

# Investigating Machine Learning Techniques for Detection of Depression Using Structural MRI Volumetric Features

Kuryati Kipli, Abbas Z. Kouzani, and Isredza Rahmi A. Hamid

**Abstract**—Structural MRI offers anatomical details and high sensitivity to pathological changes. It can demonstrate certain patterns of brain changes present at a structural level. Research to date has shown that volumetric analysis of brain regions has importance in depression detection. However, such analysis has had very minimal use in depression detection studies at individual level. Optimally combining various brain volumetric features/attributes, and summarizing the data into a distinctive set of variables remain difficult. This study investigates machine learning algorithms that automatically identify relevant data attributes for depression detection. Different machine learning techniques are studied for depression classification based on attributes extracted from structural MRI (sMRI) data. The attributes include volume calculated from whole brain, white matter, grey matter and hippocampus. Attributes subset selection is performed aiming to remove redundant attributes using three filtering methods and one hybrid method, in combination with ranker search algorithms. The highest average classification accuracy, obtained by using a combination of both SVM-EM and IG-Random Tree algorithms, is 85.23%. The classification approach implemented in this study can achieve higher accuracy than most reported studies using sMRI data, specifically for detection of depression.

**Index Terms**—MRI, brain image analysis, image feature selection, machine learning, depression detection.

## I. INTRODUCTION

Depression is the most common mental disorder worldwide and currently the fourth largest contributor to the burden of disease as reported by the World Health Organization [1]. It is estimated that by 2020, depression will remain a leading cause of disability, second only to cardiovascular disease [1]. Depression is associated with widely varying psychological and physiological features, and this heterogeneity is acknowledged within classification systems [2]. Diagnostic criteria for major depressive disorder (MDD) are currently based on clinical and psychometric assessment. The main procedures for evaluation of patients in the field of MDD are neuropsychological screening tests. Some widely used screening tests for the evaluation of depression include Hamilton Rating Scale for Depression (HRSD), Diagnostic Interview Schedule, and Hospital Anxiety and Depression Scale.

Manuscript received February 5, 2013; revised May 16, 2013. This work was supported in part by Deakin University and Ministry of Higher Education Malaysia (MoHE) through SLAB Ph.D scholarship.

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The objective of this study is to provide an automated tool to help in diagnosis of depression by differentiating between healthy and depressed patients in sMRI data. Evaluation of sMRI of the brain is usually achieved through visual ratings performed by medical experts (i.e., radiologists, neuroradiologists). However, conventional evaluation of these scans often relies on manual reorientation, visual reading, and semiquantitative analysis of certain regions of the brain. These steps are difficult, time consuming, subjective, and prone to error. In practice, no clinical expert would diagnose brain diseases only by looking at the abnormality of a single region of the brain. Instead, clinical experts carry out a comprehensive visual inspection of every part of the brain. Therefore, an automated detection system is warranted. Automated tools can be applied to anticipate the diagnosis, and avoid the inter and intra rater variability observed when pathologists give different relative importance to each of the grading criteria. The focus of this study is to investigate machine learning techniques, including attribute selection and classification. Attribute selection aims at retaining only the most relevant attributes and thus improve the generalization ability and the performance of the classifier [3].

In this study, we explore various parts of the brain using the sMRI imaging data by extracting volumetric attributes from the regions and assessing the significance of each attribute during classification. The attributes extraction has been done by the database provider [4] whereas the purpose here is to focus on the attribute selection and classification. In this work, we also compare the performance of the attribute selection and classifier algorithms by using the accuracy rate. To the authors knowledge, this is the first study that explores machine learning algorithms for depression classification from volumetric attributes. In summary, the contributions of this paper include: 1) evaluating and determining the most discriminant sMRI volumetric attributes for single-subject classification of depression 2) identifying machine learning algorithms that automatically determine relevant attributes and are optimal for depression detection.

