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Abstracts

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CONTACTS

Federal State Budgetary Scientific Institution
"Scientific Research Institute of Physiology and Basic Medicine" (SRIPhBM)
Russian Federation
630117 Novosibirsk, Timakova Str., 4
Tel: +7(383) 335-98-55
Fax: +7(383) 335-97-54
E-mail: iph@physiol.ru
URL - SRIPhBM: http://physiol.ru
URL - CSGB-2016: http://physiol.ru/csgb2016/
Organizing committee: eliseev@physiol.ru

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НИИФФМ основан в 1967 году на базе Отдела экологической физиологии человека и животных Института цитологии и генетики Сибирского отделения Академии наук СССР.

Миссия НИИФФМ: Сохранение ментального и физического здоровья населения на основе внедрения новых разработанных методов и технологий диагностики, лечения и профилактики пограничных нервно-психических и аффективных нарушений, психосоматических и нейродегенеративных заболеваний, аппаратных нейротехнологий фитнеса мозга и нефармакологической терапевтической стимуляции резистентных к фармакологическим воздействиям патологических состояний.

Направления деятельности (в соответствии с Уставом НИИФФМ):

1. Изучение молекулярно-генетических, эндофенотипических, нейрофизиологических, нейрохимических и нейроиммунных основ интегративных функций мозга и нейровисцеральных взаимоотношений в норме, при психических, психосоматических расстройствах и нейродегенеративных заболеваниях, разработка персонализированных методов их профилактики, диагностики и лечения.

2. Изучение динамики функционального состояния организма при воздействии субэкстремальных и экстремальных факторов в норме и патологии и разработка персонализированных технологий профилактики и коррекции дизадаптивных состояний.

Структура института: Два отдела (отдел экспериментальной и клинической нейронауки, отдел функциональных резервов и спортивной медицины), включающие в себя 10 лабораторий, клиника. В составе клиники - 3 стационарных отделения (психотерапевтическое отделение; отделение №1 – гастроэнтерологическое направление; отделение № 2 – кардиологическое и пульмонологическое направления), консультативно-диагностическое отделение, дневной стационар.

Кадровый состав: В штате НИИФФМ – 260 человек, в том числе 88 научных сотрудников и 29 врачей, 1 академик РАН, 29 докторов наук и 29 кандидатов наук (по данным 2016 года).

Аспирантура: В аспирантуре НИИФФМ обучается 12 аспирантов.

Публикации: НИИФФМ – лидер в области экспериментальной и клинической нейронауки, на регулярной основе публикует результаты исследований в высокорейтинговых международных журналах с высокими значениями импакт-факторов (от 2 до 43), индексируемых в мировых базах данных - Web of Science и Scopus. Сотрудники НИИФФМ проводят исследования в рамках международного научно-технического сотрудничества, Программы фундаментальных научных исследований государственных академий наук на 2013 - 2020 годы и различных грантовых систем. В 2016 г. сотрудники выполняют исследования по грантам РНФ (3), РФФИ (8), РГНФ (4), 2 программам Президиума РАН (2), проводят 15 поисковых клинических исследований, 12 международных мультицентровых фарм-трайлов, разрабатывают персонализированные нефармакологические методы терапевтической стимуляции головного мозга для лечения аффективных и нейродегенеративных расстройств.

Адрес: 6300117, Россия, Новосибирск, ул. Тимакова, 4. НИИФФМ.
Тел./факс: +7(383) 335-98-55/ +7(383) 335-97-54
URL: www.physiol.ru.ru
E-mail: iph@physiol.ru

CONTENTS

ANALYSIS OF γδT-CELL REPERTOIRE IN ALZHEIMER'S DISEASE PATIENTS AND INDIVIDUALS WITH NO MEMORY IMPAIRMENT

Aliseychik M.[1], Zolotoreva O.[1], Gusev F.[1], Grigorenko A.[1], Byragin A.[2], Andreeva T.[1], Rogaev E.[1,3,4]*

