

**TITLE OF THE PROJECT: Depression and brain biomarkers****HEAD OF THE TEAM:** Stéphane Lehericy, Brain & Spin Institute**SUMMARY****Background**

Major depression is one of the leading causes of disability worldwide. Although biomarkers are needed to refine our understanding of the pathophysiology and evolution of depressive states, promising tools such as neuroimaging have remained restricted to small, selected samples, thus yielding inconclusive results. At a brain level, functional MRI neuroimaging studies from our teams and others have found aberrant activation within the cortical midline structures to be associated with current depressive state, remitted depression and vulnerability for depression, including late-life depression, as well as with treatment response. As regards anatomical putative biomarkers, the smaller volume of hippocampus in depressed patients is a finding easy to replicate with standard methods but the multiplicity of factors moderating or mediating this “effect” makes it difficult to examine their role in samples of size typically encountered in neuroimaging research. The planned sample size for CONSTANCES subjects who will benefit from a MRI scan (i.e. 10,000), as well as the possibility of coupling these anatomical data with biographical and genetic data make CONSTANCES the ideal platform to address these questions.

**Objectives**

A cross-sectional approach will describe the brain correlates of “chronic or recurrent depressive states”. Analyses will focus on two a priori biomarkers: hippocampal volume and resting state functional connectivity within the default mode network and the cognitive control network. A longitudinal approach will confirm the ability of these biomarkers to predict future depressive states among participants free of history of depression at baseline. In addition, outputs from project ‘Depression and genetic liability’ will be used to compare brain biomarkers of depressive states with the neural correlates of genetic risk factors for depression among healthy subjects in a translational neuroscience perspective. Finally, the present project will produce synthetic inputs in order to inform the other projects of the DEDALE Research Consortium as brain functioning may explain the association of depressive states with some specific features including substance use (project Depression and addiction), cardiovascular diseases and elevated inflammation (project Depression and cardiovascular diseases) or cognitive impairment (project Depression and social outcome).

**Methods**

The cross-sectional approach will compare participants with “chronic or recurrent depressive states”, defined as repeatedly having CESD scores above validated cut-off at three years of interval, to age, gender and SES-matched control subjects with a 2:1 ratio. The longitudinal approach will compare participants with and without a depressive state at follow-up among those free of history and symptoms of depression at baseline. Hippocampal volume will be calculated based on a combination of voxel-based morphometry (VBM) with normalization by the DARTEL algorithm. As regards functional connectivity at rest, two approaches will be used. An a priori seed-based approach will be used to identify the cognitive control network and the default mode network. Further exploratory analyses will use a methodology derived from Independent Component Analysis (i.e. Multi-Scale Individual Component Clustering).

## **Perspectives**

The expected results will contribute to identify clinically relevant biomarkers of depressive states that could eventually be used in the personalized management of depressive states. Perspectives beyond the current project include the identification of brain predictors of response to antidepressant drugs thanks to a coupling with the SNIIRAM data.

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