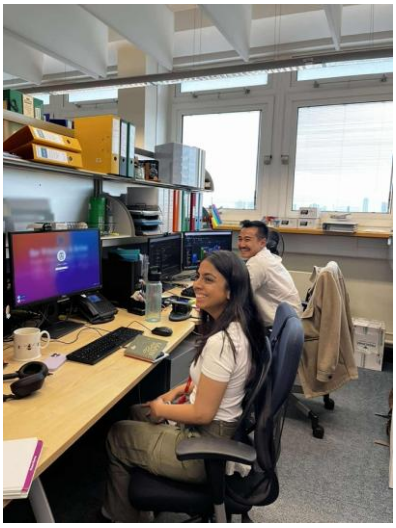
Dear Members of the European Alzheimer's Disease Consortium,

First, I would like to sincerely thank you for giving me the opportunity to undertake a four-week research placement at King's College London, within the Department of Old Age Psychiatry at the Institute of Psychiatry, Psychology and Neuroscience. I had the privilege of completing this placement under the supervision of Dr. Latha Velayudhan, a psychiatrist specializing in ageing, dementia, and general psychiatry research, and one of the department's three principal investigators.



This experience allowed me to discover a working environment that was very different from what I was used to, both in terms of the organization of space and infrastructure, as well as the team's daily rhythm and dynamics.

Although the core responsibilities of a researcher are broadly similar, the nature of the work differed significantly from what I had previously experienced. The research conducted within the department is closely integrated with clinical practice, with the primary aim of gaining a better understanding of the etiology of neurodegenerative dementias at a very early stage. The goal is to intervene upstream to prevent the progression of the disease.

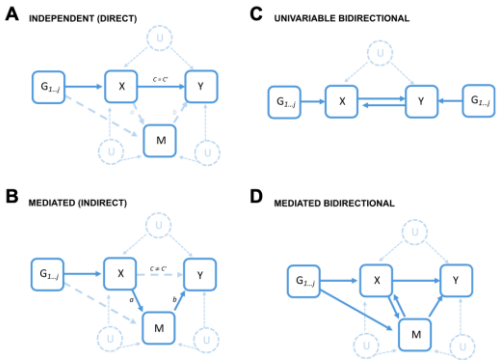
To achieve this, the teams employ advanced approaches such as the use of genetic cohorts, genomic analyses based on polygenic risk scores (PRS), Mendelian randomization, and magnetic resonance spectroscopy (MRS) — methods that are rarely, if ever, used in my home laboratory in Liège.

The diagram on the left below illustrates conceptual models of causal relationships tested using Mendelian Randomization (MR). It depicts four possible scenarios involving an exposure factor X, a potential mediator M, and an outcome Y, influenced by genetic instruments $G_{1,J}$:

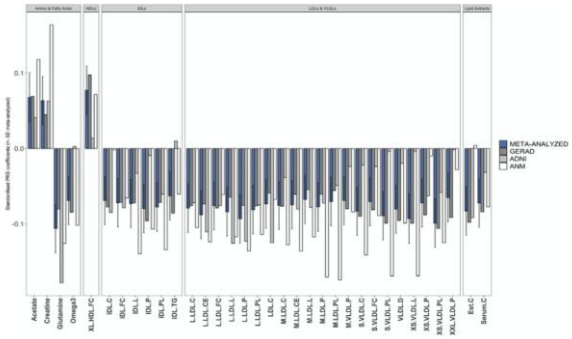
- (A) **Independent model**: a direct effect of X on Y, with no involvement of M.
- (B) **Mediated model**: the effect of X on Y is entirely transmitted through M.
- (C) **Univariable bidirectional model**: reciprocal effects between X and Y, without mediation.
- (D) **Bidirectional mediated model**: reciprocal effects between X and Y, with M acting as a mediator.

These conceptual frameworks are used in the study of (Lord et al., 2021), to analyze and distinguish between direct and indirect causal effects among blood metabolites, cognitive factors (education and cognition), and Alzheimer's disease, using both univariable and multivariable MR approaches.

