A gender-differentiated MR-Sort model for diagnosis aid of Attention Deficit Hyperactivity Disorder (ADHD)

Sarah Itani[1] and **Fabian Lecron**[2] and **Philippe Fortemps** [3]

Abstract. The present paper deals with the use of decision-making models for medical diagnosis assistance. Such a specific issue requires to consider some parameters, e.g. the nature of the pathology and the related known facts. These factors may lead to the necessity of bringing some nuances to the basic formulation of a decision-making model. In this work, we addressed Attention Deficit Hyperactivity Disorder (ADHD), a neurodevelopmental disorder for which the current agreement rate between clinicians on diagnosis is still to be improved. In that respect, we considered the MR-Sort model which is highly valued for its efficiency and readability. As previous studies report gender-based differences in the neurophysiology of ADHD, we propose a reformulation of the MR-Sort model. It provides interesting prediction rates in comparison to the recent literature.

1 Introduction

Majority Rule Sorting (MR-Sort) models [4, 5, 8] were originally introduced as a simplification of the ELECTRE Tri ones, with a particular focus on readability and efficiency. Those qualities have served the medical domain which requires that any task should be interpreted and justified, e.g. pre-anesthetic examination [11] and antibiotic prescription [3].

It would be worth considering MR-Sort models for diagnosis aid, particularly to detect disorders for which the current human diagnosis presents a high level of variability. Attention Deficit Hyperactivity Disorder (ADHD) figures among such pathologies. This neurodevelopmental disorder is currently diagnosed based on complaints reported by the child's environment, supported by the anamnesis and behavioral or self-reported measures. Thus, it might be difficult for the clinician to come to an unequivocal diagnosis. This is where decision aid plays an important role.

In our work, we apply the MR-Sort model on a sample of the ADHD-200 collection [9], a public medical dataset which compiles patients' phenotype (e.g. age, gender, intellectual quotient) and physiological data. Our aim is to determine a simple and reliable decision support model to diagnose objectively the disorder. The first objective is thus to bring clinicians to reach a certain consensus and improve their agreement on a given case. A second objective is the possible identification of a small subset of features that can be considered by neuroscientists to understand the disorder more deeply.

[1] Fund for Scientific Research - FNRS (F.R.S.-FNRS); University of Mons, Faculty of Engineering, Department of Mathematics and Operational Research, Belgium; email: sarah.itani@umons.ac.be
[2] University of Mons, Faculty of Engineering, Department of Engineering Innovation Management, Belgium; email: fabian.lecron@umons.ac.be
[3] University of Mons, Faculty of Engineering, Department of Engineering Innovation Management, Belgium; email: philippe.fortemps@umons.ac.be

2 Materials

2.1 Data

In the ADHD-200 dataset, the subjects belong either to the TD (Typically Developing) class or to the ADHD one. For soundness reason, we focus on the NYU (New-York University Child Study Center) sample, which is the most challenging one. After cleaning, this training sample includes 210 subjects (93 TD, 117 ADHD). The test sample includes 41 subjects (12 TD, 29 ADHD).

Besides the phenotype data, the physiological ones are provided in the form of Blood-Oxygen-Level-Dependent (BOLD) signals, extracted for a set of brain Regions Of Interest (ROI), measuring the oxygen consumption by the neuronal activity. The AAL90 (Automated Anatomical Labeling) atlas is considered in this work, which involves a parcellation of the brain in 90 regions of interest. Through the Athena pipeline [13], a set of 90 preprocessed signals is thus available for each patient.

Our recent studies on ADHD [6, 7] showed that :

1. the diagnosis elements are generally quite different for boys and girls: first, ADHD is more prevalent for boys [1] and second, the relevant features are gender-specific;
2. the variance of the BOLD signals are meaningful features of the brain activity: by their level of intensity, they may be interpreted as a measure of activation of the ROI;
3. some brain regions, constituting the limbic system, may be highly involved in the diagnosis of the disorder: ADHD presence is correlated with the activation of these regions.

