

Abstracts of selected publications of Assoc. Prof. Lyudmila Todorova for participation in the concourse for the academic position “Professor”

I. Publications under Indicator B4

1. Todorova, L., Vassilev, P., Hadjistoykov, P., & Surchev, J. (2012, September). Application of intuitionistic fuzzy sets for more objective comparison of Kaplan-Meier curves. In 2012 6th IEEE International Conference Intelligent Systems (pp. 212-215). IEEE.

In the present work a scheme for more objective comparison of patients, represented by Kaplan-Meier graphs, by classification separating them in groups (m in number) with "graded survivability" is proposed. The classification uses the apparatus of the intuitionistic fuzzy sets (IFS). The final result is a clear and easy to interpret table. To avoid loss of information, as well as for the obtainment of graded, sound and real evaluation of the information, contained in the Kaplan-Meier graphs the authors recommend the consideration of all possible cases, for which it is fulfilled $n < m$, where n is the number of the patient groups, represented by Kaplan-Meier survivability curves. A particular case from the neurosurgical practice is considered and analyzed. The obtained results are confirmed in practice and in the scientific literature.

2. Todorova L, Vassilev P, Matveev M, Krasteva V, Jekova I, Hadjitodorov S, Georgiev G, Milanov S. Generalized net model of a protocol for weaning from mechanical ventilation. Comptes rendus de l'Académie bulgare des Sciences, 66, 10, PUBL HOUSE BULGARIAN ACAD SCI, 2013, ISSN:1310–1331, 1385-1392

In the present work an attempt is made to evaluate objectively the ventilated patients' condition from the monitored parameters (standard physiological parameters, parameters of the ventilation and respiratory mechanics, parameters of the gas exchange and energy expenditure) in order to determine their readiness for weaning from mechanical ventilation support. This research is a step in improving the care for ventilated patients in order to decrease the period of ventilation support. In the Central Intensive Care Unit, University Emergency Hospital “N. I. Pirogov” an investigation is conducted, with stages described in detail in the paper. A generalized model represents these phases. The decision criteria and the results of their application are evaluated by the so-constructed generalized net and a validity score is updated for each rule to be used in further considerations. The accuracy of the predictive rules has been estimated by calculating the sensitivity, specificity, the positive- and negative predictive value. Due to the relatively small number of patients, the developed GN-model will be refined in the course of the continuing investigation at the Central Intensive Care Unit, University Emergency Hospital “N. I. Pirogov”.

3. Vassilev P., L. Todorova, V. Andonov. An auxiliary technique for InterCriteria Analysis via a three dimensional index matrix. Notes on Intuitionistic Fuzzy Sets, 21, 2, 2015, 71-76

In the present paper, a new auxiliary technique inspired by InterCriteria Analysis is proposed. It is also based on indexed matrices, however, since the considered estimates (again in the form of intuitionistic fuzzy pairs) are not pair-wise but triple-wise, it is three dimensional. The minimum number of required data needed to be stored, for the proposed technique, is given. The way the meaning of the obtained intuitionistic fuzzy pairs in the auxiliary method differs from that of the considered here implementation of the InterCriteria Analysis is also commented upon. Some properties of the proposed auxiliary technique are studied and possible applications are outlined.

4. Todorova, L., Ignatova, V., Hadjitodorov, S, Vassilev, P. Generalized Net Model for Monitoring the Degree of Disability in Patients with Multiple Sclerosis Based on Neurophysiologic Criteria. “Studies in Fuzziness and Soft Computing”, Springer Series, 332, Springer, 2016, ISSN:1434-9922, DOI:10.1007/978-3-319-26302-1_18, 289-303

Multiple sclerosis (MS) is a chronic disease of the central nervous system, which affects most often the young age. The disease has a social importance, as it leads to disability in active age. The course of the disease is individual and requires an adequate approach in selecting the appropriate treatment strategy. This requires periodic monitoring of the patients for early registration of the disease progression. Most commonly used tests are clinical investigation, brain MRI and other paraclinical methods, including neurophysiological assessment (usually evoked potentials). Evoked potential (EP) is a reliable method for quantifying the severity of damage to the white matter in patients with MS. The aim of this study is to develop a model for Generalized NET (GN)-registration of the direction of the course of disease based on neurophysiological evaluation of multimodal evoked potentials. Also, to make a comparison of the results obtained by the EP with the degree of disability as measured by the scale of Kurtzke (Expanded disability Status Scale-EDS S). We have followed up 48 patients with clinically definite MS over a period of 1 year. The patients were tested both clinically and neurophysiologically at Clinic of Neurology in MHAT- NHH, Sofia. The three main modalities evoked potentials were applied: visual evoked potentials with reversive pattern (VEPRP); Brainstem auditory evoked potentials (BAEP); Somatosensory evoked potentials (SSEP), taken during stimulation of median nerve. As a result it is established that the abnormalities of EP correlate significantly with the clinical findings. Based on the obtained results is developed a GN-model generating candidate predictive rules for the progression of the illness. The model has a high sensitivity (SEN), specificity (SPE), PPV (Positive predictive value) and NPV (Negative predictive value) for the disease progression.

