



Postdoctoral Position @ Paris Brain Institute, France

An international multi-registry approach to identify pre-clinical markers of neurodegenerative disease

Leveraging medical records to identify patients at risk of neurodegenerative disease

Keywords: neurodegenerative diseases, electronic health records (EHR), phenome-wide association study, risk factors, prevention, health policies, big data, international collaboration, longitudinal datasets

Topic: Neurodegenerative diseases represent one of the main public health issues in our western societies and one of the greatest challenges in drug development. Prevention policies have become essential to address these issues: primary prevention to prevent disease onset by acting on actionable risk factors, or secondary prevention to slow disease progression with very early therapeutic interventions, ideally at pre-symptomatic stages. Key to the implementation of such prevention measures is the identification of at-risk patients, at the point of care, and preferably long before disease onset.

Through a new collaboration between the Paris Brain Institute (France), the Karolinska Institute (Sweden) and the University of Queensland (Australia), we propose to use electronic health records (EHR) to identify biomedical risk factors through studying previous diagnoses (pre-clinical comorbidities), drug prescription, clinical care usage, and biological test results. This analysis will use longitudinal data in EHR registries including millions of patients who have been followed for at least 10 years before diagnosis in 4 different healthcare systems: Australia, France, the UK and Sweden and across 4 therapeutic areas: Alzheimer's disease (AD), Parkinson's disease (PD), dementia with Lewy bodies (LBD) and motor neuron diseases (MND). The objective is to identify the biomedical risk factors that are common to these diseases and the ones differentiating them.

At the Paris Brain Institute (ICM), we have started to analyse the THIN database containing medical records, prescriptions and diagnoses from 2,500 general practitioners in France and 532 general practices in the UK which covers a population of 8 million patients. Phenome-wide analysis, like genome-wide analysis, requires a very large sample size due to the number of tested associations and the possible small effect size of each association. By gathering transnational and population-based data collection from 4 different countries, we are in a unique position to address two key limitations of real-world data analysis: the usual lack of statistical power and the need to control for biases.

Role of the Postdoctoral fellow: The postdoctoral researcher will perform association testing in collaboration with consortium members, in order to identify pre-clinical markers associated with the risk of neurodegenerative disease. They will analyze the relationships between clinical diagnoses, use of prescribed medications, healthcare use, and biological test results. Analyses include disease specific (AD/PD/LBD/MND), as well as cross-disorder investigations, controlling for age, sex, socio-economic status, and disease susceptibility (e.g., family history), whenever feasible. The results for individual associations will be shared between the partners of the project to allow for meta-analyses and identification of country-specific as well as cross-country associations.

ARAMIS Team

Brain and Spine Institute (ICM)
CNRS UMR 7225 – Inserm U1127 – University Pierre and Marie Curie UM 75
Inria Paris-Rocquencourt Center
<http://www.aramislab.fr>



Examples of papers from the consortium:

- [1] Nedelec T, Couvy-Duchesne B, Monnet F, et al. Identifying health conditions associated with Alzheimer's disease up to 15 years before diagnosis: an agnostic study of French and British health records. *Lancet Digital Health* 2021; **ePub ahead of print**.
- [2] Nabais MF, Laws SM, Lin T, ... & McRae AF. (2021) Meta-analysis of genome-wide DNA methylation identifies shared associations across neurodegenerative disorders. *Genome Biology* 22:90 <https://doi.org/10.1186/s13059-021-02275-5>
- [3] Yazdani S, Mariosa D, Hammar N, Andersson J, Ingre C, Walldius G, Fang F. Peripheral immune biomarkers and neurodegenerative diseases: A prospective cohort study with 20 years of follow-up. *Ann Neurol*. 2019;86:913-926.

Team: The postdoctoral researcher will join the ARAMIS lab (www.aramislab.fr), a joint team between INRIA (the national French institute dedicated to applied mathematics and computer science) and the Paris Brain Institute (ICM), and located in the center of Paris. The Paris Brain Institute is dedicated to basic and translational neurosciences. The ARAMIS lab develops advanced statistical and computational methods to analyze imaging, electrophysiological and electronic health records data.

The postdoctoral position is **funded for one year (starting in April, 2021)** via the LeMeReND European project (EU joint program – Neurodegenerative disease research), **extensible depending on available funding**. The candidate will participate to progress report meetings and interact with our consortium partners (Prof Fang Fang at Karolinska Institute et and Dr. Allan McRae from University of Queensland).

Profile: The candidate must have a PhD in public health, epidemiology or statistics (or equivalent experiences proving a strong background in epidemiology or statistics and a good level in R or Python). They should have a strong interest in data analysis, numerical implementation and dealing with large databases. They must also possess good relational and communication skills with scientists from various disciplines and very good skills in written and spoken English. We are seeking a motivated candidate, with good track record and writing abilities, interested in working on high impact publications. Previous experience in neurodegenerative diseases research would also be valued. We encourage application from people with diverse backgrounds, including people with disability.

To apply or for further information, please send an email with CV, cover letter and two referee names, to Stanley.Durrleman@inria.fr, baptiste.couvy@icm-institute.org and Thomas.nedelec@icm-institute.org.

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