IGrC: Cognitive and Motor Changes During Symptoms Development in Parkinson's Disease Patients

Andrzej W. Przybyszewski[1](✉), Jerzy Paweł Nowacki[1], Aldona Drabik[1], Stanislaw Szlufik[2], and Dariusz M. Koziorowski[2]

[1] Polish-Japanese Academy of Information Technology, 02-008 Warsaw, Poland
{przy,jerzy.nowacki,adrabik}@pjwstk.edu.pl
[2] Department of Neurology, Faculty of Health Science, Medical University of Warsaw, Warsaw, Poland
stanislaw.szlufik@gmail.com, dkoziorowski@esculap.pl

Abstract. Cognitive symptoms are characteristic for neurodegenerative disease: there are dominating in the Alzheimer's, but secondary in Parkinson's disease (PD). However, in PD motor symptoms (MS) are dominating and their characteristic helps neurologist to recognize the disease. There are a large number of data mining publications that analyzed MS in PD. Present study is related to the question if development of cognitive symptoms is related to motor symptoms or if they are two independent processes? We have responded to this problem with help of IGrC (intelligent granular computing) approach. We have put together eye movement, neurological and neuropsychological tests. Our study was dedicated to 47 Parkinson's disease patients in two sessions: S#1 - without medications (Med_{OFF}) and S#2 after taking medications (Med_{ON}). There were two groups of patients: Gr1 (23 patients) less advanced and Gr2 more advanced PD. We have measured Gr1 in three visits every 6 months: $Gr1_{VIS1}$, $Gr1_{VIS2}$, $Gr1_{VIS3}$. Gr2 (24 patients) has only one visit (no visit number). With rough set theory (RST) that belongs to IGrC we have found from Gr2 three different sets of rules: a) general rules (G_{RUL}) determined by all attributes; b) motor related rules (M_{RUL}) – motor attributes; c) cognitive rules (C_{RUL}) determined by cognitive attributes. By applying these different sets of rules to different Gr1 visits we have found different set of symptoms developments. With G_{RUL} we have found for $Gr1_{VIS1}$ accuracy = 0.682, for $Gr1_{VIS2}$ acc. = 0.857, for $Gr1_{VIS3}$ acc. = 0.875. With M_{RUL} we have found for $Gr1_{VIS1}$ acc. = 0.80, for $Gr1_{VIS2}$ acc. = 0.933, for $Gr1_{VIS3}$ acc. = 1.0. With C_{RUL} we have found for $Gr1_{VIS1}$ acc. = 0.50, for $Gr1_{VIS2}$ acc. = 0.60, for $Gr1_{VIS3}$ acc. = 0.636. Cognitive changes are independent from the motor symptoms development.

Keywords: Neurodegeneration · Rough set theory · Intelligent granular computing

N. T. Nguyen et al. (Eds.): ACIIDS 2020, LNAI 12034, pp. 548–559, 2020.
https://doi.org/10.1007/978-3-030-42058-1_46

1 Introduction

Cognitive changes are leading in the most common neurodegenerative disease (ND) Alzheimer's disease (AD), but in Parkinson's disease (PD) they are secondary to dominating motor symptoms. In the most cases of AD neurodegeneration starts from the hippocampus and frontal cortex and it related to memory and orientation problems. With the disease progression other brain regions become also affected. In PD neurodegeneration starts from basal ganglia (substantia nigra) and is related to the lack of dopamine. Dopamine (Dopa) controls adaptation of movements to the environment. Therefore PD patients have primary motor symptoms but some of them may have also cognitive changes [1].

As SN (substantia nigra) neurodegeneration causes depletion the Dopa, in addition to the movements' problems there are also potentially emotional and cognitive decays in some PD. As and individual patient has not only a unique neurodegeneration development but also distinctive compensatory processes then as result symptoms might be various and therefore finding optimal treatment is an art for an experienced neurologist.

We have estimated disease progression in different sets of attributes in order to find if motor and cognitive symptoms have similar or dissimilar developments.

This study is an enlargement of our earlier works by using additional to our IGrC (RST) a new attributes – Trail Making Test (TMT) Part A and Part B (see below).