[1]Department of Genomics and Human Genetics, Institute of General Genetics, Russian Academy of Sciences, Moscow, Russia, [2]Immunoregulation section, National Institute on Aging, Baltimore, USA, [3] Center for Brain Neurobiology and Neurogenetics, Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia, [4] Brudnick Neuropsychiatric Research Institute, University of Massachusetts Medical School, Worcester, USA

*e-mail: evgeny.rogaev@umassmed.edu,*Corresponding author*

Key words: *Alzheimer's disease, γδT-cells, CDR3 TRG repertoires, memory*

The influence of different cytokines on nervous tissue metabolism and the cognitive functions has recently been found. Surprisingly, the producers of such cytokines may be not only glial cells but also T-cells coming from peripheral blood1. γδT-cells perform extensive regulatory functions due to production of cytokines as well as cytotoxic functions against cells presenting stress signals on their surface. The γδT-cells participate in the pathogenesis of multiple sclerosis 2, West Nile virus infection[3], and ischemic brain injury4. Neuroinflammatory process is also one of the early hallmarks in a course of Alzheimer's disease (AD). We hypothesize that the individual specific immune response to cell-stress antigens or even β-amyloid peptide, contributes to aging-related memory decline and susceptibility to neurodegeneration factors in AD. Innovative massive parallel genomic sequencing provides ultra-high resolution of TCR repertoire in AD.

We have developed and applied massive parallel sequencing assay to compare the profiles of γδTCRs in blood and cortex tissue of cohorts of AD patients and age-matched non-demented individuals. Target libraries for deep sequencing were prepared using adopted BIOMED2 consortium5 supplemented primers (primers for endogenous control and another J segment were added). Determining sequences CDR3 regions was performed using igblast, mixtcr tools. We classified the multiple γδTCRs clonotype varinats in both groups to identify the under- an over-presentation of V-segments and certain clonotypes in AD group verus controls. The data imply the presumable selection of some clonotypes in a course of AD pathogenesis. This pilot study can potentially reveal unpredicted previously immunogenic hallmarks in memory protection or decline in aging and to find principally novel biological markers and therapeutic targets for AD.

This work was supported by Russian Scientific Foundation grant № № 14-44-00077 (development of assay, immunogene repertoire blood cell DNA sequencing) and by Worcester Foundation.

References:

1. A. Filianoet al. (2016) Unexpected role of interferon-γ in regulating neuronal connectivity and social behaviour, *Nature*, **535**(7612): 425-9
2. K. Selmaj, et al. (1991) Colocalization of lymphocytes bearing gamma delta T-cell receptor and heat shock protein hsp65+ oligodendrocytes in multiple sclerosis, *Proceedings of the National Academy of Sciences of the United States of America* **88**(15):6452-6.
3. T. Welte et al. (2008) Role of two distinct gammadelta T cell subsets during West Nile virus infection, *FEMS Immunol Med Microbiol*, **53**(2):275-83.
4. T. Shichita et al. (2009) Pivotal role of cerebral interleukin-17-producing gammadeltaT cells in the delayed phase of ischemic brain injury, *Nature Medicine*, **15**(8):946-50.
5. J. Dongen et al. (2003) Design and standardization of PCR primers and protocols for detection of clonal immunoglobulin and T-cell receptor gene recombinations in suspect lymphoproliferations: report of the BIOMED-2 Concerted Action BMH4-CT98-3936, *Leukemia*, **17** (12) 2257-317

AGING AND LONGEVITY FROM GENOMIC PERSPECTIVES

Andreeva T.V.[1,2], Gusev F.E[1,2], Reshetov D.A.[1], Shagam L.I.[1], Kunizheva S.S.[1], Yigit S.[3], Geyko A.V.[1], Manakhov A.[1], Kuznetsova I.[1], Aliseychik M.[1], Lisenkova A.[1], Lukyanov E.[1], Protasova M.[1], Buzina A.N.[1], Lukiw W.J.[4], Byragin A.[5], Grigorenko A., Rogaev E.I.[1,2,6]*

