Impacts of inhaled particles on the brain

- A scoping study funded by STFC Air Quality Network (SAQN)

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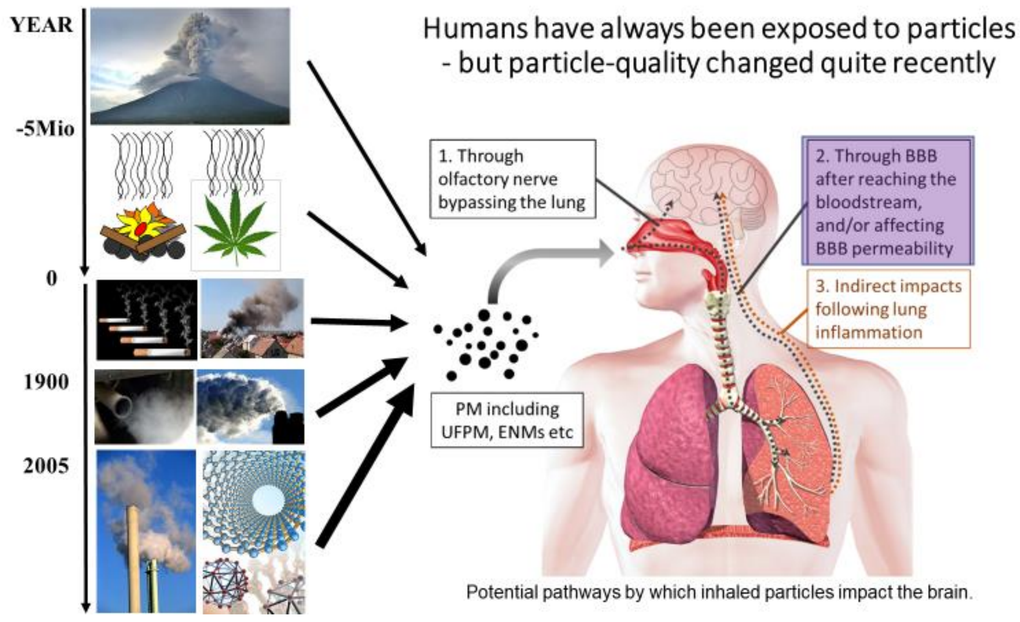
INTRODUCTION

Worldwide, around 50 million people live with dementia and this number is expected to triple over the next 30 years, representing a significant population health challenge. It is estimated that the economic impact of dementia is greater than the combination of cancer and heart disease. In the UK, the total cost of dementia, including costs to the NHS, paid social care and unpaid care, has risen to £34.7bn and will rise further to £94.1bn by 2040. In the 2020 update report of the Lancet Commission on Dementia Prevention, Intervention, and Care, **air pollution was one of the three newly added modifiable life-course risk factors for dementia**. The aetiology of dementia and other neurodegenerative disorders are complex and not fully understood, but accumulating epidemiological evidence has shown that exposure to air pollution, especially ambient particulate matter (PM), is an important environmental risk factor for neurodegenerative and other neurological disorders. Our current lack of understanding about the mechanisms by which air pollution may impact neurological health limits our ability to determine which components of air pollution could lead to these effects and therefore to design effective policy.

There has been a growing body of literature highlighting the potential impacts of traffic-generated air pollution on the central nervous system (CNS) including neuropathological outcomes in humans, which may be mediated by the inhalation of particles. The impact of inhaled particles beyond the lungs is a pressing concern gaining recognition due to the increasing acknowledgement of the systemic consequences of inhaled environmental toxicants. Some hypotheses, including those categorised as the “lung-brain axis”, suggest that effects on the brain are indirect, for example, that particles reach the blood-brain barrier (BBB) and affect the barrier integrity potentially allowing entry to other potential toxins. Other hypotheses propose direct effects and *in vivo* studies on rodents have shown that inhaled particles could impact the brain directly, since they can potentially enter the brain via the olfactory nerve or across the BBB.



Potential pathways by which inhaled particles impact the brain.

This project will utilize human cellular models to investigate the impacts of inhaled particles on BBB integrity, the translocation of particles and potential biological effects involved in the induction of neuroinflammation by using STFC facilities at CLF and ISIS. The project will also explore the liquid transport characteristics of the inhaled particles between the blood and brain Outcomes from this scoping study will enhance our understanding of mechanisms by which inhaled particles could impact upon the brain, strengthening the evidence base to inform targeted advice and policies that could improve the population’s neurological health.

UPDATE

- **Biological effects in BBB cellular model (hCMEC/D3 cells) - ongoing**

- Cytotoxicity by modified LDH assay

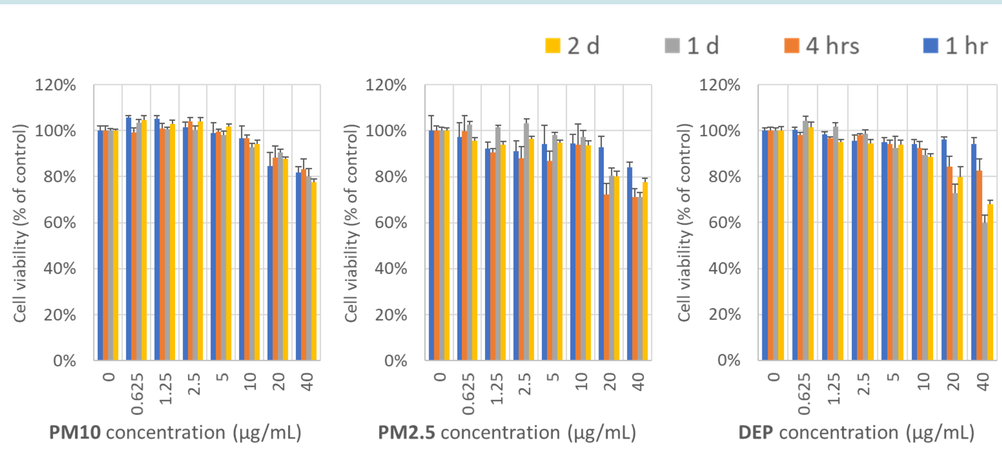


Figure 1. Cell viability of hCMEC/D3 cells after exposure to different particles.