2.2 Model

As proposed by [8], the MR-Sort model helps to assign the n instances to the k predefined ordered classes $C^h, h = 1, \ldots, k$. Assuming the instances are described by m attributes, the assignment is built on separating profiles between these classes, in an ELECTRE Tri way. For such a model, one has to determine $(k-1)$ profiles i.e. $(k-1)$ vectors $(b^h, h = 1, \ldots, k-1)$ of m evaluations on the feature set $(b^h = (b^h_1, \ldots, b^h_m))$, m weights $(w_i, i = 1, \ldots, m)$ and a coalition threshold (λ). An instance $x = (x_1, \ldots, x_m)$ is assigned to class $C^h, h = 2, \ldots, k$ if

$$\sum_{\substack{i \in \{1,\ldots,m\}: \\ x_i \geq b_i^{h-1}}} w_i \geq \lambda \quad \text{and} \quad \sum_{\substack{i \in \{1,\ldots,m\}: \\ x_i \geq b_i^{h}}} w_i < \lambda.$$

Otherwise, x is assigned to class C^1 if

$$\sum_{\substack{i \in \{1,\ldots,m\}: \\ x_i \geq b_i^{1}}} w_i < \lambda.$$

To learn these parameters from examples, one can use linear programming, mixed integer linear one [8], a meta-heuristic approach [12] or a SAT formulation [2].

3 Our proposal

Based on our previous observations, we consider the gender as a key feature to learn simultaneously a two-fold model, with one fold per gender. We summarize the BOLD signals by their variance and consider them as monotonically increasing with ADHD. This is compatible with both our observations [6] and the neurophysiological interpretation of the data [7].

In our case, we have only two ordered classes: TD $\prec$ ADHD. Thus, we need to determine only one separating profile. This order between the two classes has been chosen, since we observed that the median of signal variances on most ROIs is higher in the ADHD class than in the TD one. We restrict this first investigation on the limbic ROIs. Since ADHD is more prevalent in boys, we choose to encode the gender, such that it is equal to 0 for girls and to 1 for boys.

Our proposal is to build a two-fold model as constituted by a single profile, a single coalition threshold and two sets of weights, one per gender. The idea is to encompass the gender-based diagnosis in the only weights, i.e. not in the subject's examination but in the interpretation by the physician.

For simplicity, we start with two profile candidates, defined as the vector of medians of signal variance on the considered ROIs either for the TD class or for the ADHD one. We also develop a range of potential separating profiles built as linear combinations of these two first candidates. For each potential profile, we look for an optimal threshold and an optimal weight vector for each gender, by means of a single linear programming problem.

This LP problem minimizes the sum of the slack variables defined as violations of the MR-Sort equations (see section 2.2). For both genders, a constraint asks the sum of the related weight vector to be less or equal to one; the threshold λ has to be in $[0.5, 1.0]$.

4 Results and discussion

The best model gives a training accuracy of 75% of correct assignments, with similar results for each class; and a prediction accuracy on the ADHD-200 test set of 61%. These accuracy is comparable to the recent results of [10, 6].

Among the 27 possible features (Gender and 26 ROIs), the model needs only 6 features; the other ones have a null weight. More precisely, three features have a non-null weight for boys and three different ones have a non-null weight for girls. It means that, even if we consider a common profile for boys and girls, the model can be separated in 2 completely separated sub-profiles.Thus, this research validates the need for a gender-based model.

The small number of features in the model is certainly linked to the LP problem used to find the best weights and coalition threshold. It is very interesting in the context of medical decision support, since it limits the amount (and, in some way, the cost) of information required to support diagnosis.

Finally, the model for both the boys and the girls allows for simple interpretation. On the one hand, this is related to the internal structure of the MR-Sort model. On the other hand, the specific values of the weights simplify this interpretation.

5 Conclusion and future work

The main result of this research is the actual interest of a MR-Sort model to provide diagnosis aid. It is both efficient and readable. Moreover, it corresponds to the physician's way of working: someone may have a trouble if several indicators exceed given reference values.

For further work, it would be interesting to evaluate the model by cross-validation. Moreover, the current approach allows to identify a single profile to distinguish control from ADHD subjects. It makes sense to look for other possible profiles.

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