From: [1]Department of Genomics and Human Genetics, Institute of General Genetics, RAS, Moscow, Russia; [2]Center for Brain Neurobiology and Neurogenetics, Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia; [3]Gaziosmanpasa University Medical School, Tokat , Turkiye; [4]LSU Neuroscience Center, Louisiana State University Health Sciences Center, New Orleans, USA; Departments of Neurology and Ophthalmology, Louisiana State University Health Sciences Center, New Orleans, USA; [5]Immunoregulation section, LMBI, National Institute on Aging, Baltimore, USA; [6]Brudnick Neuropsychiatric Research Institute, University of Massachusetts Medical School, Worcester, USA

** Corresponding author: evgeny.rogaev@umassmed.edu*

Aging is a complex process of molecular and cellular decline that affects body function, and is accompanied by the development of age-related diseases. Age-related cognitive impairment is one of the most common features of human aging. Accumulating evidence links age-related memory impairment to genetic and epigenetic alterations, but fundamental molecular mechanisms of memory storage and memory decline during human aging are still unclear.

Human longevity is known to run strongly in families. Heritability estimates in twin studies range from 23% to 33%. The genetic polymorphisms identified by genome wide association studies (GWAS) can explain just a small part of heritable longevity. The GWAS methodology fails to trace rare polymorphisms or de novo mutations. The whole-genome deep sequencing (WGS) is a promising next step to search for genetic factors for the longevity trait that is not restricted by the bias for common genetic variants. Another approach of our interest is to track the epigenetic alterations (chromatin and DNA methylation) across genome in elderly subjects (in particular in cortical brain cells) that may contribute to memory and other CNS functions.

In our project we focused on an evaluation of the genetic factors related to longevity and memory in cohort of elderly people (>300 individuals of 85 years and older) including a set of centenarians. We have obtained the blood and/or saliva samples as well as detailed medical and self-lifestyle data for the human subjects from several regions of the Russian Federation. Cognitive MMSE tests were performed for the enrolled centenarians.

In our pilot study WGS for three centenarians with no signs of dementia (memory loss in elderly subjects), as well as for individual with exceptional ("infinite") memory (Russian origin), were performed on the Illumina HiSeq2000 platform resulting in a mean coverage x30-40 for every individual. The millions of single nucleotide variations (SNV) and structural variations identified in each genome were annotated and filtered for their putative biological significance. The sets of WGS data from human subject cohorts (including 1000 genomes project) and ADNI project data (including the WGS data for >800 individuals tested for the signs of sever or mild cognitive impairment) and our own WGS data from the same ethnic groups (Russia) were used as reference control sets in a search for SNV and indel variants contributing to longevity and memory. Using the WGS data of the centenarians we assessed several different theories of ageing, such as telomere length shortening, oxidative stress, insulin-like and ROS signaling pathways involvement, epigenetic regulation.

Specific mutations in genes contributing to epigenetic modifications, proteasome machinery and telomere maintenance were found more frequently in centenarian and elderly individuals than in younger groups. Several genes related to genes for the insulin/IGF1R pathway elements were found to bear mutations in the examined centenarian genomes. Our preliminary data highlights the importance of epigenetic regulation in longevity and elements related to the signaling pathways linked previously to lifespan regulation in animal models.

Acknowledgement: This work was supported by Russian Scientific Foundation grant № 14-44-00077.

THE ROLE OF Q/N-RICH REGIONS IN THE INDUCTION OF AMYLOIDOGENESIS

Antonets K.S.[1,2]*, Nizhnikov A.A.[1,2], Galkin A.P.[1,2]
[1]*Dept. of Genetics and Biotechnology, St. Petersburg State University, St. Petersburg, Russia*
[2]*St. Petersburg Branch, Vavilov Institute of General Genetics, Russian Academy of Sciences, St. Petersburg, Russia*
e-mail: kirantonez@gmail.com
**Corresponding author*

Key words: *amyloid, prion, yeast, Sup35, PSIA*

Motivation and aims: An important feature of many amyloid-forming proteins supposed to be crucial for their aggregation, is presence of compositionally biased regions, particularly glutamine (Q) and/or asparagine (N)-rich subsequences. Those regions are considered to play role not only in the formation of amyloids, but also in the interaction of different amyloids. So, overproduction of polyQ-peptide (103Q) in yeast induces aggregation of several preferably Q-rich proteins [1]. Therefore, the aim of the given research is to discover, if there exists a direct correlation between the composition of amyloid protein and the composition of proteins, which co-aggregate with amyloid.