This paper is organized as follows. Section II describes the related works. Section III explains the methods and the algorithms, as well as the selected attributes. Section IV describes the proposed experimental procedure comprising the system flowchart. Section V presents the experimental results and discusses them. The conclusions are given in Section VI.

## II. RELATED WORKS

In group-level analysis, depression is mainly characterized by volumetric reductions or increase in the hippocampus, amygdala, anterior cingulate cortex, orbitofrontal cortex,

dorsolateral prefrontal cortex, subgenual prefrontal cortex, putamen, and caudate. Also cerebrospinal fluid have been specifically associated with depression. However, the available individual depression detection studies based on sMRI (Costafreda *et al.* [5], Nouretdinov *et al.* [6], Gong *et al.* [7], Mwangi *et al.* [8], [9], Bao *et al.* [10]) have utilized different attributes for the detection. The attributes used are voxel based morphometry, brain shape and voxels value.

Attribute selection processes still have not gained much attention in the available depression detection research. There are only few studies that reported on attribute selection process. The reported studies on the investigation of attribute selection from sMRI depression data implemented ANOVA [92] and *t*-test on VBM [8]. Costafreda *et al.* [5] implemented the whole-brain analysis of variance filtering to select the areas of maximum group differences between patients and controls. Mwangi *et al.* [8] implemented an attribute selection *t*-test filter in VBM to identify the voxels that differed most in depressed patients versus healthy controls. They also investigated a wrapper method called Recursive Feature Elimination. In other brain imaging studies, Principal Component Analysis (PCA) was employed by Fu *et al.* [11] and Marquand *et al.* [12] for attribute selection. The PCA is appealing because it reduces the dimensionality of the data and therefore reduces the computational cost of analyzing new data. Mwangi *et al.* [8] used relevance vector regression (RVR) that is a sparse algorithm that employs only a fraction of its basis functions to make predictions. A study by Chyzyk *et al.* [13] employed Lattice Independent Component Analysis (LICA) and the kernel transformation hybrid with dendritic computing classifiers. These previous studies did not specifically investigate attribute selection.

At the classification, the SVM classifier was employed by Costafreda *et al.* [5], Gong *et al.* [7] and Bao *et al.* [10]. Besides the SVM classifier, Bao *et al.* [10] also investigated the K-Nearest Neighbor classifier for predicting treatment remission in MDD. Nouretdinov *et al.* [6] proposed a general probabilistic classification method to structural and functional MRI to investigate diagnostic and prognostic prediction in depression. The proposed method of classification is known as transductive conformal predictors (TCP). Mwangi *et al.* [9] used regression analysis based on relevance vector regression which is a sparse Bayesian learning method to predict brain disease. In another published study, Mwangi *et al.* [8] investigated both RVM and SVM machine learning for diagnostic purpose.

### III. METHODS

#### A. Description of the Data, Definition of ROIs and Attribute Extraction

The 3-D volumetric attributes were extracted from sMRI data provided by Neuropsychiatric Imaging Research Laboratory at Duke University called MIRIAD [4], a NIMH-supported study that has enrolled older depressed and non-depressed adult participants. A total of 115 brain data were included consisting of 88 healthy controls and 27 depressed images. Forty-four volumetric attributes were used for investigation (i.e whole brain volume, gray matter volume, white matter volume, hippocampus volume and etc). A list of attributes and their definition is available in Appendix I. The

extracted ROIs were manually traced by an expert neuroradiologist using the Analyze tool, and volumes measured using MrX tools. More detail on the pre-processing is given in ref. [14].

#### B. Attribute Selection, Ranker Search and Classifier Algorithms

Four attribute selection algorithms are used including one rule (OneR), support vector machine (SVM), information gain (IG) and ReliefF. In this study we applied default setting for the algorithms run in WEKA, a non-commercial and open-source data mining system [15].

The OneR algorithm creates one rule for each attribute in the training data, then selects the rule with the smallest error rate as its 'one rule'. To create a rule for an attribute, the most frequent class for each attribute value must be determined. The most frequent class is simply the class that appears most often for that attribute value. Finally, it chooses the attribute that offers rules with minimum error and constructs the final decision tree [16].