5. Todorova L., P. Vassilev, J. Surchev. Using Phi Coefficient to Interpret Results Obtained by InterCriteria Analysis. Advances in Intelligent Systems and Computing, 401, Springer, 2016, ISBN:3319262114, 9783319262116, 231-239

The authors propose an algorithm for assessment of the estimates of “correspondence” and “opposition” obtained by InterCriteria Analysis (ICA) in the form of intuitionistic fuzzy vector pairs. For this aim the modified Pearson coefficient of Karl Pearson, called ϕ coefficient (“mean square contingency coefficient”). The algorithm is applied on real data from neurosurgery. The statistical significance of the relations between the considered criteria is verified by data found in literature. The authors believe this approach for data exploration may prove useful in many areas.

6. Todorova, L., Ignatova, V., Surchev, J. Computerized neuropsychological test battery CogniSoft for assessment of cognition in patients with multiple sclerosis. INT. J. BIOAUTOMATION, 24, 4, 2020, ISSN:1314-2321, 371-380.

Cognitive dysfunction is a leading cause of disability in multiple sclerosis (MS) and is associated with unemployment, need of assistance with daily activities and poor quality of life. The introduction of neuropsychological testing and monitoring of cognitive status as part of the overall evaluation of MS patients in parallel with clinical and paraclinical parameters is highly recommended. Recent studies have demonstrated a better perception and preference for computerized cognitive tests than classic variants, with no significant difference in results. In accordance with global trends, a bilingual computer system CogniSoft for assessment and rehabilitation of cognitive status in persons with MS has been developed, including: 1) a set of diagnostic tests for evaluation of memory and executive functions based on the nature of Brief International Cognitive Assessment for MS (BICAMS); 2) a set of games for cognitive rehabilitation. Questionnaire for depression (Beck Depression Inventory – BDI-II) will be filled before conduction of the neuropsychological tests for differentiation of possible depression which could interfere with the results. The CogniSoft information system will incorporate two approaches for evaluation of neuropsychological

results which will allow early detection of cognitive impairments in these patients, which will initiate timely cognitive rehabilitation.

7. Todorova, L, Ignatova, V, Vassilev, P, Surchev, J. Generalized Net Model of Computer Based Registration and Rehabilitation of Cognitive Impairments in Multiple Sclerosis. Lecture Notes in Networks and Systems, 338, Springer, 2022, ISSN:2367-3370, DOI:10.1007/978-3-030-95929-6_30, 397-407.

Cognitive decline occurs along with physical disability in approximately two-thirds of persons suffering from multiple sclerosis (MS) and has devastating influence on quality of life at all stages and in all subtypes of the disease. The modern immunomodulatory therapy has a satisfactory effect on the relapse rate and disease progression, but does not improve the degree of cognitive impairment. Over the last decade, the number of studies on treatment and management of cognitive impairment in people with MS are rapidly growing. A generalized net model for registration, assessment and rehabilitation of cognitive impairment in persons with MS has been developed. The assessment of cognitive status was made on the basis of results obtained through computer-based neuropsychological tests. Based on comparison of the results from MS patients with those of healthy controls, the degree of cognitive deficit was determined. The input of the generalized net was formed by the data from patient's medical records, which were categorized according to disease duration, grade of disability, age, sex and employment. As a result of applying the InterCriteria Analysis, the output of the model provides information about the type of impaired cognitive domains and the degree of cognitive deterioration. This allows the therapist to build an appropriate rehabilitation strategy for each individual patient. The rehabilitation module contains a set of different rehabilitation games with several levels of difficulty. The frequency, as well as the degree of complexity of cognitive training is based on the patient's results and the general cognitive reserve registered at baseline. The system is implemented in a cloud infrastructure and is planned to be provided as an IT service for neurological departments and clinics. In this way, the system is available for testing and rehabilitation of unlimited number of people (both healthy controls and persons with MS) at any time. The developed GN model provides a mechanism for description and simulation of these parallel processes. In this way, the proposed model will be useful in determining the individual approach to each patient and will help optimizing the results of cognitive rehabilitation. The analysis of the model will allow outlining the future directions for therapeutic approaches on cognitive impairments in MS, which will lead to inclusion of cognitive rehabilitation and training programs in routine clinical practice within the next decade.

8. Atanassov, K., Todorova, L., Vassilev, P., Popov, E., Bozhkov, A., Slavov, C., Atanassova, V. A Variant InterCriteria Analysis Method based on Mean Value: An Application to Prostate Cancer Data. Interface Focus. (accepted)

In recent decades, multicriteria analysis methods have been increasingly used in decision-making in the field of medicine. In this work, we present a modification of an established approach for this purpose—InterCriteria Analysis. In the new algorithm, the determination of the similarity in behaviour between pairs of criteria is based on the relations of the respective pairs of objects to the mean values of the respective criteria. The proposed modification of InterCriteria analysis was applied to a dataset of 276 prostate cancer patients (obtained from a retrospective study). The obtained results for positive and negative consonance between the studied criteria are confirmed by reports in authoritative literature sources in the field of urology. The registered potential of the new method for detecting relationships between investigated criteria enables its application both independently and in combination with other methods of multicriteria analysis.

