TNA User Report

The completed and signed form below should be returned by email to
eurochamp2020@lisa.u-pec.fr

Project title	Impact of short-term air pollution exposure on cognitive function
Name of the accessed chamber	MAC-MICC
Number of users in the project	1
Project objectives (max 100 words)	The purpose of this project is to investigate the impact of air pollution (notably, Diesel Exhaust (DE)) exposure on human cognitive functioning, assuming the inflammation hypothesis as the mechanism behind these effects. Further scientific objectives seek to identify if this is prevalent in the middle-aged population (as previous research focuses on either the developing or aging brain), identify if this impact is seen after purposeful short-term air pollution exposure (as opposed to epidemiological studies which look primarily at chronic air pollution exposure, not manipulated by experimenters), and lastly using psychological tasks relevant to the inflammation hypothesis (as opposed to crude questionnaire measurements previously utilised).
Description of work (max 100 words):	The project involved human participants breathing air mixtures containing either diluted DE, or solely Filtered Air (FA) from the atmospheric chamber for one hour. Exposure to each air mix condition was controlled by having participants sit outside the chamber and inhale the air directly into the mouth and nose utilising a non-rebreather face mask with a tube attached to the chamber. After exposure, participants took part in computer tasks related to learning & memory, social cognition, and executive function. Participants were divided in two groups: Participants in the Immediate Exposure group did the cognitive task immediately after exposure to the chamber air. Participants in the Delayed Exposure group did the cognitive tasks 4 hours after exposure to the chamber air. Blood samples were collected before and after exposure for all participants. In addition, for the participants of the Delayed Exposure group, a third blood sample was collected 4 hours after exposure. Serum was extracted from blood and stored in the -80oC freezer for analysis of inflammatory markers.

Principal Investigator's and group's information	
First name	Juana Maria
Family name	Delgado Saborit
Nationality	Spanish
Activity domain[1]	Earth Sciences & Environment
Home institution	ISGlobal
Institution legal status[2]	RES
Email	Juanamaria.delgado@isglobal.org
Gender	Female
User status[3]	RES
New user	Yes

User 1 Information[4]	
First name	
Family name	
Nationality	
Activity domain	
Home institution	
Institution legal status	
Email	
Gender	
User status	
New user	

User 2 Information	
First name	
Family name	
Nationality	
Activity domain	
Home institution	
Institution legal status	
Email	
Gender	
User status	
New user	

[1] *PLEASE CHOOSE ONLY ONE DOMAIN* Physics; Chemistry; Earth Sciences & Environment; Engineering & Technology; Mathematics; Information & Communication Technologies; Material Sciences; Energy; Social sciences; Humanities.

[2] UNI= University and Other Higher Education Organisation;
RES= Public Research Organisation (including international research organisations and private research organisations controlled by public authority);
SME= Small and Medium Enterprise;
PRV= Other Industrial and/or Profit Private Organisation;
OTH= Other type of organization.

[3] UND= Undergraduate; PGR= Post graduate; PDOC= Post-doctoral researcher; RES= Researcher ENG= Engineer; ACA= Academic; TEC= Technician.

[4] Reproduce the table for each user who accessed the infrastructure

Trans-National Access (TNA) Scientific Report

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Instructions

Please limit the report to max 5 pages, you can include tables and figures. Please make sure to address any comments made by the reviewers at the moment of the project evaluation (if applicable, in this case you were informed beforehand). Please do not alter the layout of the document and keep it in Word version. The report will be made available on the eurochamp.org website. Should any information be confidential or not be made public, please inform us accordingly (in this case it will only be accessible by the European Commission, the EUROCHAMP-2020 project partners, and the reviewers). Please include:

- Introduction and motivation
- Scientific objectives
- Reason for choosing the simulation chamber/ calibration facility
- Method and experimental set-up
- Data description
- Preliminary results and conclusions
- Outcome and future studies
- References

Name of the PI: Dr Juana Maria Delgado-Saborit
Chamber name and location: MAC-MICC, Manchester
Campaign name and period: 07/10/2019-19/11/2019
Text:

• Introduction and motivation

It is known that exposure to air pollution, particularly particulate matter can interrupt the blood-brain barrier and translocate into the brain, causing release of pro-inflammatory cytokines. This promotes inflammation of the brain (neuroinflammation) similar to that of sickness, which in turn has been shown to have an impact on cognitive functions such as memory, social cognition, and executive function.