2 Methods

We have evaluated data from Parkinson Disease (PD) patients separated into two main groups with different disease duration:

- **Gr1** contained of 23 patients that received only appropriate medication (L-Dopa). As mentioned above, because PD starts with major neurodegeneration in substantia nigra that regulates the level of the dopamine, the major medications are related to the dopamine precursors or inhibitions of the dopamine reuptake.
- **Gr2** involved 24 patients also as Gr1 only on medications, but they were in the more advanced disease stage. They had longer mean disease duration, as well as their UPDRS was higher than that in Gr1 group. Also these patients went later to the surgery of DBS (deep brain stimulation) that was related to placing stimulating electrode in the basal ganglia – here in the STN (subthalamic nucleus).

All subjects were tested in two related to medications meetings: session 1 (Ses#1) was for patients that stopped taking their medications one day before our tests; session 2 was performed when patients were on their normal medications.

All PD patients had the following measurements: neuropsychological - related to the quality of life (PDQ39), sleep problems (Epworth test), depression (Beck test), and two additional TMT A&B tests; disease duration; UPDRS (Unified Parkinson's Disease Rating Scale) as basic neurological test for PD and fast eye movement tests. TMT tests present the same motor and perceptual demands, namely drawing lines to connect randomly arranged circles. TMT A has only circles with numbers (motor task). In part

B there are numbers and letters that additionally measures divided attention and mental flexibility (TMT B – cognitive task). All patients were tested in the Dept. of Neurology, Brodno Hospital, Faculty of Health Science, and Medical University of Warsaw, Poland. In this study, we have registered reflexive saccadic (RS) eye movements as validated in our earlier articles [1, 2]. In short, each subject was placed *vis-à-vis* computer monitor paying attention to screen before him/her. The experiment began as subject fixated on the spot light in the center of the computer display. The session normally started from the spot light slow movements with increasing speed and continued with random in directions (ten degrees to the right or ten degrees to the left) light spot springing that patient's eyes should followed it. This test took about 1.5 min.

We have registered instantaneous light spot and eyes positions by the clinically proven head-mounted saccadometer (JAZZ novo, Ober Consulting, Poland). In the current work, we have only analyzed fast, saccadic responses of both eyes. We have compared light spot and eyes positions and calculated the following attributes of the fast saccades (RS): the delay (*RSL*) measured as the differentiation between the initiation of the light spot and eyes movements; the amplitude of the saccadic - *RSAm*, its duration (*RSD*) and the mean speed (*RSV*) of both eyes during the saccade.

All procedures and measurements were repeated for each session also in each session patient has to perform 10 RS and means values of above-mentioned parameters were used for the analyses.

2.1 Theoretical Basis

The intelligent granular computing (IGrC) analysis was implemented in RST (rough set theory proposed by Zdzislaw Pawlak [3]) and recently extended by Andrzej Jankowski [4].

In the standard RST procedure all our results were adapted into the decision table with rows showing actual attributes' values for the dissimilar or the same subject and columns were related to different attributes. Following [3] an information system is a pair $S = (U, A)$, where U, A are nonempty finite sets. The set U is the universe of objects, and A is the set of attributes. If $a \in A$ and $u \in U$, the value $a(u)$ is a unique element of V (where V is a value set). The *indiscernibility relation IND(B)* of any subset B of A is defined after [3]: $(x, y) \in IND(B)$ *iff* $a(x) = a(y)$ for every $a \in B$ where the value of $a(x) \in V$. This relation divides A into *elementary granules* and it is the basis of RST. In the information system S set $B \subset A$ is a reduct if $IND(B) = IND(A)$ and it cannot be further reduced. Other important RST properties such as *lower approximation* and *upper approximation* were defined and discussed in [3, 5] and illustrated in [6].

In this work we have used different AI: machine learning methods (RSES 2.2) such as: exhaustive, genetic [7], covering, or LEM2 algorithms [8].