9. Vassilev, P. M., Stoyanov, T., Todorova, L. P., Marazov, A., Andonov, V., Ikonov, I. Orderings over Intuitionistic Fuzzy Pairs Generated by the Power Mean and the Weighted Power Mean. Mathematics, 11, 13, MDPI, 2023, DOI:10.3390/math11132893, 2893

In the present work, we prove a result concerning an ordering over intuitionistic fuzzy pairs generated by the power mean (M_p) for $p > 0$. We also introduce a family of orderings over intuitionistic fuzzy pairs generated by the weighted power mean (M_p^w) and prove that a similar result holds for them. The considered orderings in a natural way extend the classical partial ordering and allow the comparison of previously incomparable alternatives. In the process of proving these properties, we establish some inequalities involving logarithms which may be of interest by themselves. We also show that there exists $p > 0$ for which a finite set of alternatives, satisfying some reasonable requirements, some of which were not comparable under the classical ordering, has all its elements comparable under the new ordering. Finally, we provide some examples for the possible use of these orderings to a set of alternatives, which are in the form of intuitionistic fuzzy pairs as well as to results from InterCriteria Analysis.

10. Vassilev, P. M., Todorova, L. P., Popov, E. P., Georgieva, R. N., Slavov, Ch. K., Atanassov, K. T. Two New Modifications of the InterCriteria Analysis. *Comptes Rendus de l'Academie Bulgare des Sciences*, 76, 1, Prof. Marin Drinov Academic Publishing House, Sofia, Bulgaria, 2023, ISSN:1310-1331, DOI:10.7546/CRABS.2023.01.03, 23-34

In the present work two modifications of the InterCriteria Analysis are proposed in order to extend its theoretical foundation. The results obtained from the application of these methods over real data (from patients with prostate carcinoma) have been analyzed to determine the reliability of the calculated consonance and dissonance.

The similarity scores obtained by the modified versions of the InterCriteria Analysis are close to those given by the classical InterCriteria Analysis, as well as to the values of the correlation coefficients between the considered criteria.

This shows the reliability of the proposed modification with respect to determining the consonance and dissonance between criteria in different problems.

11. Todorova Lyudmila, Surchev Jivko, Marazov Alexander. Assessment of the factors influencing the survival of the ventricular shunt in infantile hydrocephalus. *INT. J. BIOAUTOMATION*, 27, 2, 2023, ISSN:1314-1902, DOI:10.7546/ijba.2023.27.2.000926, 107-116.

The purpose of the present research is to perform a retrospective analysis of 242 ventricular shunts implanted in childhood due to infantile hydrocephalus, submitted to a long-term follow-up (27.84 ± 6.13 years) and investigate the factors influencing the survival of the shunt, applying modern mathematical approaches. The contingent consists of 242 patients who were shunted due to infantile hydrocephalus in childhood, 55% of whom were under 6 months old when the shunt was implanted. For the entire follow-up period, patients underwent 375 revisions (average 1.55 revisions per shunt), 38% are without shunt failure, with only one revision - 26%, with two - 14%. The remaining 22% have 3 or more revisions (4.58 shunt revisions) and they make 65% of all revisions. 68.5% of all revisions are due to mechanical complications; to functional (inadequate drainage) - 7.5%. 9.1% of the patients had inflammatory complications. We found that the age at shunting (under 3 months - the worst trend) and the interval to the first revision (over 6 months - a smaller number of revisions) are of the biggest importance for the number of the following revisions. If the patient survives one year after shunting without failure, the risk of such is under 50% during the whole shunt existence.

12. Ignatova V., Todorova L., Haralanov L., Vassilev P. Early Clinical Predictors of Long-term Disability Progression in Patients with Multiple Sclerosis. *Indian Journal of Medical Specialities*, 15, 1, WOLTERS KLUWER MEDKNOW PUBLICATIONS, 2024, ISSN:0976-2884, DOI:10.4103/injms.injms_82_23, 48-52

Background: One of the unmet therapeutic needs in the treatment of multiple sclerosis (MS) is to prevent the accumulation of irreversible disability. Formulating standardized predictors of conversion in the

secondary progressive phase of the relapsing-remitting MS (RRMS) should be a step toward solving this problem.

Objective: To develop a reliable score, a predictor of physical disability worsening and secondary progression in patients with RRMS.

Materials and Methods: Seventy-four patients with RRMS were observed retrospectively for 15 years. Clinical and demographic parameters were analyzed with respect to the time of reaching Expanded Disability Status Scale (EDSS) 4 and/or EDSS 6, as well as EDSS at the end of 15 years.

Results: Almost half of the patients observed (47%) reached irreversible disability ($EDSS \geq 4.0$) and $\frac{1}{4}$ developed secondary progression ($EDSS \geq 6.0$). The statistically significant variables selected were age at onset of MS, sex, type (afferent, efferent, and combined), and number of symptoms during the first and second attacks. Based on this selection, a predictive score for the course of the disease was formed. It has a sensitivity of 86%, specificity of 89%, positive predictive value of 85%, and negative predictive value of 81%.

Conclusion: The proposed predictive score can be applied as a complementary tool in the choice of appropriate therapeutic approach at the early stages of MS, which can help avoid disability overtime.

II. Publications under Indicator I7 and I8

13. Ignatova V., Todorova L., Haralanov L., Matveev M. Dynamic Changes of Visual Evoked Potentials and Brainstem Auditory Evoked Potentials in Patients with Multiple Sclerosis.. *Comptes rendus de l'Academie Bulgare des Sciences*, 66, 4, 2013, 611-616.

