

Communiqué de presse

Press release

Identification of new risk factors or early signs of Alzheimer's disease

23/02/2021

What risk factors are associated with Alzheimer's up to 15 years before the onset of the first symptoms? This is a vital question for specialists of this neurodegenerative disease – which develops over many years before becoming clinically visible – who aim to improve early prevention for at-risk patients. A multidisciplinary team of researchers from the Paris Brain Institute's (INSERM/CNRS/Sorbonne University) Aramis project led by Stanley Durrleman (Inria), from INSERM/University of Bordeaux, and from Cegedim Health Data, analysed the anonymised health records of nearly 80,000 patients consulting general practitioners in France and the United Kingdom, taken from the THIN® database. The scientists identified ten pathologies developed more frequently by patients reporting Alzheimer's dementia within 15 years than by other patients of the same age. Their results are published in the prestigious journal *The Lancet Digital Health*.

Despite the growing number of findings, our knowledge of the risk factors and early symptoms of Alzheimer's disease remains patchy and based on specific risk factor approaches. Until now, there has been no exhaustive, agnostic study conducted on a very large sample of patients that analyses possible risk factors well ahead of the Alzheimer's diagnosis.

For the first time, a team of researchers has accessed the anonymised medical data of nearly 40,000 patients with Alzheimer's disease and of the same number of control subjects who did not develop neurodegenerative diseases over the period studied. The data was extracted from the THIN® (The Health Improvement Network) database owned by Cegedim Group, an innovative technology and services company specializing in healthcare data.

The Aramis team's expertise in mathematical modelling made it possible to perform an analysis without predefined hypotheses, and test the possible link between the onset of Alzheimer's disease and 123 health factors. Statistical explorations of historical medical records yielded a list of the 10 most common conditions experienced by patients who go on to develop Alzheimer's disease within 15 years. Depression topped the list, followed by anxiety, exposure to high stress, hearing loss, constipation, cervical spondyloarthritis, memory loss, fatigue (and discomfort), and finally falls and sudden weight loss. "*The connections made allowed us to confirm known associations, such as hearing problems or depression, and other less known factors or early symptoms, such as cervical*

spondylosis or constipation. However, we are only reporting statistical associations. These will have to be the subject of further studies to understand the underlying mechanisms,' says researcher Thomas Nedelec, from the Aramis team, "The question remains as to whether the health problems encountered are risk factors, symptoms, or warning signs of the disease".

Epidemiologist and Inserm research director Carole Dufouil, and neurologist Stéphane Epelbaum, helped validate the methodology and interpret the relevance of these statistical associations. Although these results still need to be refined, they are already valuable for health professionals and all those involved in prevention, who could try to address these risk factors as soon as they are detected and hope to prevent the disease.

This work opens up several prospects, the first of which will be to expand and diversify the corpus of data studied. A grant from the European programme for the study of neurodegenerative diseases (Joint Programme - Neurodegenerative Disease Research) will enable the Aramis researchers to add data from Sweden and Australia to the existing pool and thus to extend their analyses to more than 26 million data from anonymised health records. This will also enable research to be extended to other degenerative diseases (Parkinson's, Charcot's disease, multiple sclerosis, etc.). *"We hope, through this approach, to identify the common basis of these diseases and the specificities associated with each one,"* concludes Stanley Durrleman.

Source

Identifying health conditions associated with Alzheimer's disease up to 15 years before diagnosis: an agnostic study of French and British health records, *The Lancet Digital Health*, February 23 2022. [https://www.thelancet.com/journals/landig/article/PIIS2589-7500\(21\)00275-2/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500(21)00275-2/fulltext)

Thomas Nedelec, PhD (1) ; Baptiste Couvy-Duchesne, PhD (1,3) ; Fleur Monnet, MSc (4), Timothy Daly, MPhil (5) ; Manon Ansart, PhD (1) ; Laurène Gantzer, MSc (4) ; Béranger Lekens, MSc (4) ; Stéphane Epelbaum, PhD (1,2) ; Carole Dufouil, PhD (6,7)* ; Stanley Durrleman, PhD (1)*

(1) Paris Brain Institute, ICM, Inserm U 1127, CNRS UMR 7225, Sorbonne Université, Inria, Aramis project team, F-75013, Paris, France

(2) AP-HP, Hôpital de la Pitié Salpêtrière, Institute of Memory and Alzheimer's Disease (IM2A), Centre of Excellence for Neurodegenerative Disease (CoEN), Department of Neurology, F-75013, Paris, France.