The SVM evaluates the worth of an attribute by using an SVM classifier [17]. The SVM is that the weights of the decision function are a function only of a small subset of the training examples, called "support vectors". Those are the examples that are closest to the decision boundary and lie on the margin. The existence of such support vectors is at the origin of the computational properties of the SVM and its competitive classification performance.

The IG evaluates the worth of an attribute by measuring the information gain with respect to the class. The information gain is equal to the total entropy for an attribute if for each of the attribute values a unique classification can be made for the result attribute.

The ReliefF evaluates the worthiness of an attribute by repeatedly sampling an instance and considering the value of the given attribute for the nearest instance of the same and different class [18]. It can operate on both discrete and continuous class data.

The Ranker Search algorithm is an extension of the standard forward selection/best first that allows for either a fixed set (i.e. select no more than *n* attributes) or a fixed width (consider only adding an attribute from the top *n* ranked attributes to the current subset at each step) approach to be used. Both these options result in a faster search than standard forward selection (they give similar and sometimes better results due to less overfitting) [15], [19].

There are many classification algorithms that can be used for classification. In this paper, we used ten different classifiers: Naïve Bayes, SVM RBF, SVM Sigmoid, J48, Random Forest, Random Tree, VFI, LogitBoost, Simple KMeans Classification Via Clustering (KMeans), and Classification Via Clustering EM (EM).

### IV. EXPERIMENTAL PROCEDURES

The experiments are conducted using WEKA, a non-commercial and open-source data mining system [2], [3]. WEKA contains tools for data pre-processing, classification, regression, clustering, association rules, and visualization. It is also well suited for developing new machine learning schemes. Attributes selection is performed using a cross validation strategy with 10 folds and 1 seed.

- 1) Volumetric attributes are selected (see Appendix I) from the sMRI dataset (44 attributes are selected in this work). From the selected attributes we constructed a data matrix.
- 2) Class values are assigned as nominal/binary (0, 1) values; 0 represents healthy subjects and 1 stands for depressed subjects.
- 3) All the attributes are ranked using four attribute selection methods.
- 4) The attribute rankings are tabulated from highest to lowest for the four methods.
- 5) New datasets are created from each attribute ranking result; A total of 17 new matrixes are formed out of the original data matrix as follows: Top 1, Top 2, Top 3, Top 4, Top 5, Top 6, Top 7, Top 8, Top 9, Top 10, Top 15, Top 20, Top 25, Top 30, Top 35, Top 40, and Top 43.
- 6) The new data subsets are named according to format; Top <Ranking No.>\_<Attribute Selection Name>. Each attribute selection has 17 sets, thus, there are 68 new dataset formed from this combination.
- 7) Ten classifiers are selected for the classification: Naïve Bayes, SVM RBF, SVM Sigmoid, J48, Random Forest, Random Tree, VFI, LogitBoost, Simple KMeans Classification Via Clustering, and Classification Via Clustering EM. The classification experiments were designed as training/test of 70/30. All together we have  $68 \times 10 = 680$  possible combination. Instances were "arranged to ensure balanced no of class in each sub set". The classification rule set to follow the initial arrangement (with order preserved).
- 8) The accuracies percentages for the classification were automatically calculated by WEKA. The results are ranked in descending order using the accuracy percentage.

significantly small number of attributes,  $N=7$  needed for the classification. Overall, it can be seen that the EM, J48, Random Forest and Random Tree classifiers achieved good performances and have the potential for depression detection classification problem. However, the Naïve Bayes and the VFI performances were very sensitive to the attribute selection used.

Finally, the proposed attribute selection was compared against the previous works [5], [8] which used statistical filter method (ANOVA and  $t$ -test). The classification accuracy in ref. [5] is 67.6%, which is smaller than the accuracy of the proposed attribute selection. However, the classification accuracy in [8] is 87.1%, which is slightly higher than the accuracy of the proposed attribute selection. The performance difference may also be due to the difference in the attributes used.