Evoked potentials are widely used in diagnosis of multiple sclerosis (MS), but not sufficient data are available for their prospective role in the course of disease. The presentation is a longitudinal study in the Clinic of Neurology at MHAT - NHH - Sofia from Aug 2009 to Mar 2012. It includes 52 patients with clinically definite multiple sclerosis according to revised MacDonald criteria (2005/2010). Paternal visual evoked potentials (PVEP) and brainstem auditory evoked potentials (BAEP) were examined consecutively during the study and these results were compared with the grade of disability according to Expanded Disability Statement Scale (EDSS). The follow-up was done at registered relapses and also at patients without new complaints - one or two years since the initial examination. For quantitative assessment of pathological EP changes, a total evoked potential (EP) score was formulated. This score is a sum of the individual PVEP and BAEP scores. The time interval to the first change of total EP score and the time interval to the first change in EDSS were assessed. The results were compared to Kaplan–Meier survival curves. We found more prominent sensitivity of the total EP score compared to EDSS in the course of disease. Our study concludes that the neurophysiologic method is more sensitive test than EDSS for earlier detection of deterioration and disease progression.

14. Ignatova, V., L. Todorova, L. Haralanov. Multimodal evoked potentials in the monitoring of multiple sclerosis. *Comptes rendus de l'Académie bulgare des Sciences*, 2014, ISSN:ISSN 1310–1331 (Print) ISSN 2367–5535

Neurologists are still arguing about the reliability of evoked potentials (EP) in the diagnosis and monitoring of patients with multiple sclerosis (MS). The recent paper is devoted to this problem through follow up of 38 patients with definite multiple sclerosis (McDonald 2010). We have followed up the dynamics of clinical and neurophysiological parameters of this sample for a period of one year. Clinical assessment was made by using Expanded Disability Status Scale (EDSS) and neurophysiologic examination was performed with multimodal evoked potentials (MMEP). The degree of neurophysiological impairment was determined by

total EP-score, introduced by the authors. The total EP-score is a sum of 6-graded individual evoked potentials score from the following modalities: visual, brainstem auditory and somatosensory. Our study revealed that the total EP-score changed in two thirds of patients during the one-year follow up period, while EDSS-score changed in only 1/3 of them. These results indicate that the neurophysiological deterioration precedes the deterioration of disability, i.e. MMEP have an important place in follow up of patients with MS.

15. Surchev, J., L. Todorova. *Mathematical Index for Comparing the Survival of Homogenous Groups of Ventricular Shunts. Comptes Rendus De L Academie Bulgare Des Sciences, 2013, ISSN:ISSN 1310–1331 (Print) ISSN 2367–5535 (Online), 1211-1218.*

In literature there are no unified criteria for evaluation and comparison of the overall survival of cerebrospinal fluid shunts in different groups of patients by one or more different authors, which makes the differentiation of essential factors influencing the complications frequency difficult. Commonly used "Kaplan–Meier survival curves" visualize the frequency only of the first failure (revision) in patients with shunts. The following complications remain "underlying", but such occur in most shunts. It is more correct to use the term "survival" if we have in mind all complications during the entire shunt follow-up period.

The present study suggests mathematical index for comparing the survival of ventricular shunts group during the entire study period. In literature there is no such index up to now. Elaborating this index is an answer to the necessity to compare the survival of different shunts groups. The aim of this comparing is to specify the optimal conditions for surgery (shunting) – age, type of cerebrospinal fluid shunt surgery, type of valve system, etc. The higher value of the index correlates with better survival during entire shunt follow-up period in each group, which has a predictive (prognostic) value.

The suggested index can be used for comparing the survival of different patients' groups in one study or materials of different authors.

16. Surchev, J., L. Todorova. *Prognostic value of the interval from implantation to first revision for the number of following complications in shunt dependent patients. Comptes Rendus de L'Academie Bulgare des Sciences, 2014, ISSN:ISSN 1310–1331 (Print), ISSN 2367–5535 (Online), 1287-1294.*

Hydrocephalus modern treatment is based on shunt surgeries, which are followed by post surgery complications in not low percentage of the patients (35–80%). Many researchers relate the number and the type of complications to the time interval from valve implantation to the first revision. The present research is retrospective and follows up 242 patients with valves implanted for hydrocephalus; 151 of them have undergone at least one revision. We analyzed the dependence “number of revisions – interval from implantation to first revision”.

In our material 40% of all revised patients undergo first revision up to one year after implantation. Among the patients with 3 and more revisions during the whole shunt existence, 47% are revised for the first time up to 6 months after implantation, while only 22% of the patients “with 1 and 2 revisions” have undergone first revision in the same interval ($p < 0.05$). The present research shows that the shorter the interval from shunting to first revision, the larger the number of following revisions ($p < 0.05$).

17. Surchev, JK, Nachev, S., Todorova, L., Marinov, M. *Optic Nerve Glioma in Two Sisters with Family History of Neurofibromatosis Type 1. Journal of Neurological Surgery Part A: Central European Neurosurgery, 79, 3, 2018, ISSN:2193-6315, DOI:10.1055/s-0037-1608869, 268-272.*

Optic nerve glioma (ONG) is associated in 10% of patients with neurofibromatosis (NF) type 1. To date no consensus has been reached regarding the therapeutic approach and prevention of visual impairment in these patients. Reports in the literature vary from a conservative approach (observation) to the use of single treatment modalities or multimodality protocols of surgical removal, radiotherapy, and/or chemotherapy. We present our experience with two siblings with ONG whose mother carries cutaneous stigmata of NF

type 1. The younger sister was diagnosed 3 years after the treatment of the older sibling following recommended imaging for screening. Postoperative follow-up for 11 and 15 years, respectively, demonstrated lack of tumor regrowth and preserved vision in the contralateral eye. We discuss the treatment strategy in pediatric patients with orbital ONG associated with NF type 1.

