurement of the perceived stress, mood and sleep quality of the participants calls the quality of the data into question. The different mental health ratings were self-reported and thus, a more objective measure of stress, mood and sleep quality should be employed in future studies. It would also be beneficial to replicate the current findings with validated measures of mood and sleep quality. This third limitation represents a peculiar challenge in conducting a research study in which participants were also involved in designing the study. As such, participants wanted to study several cognitive and mental health outcomes but without having to devote too much time in answering questions every day, which drove researchers to avoid integrating validated questionnaires such as the Positive and Negative Affect Schedule or the Perceived Stress Scale since they are longer to complete. Other than the questionnaires or test, we would recommend taking advantage of wearable technologies that could offer proxy data of these outcomes such as total time of sleep, heart rate, blood pressure, etc. Fourth, linked to our previous discussion about the issues with NO_2 exposure measurements, some aspects of our BC and $PM_{2.5}$ exposure measures may have impeded a representative exposure to these pollutants. For BC and $PM_{2.5}$ exposure measures, we had no hourly measures and therefore, part of the exposure measured occurred after the participants performed the cognitive test and completed the mental health questionnaire. Also, for $PM_{2.5}$ and BC measures, we only had access to the data from six and one station in Barcelona, respectively. Fifth, to examine the association between air pollution and sleep quality, we did not account for indoor air pollution exposure. Considering that people spend almost a third of their day sleeping, the bedroom represents a microenvironment in which indoor air quality may play an important role in sleep quality (Canha et al., 2021). Sixth, the way we assessed noise exposure was not exhaustive and therefore we likely misattributed the noise exposure levels in some of our participants. For instance, it was not possible to know if the residence was actually facing the street assigned, what floor the residence was located, nor we were able to identify if the bedroom had windows facing the street. Lastly, even after controlling for multiple factors in our analysis, there is a possibility of residual bias due to unmeasured confounders, especially with respect to time-varying factors.

5. Conclusions

Our panel study indicated that short-term air pollution exposure may be related to small non-pathological alterations in cognitive and mental functions in adults, more specifically on attention, perceived stress and sleep quality. The presence of natural spaces around the residence may modify the relationship between air pollution and attention performance. Also, the daily average levels of NO_2 observed in this study exceeded those recommended by the WHO, which adds to the concern about health risk of air pollution in cities with heavy traffic like Barcelona. From a research perspective, our study warrants future investigations on acute exposure to air pollution using valid tests along with wearable technologies to study several cognitive and mental health domains. All in all, our findings add to the evidence of the acute impact of poor air quality on cognition, perceived stress and sleep quality as well as provide further incentives to design urban areas for the benefits of people's brains.

CRediT authorship contribution statement

Florence Gignac: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Data curation, Visualization. **Valeria Righi:** Conceptualization, Methodology, Investigation, Resources, Writing – review & editing. **Raül Toran:** Investigation, Writing – review & editing, Funding acquisition. **Lucía Paz Errandonea:** Conceptualization, Methodology, Investigation, Resources, Writing – review & editing. **Rodney Ortiz:** Investigation, Writing – review & editing, Project administration. **Bas Mijling:** Data curation, Writing – review & editing. **Aytor Naranjo:** Data curation, Writing – review & editing. **Mark Nieuwenhuijsen:** Conceptualization, Writing – review & editing, Funding acquisition. **Javier Creus:** Conceptualization, Investigation, Resources, Writing – review & editing, Funding acquisition. **Xavier Basagaña:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2022.107284.

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