Methods: To perform a search for candidates for novel amyloids, we used proteomic method, PSIA (Proteomic Screening and Identification of Amyloids) [1], recently developed by us, with some modifications including high-performance liquid chromatography for separation of tryptic peptides [2].

Results: We used two variants of prion-forming domain (PrD) of yeast protein Sup35 – the wild-type variant, which was Q-rich, and the variant with all Qs substituted with Ns, which was N-rich. As a result, the overproduction of wild-type Sup35 PrD induces formation of detergent-resistant aggregates of 4 proteins, while the N-substituted variant induces aggregation of 11 proteins, and only 2 proteins of this set are overlapped. The most important is that only 2 of all 13 found proteins are Q/N-rich.

Conclusion: Though the presence of compositionally different amyloids in the cell induces aggregation of dissimilar sets of proteins, there is no strong correlation between the composition of the corresponding amyloid-forming protein and the composition of proteins, whose aggregation is induced by him.

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References:

1. Nizhnikov A.A. et al. (2014) Proteomic screening for amyloid proteins, PLoS One, 9: e116003.
2. Antonets K.S. et al. (2016) Proteomic Analysis of Escherichia coli Protein Fractions Resistant to Solubilization by Ionic Detergents, Biochemistry(Mosk), 81:34-46.

HUMAN AUTHENTICATION USING ELECTROCARDIOGRAM

Bogdanov M.R.*
M. Akmullah named after Bashkir State Pedagogical University, Ufa, Russia
e-mail: bogdanov_marat@mail.ru
**Corresponding author*

Key words*: electrocardiogram, biometric authentication, wavelet analysis*

Motivation and Aim: Biometric methods of human identification are discussed. The mathematical aspects of human identification based on electrocardiogram are considering. Results of electrocardiogram recognition with wavelet analysis are presented.

Methods and Algorithms: wavelet analysis.

Results: 97% accuracy while biometric identification was achieved.

Conclusion: Biometric methods of identification are all wider application in our lives. Such methods of identification like fingerprint recognition, iris, voice, or palms recognition gradually enter a phase of maturity and are increasingly beginning to be used in a variety of mobile, web and other applications, however, the evidence suggests that the traditional methods of identification inherent vulnerability. Yield is seen in the development of multi-modal identification systems using biometrics such as, for example, an electrocardiogram, an electroencephalogram and DNA. The most preferred option in our opinion, is the use of the ECG.

Availability: The technology may be used in various security applications.

References:

1. Bogdanov M.R. Using of wavelet analysis under Electrocardiogram Recognition. ITIDS'2015. The 3 rd International Conference on Information Technologies for Intelligent Decision Making Support. Ufa, Russia. May 18 - 21, 2015.
6. Bogdanov M.R. Unconventional encryption algorithm [Netradicionnyj algoritm shifrovaniya]. Electronic scientific journal "Computer facilities and software" [Elektronnyj nauchnyj zhurnal "Vychislitelnaya tehnika i programmnoe obespechenie"]. 2014, Release 1(1) January-April, pp. 17-23. [Online]. Available at: http://www.computer-facilities-andsoftware.ingnpublishing.com/archive/2014/release_1_1_january-april/bogdanov_m_r_netradicionnyj_algoritm_shifrovaniya/ Received: 2014-03-12 Accepted: 2014-04-23 Published on-line: 2014-04-30.
7. Bogdanov M.R., Zakharov A.V., Gabidullin Ju.Z., Dumchikov A.A.Unconventional encryption algorithms.. ISSN: 2319. 5967. ISO 9001:2008 Certified. International Journal of Engineering Science and Innovative Technology (IJESIT). Volume 3, Issue 5, September 2014.
8. Bogdanov M.R., Gabidullin Ju.Z., Dumchikov A.A., Zakharov A.V., Gorbunova V.Ju. Method for recognition of bird's voices with wavelet analysis. Russian Patent #2014611697. 07.02.2014.
9. Bogdanov M.R. The way of researching of biological diversity of ornitophauna with wavelet analysis. Proceedings of Samara Scientific Centre of RAS. #3(4). 2013. P. 1232-1236.