18. Surchev, J, Todorova, L, Ignatova, V. Intraventricular intraoperative prophylaxis with vancomycin - a factor for reducing infections in shunt operations. *Comptes rendus de l'Académie bulgare des Sciences*, 72, 11, 2019, ISSN:1310-1331, DOI:10.7546/CRABS.2019.11.17, 1585-1591.

Shunt operations are a main method of treating internal hydrocephalus. According to literary data, 8–10% of the ventricular peritoneal shunts suffer infections. Approaches to minimize the risk of inflammatory complications are sought. For a period of 9 years (2008–2016) 295 children aged 0 to 18 years have undergone implantation of shunt for infantile hydrocephalus. For the purposes of this study, they were divided into three groups according to the type of antibiotic intraoperative prophylaxis: Group A – dissolving amino-glucosid antibiotic into the serum with which the valve is irrigated and injected into it. Intraventricularly, the team does not administer an antibiotic. Group B – non-systemic use of amino-glucoside antibiotic in the serum with which the valve is irrigated and filled, without intraventricular administration of an antibiotic Group C – intraoperative prophylaxis with vancomycin intraventricularly. Through the ventricular catheter, vancomycin is injected intraventricularly, and through the distal catheter – into the peritoneal cavity or the right atrium. In Group C, no case of infection was recorded for the whole period considered. In Group A 12 patients out of 202 are infected. The highest incidence of infections is in Group B – every sixth patient. There is a statistically significant difference in the comparison of infection rates among the groups, between the A and C Groups ($p < 0.001$) and between the B and C Groups ($p < 0.01$). Intraventricular intraoperative administration of vancomycin bypasses the blood-brain barrier, prevents bacterial sowing and significantly reduces infections in fluid shunt surgeries.

19. Ignatova V, Stoyanova T, Haralanov L, Surchev J, Todorova L. Depression and anxiety in patients with multiple sclerosis. Comparison with grade of disability. *Comptes rendus de l'Académie bulgare des Sciences*, 72, 10, 2019, ISSN:1310–1331, DOI:10.7546/CRABS.2019.10.17, 1433-1440.

Both depressive symptoms and anxiety take grater prevalence rates in MS patients than in the general population which is an argument to search a relationship with grade of physical disability. Our study included 26 healthy controls and 55 patients with clinically definite MS according to the revised McDonald criteria from 2010. Emotional condition was assessed through Beck Depression Inventory – second revision (BDI–II) and Generalized Anxiety Disorder (GAD–7). According to grade of physical disability the MS subjects were divided into two groups: patients with EDSS < 3.5 and patients with EDSS = 3.5. There is a trend of increasing BDI score in patients compared to controls, but statistically significant correlation ($p < 0.01$) regarding depressive levels was found only between controls and MS persons with high physical disability. Our results revealed depressive states at a much higher rate in MS subjects – 47% in patients with EDSS < 3.5 ($p < 0.05$) and 70% in patients with EDSS > 3.5 ($p < 0.01$) compared to healthy controls (19%). Generalized anxiety was registered at higher extent in patients than in healthy persons, but the difference is not statistically significant. Our study revealed moderate correlation ($r = 0.61$) between depression and generalized anxiety levels.

Regardless of whether or not there is a relationship between EDSS, depression and anxiety, these indicators negatively impact patients' quality of life. The early detection of depressive and anxiety symptoms, the search for and application of effective pharmacological and rehabilitative approaches should be among the main priorities in the care for these patients.

20. Mermeklieva E., Cherninkova S., Chernodrinska V., Solakov D., Grozeva G., Tomova M., Todorova L. Combined electrophysiological method for early diagnostics of functional changes in the visual analyzer in patients with diabetes mellitus without diabetic retinopathy. *Comptes rendus de l'Académie*

bulgare des Sciences, 72, 5, 2019, ISSN:ISSN 1310–1331, DOI:DOI: 10.7546/CRABS.2019.05.16, 674-682.

The aim of the study is to explore objectively the function of the visual analyzer by simultaneously performed pattern electroretinography (PERG) and visual evoked potentials (PVEPs) in patients with diabetes mellitus (DM) without diabetic retinopathy, detected with the specialized ophthalmological exams. A group of 112 people (224 eyes) were studied. The control group consisted of 47 healthy controls (94 eyes). The patients with DM were 65 (130 eyes). Two types of objective electrophysiological (EF) methods were performed - PERG and PVEPs. The main variables that were considered in the results analysis were the latency and amplitudes, reflecting the configuration of the wave forms. The comparative analysis of components of the two EF studies between patients with DM without DR and controls demonstrated significant differences. The two groups statistically differed in P50 amplitude and latency of PERG. PVEPs had also statistically significant prolonged latencies and lower amplitudes in the diabetic group. EF studies could be used as an objective method for registration of early changes in the visual analyzer's function associated with DM. Also, to monitor the dynamics of changes as they are non-invasive, harmless, faster and less expensive than fluorescein angiography (FA), optical coherent tomography (OCT) and angio-OCT.

21. Ignatova V., Todorova L., Haralanov L. Exogenous temporal factors for stroke onset. Comptes rendus de l'Academie bulgare des Sciences, 74, 9, 2021, ISSN:1310–1331, DOI:10.7546/CRABS.2021.09.16, 1397-1405.