Only one previous experiment is thought to have used an atmospheric chamber to identify the impact of purposeful short-term DE exposure on human participants to identify changes to human cognition, focusing solely on electroencephography readings to identify changes in brain function as opposed to human behaviour alone (Crüts et al, 2008). With this in mind, this project has a number of unique/innovative aspects.

If it is identified that learning and memory, social cognition, and executive function processes are affected by short-term exposure to air pollutants, specifically DE constituents such as nitrogen dioxide (NO2) and fine particulate matter (PM2.5), then air quality in both educational institutions

and workplaces is crucial. Results could suggest that children attending schools in pollution-rich areas may show performance deficits compared to those attending schools in cleaner areas. Elucidation of the cognitive costs of exposure to poorer quality air may allow for development of interventions to reduce these effects. This study will also support policy makers with evidence for changing legislation regarding DE emission limits and indoor air quality limits in workspaces to ensure productivity of staff. Additionally, industries with workforce exposed to DE (e.g. taxi drivers) will gain knowledge useful to design adequate measures to ensure that cognitive abilities and productivity of their staff are not compromised during the work shift (short-term) as well as reducing long term exposure effects on cognition on their workforce. Ultimately, further information on this topic can be used to ensure the gravity of impact of air pollution exposure is taken into consideration when new laws are made and pressure is needed to combat the continued rise of pollution in urban areas.

This experiment was designed, organised and implemented in conjunction with colleagues from the University of Birmingham: Mr Thomas Faherty and Professors Kim Davis, Janet Raymond and Rob Mackenzie in a 3-way collaboration. I was the only TNA participant.

• Scientific objectives

The purpose of this project is therefore to investigate the impact of air pollution (notably, Diesel Exhaust (DE)) exposure on human cognitive functioning, assuming the inflammation hypothesis as the mechanism behind these effects. Further scientific objectives seek to identify if this is prevalent in the middle-aged population (as previous research focuses on either the developing or aging brain), identify if this impact is seen after purposeful short-term air pollution exposure (as opposed to epidemiological studies which look primarily at chronic air pollution exposure, not manipulated by experimenters), and lastly using psychological tasks relevant to the inflammation hypothesis (as opposed to crude questionnaire measurements previously utilised).

• Reason for choosing the simulation chamber/ calibration facility

This selected chamber has been chosen for a variety of reasons

- Ability to mix air prior to participants breathing it, therefore allowing to double check the air quality
- Using the diesel engine at all times within participant view, so there are no effects of smell or visual cues between conditions
- Use of lights to control temperature and light conditions for all participants to avoid impact of photochemical reaction to the air mix
- Ability to constantly monitor the air quality in the chamber in order so as not to commence exposure if concentrations are introduced above ethically accepted limits

• Method and experimental set-up

The technical work plan has been approved by the University of Birmingham Ethics Committee (Reference number ERN_18-1613).

The project involved human participants breathing air mixtures containing either diluted DE, or solely Filtered Air (FA) from the atmospheric chamber for one hour. Exposure to each air mix condition was

controlled by having participants sit outside the chamber and inhale the air directly into the mouth and nose utilising a non-rebreather face mask with a tube attached to the chamber.

NOx levels in DE were controlled by injection from a cylinder into the charge line and a high capacity ozone generator controls initial ozone concentrations as well as serving as a cleaning agent during flushing between experiments. Cycling between air mix conditions is facilitated by full computer control and monitoring of key chamber conditions. This enables full control of the conditions throughout the experiment. Pollutants were introduced into the chamber at the start of the charging procedure prior to any exposure of participants. Pollutant levels (including NO_2, CO, BC and $PM_{2.5}$) were measured during this procedure and continuously monitored by computers and human operators thereafter during testing, ensuring safe levels are maintained at all times. During the exposures, air was continuously monitored for NOx, CO, BC, $PM_{2.5}$, and total hydrocarbons. The temperature and humidity in the chamber was controlled (suggested at 20° C and 50%, respectively to avoid uncomfortable breathing conditions). As the mix of air is pre-prepared from a known injection of exhaust and a known dilution volume, the concentration of the pollutants of interest (PM2.5 and NOx) is directly measured before any of the participants breathes from the chamber and there is no means by which the pollutant concentration can increase throughout the exposure period.

After exposure, participants took part in computer tasks related to learning & memory, social cognition, and executive function. Participants were divided in two groups: Participants in the Immediate Exposure group did the cognitive task immediately after exposure to the chamber air. Participants in the Delayed Exposure group did the cognitive tasks 4 hours after exposure to the chamber air.