THE OPPOSING EFFECTS OF SHORT- AND LONG-TERM SOCIAL STRESS ON PREFRONTAL CORTEX TRANSCRIPTOME

Bondar N.P.[1]*, Bryzgalov L.O.[1], Ershov N.E.[1,3], Gusev F.E.[3,5], Reshetnikov V.V.[1], Avgustinovich D.F.[2], Tenditnik M.V.[4], Rogaev E.I.[3,5], Merkulova T.I.[1]

[1]Laboratory of Gene Expression Regulation, Institute Cytology and Genetics, SB RAS, Novosibirsk, Russia
[2]Laboratory of Molecular Mechanisms of Pathological Processes, Institute Cytology and Genetics, SB RAS, Russia
[3]The Center of Brain Neurobiology and Neurogenetics, Institute Cytology and Genetics, SB RAS, Russia; [4] Laboratory of Experimental Models of Emotional Pathologies, Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia
[5]University of Massachusetts Medical School, USA
e-mail: nbondar@bionet.nsc.ru
**corresponding author*

Key words: *social defeat stress, depression, RNA-seq, prefrontal cortex*

Motivation and Aim: Chronic social defeat stress is a well-validated murine model of depression. However, little is known about the gene activity dynamics during the development of a depression-like state.

Methods and Algorithms: We analyzed the effects of social defeat stress of varying duration (10 and 30 days) on the behavioral patterns and prefrontal-cortex transcriptome in C57BL/6 mice.

Results: Commonly used 10-day exposure to social defeat stress resulted in a high level of social avoidance with no sign of depression-associated behavior. Contrariwise, most animals exposed to 30-day stress demonstrated clear hallmarks of depression, including higher level of social avoidance, increased immobility in the forced swim test, and anhedonic behavior. The monitoring of transcriptome changes revealed massive alterations in gene expression on the 10th day. Surprisingly, expression of a few genes was only affected on the 30th day of stress, apparently, due to a reversal of the majority of the early stress-induced changes to the original basal state. Moreover, we have found that glucocorticoid-sensitive genes are clearly enriched targets on the 10th day of stress, but these genes stop responding to the elevated corticosterone level after the 30th day of stress. The majority of genes altered by 30-day stress were downregulated, with the most relevant ones participating in chromatin-modifications and neuroplasticity (e,g, guanine nucleotide exchange factors (GEFs) of Rho-family GTPases).

Conclusion: Taken together, our data suggest that depression may be caused by weakening of the response to the stressful environmental factors in terms of both behavior and gene expression. Our results also support the hypothesis that major depressive disorder is associated with defective cell adhesion and impaired neuronal plasticity.

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DRUG-INDUCED DYSKINESIA AND POLYMORPHISMS OF SGK1 GENE IN RUSSIAN SCHIZOPHRENIC PATIENTS

Boyarko E.G.*, Fedorenko O.Y., Semke A.V., Ivanova S.A.
Mental Health Research Institute, Tomsk, Russia
e-mail: egboyarko@mail.ru
**Corresponding author*

Key words: *gene polymorphism, schizophrenia, dyskinesia*

Motivation and Aim: Extrapyramidal symptoms (including tardive dyskinesia) were observed in 20-30% of patients receiving conventional antipsychotics [1]. Antipsychotics change dopaminergic neurotransmission, which in turn may cause extrapyramidal disorders. An important influence of potassium channels on dopaminergic neurotransmission is well documented [2]. Studies show that serum and glucocorticoid-regulated kinase 1 (SGK1) modulate the activity of neuronal potassium channels [3]. The aim of our study was to investigate the association of polymorphisms of SGK1 (rs1743964, rs1057293, rs1009840) gene with drug-induced dyskinesia in Russian schizophrenic patients.