An extension of the information system is the decision table as a triplet: $S = (U, C, D)$ where attributes A are divided into C and D as condition, and decision attributes [9]. As in a single row there are many condition attributes and one decision attribute related to a particular measurement of the individual subject we can interpret it as unique rule $if(condition\text{-}attribute_1 = value_1 \& \ldots) => (decision\text{-}attribute_n = value_n)$. If we gather all such rules (measurements) for a single patient they might be basis for so-called *precision (personalized) medicine* with one condition that they are not contradictory. As in our

decision table we have measurements of different patients in several conditions our main purpose is to find *universal rules*. This is a possible thanks to IGrC implemented in RST that generalize all specific rules into the knowledge with proposals that are always true as it is related to the *lower approximation,* and others are only partly true that is related to the *upper approximation*. Notice that the decision attribute (in our case UPDRS) is the result of tests performed by the neurologist specialized in the Parkinson's disease. Therefore, *the supervised machine learning with a doctor as the teacher determines our knowledge.*

Even for very experienced neurologist finding optimal treatment is difficult and it is related to differences between patients and dissimilar effects of similar treatments. It is connected to differences between individual patients, as the neurodegenerative processes begin many years earlier than first symptoms in PD and during this time plastic compensatory processes in each brain are distinctive.

Our algorithms are related to IGrC that takes into account individual patients differences, but thanks to RST we can obtain abstraction and generalization of our rules that might simulate intuitions of an experienced neurologist. Also we would like to mention that our IGrC mimics such advanced processes in the brain as for example complex objects recognition [10]. We have recently demonstrated that RST can describe processes in the visual brain that are related to different objects classification [10]. Therefore, we might assume that our IGrC rules are sufficiently flexible, abstract and universal (like a visual brain) to resolve Parkinson's disease progressions issues related to different disease stages and various treatments.

We have used as IGrC the RSES 2.2 [11] that generalizes rules from decision table to treat diverse patients. In our earlier work, we have demonstrated that the RST application provides enhanced results than proposed by others AI algorithms [1].

3 Results

As explained above in the Methods section we had two groups of patients: Gr1 of less advanced PD (23 patients) and more advanced group (24 patients). Both group were tested in two sessions: Ses#1 – without medications and in Ses#2 on medications.

Statistical Results

Patients from group Gr1 had three visits: $Gr1_{VIS1}$, $Gr1_{VIS2}$, $Gr1_{VIS3}$ every 6 months. Their mean age was 58 ± 13 (SD) years with mean disease duration of 7.1 ± 3.5 years.

For $Gr1_{VIS1}$ mean total UPDRS in Ses#1 was 48.3 ± 17.9, in Ses#2 was 23.6 ± 10.3 (statistically different with $p < 0.0001$).

For $Gr1_{VIS2}$ mean total UPDRS in Ses#1 was 57.3 ± 16.8, in Ses#2 was 27.8 ± 10.8 (statistically different with $p < 0.0005$).

For $Gr1_{VIS3}$ mean total UPDRS in Ses#1 was 62.2 ± 18.2, in Ses#2 was 25 ± 11.6 (statistically different with $p < 0.0001$).

For Gr2 patients their mean age was 53.7 ± 9.3 years, and they have 10.25 ± 3.9 years disease duration. Their total UPDRS in Ses#1 was 62.1 ± 16.1, and in Ses#2 29.9 ± 13.3.

3.1 IGrC for Reference Gr2 Group

We have placed Gr2 data in the following information table (Table 1).

Table 1. Part of the decision table for three Gr2 patients

P#	dur	S#	PDQ39	Epw.	RSL	RSD	RSAm	RSV	Beck	TrA	TrB	UPDRS
45	13.3	1	56	10	212	46	9.5	407	19	49	90	76
45	13.3	2	56	10	284	47	9.69	402	19	49	90	42
46	7.3	1	48	0	202	55	4.7	168	19	49	60	53
46	7.3	2	48	0	386	49	9.8	367	19	49	60	18
47	9.3	1	94	6	360	60	10.1	353	37	63	333	70
47	9.3	2	94	6	206	50	9.6	337	37	63	333	33

The complete Table 1 has 48 rows (24 PD each in two sessions). There are the following condition attributes: P# - number given to each patients, S# - session number (1 or 2), dur –duration of the disease, PDQ39 – quality of life test result, Epworth test (quality of sleep) results, RS parameters (as describe in the Methods section): RSL – delay. RSD – duration, RSAm – amplitude, RSV – velocity. The last attribute (called decision attribute) was UPDRS (total UPDRS) as described above.