Blood samples were collected before and after exposure for all participants. In addition, for the participants of the Delayed Exposure group, a third blood sample was collected 4 hours after exposure. Serum was extracted from blood and stored in the -80oC freezer for analysis of inflammatory markers.

• Data description

Data has been collected from 88 participants in total. There were 90 participants originally taking part in the experiments, however 2 participants withdraw before exposure due to fainting at blood collection stage.

There were 4 groups of participants according to their exposure to diesel or clean air, and according to completing the cognitive test immediately after exposure, or 4 hours after exposure. The distribution of participants in each group is as follows:

Diesel Exhaust

- Tests done immediately after 1 hour exposure (20 participants)
- Tests done 4 hours after 1 hour exposure (23 participants)

Clean Air

- Tests done immediately after 1 hour exposure (22 participants)

- Tests done 4 hours after 1 hour exposure (23 participants)

All the participants were tested in 2 cognitive domains, such as Social Cognition and Episodic Memory. Each of the cognitive tests is described hereunder:

Social Cognition

Participants look at a fixation cross in the centre of the screen and are tasked with reporting the gender of a target face (left or right of the fixation cross) whilst ignoring a distractor face. Target & distractor faces are either frowning or happy faces (1/3 of distractors are scrambled / non-faces to get a 'baseline' performance). An example of a Social Cognition test is displayed in Figure 1.

Figure 1. Social Cognition test example

Episodic Memory (Sequential / Temporal & Spatial)

Participants are shown a circle populated by images every 10 seconds (Figure 2). They are asked to utilise a story to remember the location and order of these images
After 2 minutes of arithmetic (to distract participants and remove information from working memory) participants drag images from outside circle to their correct location, as shown in Figure 3 (order not tested).