Methods: Blood samples were taken from 443 Russian Caucasian patients (61,4% male and 38,6% female) with a clinical diagnosis of schizophrenia (ICD-10: F20). The average age of patients 38 ± 14,5 years; duration of the disease at the time of the survey 23 ± 8,9 years. The drug-induced dyskinesia was assessed using standard international scale AIMS.

Results: When comparing the group of patients with and without dyskinesia we did not find any associations between polymorphic variants of SGK1 gene and tardive dyskinesia. Additional comparison was carried out in groups of men and women. In the group of men, we identified the association of A allele ($\chi2 = 3,80$, $p = 0,049$) and AA genotype ($\chi2 = 6,17$, $p = 0,046$) of rs1057293 in SGK1 gene with drug-induced dyskinesia. In the group of women, we identified the association of AA and GG genotypes of rs1743964 in SGK1 gene with dyskinesia ($\chi2 = 6,006$, $p = 0,049$). To assess clinical heterogeneity of tardive dyskinesia we subdivided group of patients with extrapyramidal disorders into groups of patients with orofaciolingual symptoms and patients with limb-truncal symptoms. It was found that orofaciolingual form was associated with AA and CC homozygous genotypes of rs1009840 in SGK1 ($\chi2 = 5,818$, $p = 0,049$) (in the group of women).

Conclusion: Thus, SGK1 gene are involved in the development of tardive dyskinesia induced by long-term therapy with neuroleptics and phenotypically different forms of tardive dyskinesia - orofaciolingual and limb-truncal - characterized by different genetic features. Acknowledgements: The study was supported by a Russian Science Foundation № 14-35-00023.

References:

1. Loonen, A.J., van Praag, H.M. 2007 Measuring movement disorders in antipsychotic drug trials: the need to define a new standard. Journal of Clinical Psychopharmacology, 27(5): 423-430.
2. Zhang, H., Rodgers, E.W., Krenz, W.D., Clark, M.C., Baro, D.J. 2010 Cell specific dopamine modulation of the transient potassium current in the pyloric network by the canonical D1 receptor signal transduction cascade, J Neurophysiol, 104: 873–884.
3. Lang, F., Boehmer, C., Palmada, M., Seebohm, G., Strutz-Seebohm, N., Vallon, V. 2006 (Patho) physiological significance of the serum- and glucocorticoid-inducible kinase isoforms, Physiol Rev 86(4): 1151-1178.

METAGENOMIC ANALYSIS OF VIRAL COMMUNITIES IN LAKE BAIKAL

Butina T.V.[1], Bukin Y.S.[1], Tupikin A.E.[2], Kabilov M.R.[2], Belykh O.I.[1]
[1]*Limnological Institute SB RAS, Irkutsk, Russia*
[2]*Genomics Core Facility, Institute of Chemical Biology and Fundamental Medicine SB RAS, Novosibirsk, Russia*
e-mail: tvbutina@mail.ru

Key words: *viral community, metagenomics, virome, genetic diversity, Lake Baikal*

Viruses have a significant impact on numerous biogeochemical processes in aquatic environments and effectively regulate the abundance and diversity of bacteria and phytoplankton [1]. This study was aimed at elucidating diversity of viral communities in Lake Baikal. The basic approache in our research was metagenomic analysis that is the study of total viral genetic material (virome) using the next-generation sequencing and bioinformatic analysis. Metagenomic studies of freshwater environments are not numerous. Therefore, available descriptions of genetic diversity of marine viruses far exceed those from freshwaters. Viral communities of the largest and oldest freshwater lakes remain poorly studied.

Water samples were collected from the main pelagic sites in the southern and central basins of Lake Baikal. Sample processing (filtration, concentration of viral particles, isolation of DNA) was performed as described before [2]. Genetic material of DNA-viruses was sequenced on the platform of Illumina MiSeq. Bioinformatic analysis of the resulting data set was carried out using special programs and applications (FLASH, FastQC, BLASTn, BLASTx etc.).