Table 2. Discretized-table extract for above (Table 1) Gr2 patients

P#	dur	S#	PDQ39	Epw.	RSL	RSD	RSAm	RSV	Beck	TrA	TrB	UPDRS
45	"(8.5,Inf)"	1	"(-Inf,58.5)"	*	"(-Inf,219)"	*	*	*	"(12.5,Inf)"	*	*	"(54,Inf)"
45	"(8.5,Inf)"	2	"(-Inf,58.5)"	*	"(219,Inf)"	*	*	*	"(12.5,Inf)"	*	*	"(18.5,43)"
46	"(-Inf,8.5)"	1	"(-Inf,58.5)"	*	"(-Inf,219)"	*	*	*	"(12.5,Inf)"	*	*	"(43.0,54)"
46	"(-Inf,8.5)"	2	"(-Inf,58.5)"	*	"(219,Inf)"	*	*	*	"(12.5,Inf)"	*	*	"(-Inf,18.5)"
47	"(8.5,Inf)"	1	"(58.5,Inf)"	*	"(219,Inf)"	*	*	*	"(12.5,Inf)"	*	*	"(54,Inf)"
47	"(8.5,Inf)"	2	"(58.5,Inf)"	*	"(-Inf,219)"	*	*	*	"(12.5,Inf)"	*	*	"(18.5,43)"

Table 2 is a discretized table for three patients: 45, 46, and 47 in two sessions: S#1 (session 1), and S#2 (session 2). Significant parameters were: disease duration (dur), session number, PDQ39, RSL (saccade delay), Beck depression test results, and UPDRS. Not significant were: Epworth test results, RSD, RSAm, RSV – saccades parameters, and Trail A and B results.

We have used RSES 2.2 for an automatic discretization of the Gr2 measurements. We have found that UPDRS has 4 ranges: "(-Inf, 18.5)" , "(18.5, 43.0)", "(43.0, 54.0)", "(54.0, Inf)".

We had obtained 70 rules for Gr2 patients, and after filtering reduced them to 8 rules. As an example we present below 4 rules filled by the most cases:

$$(dur="(8.5,Inf)")\&(Ses=1)\&(Beck="(12.5,Inf)")=>(UPDRS="(54.0,Inf)"[8])\ 8 \quad (1)$$

$$(Ses=1)\&(RSLat="(219,Inf)")\&(Beck="(12.5,Inf)")=>(UPDRS="(54.0,Inf)"[6])\ 6 \quad (2)$$

$$(dur="(8.5,Inf)")\&(Ses=1)\&(PDQ39="(58.5,Inf)")=>(UPDRS\ \ ="(54.0,Inf)"[5])\ \ 5 \quad (3)$$

$$(Ses=2)\&(PDQ39="(58.5,Inf)")\&(Beck="(12.5,Inf)")=>(UPDRS\ ="(18.5,43)"[5])\ 5 \quad (4)$$

We can interpret rules as following: Eq. 1 claims for 8 cases that if disease duration was longer than 8.5 years and patients were without medications with Beck test above 12.5 (indicating depression) then his/her total UPDRS was above 54. Previously by addition the depression results we have obtained higher accuracy than without Beck depression attribute [12], but in this study we do not see very strong influence of the depression (compare Eqs. 2 and 3). In Eq. 4 patients were on medication with not good quality of life and depressive but his/her UPDRS was medium (between 18.5 and 43).

3.2 IGrC for Estimation of General Disease Progression for Gr1 Group

We have used above general rules from Gr2 to predict UPDRS of Gr1 (Table 3).

Table 3. Confusion matrix for UPDRS of $Gr1_{VIS1}$ group by rules obtained from Gr2-group

		Predicted				
		"(54.0, Inf)"	"(18.5, 43.0)"	"(43.0, 54.0)"	"(-Inf, 18.5)"	ACC
Actual	"(54.0, Inf)"	7. 0	0.0	0.0	0.0	1.0
	"(18.5, 43.0)"	2.0	8.0	0.0	0.0	0.8
	"(43.0, 54.0)"	3.0	1.0	0.0	0.0	0.0
	"(-Inf, 18.5)"	0.0	1.0	0.0	0.0	0.0
	TPR	0.6	0.8	0.0	0.0	

TPR: True positive rates for decision classes; ACC: Accuracy for decision classes: the global coverage was 0.48 and the global accuracy was 0.68, the coverage for decision classes was 0.8, 0.45, 0.57, 0.125.

