Data Mining Using SPECT Can Predict Neurological Symptom Development in Parkinson's Patients

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We have compared in Parkinson's diseases patients neurological data with the local cerebral blood flow measured by the Single-Photon Emission Computed Tomography. Most of our patients underwent Deep Brain Stimulation surgery or were qualified for one in relation to the advanced disease progression. Local cerebral blood flow in different areas has correlated to the Unified Parkinson's Disease Rating Scale (UPDRS). We have used two different data mining methods: WEKA and Rough Set Exploration System to explore these correlations. We have demonstrated that cerebral blood flow changes gave good predictions for the UPDRS IV (84 %) that suggest that a general state of Parkinson Disease are stronger related to the cerebral blood flow than to only motor symptoms.

Deep brain stimulation, Parkinson Disease, SPECT, UPDRS

I. INTRODUCTION

Parkinson Disease (PD) is the second major neurodegenerative disease related to the population ageing. Currently we are not able to cure this and other neurodegenerative diseases. The most popular treatments are pharmacological and in more advanced cases - the deep brain stimulation (DBS). Although PD is known for quite long time, symptom developments in individual patients show great variability.

Our purpose was to estimate PD symptoms by extracting relevant attributes from the local CBF changes and to apply data mining and machine learning methods in order to help neurologists in an objective estimation of the disease progression. In the standard approach, PD progression is estimated on the basis of subjective patient's reports and also partly subjective doctor's measurements (Unified Parkinson's Disease Rating Scale – UPDRS).

In this work, we have analyzed two sets of data: one related to the local CBF: SPECT data and the other neurological data acquired obtained by patients and neurologist classified into different UPDRS parts.

SPECT is known imaging method which have been used in analysis of PD symptoms in previous studies. It provides information about blood flow in given regions of brain. In earlier study [1] it was demonstrated that the SPECT analysis of PD during 4-year period regarding symptom progression correlated to tracker uptake values acquired from the imaging procedure. It showed that SPECT uptake values decline in patients by 11% per year.

Another study found SPECT correlation with PD symptoms [2] . In this work PD patients were compared to the control group. This result correlates with our initial SPECT data, which shows decrease in uptake values after DBS that general correlates with PD symptoms.

The following papers [3], [4] studied 29 PD patients and 38 healthy volunteers as control group. In comparison to [2] they found that putamen as a region of interest can be used in diagnostics of early PD with high accuracy. In addition to the local CBF in the putamen in both papers were also analyzed caudate uptake correlations.

SPECT analysis was found useful in order to predict the early parkinsonism [5]. In this work SPECT data was applied to diagnose PD patients with unilateral symptoms before manifestation of motoric dysfunctions.

There are many examples of data mining techniques application in order to improve PD classification and assessment quality of symptoms or side effects that are usually