A total of 1.3 and 4.7 % sequences from Southern and Central Baikal, respectively, were identified as viral. Defined sequences belonged to 23 viral families. Six families of viruses (Myoviridae, Siphoviridae, Poxviridae, Mimiviridae, Podoviridae, Phycodnaviridae) dominated in both water samples, amounting to more than 90% of identified sequences. In general, the viral community composition in two basins of Lake Baikal were similar; however, the percentage ratio of the families differed. Viruses from revealed families and genera affect a wide range of organisms, including bacteria and cyanobacteria, archaea, algae, amoebae, flagellates, fishes, amphibians, insects, and mammals.

In conclusion, our study revealed a high diversity of viral communities (virome) in the pelagic zone of Lake Baikal and demonstrated appropriateness of the chosen approach for future investigations of viruses in the lake ecosystem.

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References:

1. Suttle C.A. (2007) Marine viruses – major players in the global ecosystem, Nat. Rev. Microbiol. 5: 801– 812.
2. Butina T.V., Bukin Yu.S., Kabilov M.R. et al. (2015) Taxonomic diversity of virioplankton of the littoral zone of Lake Baikal, Topical scientific problems of Pribaikalye, 1: 51–55.

COMPUTER ANALYSIS OF GENOME CO-LOCALIZATION OF TRANSCRIPTION FACTOR BINDING SITES BASED ON CHIP-SEQ DATA

Dergilev A.I.[1,2], Svichkarev A.V.[2], Orlov Y.L.[1,2]*
[1]*Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia*
[2]*Novosibirsk State Medical University*
e-mail: orlov@bionet.nsc.ru
** Corresponding author*

Key words: *transcription factors, ChIP-seq, gene expression*

Motivation and Aim: Analysis of gene regulation in brain by transcription factors needs bioinformatics support. A scientific problem being solved is to study transcription factor binding sites (TFBS) co-localization in genomes using ChIP-seq data. Technology ChIP-seq, which combines chromatin immunoprecipitation (ChIP) and highly efficient DNA sequencing, allows to determine transcription factor binding sites in genome scale.

Methods and Algorithms: The tasks of analyzing genome-wide ChIP-seq data rises are to identify the coordinates of TFBS and to compare their location with genomic annotation (relative location and distance to gene transcription start sites, promoter regions etc.). In addition to determining the location of binding sites for a transcription factor, there are problems of determining the cluster sites of different transcription factors, clusters together or located at a short (100-200 nt) distances on chromosomes assuming similar function and regulatory mechanisms. Programs processing huge amounts of text data (bed, wig files) identifying areas of intersection of genomic annotations (coordinates), adapted to the respective model genomes are technically necessary.

Results: We developed set of programming script for TFBS location analysis. The study of clusters of sites ChIP-seq data on the status of binding sites of 15 different transcription factors in the mouse genome were used [1]. The computer program in C ++ language is developed to calculate the relative position of the coordinate TFBS and their clusters. Methods of establishing complex signals and patterns of the algorithm "Discovery" (program GeneDiscovery), previously developed in the framework of the theory of data analysis (Data Mining, Knowledge Discovery) in the context of signals DNA segments were used for the analysis of clusters of binding sites. We confirmed separation of TFBS clusters in mouse genome (embryonic stem cells) onto classes presented by Oct4, Nanog, Sox2 from one side, and c-Myc from another side. This analysis was extended to exact location of nucleotide motifs in ChIP-seq peaks relative to each other and iterative correction of such motifs.

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References:

1. Chen X. et al. 2008 Integration of external signaling pathways with the core transcriptional network in embryonic stem cells, *Cell*, 133(6):1106-1117.

BEHAVIORAL PATTERNS OF INTELLIGENT AGENTS IN A MODEL OF COMPETITIVE FORAGING

Donskikh V.A.*, Titov I.I.
Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia
e-mail: dumai-spb@mail.ru
**Corresponding author*

Key words: *population modelling, intelligent agent, adaptive landscape, clustering*

Motivation and Aim: Multiagent models are used to study various complex systems such as groups of cells, populations of animals or social networks. Identification of behavioral patterns is a necessary prerequisite for understanding the multiagent dynamics and finding the successful strategies.