Table 4. Confusion matrix for UPDRS of $Gr1_{VIS2}$ group by rules obtained from Gr2-group

		Predicted				
		"(54.0, Inf)"	"(18.5, 43.0)"	"(43.0, 54.0)"	"(-Inf, 18.5)"	ACC
Actual	"(54.0, Inf)"	6.0	0.0	0.0	1.0	1.0
	"(18.5, 43.0)"	1.0	7.0	0.0	0.0	0.875
	"(43.0, 54.0)"	2.0	2.0	0.0	0.0	0.0
	"(-Inf, 18.5)"	0.0	0.0	0.0	0.0	0.0
	TPR	0.7	0.8	0.0	0.0	

TPR: True positive rates for decision classes; ACC: Accuracy for decision classes: the global coverage was 0.39 and the global accuracy was 0.72, the coverage for decision classes was 0.46, 0.5, 0.4, 0.0.

Table 5. Confusion matrix for UPDRS of $Gr1_{VIS3}$ group by rules obtained from Gr2-group

		Predicted				
		"(54.0, Inf)"	"(18.5, 43.0)"	"(43.0, 54.0)"	"(-Inf, 18.5)"	ACC
Actual	"(54.0, Inf)"	7.0	0.0	0.0	0.0	1.0
	"(18.5, 43.0)"	0.0	7.0	0.0	0.0	1.0
	"(43.0, 54.0)"	1.0	1.0	0.0	0.0	0.0
	"(-Inf, 18.5)"	0.0	1.0	0.0	0.0	0.0
	TPR	0.9	0.8	0.0	0.0	

TPR: True positive rates for decision classes; ACC: Accuracy for decision classes: the global coverage was 0.37 and the global accuracy was 0.82, the coverage for decision classes was 0.5, 0.438, 0.29, 0.11.

Results from Table 3 to 5 we interpret that with the disease development in time patients from Gr1 become more similar to patients from Gr2 as predictions of their symptoms become more precise from 0.68 to 0.82.

3.3 IGrC for Estimation of Motor Disease Progression for Gr1 Group

We have used the following attributes in order to predict UPDRS of Gr1 group on the basis of motor attributes such as Trail A rests (time of number connecting), eye movements results (RL – latency of saccades) and in addition disease duration and quality of sleep (Epworth test results). In this case, we have obtained from Gr2 33 rules, as examples:

$$(Ses=1)\&(TrailA="(42.0,Inf)")\&(dur="(5.695,Inf)")\&(Epworth="(-Inf,14.0)")\ \&(RSLat="(264.0,Inf)") \Rightarrow (UPDRS="(63.0,Inf)"[4])\ 4 \tag{5}$$

$$(dur="(5.695,Inf)")\&(Ses=2)\&(RSLat="(-Inf,264.0)")\&(Epworth="(-Inf,14.0)")\&(TrailA="(-Inf,42.0)") \Rightarrow (UPDRS="(-Inf,33.5)"[4])\ 4 \tag{6}$$

$$(dur="(5.695,Inf)")\&(Ses=2)\&(TrailA="(42.0,Inf)")\&(RSLat="(-Inf,264.0)")\ \&\ (Epworth="(14.0,Inf)") \Rightarrow (UPDRS="(-Inf,33.5)"[3])\ 3 \tag{7}$$

Notice that these rules Eqs. 5–7 describe UPDRS in two ranges: below 33.5 or above 63. In the consequence in Tables 6, 7 and 8 (below) there is no prediction for other ranges of UPDRS. Equation 5 says that for patients without medication, with disease duration above 5.7 years with long delay of saccades and slow Trail A then their UPDRS was above 63. Even with similar disease duration as in Eq. 6 if patients were on medications and had a short saccadic delay then their UPDRS was below 33.5 (Eq. 7).

Table 6. Confusion matrix for UPDRS of $Gr1_{VIS1}$ group by motor rules obtained from Gr2-group

		Predicted				
		"(63.0, Inf)"	"(33.5, 43.0)"	"(43.0, 63.0)"	"(-Inf, 33.5)"	ACC
Actual	"(63.0, Inf)"	2.0	0.0	0.0	0.0	1.0
	"(33.5, 43.0)"	0.0	0.0	0.0	0.0	0.0
	"(43.0, 63.0)"	1.0	0.0	0.0	0.0	0.0
	"(-Inf, 33.5)"	0.0	0.0	0.0	2.0	1.0
	TPR	0.7	0.0	0.0	1.0	

TPR: True positive rates for decision classes; ACC: Accuracy for decision classes: the global coverage was 0.22 and the global accuracy was 0.5, the coverage for decision classes was 0.7, 0.0, 0.08, 0.08.