The graph on the right displays effect bars of metabolic polygenic risk scores (PRS) on Alzheimer's disease (AD) diagnosis.
This figure shows the standardized effects (blue bars) of PRS for 34 metabolites significantly associated with AD ($p < .05$), based on three cohorts (GERAD1, ADNI, ANM) and their meta-analysis. These associations suggest a shared genetic basis between certain lipid-related metabolites—particularly subfractions of HDL, LDL, and VLDL—and AD risk, although only glutamine and free cholesterol in extra-large HDL particles (XL.HDL.FC) demonstrated a robust protective causal effect in subsequent Mendelian Randomization (MR) analyses.

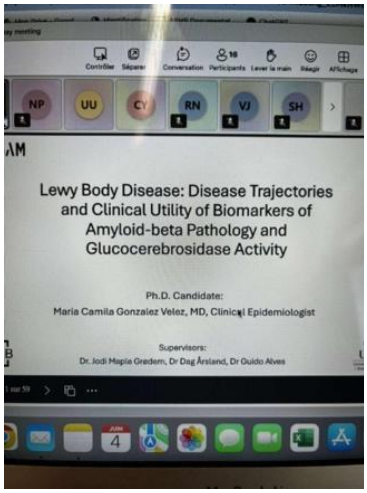


(Lord et al., 2021)



(Lord et al., 2021)

In addition, in this laboratory, numerous neuropsychological assessments are conducted, particularly as part of studies on the progression of Parkinson's disease dementia and Lewy body dementia, with close and continuous patient follow-up. This laboratory offers a compelling example of the integration between clinical research and clinical practice — an aspect that was especially enriching for me to explore as a psychologist and clinical neuropsychologist currently pursuing a PhD in neuroscience. My research focuses on the functional role of the transentorhinal cortex, a brain region affected at an early stage of Alzheimer's disease.



During this experience, I had the opportunity to attend weekly presentations by the lab's PhD students on their thesis projects. I was also able to follow procedures related to the retrieval of 7T MRI data in DICOM format from a dedicated server. These activities allowed me to meet and interact with neuroimaging professionals and researchers during various meetings.

Moreover, joining an English-speaking laboratory was a real challenge, but also an incredibly rewarding experience, especially since I did not have a strong command of English at the outset. This immersion allowed me to reconnect with the language and revisit concepts I had not had the opportunity to practice during my psychology studies at the University of Liège.

If I may offer a slightly critical remark about this experience, it would concern the organization prior to the placement. When I initially contacted Dr. Latha Velayudhan, she was not aware of the EADC exchange fellowship. Nevertheless, she warmly welcomed me into her lab and designated one of her PhD students (Sajini Kuruppu) as my main contact, who proved to be an excellent and supportive guide throughout my stay.

However, due to the short duration of the placement, I was unable to participate in hospital-based patient follow-up activities (which require vaccination) or to obtain an institutional login granting access to a workstation. This made certain tasks, such as managing the MRI data that had been proposed for analysis, more complicated. While I was able to follow the workflow and meet professionals in neuroimaging, my limited access to necessary software on my personal laptop meant I lacked autonomy to carry out a more substantial contribution.
Perhaps with more advance planning and clearer communication prior to the visit, these logistical challenges could have been avoided, and I might have been able to engage more fully in the lab's research efforts.

Finally, this research placement has significantly enriched my academic and methodological background. It provided me with valuable theoretical foundations in areas of research very different from those I was previously familiar with, such as genetic epidemiology and polygenic approaches. I also had the opportunity to become acquainted with innovative analytical methods like Mendelian Randomization, which broadened my perspective on causal inference in neurodegenerative diseases. This exposure to new scientific paradigms will shape the future direction of my doctoral research. Furthermore, this immersion in an English-speaking laboratory greatly improved my English skills, both spoken and written, and allowed me to expand my professional network by meeting researchers from various disciplines.

References:

Lord, J., Green, R., Choi, S. W., Hübel, C., Aarsland, D., Velayudhan, L., Sham, P., Legido-Quigley, C., Richards, M., Dobson, R., & Proitsi, P. (2021). Disentangling Independent and Mediated Causal Relationships Between Blood Metabolites, Cognitive Factors, and Alzheimer's Disease. *Biological Psychiatry Global Open Science*, *2*(2), 167-179. https://doi.org/10.1016/j.bpsgos.2021.07.010