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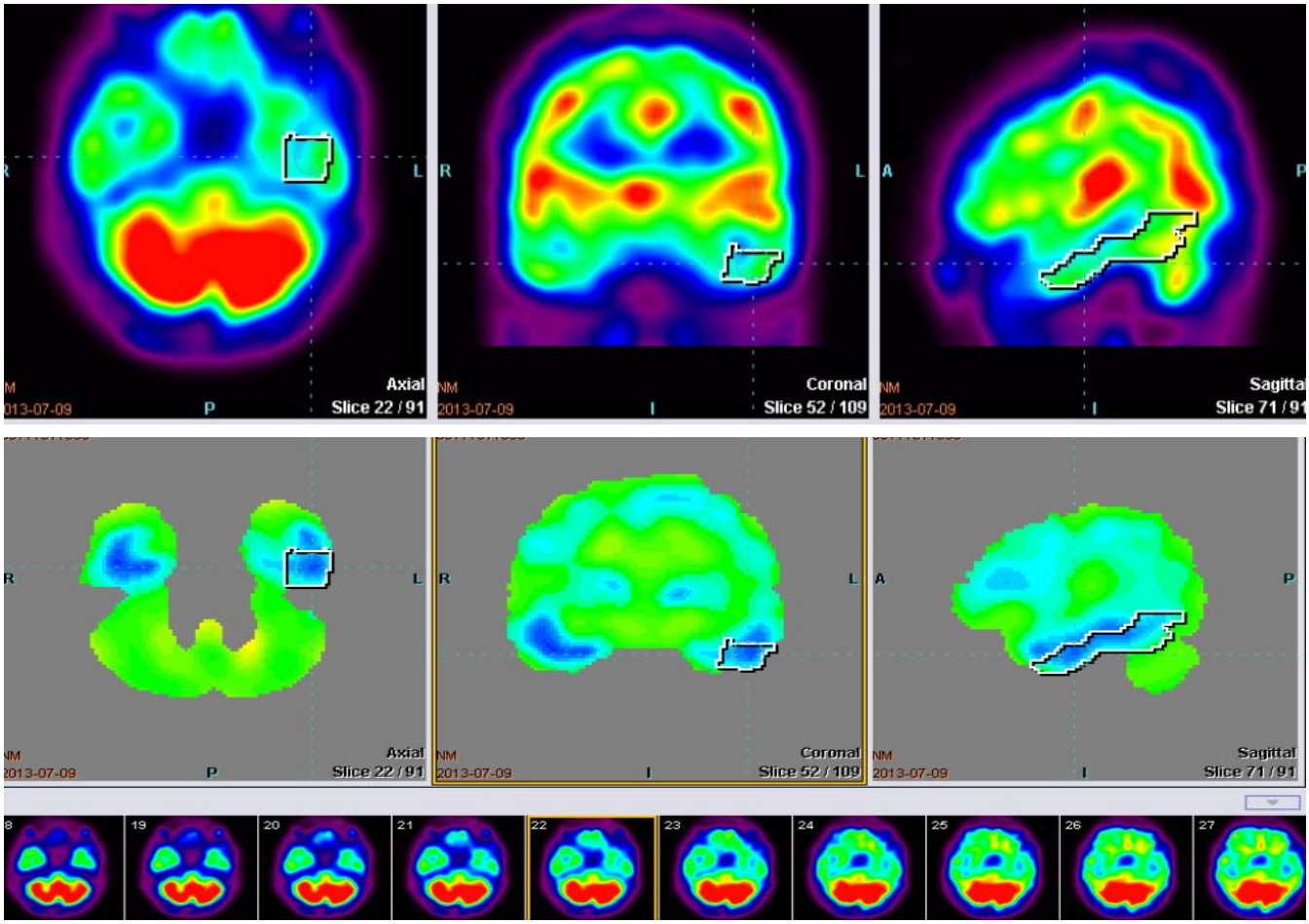

Fig. 1. Example SPECT imaging data for inferior temporal gyrus (ROI marked in slice views). Two upper rows present different color maps for uptake values of the tracker. And bottom row present axial slices of uptake values.

difficult to evaluate in objective way. In our previous study, we have applied and predicted DBS parameters in PD based on the Diffusion Tensor Imaging data (anatomy) correlated with neurological symptoms based on UPDRS. [6]

Our present approach is an extension of above-mentioned studies but is based on different data sets. Our goal was to develop method, which could give us highly objective system to compare symptoms in individual related different types of treatments.

II. METHODS

A. SPECT data

We have collected data from the Single-photon emission computed tomography (SPECT) analysis for 17 patients. Only part of the test group had data before and after the DBS, so partially we had only data from pre DBS stage. This type of nuclear medicine procedure gives information about cerebral blood flow (CBF) in a given region of interest (ROI). It is based on injecting into subject's bloodstream tracer, which emits gamma radiation. In the SPECT, the direct radiation emitted by the tracker is measured and uptake is calculated in order to extract the local blood flow. The resolution of the SPECT imaging is in the range of 1 cm. Gamma radiation is measured by providing minimum, maximum and mean uptake of the tracker for given region of interest.

Our SPECT analysis consists of 75 measurements from different regions of interest (ROI). Each ROI has measurements for both hemispheres. This creates challenging number of attributes for each session in individual patient, which with certain data mining methods could lead to over fitting issue thus may decrease classification's accuracy. We have decided to narrow down number of parameters used in this study. We will focus on three areas especially important in PD [7], [8] that already were used with analysis of SPECT data [9]:

- Basal ganglion
- Caudate nucleus
- Supplementary motor cortex

These areas are known to play key roles in PD pathology and they are indirectly stimulated by the DBS. Also the supplementary motor cortex has somatotopic connections with the primary motor cortex that is affected in PD. Therefore, we

can expect the correlation between SPECT and Unified Parkinson Disease Rating Scale (UPDRS).

B. Neurological data

In addition to SPECT measurements we gathered neurological information, which were collected from patients in four sessions. Each session was based on two attributes: best medical treatment (BMT) and deep brain stimulation (DBS) being either on or off. We had following four sessions numbered from 0 to 3:

- 0: BMT off, DBS off
- 1: BMT off, DBS on
- 2: BMT on, DBS off
- 3: BMT on, DBS on

Every session has additional attribute called "Type of Visit" (Tab.1). This attribute gives information about time in relation to DBS that given session was measured. Meaning that we have multiple sessions of the same type for one patient being collected in different periods, for example 3 months after DBS, 6 months after DBS or 12 months after DBS (Tab.1).