The aim of the current study is to underline the influence of exogenous temporal factors on stroke onset in a Bulgarian population and look for a relationship between temporal variation and conventional vascular risk factors on the course of the disease.

We tracked retrospectively 675 individuals diagnosed with stroke in 2018 who were admitted at the Clinic of neurology at National Cardiology Hospital Sofia. The stroke types were distributed in three groups: ischemic stroke (92%), brain hemorrhage (6%) and subarachnoid hemorrhage (2%).

No seasonal dependence was registered, but the peak of incidence rate was recorded in June and minimal incidence was found in July and October ($p < 0.05$). Similarly to other studies, we report a relatively high incidence of morbidity at the beginning (Tuesday) and the end (Saturday) of the working week.

The present study is devoted to determining the specific temporal patterns of stroke onset in a Bulgarian cohort and discovering a relationship between cyclic temporal variations and traditionally accepted vascular risk factors. Considering the huge advances in circadian biology in recent decades, which allow systematic studying of the links between impaired endogenous circadian rhythms and exogenous temporal influences on them, we examined the 24-hour pattern of variation in the frequency of stroke onset and found that it was highest in the morning and lowest at night. As a result, we recommend that the cyclic temporal pattern of stroke onset should be considered in the chrono-therapy of risk factors for avoiding cerebrovascular diseases.

22. Mermeklieva, E., Cherninkova, S., Grozeva, G., Tomova, M., Solakov, D., Haralanov, L., Tankova, Ts., Todorova, L., Damianov, V., Asenova, R. Combined electrophysiological method for early diagnostics of functional changes in the optical analyzer in human with newly-diagnosed diabetes mellitus. General Medicine, 19, 4, 2017, 3-8.

The aim of the study is to explore objectively the function of the visual analyzer by simultaneously performing pattern electroretinography (PERG) and visual evoked potentials (PVEPs) in patients with newly-diagnosed diabetes mellitus (DM). A group of 81 people, 162 eyes, of whom 47 healthy controls - 94 eyes, were studied. Patients with DM are 34-68 eyes. Two types of objective electrophysiological (EF) methods were performed - PERG and binocular PVEPs. The main indicators that are taken into account in the analysis of the results are the latency, amplitudes and amplitude ratios, reflecting the configuration of the waveforms. The comparative analysis of the components of the two EF studies between patients with

newly-diagnosed DM and controls revealed significant differences. In PERG, the two groups statistically differ in P50 amplitude, lower in diabetics. PVEPs have statically significant prolonged latencies of all components except N145 in the diabetic group. EF studies could be used as an objective method for registration of early changes in the visual analyzer function as a complication of DM. Also, to monitor changes in dynamics as they are non-invasive, harmless, faster, and cheaper than fluorescein angiography (FA), OCT and angio-OCT.

23. Mermeklieva, E., Grozeva, G., Tomova, M., Solakov, D., Haralanov, L., Damianov, V., Asenova, R., Todorova, L. A comparison of the electrophysiological tests of the visual analyzer indicators and the duration of diabetes mellitus. *General Medicine*, 20, 2, 2018, ISSN:1311-1817, 33-36.

Aim: The aim of the study was to compare the values of the components of pattern electroretinography (PERG) and visual evoked potentials (PVEPs) in patients with diabetes mellitus (DM) and the duration of DM. **Material and methods:** A group of 135 diabetic patients (270 eyes), were studied, with mean age 51 ± 13.72 , 57 males and 78 females. Patients with DM type 1 were 55 and with type 2 DM - 80. Two types of objective electrophysiological (EF) methods were performed - PERG and binocular PVEPs. The main indicators that were considered in the results analysis were the latency, amplitudes and amplitude ratios, reflecting the configuration of the wave forms. **Results:** The correlative analysis between the values of the components of the two electrophysiological (EF) studies and the DM duration, demonstrated absence of correlation between the degree of electrophysiological changes and the DM duration. **Conclusion:** EF studies are an objective method for examination of changes in the visual analyzer function as a DM complication. The severity of their alterations does not correlate with the duration of DM. Perhaps the DM compensation, the presence of risk factors such as AH, obesity, etc., as well as the DM complications, influence the severity of impairment of the visual analyzer function.

24. Vassilev, P., Todorova, L., Marinov, E. On intuitionistic fuzziness. Book series *Studies in Computational Intelligence, Research in Computer Science in the Bulgarian Academy of Sciences*, 934, *Studies in Computational Intelligence*, 2021, DOI:10.1007/978-3-030-72284-5_11, 227-254.

In the present work we try to provide an overview of the main results related to intuitionistic fuzzy sets and related concepts contributed by scientists from the Bulgarian Academy of Sciences from the very birth of the concept to present day.

Of course, it is impossible not to mention briefly the contributions of other authors but we will try to keep the focus of our exposition on the results of the groups that have worked within the Academy.

25. Ignatova, V, Todorova, L. Computer-Based Rehabilitation of Cognitive Impairments in Patients with Multiple Sclerosis. *Lecture Notes in Networks and Systems*, 374, Springer, 2022, ISSN:2367-3370, DOI:10.1007/978-3-030-96638-6_4, 39-49.

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system, which leads to demyelinating lesions in brain and spinal cord and further neurodegeneration. It results in manifestation of motor, cognitive and neuropsychological symptoms, which can occur simultaneously or independently of each other. Approximately 2/3 of people with MS suffer from cognitive impairment which lead to deteriorated quality of life.

