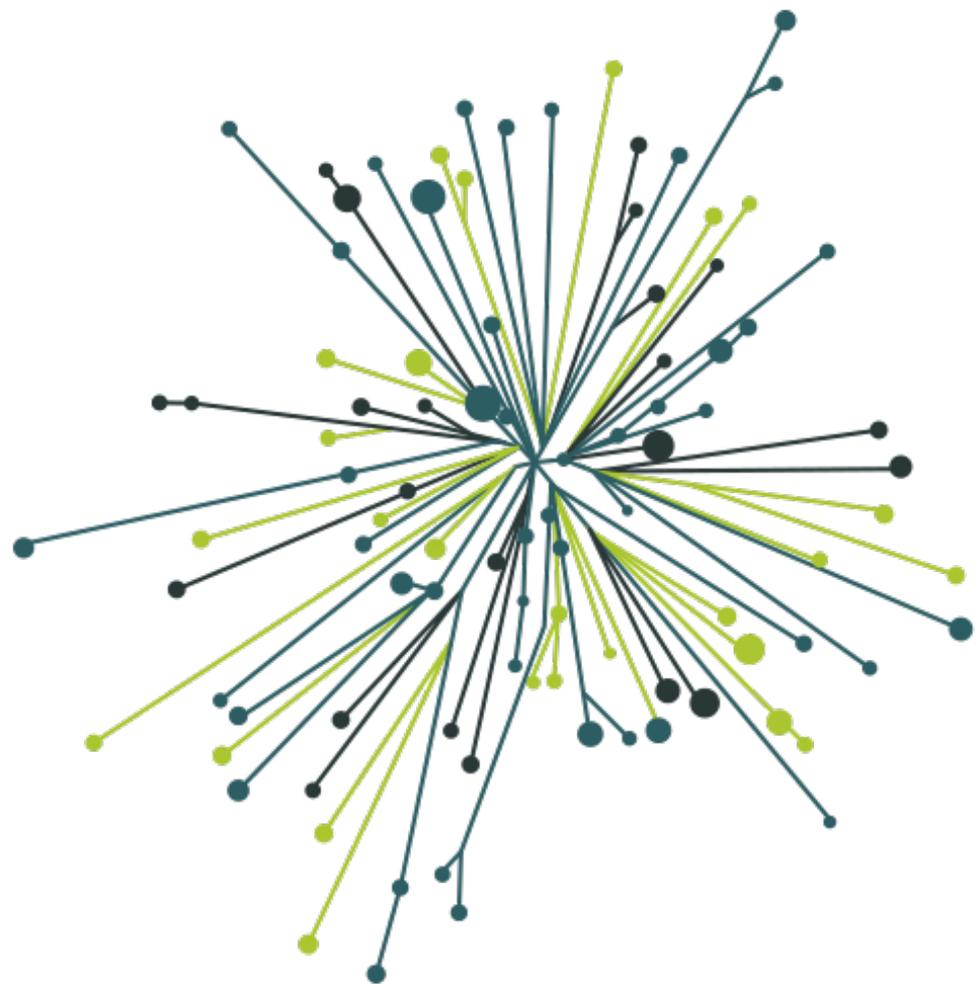


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# Identification of genetic variants contributing to late-onset Alzheimer's disease risk and correlation with cerebral activity of patients

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## Background

Alzheimer's disease (AD), the most common form of dementia in the elderly population, is clinically defined by a slowly progressing memory loss, together with deficits in higher intellectual functions and cognitive abilities across different domains [1]. Differential diagnosis of dementia due to AD is, however, difficult to establish mainly in early stages of the disease. In an attempt to characterize more accurately neural dynamics in mild cognitive impairment, members of our team have previously shown a significant slowing of electroencephalography (EEG) activity and several significant alterations in spectral fluctuations of AD patients when compared to controls [2]. At the genetic level, mutations in three genes have been identified as responsible for early-onset AD: the gene encoding for the amyloid precursor protein peptide (*APP*) [3-5], and the *presenilin 1* (*PSEN1*) and *presenilin 2* (*PSEN2*) genes [6]. A more complex genetic etiology seems to underlie the most common form of the disease- late onset AD (LOAD) with the first symptoms appearing at an age >70 years old. To date, *apolipoprotein E epsilon4* allele has been the major genetic risk factor described for its development [7], although approximately other 20 susceptibility genes with common variants have been suggested to contribute to LOAD risk.

## Objectives

- To identify novel LOAD candidate genes
- To characterize the population regarding coding and regulatory variants within genes at the previously identified LOAD *loci*
- To associate different cerebral activities to each of the four disease stages
- To correlate variants in candidate genes and disease progression (assessed by neuroimaging)

## Subjects

### LOAD patients:

100 from North Portugal



100 from the Spanish community of Castile and León



**CONTROLS:** 50 controls (individuals aged >70 with no signs of cognitive deficit):  
25 from North Portugal and 25 from the Spanish community of Castile and León

From both populations, we will analyze 25 patients from each of the

### 4 general stages of LOAD



This project has been approved by the Ethics Committee of the University of Porto (CEUP)

## Strategy

- Characterization of neural dynamics in all patients and healthy controls: **cerebral activity will be assessed by electroencephalography (EEG)**
- Analysis of EEG patterns and disease severity based on the time of clinical evolution



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- Oral sample collection through a **non-invasive procedure**: saliva samples collected in Oragene OG500 tubes containing a solution to stabilize the DNA for long-term storage at room temperature, followed by DNA extraction

- **Exome-wide analysis** through SureSelect Human All Exon V6

We expect to find a non-invasive approach to assess early stages of cognitive decline, and improve the accuracy of LOAD diagnosis

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