TABLE I: AVERAGE ACCURACY (ACC), NUMBER OF ATTRIBUTES (N), F-MEASURE AND AREA UNDER THE CURVE (AUC)

Evaluator	Classifier	N	Accuracy	AUC
SVM	EM	7	85.2941	0.6875
IG	RandomTree	15	85.2941	0.6875
ReliefF	J48	30	82.3529	0.4856
IG	J48	35	82.3529	0.4856
SVM	Kmeans	1	82.3529	0.6683
SVM	Kmeans	7	82.3529	0.6683
All	NaiveBayes	44	82.3529	0.5962
SVM	RandomForest	8	82.3529	0.7163
IG	RandomForest	6	82.3529	0.7188
IG	RandomForest	15	82.3529	0.6875
ReliefF	RandomTree	3	82.3529	0.6250
ReliefF	RandomTree	5	82.3529	0.6250

## V. RESULTS AND DISCUSSIONS

### A. Classification Performances

Table I shows the accuracy rates (percentage of correctly classified samples) and the average area under the receiver operating characteristic curve (AUC), respectively, for the combination that achieved accuracy greater than or equal to 80%. The results are sorted from the highest to lowest accuracies. It can be seen that the hybrid evaluator SVM and the filter evaluator IG has the highest accuracy.

The best accuracy for the attribute selection-classifier is displayed in Fig. 1. When the presented attribute selection methods were used in combination with an SVM RBF/Sigmoid, the results were consistent regardless of the attribute selection used. The evaluator OneR in combination with SVM RBF classifier produced slightly higher accuracy of 79.41% compared to the other methods. These results were comparable or better than those reported in previous works [5], [7], [8], [10] using the SVM. The existing works reported accuracies between 58.70% to 87.1% when using the SVM, while our classification showed stable results between 76.47% to 79.41%. However, the accuracy increased when an EM or Random Tree classifier was applied instead of the SVM. The hybrid evaluator SVM in combination with the EM classifier and the filter evaluator IG in combination with the Random Tree classifier recorded highest accuracy of 85.29%. The good performance of the EM classifier here attributed to the

### B. Evaluation of Attributes/Features

The attributes of the final set are different for each classification pair and each attribute selection method. Table II shows the most frequent selected attributes at certain achieved accuracy. The table tabulates the attributes with its corresponding frequency and ranked in descending order. From Table II, it can be seen that the Top 2 attributes contributed to  $accuracy \geq 75-85$  are the same and the Top 4 attributes contributed to  $accuracy \geq 75$  and 80 are the same. For the accuracy score of 75 or above, the Top 1 (ltotgm) in the ranking doubled the frequency for attributes on ranked number 11 (rhippoc) and 12 (rtotgm).

Specifically, when the  $accuracy \geq 80$ , the Top 1 and 2 have significantly higher frequencies compared to the rest. The frequency reduced significantly from Top 2 to Top 3 attributes. Interestingly, for higher accuracy (85%), we could perceive that only 18 attributes contributing and the frequency for the Top 4 attributes is actually doubled the remaining. Specifically for  $accuracy \geq 85\%$ , left-brain dominated the contribution with total frequency of 14 frequencies. Fig. 2 illustrates the most important brain attributes for the  $accuracy \geq 85\%$ . This result is in accordance to reported works in depression at group-level statistical analysis. For example, previous studies have shown a morphometric reduction of the hippocampus (bilateral hippocampus, left and right hippocampus, and hippocampus

grey matter) in patients with depression compared to healthy controls [20]. It can be seen that on overall, the most important attribute was ltotgm.