Confusion Tables 6, 7 and 8 shows that the motor symptoms give very accurate estimation of the UPDRS with accuracy from 0.8 to 1. There is only problem that coverage is small between 0.11 and 0.32. On the basis of motor attributes, we have very precise predictions but only for a small percentage of the population subjects.

Table 7. Confusion matrix for UPDRS of $Gr1_{VIS2}$ group by motor rules obtained from Gr2-group

		Predicted				
		"(63.0, Inf)"	"(33.5, 43.0)"	"(43.0, 63.0)"	"(-Inf, 33.5)"	ACC
Actual	"(63.0, Inf)"	3. 0	0.0	0.0	0.0	1.0
	"(33.5, 43.0)"	0.0	0.0	0.0	0.0	0.0
	"(43.0, 63.0)"	1.0	0.0	0.0	0.0	0.0
	"(-Inf, 33.5)"	0.0	0.0	0.0	11.0	1.0
	TPR	0.8	0.0	0.0	1.0	

TPR: True positive rates for decision classes; ACC: Accuracy for decision classes: the global coverage was 0.33 and the global accuracy was 0.6, the coverage for decision classes was 0.86, 0.25, 0.33, 0.0.

Table 8. Confusion matrix for UPDRS of $Gr1_{VIS3}$ group by motor rules obtained from Gr2-group

		Predicted				
		"(63.0, Inf)"	"(33.5, 43.0)"	"(43.0, 63.0)"	"(-Inf, 33.5)"	ACC
Actual	"(63.0, Inf)"	1.0	0.0	0.0	0.0	1.0
	"(33.5, 43.0)"	0.0	0.0	0.0	0.0	0.0
	"(43.0, 63.0)"	0.0	0.0	0.0	0.0	0.0
	"(-Inf, 33.5)"	0.0	0.0	0.0	8.0	1.0
	TPR	1.0	0.0	0.0	1.0	

TPR: True positive rates for decision classes; ACC: Accuracy for decision classes: the global coverage was 0.24 and the global accuracy was 0.64, the coverage for decision classes was 0.45, 0.13, 0.3, 0.11

3.4 IGrC for Estimation of Cognitive Disease Progression for Gr1 Group

We have used the following attributes in order to predict UPDRS_T of Gr1 group on the basis of motor attributes such as Trail B rests (time of number and letters connecting), eye movements results (RL – latency of saccades) and in addition session number and quality of sleep (Epworth test results). In this case, we have obtained from Gr2 rules, as examples are:

$$(TrailB="(127.5,Inf)")\&(Ses=1)\&(Epworth="(-Inf,7.5)")=>(UPDRS="(63.0,Inf)"[4])\ 4 \quad (8)$$

$$(Ses=1)\&(RSLat="(244.5,Inf)")\&(Epworth="(-Inf,7.5)")=>(UPDRS="(63.0,Inf)"[3])\ 3 \quad (9)$$

$$(TrailB="(127.5,Inf)")\&(Ses=2)\&(RSLat="(-Inf,244.5)")=>(UPDRS="(18.5,\ 43.0)"[3])\ 3 \quad (10)$$

$$(TrailB="(-Inf,52.0)")\&(Ses=1)=>(UPDRS\ ="(43.0,63.0)"[2])\ 2 \quad (11)$$

The Eq. 8 described the rule for 4 cases when patients were without medications (Ses = 1) and cognitively slow (Trail B time longer than 127.5 s) and without sleep problems (Epworth below 7.5) then UPDRS was above 63 (Eq. 8). In the next Eq. 9 there were similar condition attributes (no medications, no sleep problems), but slow cognitive was replaced but slowness in the reflexive saccades (long latency) that determined an advanced (above 62) UPDRS.

Equation 10 demonstrated that if patient was on medication and had a short saccadic latency, even if his/her Trail B was slow, the UPDRS was in medium range. But without medications even if Trail B was good his/her UPDRS was high (between 43 and 63) (Eq. 11).