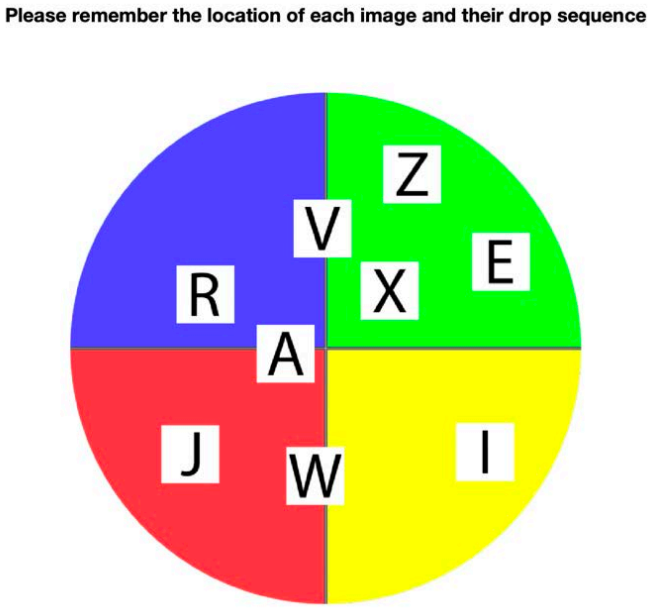


Figure 2. Episodic Memory display of images

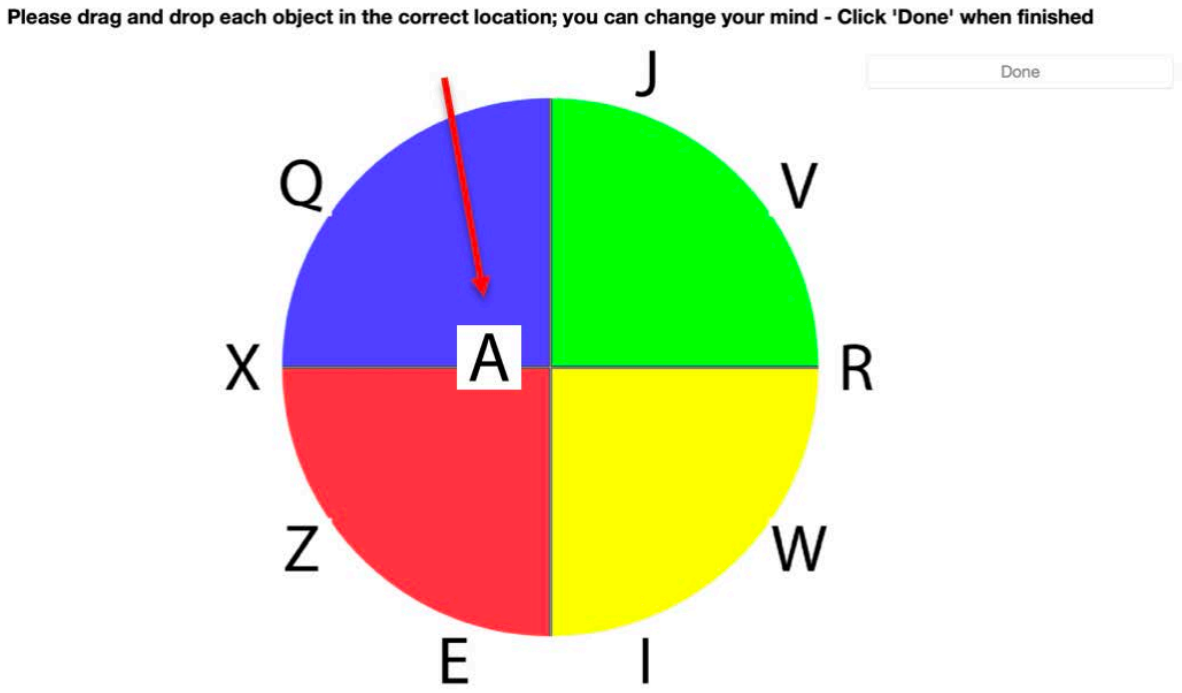


Figure 3. Episodic Memory (Spatial test)

Secondly, participants drag images to their correct order on a line below the circle

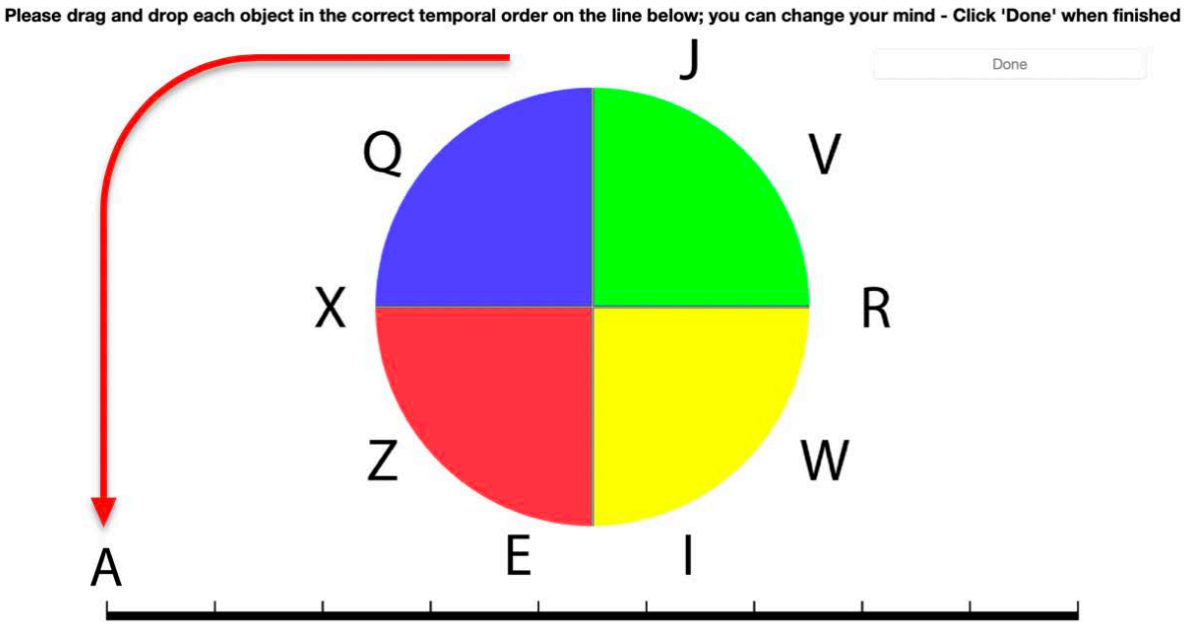


Figure 4. Episodic Memory (Temporal test)

A total of 125 serum samples were retained from blood samples collected. These were collected from the following participants groups:

Clean Air

- 22 Pre Exposure & Immediate Post-Exposure
- 11 Delayed Post-Exposure

Diesel Exhaust

- 29 Pre-Exposure & Immediate Post-Exposure
- 12 Delayed Post-Exposure

• Preliminary results and conclusions

Social Cognition

The results from the Social Cognition tests will be analysed to work out overall reaction times according to pollution exposure. This information will allow us to identify if diesel exhaust exposure causes psychomotor slowing. We will also analyse the results of this experiment to identify if certain emotions are more distractable after pollution exposure compared to clean air exposure.

