Machine-Learning for Neuroimaging

Authors: SALHI Laila and TRASSOUDAINE Clément

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Introduction

Data-science and medical 3D imaging techniques appeared very recently and went very common nowadays with substantial improvement in techniques and use cases. A lot of research was made for both of those fields independently. Two decades ago, it went obvious that machine-learning would be very useful for research in medical-imaging and more specifically in neuroimaging: a lot of data was extracted from a huge quantity of patients, split into disease or functionality-oriented datasets. Machine-learning techniques are then very useful to isolate characteristics of brain-areas, diseases, brains networks, and so forth.
This article aims to draw a state of the art of the Machine-learning methods and use cases in the neuroimaging field.
Both article source files and the *Jupyter notebooks* used to reprocess paper results (use cases) are available on Github (https://github.com/intv0id/ADST2018)

1. Data acquisition and cleaning

1.1 Acquisition techniques

In this article, we will focus on Nuclear Magnetic Resonance Imaging results. This includes the conventional MRI imaging which is a static method to acquire brain topology (in 3D) such as a Gray Matter Density (GMD) map, and the functional MRI (fMRI) which encodes the evolution of the brain state, usually the hemodynamic response (resulting a 4D encoded file). These techniques are yet known for only a few decades and to go a bit into the technical details of the acquisition, the elementary principle consists in emitting iteratively a brief (and intense) pulse of radio (well defined) frequency to excite hydrogen atoms, resulting a short faint signal response detected by the machine. Processing all of those responses gives approximately (with a typical 1cm3 resolution) the location of the hydrogen atoms and their state. Other 3D and 4D imaging techniques exists such as Positron Emission Tomography (PET) scan. We chose not to mention it in our article as far as the Machine-Learning techniques used for such imaging techniques are similar.

1.2 Basic processing

In order to reduce artifact and noise-related signal components, we have to perform series of operations on raw functional datasets prior to statistical analysis. Preprocessing can include motion correction, slice timing correction, co-registration with an anatomical image or normalization to a common template.

1.3 Data accuracy

Before a machine-learning based analysis is made, this is important to have a statistical analysis made on subjects. The datasets are commonly very limited in terms of patients (it is very rare that a dataset length is more than a hundred subjects) therefore we have to check whether or not the patients and control subjects have the same social background (including language fluency, level of studies, ...) and are representative of the population studied (age, gender, ...). In order to have a better training on a few elements, it is also common to use the KFold cross-validation (the training/test data loops over the dataset). However, a lot of studies are conducted over multiple datasets that may have aimed to different observations. This leads to be critical over the reverse inference issues that we will go into the details later in this article.

2. Neuroimaging Analysis

2.1 Clustering: extracting networks

It has been shown that brain activation exhibits coherent spatial patterns during rest. These correlated voxel activations form functional networks that are consistent with known task-related networks. Predictive modeling can be useful, as it could be applied to diminished subjects that cannot execute a specific task. Resting state fMRI is unlabeled data in the sense that the brain activity at a given instant in time cannot be related to an output variable. To extract functional networks or regions, we can use unsupervised methods learning methods that group together similar voxels by comparing their time series. In neuroimaging, the most popular method is Using Independent Component Analysis (ICA).

2.2 Regression and classification

Regression vs classification

The main difference between them is that a regression is predicting a continuous variable whereas the regression works with discrete values and predicts probabilities for each element of the set of values. In neuroimaging, the goal is to predict phenotypic elements which can be continuous (age) or discrete (disease). Nevertheless, when talking about emotion rating, both of these cases can happen: emotions and feelings can be discriminated between them and their strength can be rated. It is then very important to first have a good understanding of what the outputs should be for studies.

Techniques

As far as the acquisition process is returning a huge number of voxels (hundreds of thousands for each patient), it is necessary to select first the most relevant voxels for our study. This process is going with the dimension reduction one performed to ease the computation (going from a 3D model through a 2D one with only selected voxels). There are multiple algorithms to perform this operation. The two most used for neuroimaging are currently K-best (selecting the k voxels with the higher variance, taking the risk that the huge differences between those voxels are not linked to the study parameter, cf. reverse-inference issues) Then, once the valuated voxels are extracted, two techniques can be used, namely Support Vector Machine (SVM) (aiming to statistical Multi-Voxel Pattern Analysis (MVPA)) and Logistic Regression (LR)).

3. Limits

3.1 Voxel-based morphometric analysis

Voxel-based morphometric analysis is very limited in characterizing morphological differences between groups, and it is significantly biased toward group differences that are highly localized in space and of linear nature, whereas it is significantly reduced in cases with group differences of similar or even higher magnitude, when these differences are spatially complex and subtle. The complex and often nonlinear ways in which various factors, such as age, sex, genotype and disease, can affect brain morphology, suggest that alternative, unbiased methods based on machine learning theory might be able to better quantify brain changes that are due to a variety of factors, especially when relationships between brain networks, rather than individual structures, and disease are examined.

3.2 Reverse inference

Reverse inference is a process of induction entailing reasoning backwards from the observed brain activity to a particular cognitive process not directly tested, but perhaps linked to the task used, drawing on other research implicating that brain area with that cognitive process. It is not a correct reasoning process but works according to Bayes theory.

4 Case studies

4.1 Cognitive process recognition[i]

Using the Blood-Oxygen-Level-Dependent (BOLD) fMRI technique, it is possible to extract parts of the brain dealing with bad emotions and to predict their pain-level. The Neurovault dataset col. 503 was taken from 182 subjects facing iteratively 30 pictures (neutral, violence, injuries). We then observe that the prediction is far more accurate using the Searchlight selection algorithm than K-best because it is far more accurate at removing "noise voxels". Searchlight goes through all the voxels and calculate the variance, but also includes the neighbor voxels, eliminating physical noise due to the morphometry issues.

4.2 MRI-based Age prediction[ii]

Some areas in the brain can be used as a marker for the aging of the subject. This is due to the Gray Matter Density that decreases all over our life on these areas. The oasis Dataset was aiming to predict age and Dementia (based on the Mini-mental score examination). The computation is processed using K-best selection and a SVM regressor.

Conclusion

Though, techniques used in machine learning for neuroimaging may have some limits, its benefits and perspectives are huge. And this will be used for analysis and diagnosis for diseases such as ADHD and schizophrenia very soon. Thus, specific libraries to neuroimaging will be further developed aiming also to be used in research projects such as the European Brain Project in which several computer science institutes (such as the INRIA) take part.

References

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[i] https://github.com/intv0id/ADST2018/blob/master/SentimentAnalysis/Classifyer.ipynb
[ii] https://github.com/intv0id/ADST2018/blob/master/AgePrediction/AgePrediction.ipynb