(3) Institute for Molecular Bioscience, the University of Queensland, St Lucia, Queensland, Australia

(4) Cegecim R&D, Boulogne-Billancourt, France

(5) Sciences, Normes, Démocratie (UMR 8011), Philosophy Department, Sorbonne Université, Paris, France

(6) Univ. Bordeaux, Inserm, UMR 1219, Inserm, CIC1401-EC, F-33000 Bordeaux, France.

(7) Pole de Santé Publique Centre Hospitalier Universitaire (CHU) de Bordeaux, F-33000 Bordeaux, France

*equal contributions

Find out more

About Paris Brain Institute

Created in 2010, the Paris Brain Institute is an international scientific and medical research centre of excellence, located in Paris at the heart of the Pitié-Salpêtrière Hospital. Its innovative model brings together patients, doctors, researchers and entrepreneurs with a common goal: to understand the brain and accelerate the discovery of new treatments for nervous system diseases. The Institute thus includes a network of more than 700 researchers and clinicians (AP-HP, Sorbonne University, Inserm and CNRS), 10 cutting-edge technological platforms, 1 clinical investigation centre, 1 training organisation and more than 2,000m² dedicated to incubating startups. Since 2017, it has also been the health partner of Station F; this location gives it a competitive advantage in the field of connected health. In 2020, the Paris Brain Institute celebrated its tenth anniversary.

institutducerveau-icm.org

About University of Bordeaux

With more 54,000 students, 3,200 researchers and teachers, and 2,800 staff members, the University of Bordeaux is one of the leading French public research and higher education institutions, located in a dynamic and culturally rich, fast-developing region.

Ranked among the top universities in France, the University of Bordeaux is renowned for the quality of its academic courses and research. It is a multi-disciplinary, research-focused institution with a strong ambition to develop as a leading, international campus. The University of Bordeaux is leading an ambitious, competitive development program in partnership with local higher education institutes and national research organizations, in order to promote Bordeaux as a “Campus of Excellence”.

About Inria

Inria is the French national institute for research in digital science and technology. World-class research, technological innovation and entrepreneurial risk are its DNA. Within 200 project-teams, most of which are shared with major research universities, more than 3,500 researchers and engineers explore new avenues, often in an interdisciplinary manner and in collaboration with industrial partners, to meet ambitious challenges. As a technological institute, Inria supports the diversity of innovation paths: from open source software publishing to the creation of technological startups (Deeptech).

About THIN®

THIN® (The Health Improvement Network) is a large European database of anonymized Electronic Health Records collected at the physicians' level, owned by Cegecim group. THIN® anonymized longitudinal patient data currently covers large populations of over 69 million patients across several European countries (France, the UK, Spain, Italy Belgium and Romania). It aims at enabling advancements in patient care and outcomes by assisting leading healthcare authorities, academics and research centers with healthcare research and analysis.

About Cegecim Health Data

Cegecim Health Data is part of the Cegecim Group, an innovative technology, services and real world data group that has specialized in healthcare for more than 50 years. Cegecim Health Data provides anonymized Real-World Data and Evidence (RWD-E) platforms and advanced studies to drive cutting-edge improvements in patient outcomes in the interests of public health. Through THIN® (The Health Improvement Network), a data history of over 25 years and millions of anonymized patient records are immediately accessible. Our life science users can use THIN® data across the pharma value chain, from R&D, market access, and medical, to marketing.

Press contact

Paris Brain Institute

Astrid Crabouillet

+33 (0)1 57 27 40 22

astrid.crabouillet@icm-institute.org