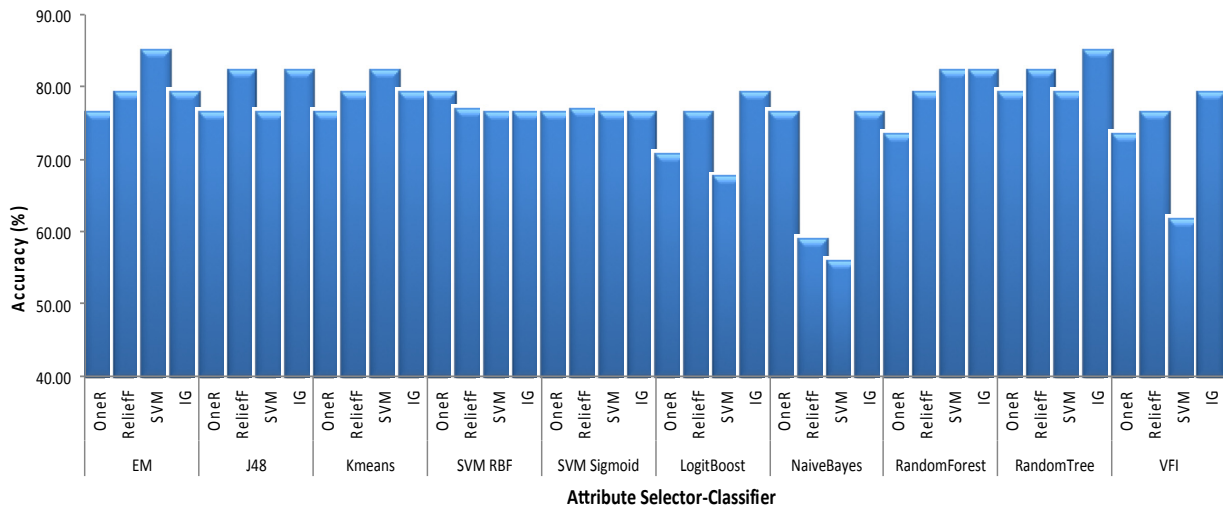


Fig. 1. Best classification accuracy of attribute selection-classifier combination.

TABLE II: THE MOST FREQUENT SELECTED ATTRIBUTES AND THE CORRESPONDING FREQUENCY

ACC≥75			ACC≥80		ACC≥85	
No	Attributes	f	Attributes	f	Attributes	f
1	ltotgm	204	ltotgm	10	ltotgm	2
2	lhemis	194	lhemis	9	lhemis	2
3	lnonlgm	182	lnonlgm	7	ltotcsf	2
4	ltotcsf	145	ltotcsf	7	nvcsf	2
5	wholebr	144	nvcsf	7	lnonlgm	1
6	cerebrm	131	wholebr	6	wholebr	1
7	tothippoc	128	nvcsf	5	nvcsf	1
8	nvcsf	127	lvent	5	lvent	1
9	nvcsf	116	rhippoc	5	rhippoc	1
10	lvent	113	ltotwm	5	ltotwm	1
11	rhippoc	109	lgmles	4	lgmles	1
12	rtotgm	96	totgm	4	totgm	1
13	ltotwm	91	lnonlgm	4	lnonlgm	1
14	lgmles	91	lnonlwm	4	lnonlwm	1
15	totgm	84	totvent	4	totvent	1
16	totcsf	82	cerebrm	3	ltotles	1
17	lnonlgm	80	tothippoc	3	rgmles	1
18	rgmltc	78	ltotles	3	lwmlcs	1
19	lnonlgm	76	rgmles	3	cerebrm	0
20	ltotles	75	lwmlcs	3	tothippoc	0