Table 9. Confusion matrix for UPDRS of $Gr1_{VIS1}$ group by cognitive rules obtained from Gr2-group

		Predicted				
		"(63.0, Inf)"	"(18.5, 43.0)"	"(43.0, 63.0)"	"(-Inf, 18.5)"	ACC
Actual	"(63.0, Inf)"	2.0	0.0	0.0	0.0	1.0
	"(18.5, 43.0)"	3.0	1.0	0.0	0.0	0.3
	"(43.0, 63.0)"	2.0	0.0	2.0	0.0	0.5
	"(-Inf, 18.5)"	0.0	0.0	0.0	0.0	0.0
	TPR	0.3	1.0	1.0	0.0	

TPR: True positive rates for decision classes; ACC: Accuracy for decision classes: the global coverage was 0.22 and the global accuracy was 0.5, the coverage for decision classes was 0.7, 0.0, 0.08, 0.08.

Table 10. Confusion matrix for UPDRS of $Gr1_{VIS2}$ group by cognitive rules obtained from Gr2-group

		Predicted				
		"(63.0, Inf)"	"(18.5, 43.0)"	"(43.0, 63.0)"	"(-Inf, 18.5)"	ACC
Actual	"(63.0, Inf)"	5.0	0.0	0.0	0.0	0.8
	"(18.5, 43.0)"	1.0	3.0	0.0	0.0	0.8
	"(43.0, 63.0)"	4.0	0.0	1.0	0.0	0.2
	"(-Inf, 18.5)"	0.0	0.0	0.0	0.0	0.0
	TPR	0.5	1.0	0.5	0.0	

TPR: True positive rates for decision classes; ACC: Accuracy for decision classes: the global coverage was 0.33 and the global accuracy was 0.6, the coverage for decision classes was 0.86, 0.25, 0.33, 0.0.

Tables 9, 10 and 11 demonstrated that cognitive changes were not changing so fast with disease development as general or motor changes. They are more stable than other changes and not in the main stream of the neurodegeneration processes in PD. It is related to the fact that accuracy of cognitive changes (from 0.5 to 0.64) was significantly lower in comparison to general (from 0.68 to 0.88) or to motor (from 0.8 to 1.0) symptoms development during disease progression.

Table 11. Confusion matrix for UPDRS of $Gr1_{VIS3}$ group by cognitive rules obtained from Gr2-group

		Predicted				
		"(63.0, Inf)"	"(18.5, 43.0)"	"(43.0, 63.0)"	"(-Inf, 18.5)"	ACC
Actual	"(63.0, Inf)"	4.0	0.0	1.0	0.0	0.8
	"(18.5, 43.0)"	0.0	2.0	0.0	0.0	1.0
	"(43.0, 63.0)"	2.0	0.0	1.0	0.0	0.3
	"(-Inf, 18.5)"	0.0	1.0	0.0	0.0	0.0
	TPR	0.7	0.7	0.5	0.0	

TPR: True positive rates for decision classes; ACC: Accuracy for decision classes: the global coverage was 0.24 and the global accuracy was 0.64, the coverage for decision classes was 0.45, 0.13, 0.3, 0.11.

4 Discussion

We have used IGrC for evaluation of disease development in our longitudinal study of patients with Parkinson's disease (PD). We applied IGrC (intelligent granular computing with RST [3] that looks into "crisp" granules and estimates objects by upper and lower approximations that determine precision of the description as dependent from properties

of granules [3]. In order to follow time changes we have used similarities measured by estimating accuracy between more advance group of patients (Gr2) and another group Gr1 measured three times every 6 months. General and motor symptoms are following disease progression in contrast to cognitive changes that have lower accuracies that might suggest that there different mechanisms of neurodegeneration even if there are some similarities between Parkinson's and Alzheimer's diseases. The next interesting step might be to look into emotional developments during disease progression if they progress like motor symptoms or are relatively low like cognitive changes? In our previous work [13] we have proposed that in analog to the Model of different objects learned in the visual brain we can think about the Model of the Parkinson's disease in the advanced stage of the disease. Therefore, we can take the group Gr2 as a Model and look into similarities between disease time developments of Gr1. For general and motor symptoms similarity (accuracy of rules) increases to near 1 with disease development. But for the cognitive change it is not exactly the case. Therefore Gr2 is not good model for cognitive developments in time for Gr1. It might be related to large interindividual variability in cognitive decay between PD patients. However, the most data mining studies related to Parkinson's disease concentrate on motor symptoms such as gait [14] or speech articulation [15].

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