Neurological data consisted of many attributes, among them: the Hoehn and Yahr (H&Y) scale, the Schwab and England scale, UPDRS classification for both side of the body for specific symptoms. UPDRS sections covered were:

- I: Mentation, behavior and mood
- II: Activities of daily living
- III: Motor examination
- IV: Complications of therapy

C. Data mining - RSES

We have analyzed our data with the Rough Set Exploration System (RSES) version 2.2, which is data mining tool developed in java and implements rough set theory proposed by Pawlak [10].

TABLE I. EXCERPT FROM DECISION TABLE

Session #		2	1	2	0	2
Patient #		59	47	51	53	61
Type of visit		6	0	12	6	6
Mean uptake	**Basal ganglia L**	28607	13398	19404	18339	14259
	Basal ganglia R	31026	14277	19337	18670	13747
	Supplementary motor L	30470	13917	18532	16301	13587
	Supplementary motor R	30378	14753	19054	16521	13551
	Caudate nucleus L	22643	10039	17088	16629	11920
	Caudate nucleus R	25365	11619	15706	17238	11551

In order to apply rough set theory we have properly structured our data, defined as the information system or a decision table. As in Pawlak original work [10] we define an information system as S = (U, A), where sets U is set of cases and A is a set of attributes. Both are nonempty and finite. The decision table defines function *p* which maps a product of U and A into set of values. Let B be a nonempty subset of set A of all attributes. The indiscernibility relation IND(B) is a relation on U defined on x,y ∈ U as follows:

$$(x, y) \in IND(B) \text{ if and only if } \rho(x, a) = \rho(y, a) \text{ for all } a \in B \quad (1)$$

Afterwards we define the notion of reduct B⊂A based in indiscernibility relation as a reduct of information system if IND(B) = IND(A) and there aren't any other subsets having this property. We name a decision reduct of a decision table as a set B⊂A which attributes cannot be further reduced and IND(B) ⊂ IND(D). We distinguish two sets of attributes in the system: C – conditional attributes and attribute D – decision attribute. For any decision attribute D, if an object in a set satisfy given subset of C attributes it is automatically classified based on given reducts.

In this work we have created decision rules from two subsets of data. First was neurological data from patient examination and second data acquired from SPECT. Both data sets were explained above.

We have divided the decision table into the training and the test subsets. On the basis of the training set derived from the decision table, we have created decision rules and used them to classify in the next step test set of data. The number of decision rules in given data set can be very extensive so the reduct set was used which reduced redundant decision rules conditions in classification. In order to do this we applied several algorithms techniques for example by using discretization function on data, creating ranges of values for given decision class for given attribute. We have few algorithms available in RSES for creating those, among them LEM2 algorithms, covering algorithms, genetic algorithms and exhaustive algorithms. We have used exhaustive algorithm [6].

Since not all the fields were always filled with data, especially in neurological data where not all dimensions were always relevant for assessment in given period we needed to handle them appropriately. In RSES we have few options to do this, namely: fill empty values with most common value for given attribute, fill empty values with most common value for given decision class, analyze data without taking into account empty values or treating missing values as information. In this paper we use the last option so treating missing value as information.

D. Data mining – WEKA Random Forest

As a second tool to compare our data mining results we choose WEKA framework and specifically random forest implementation.

TABLE II. PREDICTION ACCURACY RESULTS FOR RSES AND WEKA RANDOM FOREST ALGORITHM

SPECT data attributes set	Decision attribute	RSES		WEKA
		Accuracy	Coverage	Accuracy
Mean uptake from all regions	I	71,9	81	61,07
Mean uptake from all regions	II	48,1	81	50,72
Mean uptake from all regions	III	15,1	90	27,29
Mean uptake from all regions	IV	83,7	84	54,01
Mean uptake from all regions	Total	12,3	97	39,31
Mean uptake from all regions	HY	51,2	86	37,07
Mean uptake from all regions	SE	65,2	79	42,61
Parahippocampal gyrus and supramarginal gyrus	I	80,4	72	60,59
Celeberum	I	80,8	79	58,77

Motivation behind choosing exactly this algorithm was decent accuracy, capabilities to handle a lot of attributes and effective method for estimating missing data.