In unison with the global world tendencies, for the first time in Bulgaria a computer system Rila Cogni Soft for assessment and rehabilitation of cognitive impairment has been developed. The system is composed of 3 modules: 1) electronic record of demographic and clinical data; 2) module for assessment of the cognitive status and 3) module for rehabilitation of the registered cognitive impairment. The rehabilitation training programs are developed on the basis of established international standards. Based on the affected cognitive domains and degree (severity) of damage, the therapist administers individual rehabilitation programs.

Using the system, we create our own norm (based on results from 70 healthy persons) for each of the diagnostic tests. A statistically significant difference ($p < 0.05$) in the level of cognition was found between healthy controls and individuals with MS ($n = 23$). InterCriteria Analysis was used to study the relationships between the degree of cognitive impairment and clinical features. Improved cognitive functions were registered after 3-month period of rehabilitation ($p > 0.05$).

26. Lubich, M., Popov, E., Georgieva, R., Dmitrenko, D., Bojkov, B., Slavov, Ch., Todorova, L., Atanassova, V., Vassilev, P., Atanassov, K. A Generalized Net Model of Some Nephrological Diseases. *Lecture Notes in Networks and Systems*, Springer, 2023, ISSN:23673370, DOI:10.1007/978-3-031-45069-3_18, 200-206.

This paper describes a generalized net model of the process of diagnostic work-up of the basic nephrological diseases and conditions: AKI, oliguria, proteinuria, hematuria, and its implementation in everyday clinical practice for education, differential diagnosis and multidisciplinary collaboration.

27. Popov, E., Georgieva, R., Dmitrenko, D., Bojkov, B., Slavov, C., Lubich, M., Vassilev, P., Atanassova, V., Todorova, L., Atanassov, K. Generalized Net Model of the Prostate Cancer Early Stages of Development. *2nd International Symposium on Bioinformatics and Biomedicine, BioInfoMed 2022. Lecture Notes in Networks and Systems*, 658, Springer, 2023, ISBN:978-303131068-3, DOI:10.1007/978-3-031-31069-0_24, 246-252.

A generalized net model of the prostate cancer early stages of development is described. The relationship of the prostate with the human body respiratory, blood and circulatory, and endocrine systems are represented.

28. Vassilev, P., Zhivkova, K., Atanassova, V., Todorova, L., Petkova, D. On some new geometrically motivated operators over intuitionistic fuzzy sets. *Notes on Intuitionistic Fuzzy Sets*, 31, 4, Prof. Marin Drinov Academic Publishing House, 2025, ISSN:1310-4926, DOI:10.7546/nifs.2025.31.4.448-457, 448-457.

We consider four new geometrically motivated operators acting in the interior of the interpretation triangle used to depict intuitionistic fuzzy sets. The first operators uses the points resulting from the classical “necessity” and “possibility” operators, in combination with the point $\langle 0, 0 \rangle$. The definition of the second operator employs the projections of the considered point onto the sides of the triangle, as viewed from the vertices $\langle 0, 0 \rangle$, $\langle 0, 1 \rangle$, and $\langle 1, 0 \rangle$. The remaining two operators combine two of these projections with the result of the modal operators of the internal point. We also consider operators obtained as linear combinations of some of these four operators.

29. Vassilev, P., Todorova, L., & Kosev, K. (2014, September). Note on the (μ, ν) -coherence relation, defined over intuitionistic fuzzy sets. In *Proc. of 10th Int. Workshop on Intuitionistic Fuzzy Sets, Banská Bystrica (Vol. 29, pp. 7-9)*.

In the present paper, a new relation between intuitionistic fuzzy sets defined over a universe set X is proposed. Some properties of the newly defined relation are studied. It is proved that the relation introduces an equivalence class generated by a fixed intuitionistic fuzzy set.

30. Matveev M, Krasteva V, Jekova I, Georgiev G, Milanov S, Prokopova R, Todorova L. Profile of Autonomic Cardiac Control in Patients who are Not Considered Ready for Weaning from Mechanical Ventilation. *Computing in Cardiology*, 39, IEEE, 2012, ISSN:2325-8861, 625-628.

This study tracks the global tendency of the heart rate variability (HRV) profile over five ventilation modes, aiming to find evidences on the hypothesis that patients who failed during the weaning process manifest important differences in the autonomic nervous system activity. This preliminary study enrolls 17 patients (7 successful (S), 10 failure (F)) who underwent weaning with AVEA ventilator. Time- and frequency-domain HRV analysis is applied over 5-min ECG episodes recorded at the beginning of 5 ventilation modes: (1) controlled mechanical ventilation (CMV) on a sedated patient; (2) CMV on a sedated and paralyzed patient; (3) Pressure support ventilation with zero back-up pressure PSV(0); (4) PSV at 12-25 cmH₂O; (5) Spontaneous breathing trial (SBT) at 8 cmH₂O. Our results support the finding of other authors that during SBT, the patients who succeed in weaning show a prevalently sympathetic modulation, while relatively increased vagal activity is typical for the F-group. PSV(0) is however an outstanding test for which F-patients manifest about 3 to 20 fold increased sympathetic and vagal activity compared to the S-group.

