Learning to predict the response to antidepressant drugs

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Abstract

Depression affects more and more people worldwide. Often depressive individuals are prescribed targeted drugs, which may or may not be effective. Since depression is a complex illness, the response to a particular drug is hard to predict in advance in the clinical practice. Several studies are now advocating the use of modern data mining and machine learning techniques to identify potential reliable biomarkers, which are easy to collect, to assess in advance whether a particular drug would be effective for a given patient.

In this project, we will design, run, and interpret several machine learning models on a clinical dataset collected by the CHRU Tours. The objective is to judge at which level and with which accuracy we can expect to predict drug effectiveness in depressive individuals.

Keywords: Machine Learning, antidepressant drug resistance, biomarkers, data mining

Project description

An estimated 3.8% of the global population experience depression. It represents approximately 280 million people worldwide. Major depressive disorder (MDD) is diagnosed when an individual has a persistently low or depressed mood, anhedonia or decreased interest in pleasure activities, feelings of guilt or worthlessness, lack or energy, poor concentration, appetite changes, psychomotor retardation or agitation, sleep disturbances, or suicidal thoughts. The lifetime risk of MDD is almost 1 in 5 people experiencing one episode at some point in their life (15-18%). The treatment for MDD usually consists of psychological therapy, pharmacotherapy or both. For moderate and severe major depressive episodes (MDE), the French national authority for health (Haute Autorité de Santé HAS) recommends the use of monoaminergic-based antidepressants medication, such as selective serotonin reuptake inhibitors (SSRI).

Despite the wide range of antidepressant therapies available, a significant number of patients do not respond to the treatment. They either respond partially without remission, or not at all. Between one third and half of the patient do not respond to the first round of antidepressants, and even after multiple rounds of treatment, up to one third of the patients will become treatment resistant. This is known as treatment resistant depression (TRD).

Nevertheless, our knowledge of the precise mechanisms by which antidepressants induce remission is incomplete. Various potential predictors of resistance to antidepressants have been identified, but despite evidence of potential biomarkers, the diagnosis of depression relies so far on clinical criteria reported by patients and observed by clinicians, rather than objective biological or sensory measurements. There is therefore a need for finding objective and reliable biomarkers of depression and of response or non-response to treatment. However, depression is a complex illness that can have many underlying causes and involve a variety of physical and psychological mechanisms. For this reason, Machine Learning has been advocated as a pertinent approach to analyse multiple clinical data and identify reliable biomarkers.

The present project aims at continuing this search for depression and treatment response biomarkers. For that, we will use the clinical dataset collected during the BIORESA (BIOmarqueurs de la RESistance

aux Antidépresseurs) study conducted at the CHRU Tours. The dataset contains variables including metabolomics data (screening methods developed at the CHRU Tours), tissue pulsatility imaging (TPI) measurements, olfactory capacity analysis and routine blood and physiological data from depressive patients. To our knowledge, no study has evaluated the predictive power of TPI measurements and olfactory data in depression using machine learning algorithms. Moreover, the metabolomics variables are a result of screening pipelines developed at the CHRU Tours and could provide new insights compared to previous studies.

Data and resources

The student will work at ENSTA Paris, in the department of applied mathematics, supervised by Andrea Simonetto (PhD), professor of optimization and data science, and they will have access to the anonymised BIORESA dataset to run their machine learning models. The dataset contains 52 patients and 2066 variables. The design and interpretation of the models will be done in cooperation with Wissam El Hage (MD, PhD), professor of adult psychiatry, director of the CIC1415 Centre d'Investigation Clinique, co-director of the "Psychiatrie Neurofonctionnelle" team of the INSERM iBrain U1253, at CHRU Tours and Helene Clogenson (PhD), scientific specialist and member of the CIC-IT of the CHRU Tours.

Required skills

Good programming skills in python and/or R; good knowledge of machine learning. Willing to work in a multi-disciplinary team.

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