Random forest bases on the combination of tree predictors where each tree depend on values from random vector sampled for all trees in the forest. Vector is sampled independently and with the same distribution. Having the decision sub trees based on training set we are applying the decision trees to an object we want to classify, and each decision sub tree is used to predict the decision class.[11]

To classify objects by multiple decision trees we have counted results and made prediction according to a value that was selected by majority of them.

In our experiments we have run tests with 10 decisions trees selected from the testing set.

III. RESULTS

We have gathered data from 17 patients, each patient having multiple sessions as well as being examined during different time periods after the DBS surgery. In total our information system consisted of 104 objects to be analyzed and classified in course of data mining process.

Initially we started in extracting mean SPECT tracer uptake values for all available regions for both hemispheres. This gave us decision table that has 167 attributes: 3 attributes related to patient and session information, 130 attributes from SPECT data and 34 scales related attributes, including UPDRS, H&Y and Schwab and England scale. 167 attributes from SPECT data consist of different predefined ROI's captured by Siemens Scenium Analysis, this consist of roughly 80 brain areas, most of them with measurements for both hemisphere. Part of this data table can be seen on Tab I.

Brief statistics regarding the data objects, mean patient age was 58.06 ± 21.06, mean total UPDRS for specific session was: S0: 68 ± 40, S1: 33.78 ± 29.78, S2: 48.64 ± 31.35 and S3: 25.4 ± 20.4.

As these numbers of attributes were too big to be used with our data we need to reduce number of it. In order to do this we have performed first round of classification in RSES of full data set with tenfold cross validation method. We have acquired results as can be seen in Tab II. We have observed particularly good accuracy for predictions of UPDRS I and IV being respectively 71.9% and 83.7%. Moderate results were acquired for predicting UPDRS II, H&Y and Schwab and England scale averaging around 55%. The poorest results were acquired for UPDRS III with 15.1% of accuracy.

Next round of testing consisted of tests for well-known brain areas which were already described in previous papers [1], [9] as one which are known to be correlated with PD progression. Those areas include: basal ganglia, caudate nucleus, putamen and supplementary motor cortex. By narrowing down SPECT attributes to only the ones responsible for previously mentioned measurements we have created information system with 11 condition attributes. Best results using this setup were acquired for UPDRS I and IV, respectively estimated to 80.2% and 88.4% in RSES.

After preliminary results from full information system in order to narrow down the number of attributes we have examined reducts generated by RSES in order to classify objects. Especially interesting case was found in UPDRS I where we have observed 3 reducts which were at the same time the biggest decision set and included SPECT areas:

{ Patient #, TypeOfVisit, "Supramarginal gyrus_L+First*(mean_uptake)" }

{ Session, TypeOfVisit, "Parahippocampal gyrus_R+First*(mean_uptake)" }

{ Patient #, TypeOfVisit, "Parahippocampal gyrus_R+First*(mean_uptake)" }

In conclusion that both parahippocampal gyrus and suppramarginal gyrus were very often used in predicting this decision attribute.

In next step we have extracted dataset only with following two regions, leaving rest of our decision table as it was in previous stage and rerun the classification for UPDRS I. The results was 80.8% of accuracy and 72% of coverage. This gave us improvement by 8.5% in accuracy but decline in coverage by 9% in comparison to the first stage classification.

TABLE III. PREDICTION ACCURACY RESULTS FOR SPECYFIC PD SYMPTOM - TREMOR

Decision attribute	RSES		WEKA	
	Acc.	Cover.	Acc.	Cover.
UPDRS 20 Face Lips Chin	82,8	83	80,89	94,38
UPDRS 20 RHand	48,7	84	48,31	82,02
UPDRS 20 LHand	54,8	85	51,68	88,76
UPDRS 20 RFoot	71,1	87	76,4	89,88
UPDRS 20 LFoot	71,5	85	75,28	89,88

After additional examination we noticed that a lot of reducts for UPDRS I depends on attributes connected to uptake in celebellum. Following that we have extracted another subset of attributes from our main data table and re-run all tests. This time we were able to acquire 80.8% of accuracy and 79% of coverage. This gave a small improvement in the accuracy of 0.4% and increased coverage by 7%.

After performing the data exploration and classification in RSES we rerun all the tests in WEKA using earlier mentioned random forest algorithm.

Summary of results can be found in Tab II. We see that random forest algorithm was better in predicting UPDRS II, III and total UPDRS. But in general, it gave not as good classification results as RSES.