Episodic Memory (Sequential / Temporal & Spatial)

The results of the Episodic Memory task will be analysed to evaluate participant's performance in the domains of episodic memory for sequences as well as spatial location. This information is relevant to daily life tasks such as remembering a shopping list or navigating through a supermarket.

We aim to analyse the blood samples to identify any changes in inflammatory proteins, cortisol, and other measures both immediately and 4 hours after exposure to pollution compared to clean air.

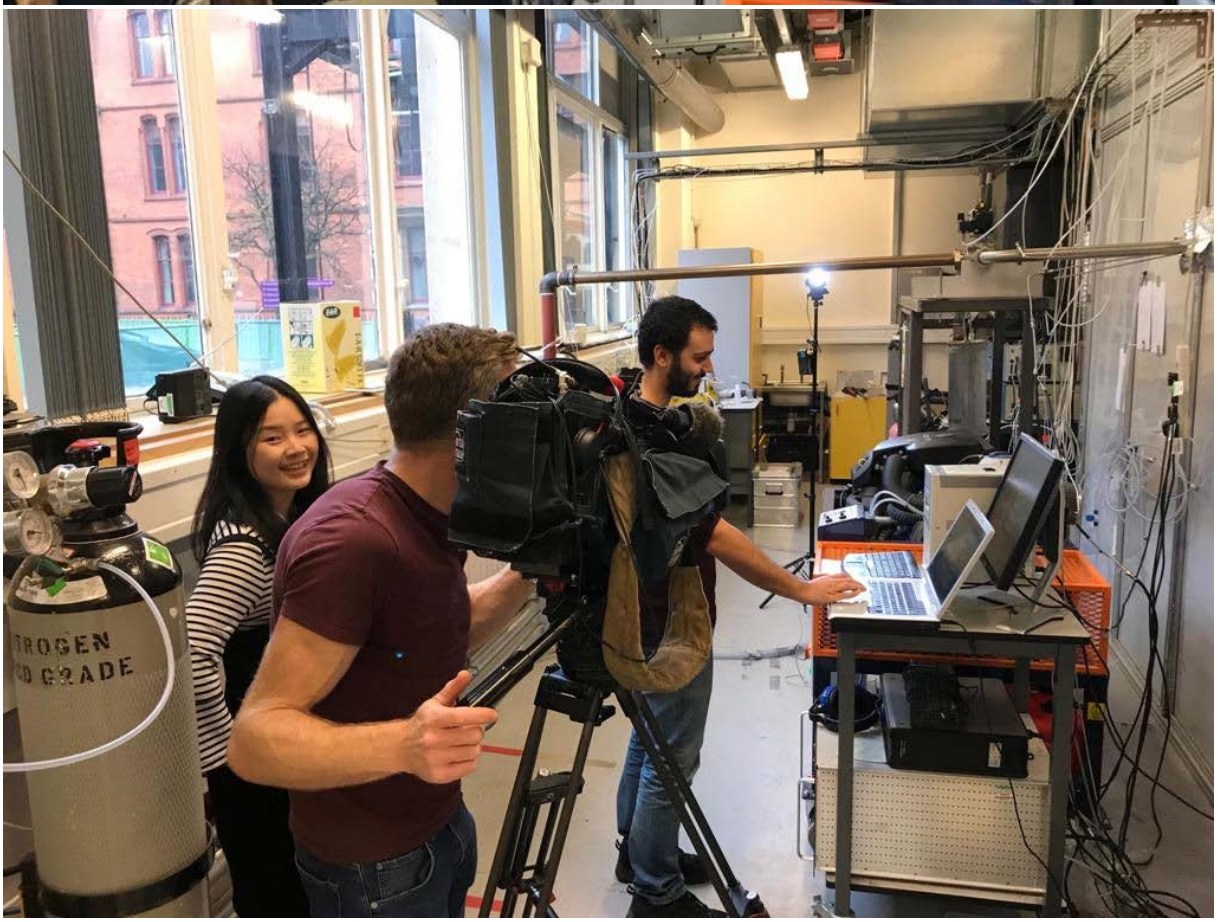
• Outcome and future studies

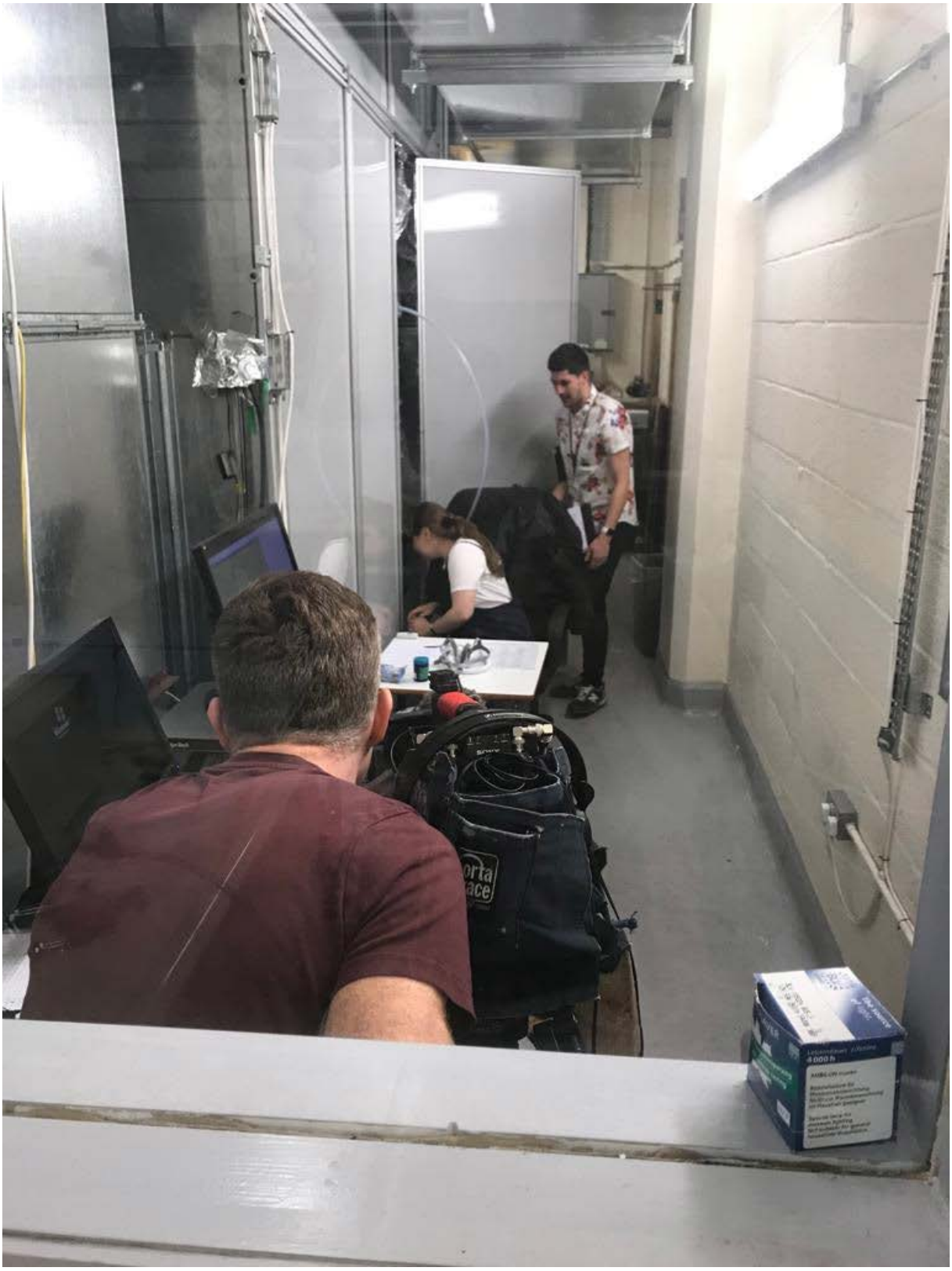
The results of the cognitive tests and the blood biomarkers are subject of ongoing analysis that will be written up for open access peer-reviewed publication within early 2020.

Once the results of the current experiment are fully analysed, I will engage with the partners in this experiment to design a follow up study.

The experiment was featured in one of the ITV programmes on science outreach. It has yet to be broadcasted on television. I enclose below some of the pictures taken during the date that the ITV crew members visited the laboratory.

Integration of European Simulation Chambers for Investigating Atmospheric Processes. Towards 2020 and beyond





The experiment was also showcased to the local Member of British Parliament.

• **References**

N/A