\*ACC: accuracy

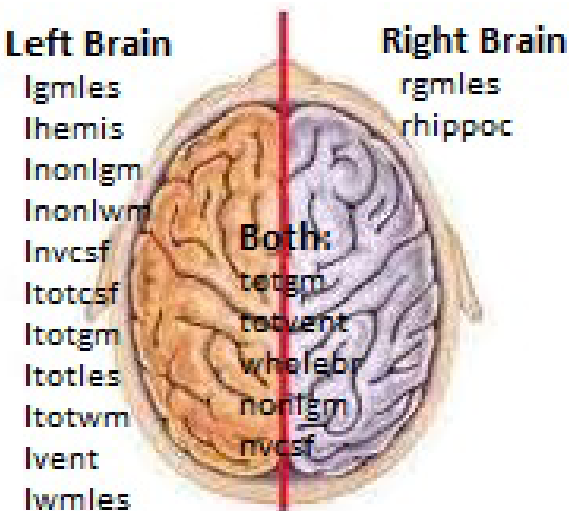


Fig. 2. The most important brain attributes (ACC≥85%).

## VI. CONCLUSION

In this study, several machine learning techniques for attribute selection and classification were examined for depression detection using the brain volumetric attributes. The potential of attributes extracted from the brain sMRI volumetric calculation was explored and the diagnostic value of each attribute was investigated. The performance results highlight the potential of depression detection from sMRI volumetric attributes. The SVM evaluator in combination with the EM classifier and the IG evaluator in combination with the Random Tree classifier have achieved the highest accuracy. However, the small sample sizes limits the ability to draw firm conclusions. Thus, further studies with larger datasets are necessary to generalize the results and improve the performance of the whole detection system.

## APPENDIX

### APPENDIX I: VOLUMETRIC ATTRIBUTES DESCRIPTIONS

No	Attributes	Description
1	nonlgm	Non-lesion gray matter (GM) volume in whole brain
2	gmles	Subcortical gray matter lesion (GML) volume in cerebrum
3	totgm	Total GM volume
4	nvcsf	Non-ventricular CSF volume in the whole brain
5	totvent	Total Lateral ventricle volume
6	totcsf	Total CSF volume
7	nonlwm	Non-lesion white matter (WM) volume in whole brain
8	wmlcs	WM lesion volume in the cerebrum
9	totwm	total WM volume
10	totles	total lesion volume
11	wholebr	whole brain volume
12	lnonlgm	Non-lesion GM volume in left cerebral hemisphere
13	lgmles	Subcortical GML volume in the left cerebral hemisphere
14	ltotgm	left hemisphere total GM volume
15	lnvcsf	Non-ventricular CSF volume in left cerebral hemisphere
16	lvent	Lateral ventricle volume in left cerebral hemisphere
17	ltotcsf	left hemisphere total CSF volume
18	lnonlwm	Non-lesion WM volume in left cerebral hemisphere
19	lwmlcs	WML volume in the left cerebral hemisphere
20	ltotwm	left hemisphere total WM volume
21	ltotles	left hemisphere total lesion volume

22	lhemis	left hemisphere volume
23	rnonlgm	Non-lesion GM volume in right cerebral hemisphere
24	rgmles	Subcortical GML volume in the right cerebral hemisphere
25	rtotgm	right hemisphere total GM volume
26	rmvcsf	Non-ventricular CSF volume in the right cerebral hemisphere
27	rvent	Lateral ventricle volume in the right cerebral hemisphere
28	rtotcsf	right hemisphere total CSF volume
29	rnonlwm	Non-lesion WM volume in right cerebral hemisphere
30	rwmls	WML volume in the right cerebral hemisphere
31	rtotwm	right hemisphere total WM volume
32	rtotles	right hemisphere total lesion volume
33	rhemis	right hemisphere volume
34	cerebrm	cerebral volume
35	lgmtc	Left caudate GM volume
36	lgmltc	Left caudate lesion volume
37	rgmtc	Right caudate GM volume
38	rgmltc	Right caudate lesion volume
39	lputamn	Left putamen volume
40	rputamn	Right putamen volume
41	lhippoc	Left hippocampus volume
42	rhippoc	Right hippocampus volume
43	totputamn	total putamen volume
44	tothippoc	total hippocampus volume

#### ACKNOWLEDGMENT

We thank the Duke University NIRL for making the MIRIAD MRI data available. ”

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