On the basis of information table, we also run data mining process in both Weka and RSES for specific UPDRS III attributes that in connection with previous data described patient particular symptoms like hand tremor in a given time period for the given session. Additionally we narrowed down SPECT regions to the basal ganglia and supplementary motor cortex, regions involved in motor functions, as most of the specific UPDRS in our data set is related to these functions [7]. We obtain the best results for UPDRS 20, which is a subsection of UPDRS III. It describes the tremor at rest and it is measured for different body parts, specifically for left and right hand, for foot, lips, chin and face. Best result was acquired for predicting face, lips and chin tremors and it was estimated to 82.2% in RSES and 80.89% in Weka by using random forest algorithm. Full result can be seen on Tab III.

We note that Weka has better accuracy in predicting summarized symptom assessments for numeric attributes like total UPDRS, UPDRS III, H&Y scale, but RSES was in most cases better in predicting attributes with limited subset of possible values like specific UPDRS symptoms or UPDRS sections with limited range of values. Summarized scale results were expressed as numeric values and specific UPDRS symptoms were defined as symbolic values which can take only values from 0 to 4, as 0 is a normal, and 4 is the most sever. We conclude that RSES is better in predicting small subset of values, but receiving poor results for numeric values. On the other hand Weka random forest reached insignificantly inferior to RSES results in most symbolic attributes predictions but were much more efficient in predicting numeric values for total UPDRS and other general scales.

In all tests with coverage greater than 80%, Weka gave better results than RSES with mean coverage of 88.98% for specific UPDRS, and RSES reaching 84.8%. We have also compared coverage for the specific UPDRS.

Until this point all our experiment was conducted on SPECT data and neurological data only. In the next step, we have repeated our analysis in relationship to additional attributes such as DBS-on, DBS-off or BMT-on, BMT-off and another patient-related attributes. . This created situation that for one set of SPECT measurements we had several feature sets from neurological data being gathered in regard to BMT. Our anlysis included splitting this data into two subsets, one containing only rows with BMT-on, and another with BMT-off. This created two separate tables with 52 data objects each.

We have rerun selected tests that gave promising results in previous experiments and it turned out that BMT-on and

TABLE IV. RESULTS FOR PREDICTING DIFFERENT SUBSETS OF DATA IN REGARD OF BMT ATTRIBUTE

Subset	SPECT data attributes	Decision attribute	RSES		WEKA	
			Accurancy	Coverage	Accurancy	Coverage
BMT Off	all mean	I	55	62	32,69	61,53
	parahippocampal, supramarginal	I	49,8	62	42,31	76,92
	all mean	II	2,5	50	17,31	32,69
	all mean	IV	55	56	21,15	50
		Mean total:	**40,58**	**57,50**	**28,37**	**55,29**
BMT On	all mean	I	56,7	64	32,69	76,92
	parahippocampal, supramarginal	I	61,7	66	36,53	86
	all mean	II	11,7	48	15	n/a
	all mean	IV	50,2	56	17,3	55,76
		Mean total:	**45,08**	**58,50**	**25,38**	**72,89**

BMT-off data limitations decreased accuracy of the model. We have obtained the maximum accuracy with RSES for predicting UPDRS I of 55% with 62% coverage. Both accuracy and coverage dropped in comparison to previously constructed information system. Also we observed decline in both accuracy and coverage, for BMT-on: the mean accuracy was 45.08% and coverage was 58.50%. For sessions with BMT-off we got accuracy of 40,58% and coverage was 57.70%. Full results are shown in Tab IV.

Also we notice that in this experiment WEKA results were significantly worse than RSES, reaching maximum of 42.31% in accuracy with mean 28.37% for BMT-on and 25,38%. For BMT-off

IV. DISCUSSION

We have demonstrated that on the basis of local CBF measured by SPECT one can predict symptoms of Parkinson Disease. We have presented how to improve accuracy classification by data exploration and selecting appropriate ROI's.

On the other hand, different data mining methods have different advateges/disadvanteges., WEKA was better to assess general numeric attributes where RSES had better accuracy with symbolic attributes but with narrow subset of possible predictions. We have got similar results in our previous works [6].

Further work should include broadening available data set as well as exploring more data mining and exploration methodologies. We have demonstrated that two proposed methods we can acquire significantly different results when applying dedicated algorithm for a given task.

From physiological point of view it would beneficial to acquire more sessions of SPECT measuremets to see how results are related to the time after the DBS surgery. Similar studies was already conducted but it was based on patients that did not undergo DBS treatment. An important clinical conclusion from this study is that the CBF changes are stronger related to UPDRS I and IV and not to movement symptoms measured by UPDRS III. In consequence the local CBF can be more sensitive biomarker that mostly used motor disorders.

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