- **Using FIB-SEM in correlation with Confocal microscopy at CLF to observe particles directly at Blood-brain-barrier (BBB) - planned**

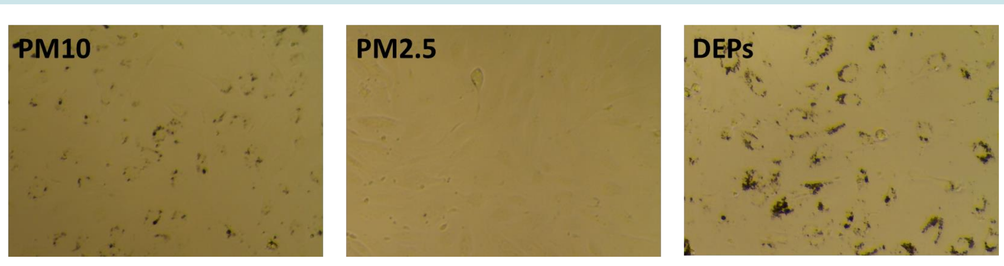
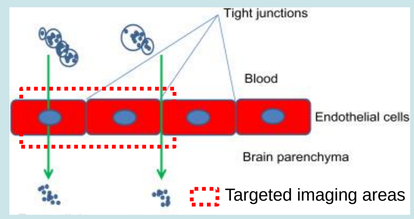


Figure 2. hCMEC/D3 cells after exposure to different particles (10 µg/mL).

- Experiments to be carried out in May - July 2022



- **Using Neutron spectroscopy at ISIS to identify the lipid dynamics after exposed to particles at Blood-brain-barrier (BBB)**

- Xpress experiment has been carried out for validation of this technique application

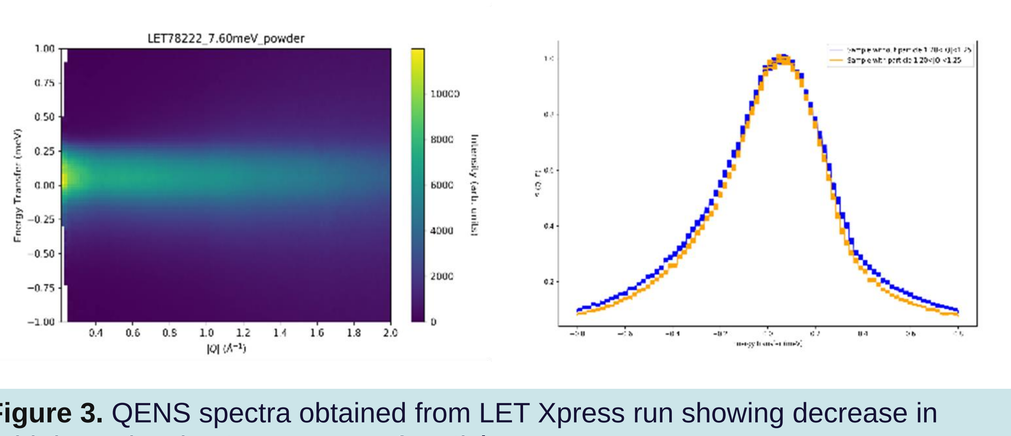


Figure 3. QENS spectra obtained from LET Xpress run showing decrease in lipid dynamics due to presence of particles.

- **A UKHSA PhD studentship (2022-2025) was awarded with collaborative efforts**

- The project will follow and expand upon this scoping study project, with collaboration and support from CLF and ISIS.

Project title: How Might Air Pollution Hurt the Brain? – Understanding the Impacts of Inhaled Particulate Matter on Neurological Health

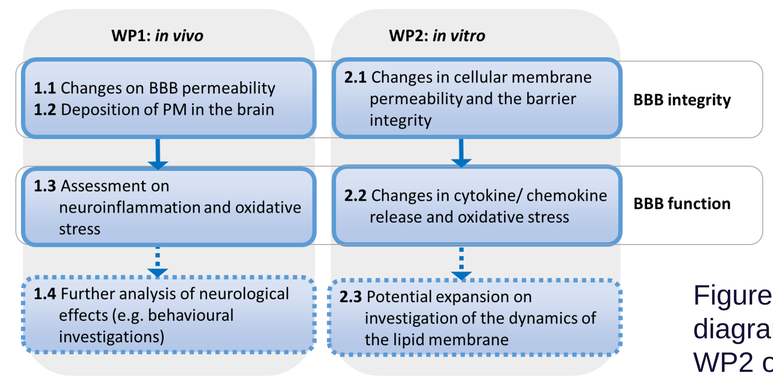


Figure 4. The workflow diagram for WP1 and WP2 of the PhD project.

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- Dr Sarah Moller and Fleur Hughes from SAQN

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