TITLE OF THE PROJECT: Depression and genetic liability

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SUMMARY

Background

Major depression is one of the leading causes of disability worldwide. Several factors are involved in the etiology of major depression, including genetic and environmental factors, as well as their interplay through gene by environment (G x E) interactions. However, most of previous longitudinal studies were underpowered to look for additional moderation by age, gender or socio-economic status (SES). As regards age, previous G x E interaction studies addressing the risk of depressive disorders have mainly focused on adulthood and studies addressing late-life depression are rare. In the context of population aging, major depression in the elderly represents an increasing public health issue. Data are lacking regarding the interplay of age-related environmental risk factors, such as bereavement or retirement, with genetic vulnerability for depression.

Objectives

The present project will encompass both a both a cross-sectional and a longitudinal approach and examine the following potential moderating factors: age, gender and SES. Given the rapid aging of the French population, specific attention will be paid to late-life depression. The cross-sectional approach will describe how selected genetic variants are associated with current depressive states. The longitudinal approach will describe how G x E interactions might predict the incidence of new depressive states as well as the following outcomes: hospitalization for depression or suicidal attempt, suicide. As regards late-life depression, specific attention will be paid to the role of age-related life events such as retirement and bereavement.

Methods

Depressive states will be measured at baseline and every three years by the CESD scale. Genetic data will be extracted for a subsample of 20,000 participants whom parents were born in Europe. This subsample will be determined to optimize statistical power (i.e. oversampling those participants with depressive states, those reporting stressful life events on the first follow-up questionnaire, those with comorbid substance use disorders and those aged ≥60 years; see also project Depression and addiction) and to include participants with brain MRI data (see also project Depression and brain biomarkers). DNA extraction will be automatized. We already selected candidate SNPs based on the literature. Genotyping will be performed by using real-time PCR. The status of the Hardy-Weinberg equilibrium for the markers will be computed in the control subjects at least to avoid any error of the allele calling during the genotyping. We will format the data to fit with the database of the DEDALE Research Consortium and to transmit them to the other teams of the consortium. Analyses will be computed according to the genotypes for each variant to allow comparing additive effects and dominant models. We will also carry out haplotype analysis, which corresponds to the combined study to several SNPs encompassing the same gene and, in case of association, reinforces the discovery. Furthermore, we will compute epistatic effects which correspond to SNP x SNP interaction(s) studies.

Perspectives

Besides gaining knowledge about the genetic determinants of depressive states in the general population, the results of this project may eventually be used in personalized medicine as predictors of individual risk or clinical course. Perspectives include the use of the identified risk genetic markers in the other project of the DEDALE Research, looking for shared genetic liability with addiction (project Depression and addiction) and cardiovascular diseases (project Depression and cardiovascular diseases) for instance. Perspectives also include avenues of research in pharmacogenetics thanks to coupling with the SNIIRAM database.

Note: this project is part of the research consortium 'DEDALE - Déterminants et évolution des états dépressifs : approche longitudinale en épidémiologie intégrative'