31. Ignatova V., Surchev J., Stoyanova Ts., Vassilev P., Haralanov L., Todorova, L. Social cognition impairments in patients with multiple sclerosis. Comparison with grade of disability. *Neurology India*, 68, 1, 2020, ISSN:19984022, 94-98.

Objectives: Social cognitive impairments are an essential aspect of general disability in patients with multiple sclerosis (MS). They can manifest independently or in addition to physical deficits.

Aim: To examine the impairment of social cognition and its potential relationship with the grade of disability in MS patients.

Settings and Design: Our study included 17 healthy controls and 36 patients with clinically definite MS (relapsing-remittent form) according to the McDonald Criteria (2010). The patients were divided into two groups – patients with Expanded Disability Status Scale (EDSS) <3.5 (N = 18) and those with EDSS ≥3.5 (N = 18). The neuropsychological battery included empathy assessment (Self-Compassion, “Reading the Mind”) and theory of mind tests – ToM (Faux pas, cartoons).

Results: We did not register a change in self-assessment empathy in MS. Reading the Mind in Eye test showed a clear tendency for deterioration with increasing physical disability. The statistically significant difference ($P < 0.05$) between the results of controls and patients with EDSS ≥3.5 was registered. The tests for interpreting stories perceived in an auditory manner (“faux pas”) showed a clear trend toward “failure” among patients ($P < 0.05$). The results of patients with high disability in ToM cartoons task were statistically worse ($P < 0.01$) both in comparison to those of controls and patients with EDSS <3.5.

Conclusion: Our study found that, during the course of MS, deterioration of both social cognitive skills and basic cognitive abilities occurs, which is parallel to physical disability.

32. Vassilev, Peter, Ribagin, Simeon, Todorova, Ludmila. On an aggregation of expert value assignments using index matrices. *Notes on Intuitionistic Fuzzy Sets*, 23, 4, 2017, ISSN:Print ISSN 1310-4926, Online ISSN 2367-8283, 75-78

We elaborate on an idea firstly proposed by V. Traneva. We extend the approach by considering new possibilities for aggregation based on what we name “total relevance”. This allows for better knowledge discovery and selection of the most influential input.

33. Lubich, Martin, Papazov, Velimir, Popov, Elenko, Georgieva, Radostina, Dmitrenko, Dmitrii, Bojkov, Borislav, Slavov, Chavdar, Vassilev, Peter, Atanassova, Vassia, Todorova, Lyudmila, Atanassov, Krassimir T. A Generalized Net Model of the Prostate Gland's Functioning. *Mathematics*, 10, 3, MDPI, 2022, DOI:10.3390/math10030479, 479.

Over the last 20 years, many Generalized Net (GN) models of the ways of functioning of the different systems and organs in the human body and models related to the description of biomedical processes in living organisms have been constructed. In this paper, a GN model of the prostate gland's functioning was developed, as a continuation of the previous research. The model provides the possibility to trace the logical

relations of the interactions of the prostate gland and various individual organs in the human body. The model shows the possibility for the existence of currently unknown feedback loops.

34. Ignatova V, Todorova L, Surchev J. Social Cognition Impairments in Patients with Multiple Sclerosis and Comparison with Imaging Studies, Disease Duration and Grade of Disability. Trending Topics in Multiple Sclerosis, In Tech, 2016, ISBN:978-953-51-2656-0, DOI:10.5772/63465, 29, 227-255

Cognitive impairments in multiple sclerosis (MS) are heterogeneous and their rate varies between 43% and 70%. A less studied aspect of cognition is social cognition, which is not a uniform theoretical construct. It includes emotion perception, prosody, empathy, theory of mind (ToM) and assessment of mood. In addition to progressive physical disability, social cognitive impairments are a reason for job loss in 24–80% of patients with MS, increased divorce rate, dissolution of partnerships and social communication difficulties. Social cognitive impairments are the result of disruptions in the mentalization network at the neuroanatomical, neurochemical and/or genetic level, which can lead to malfunctions in the dopaminergic-serotonergic system and to compromising the development of neuroanatomical targets within the network. The wide dissemination of demyelinating lesions and cortical thinning typical of patients with MS often lead to anatomic and functional disorders of the above-mentioned specific brain structures. A correlation has been established among specific cortical areas involved in emotion identification from facial expression (right and left fusiform face area, frontal eye), emotion processing (right entorhinal cortex) and socially relevant information (left temporal pole). The most active brain region involved in social cognitive processing is the medial frontal cortex (MFC), which is described as the brain's social cognitive center. During performance of various socio-cognitive tasks for mental state attribution, common areas of increased activation in the medial prefrontal gyrus and the temporoparietal junctions are registered bilaterally, while the area of the medial prefrontal cortex (the paracingulate cortex) is the only region uniquely activated by the performance of ToM.

Most MRI studies of patients with MS found a correlation between the cognitive and/or affective disorders, on the one hand, and lesion localization, total lesion load, or cerebral atrophy, on the other. A significant correlation was also reported between abnormal activities in specific cortical zones on fMRI, on the one hand, and clinical manifestation, conventional MRI findings and behavioral changes, on the other. Altered patterns of brain activity were found in all clinical phenotypes of MS, including when cognitive abilities were intact and/or restored, social cognitive dysfunction in MS actually affects all stages of the disease and all types of clinical course. The cortical plastic changes are a dynamic phenomenon that can be modulated by external factors. This phenomenon would facilitate the mapping of individual strategies for adequate treatment and rehabilitation of each patient.