TITLE OF THE PROJECT: **Drugs and cognitive ageing**

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SUMMARY

Background

In France, a person consume on average 48 boxes of medicines per year. Among these medicines, some substances prescribed for an indication unrelated to cognitive function may however modify cognitive ageing. Some can stimulate the cognitive abilities and/or slowing down cognitive decline with age, others may alter cognitive function and/or accelerate cognitive decline.

It is fundamental to identify these substances and to argue such effect for two reasons.
First, identification of these substances in observational cohort studies could lead to new hypotheses concerning preventive treatments potentially able to slow the onset of symptoms leading to dementia (such hypotheses have to be further confirmed by RCT in targeted populations).
Even if some candidate treatment have already been explored without success (Statins; Antihypertensive; NSAID (Non-steroidal anti-inflammatory drugs) ; Aspirin ; Gonadal steroide), the range of treatments used in France is very large and many others hypotheses can still be explored.

In other hand, this kind of study can also highlight some cognitive side effects of substances likely to accelerate the physiopathological process leading to dementia, and/or diminishing the cognitive reserve of patient with cognitive impairment (ex: benzodiazepine treatment, drugs with anticholinergic properties or cancer chemotherapy). These cognitive side effects have to be analyzed in their context considering the risk / benefit ratio and the possibility of substitution for each treatment.

Objectives

General objective of our project is to analyze the association between commonly used drugs and cognitive ageing. Specific aims of our project will focus on the following themes:

1. Exploration of the cognitive impact of drugs with anticholinergic properties.

2. Exploration of the Interaction between different drugs with known cognitive effect (benzodiazepines, drugs with anticholinergic properties).

3. Exploration of the cognitive impact of oral antidiabetic drug

4. Analysis of drug use and cognitive aging using exploratory statistical methods of data mining.

Methods

For our project, we will performed analyzes on subject aged from 45 to 75 years in one of the 17 Social Security Health Screening Centers (HSCs) involved in the cohort. We will use baseline scores at neuropsychological tests for cross-sectional analysis, and the 5 years follow-up measures for longitudinal study of the cognitive decline. Drug consumption history will be obtained through the data base of the health insurance system: SNIIRAM ("Système national d'information inter-régime de l'Assurance maladie"). This recording allows a detailed analysis of the dose effect of the treatment, considering simultaneously time of exposition and level of exposition. All Analyses will be adjusted for available confounders.
For the fourth specific aim, we will use exploratory methods, such as multiclass linear discriminant analysis (LDA) and classification and regression trees (CART), which provide flexible ways to examine data without preconceptions.

Perspectives

The Cohort Constances shows two major advantages for the analysis of this theme. First, the continuous recording of the drugs prescription via the SNIIRAM, allows a reliable and comprehensive measure of the exposures. Secondly, the size of the cohort allows the study of rare exposure. These arguments are warranty for some original and valuable research.

Note: this project is part of the research consortium 'PRESAGE – PREparing Successful AGEing'