Methods and Algorithms: We consider a model, in which the agents travel inside a circle colliding with each other [1]. An agent replenishes its energy reserve by sequential visiting a center and a border of the area and spends it on actions and collisions. If the agent's energy is exhausted, it retrains by copying the successful agents with errors. A cognitive system of an agent is represented by a response matrix and determines its individual strategy.

Results: We identified four stable behavioral patterns, characterized them by their response matrices, by physical parameters and by the number of the receptors used and modeled them by automata. We show that the IA behavior pattern is more precisely identified by the physical properties of populations rather than by the temporal sequences of actions. We found that more successful strategies use more physical receptors and determine more complex behavior. Reducing the agent representation in their configurational space we construct the adaptive landscape where the transitions between the strategies could be traced through the population trajectories.

Conclusion: We created a toy model for solving the problem of IA behavior classification, of finding its optimal strategy and simulation of IA evolution. We developed a combined view on IA dynamics in terms of population genetics and chemical kinetics.

References:

1. Burtsev M., Turchin P. 2006 Evolution of cooperative strategies from first principles, *Nature,* 440: 1041-1044.

ASSOCIATION STUDY OF THE ENDOTHELIAL NITRIC OXIDE SYNTHASE GENE POLYMORPHISMS AND METABOLIC SYNDROME IN RUSSIAN PATIENTS WITH SCHIZOPHRENIA

Fattakhov N.S.[1,2,*], Smirnova L.P.[2], Parshukova D.A.[2], Skuratovskaia D.A.[1], Litvinova L.S.[1], Semke A.V.[2], Ivanova S.A.[2]
[1]*Immanuel Kant Baltic Federal University, Kaliningrad, Russia*
[2]*Mental Health Research Institute, Tomsk, Russia*
e-mail: NiFattakhov@kantiana.ru
**Corresponding author*

Key words*: schizophrenia, metabolic syndrome, endothelial nitric oxide synthase, single nucleotide polymorphism*

Motivation and Aim: Incidence rates of metabolic syndrome (MetS) are significantly higher in patients with schizophrenia compared to the general population [1]. Genetic variation within the endothelial nitric oxide synthase gene (NOS3) may result in impaired endogenous nitric oxide formation and has been associated with cardiovascular diseases [2]. There is growing evidence that polymorphisms in NOS3 influence the development of MetS, however, there is also a controversy regarding the association of polymorphisms in the gene encoding NOS3 and MetS in patients with schizophrenia [3]. In this study, we aimed to evaluate the effects of NOS3 polymorphisms on MetS risk in Russian patients with schizophrenia.

Methods and Algorithms: 70 Caucasian patients with schizophrenia and MetS and 127 schizophrenic patients with normal BMI were enrolled in the study and genotyped for T-786C (rs2070744), G894T (rs1799983) and C774T (rs1549758) in NOS3. MetS was diagnosed using International Diabetes Federation (IDF) criteria.

Results: The allelic and genotypic frequencies of rs2070744 (promoter region) polymorphism in schizophrenic patients with MetS were significantly different from those in schizophrenic patients with normal BMI. These patients had significantly higher frequencies of rs2070744 T allele ($\chi2$=6.80; p=0.009, OR=0.59; 95%CI: 0.40-0.88), rs2070744 C allele ($\chi2$=6.80; p=0.009, OR=1.69; 95%CI: 1.14-2.51) and rs2070744 TT genotype (p=0.006, OR=0.45; 95%CI: 0.25-0.82). Strong linkage disequilibrium between rs1799983 and rs1549758 was observed (D' > 0.9). No association was observed between NOS3 haplotypes and MetS risk in patients with schizophrenia.

Conclusion: Our results point to a role for NOS3 polymorphisms in MetS in Russian patients with schizophrenia. These findings indicate that rs2070744 polymorphism may serve as a prognostic biomarker for MetS among Russian schizophrenic subjects.

References:

1. Malan-Müller S. et al. 2015 A systematic review of genetic variants associated with metabolic syndrome in patients with schizophrenia, *Schizophr Res,* 170(1) 1-17.
2. Uthor A., More O.N.E. 2003 Title of the paper, *Journal,* 12 13-16.
3. Huang P.L. 2009 eNOS, metabolic syndrome and cardiovascular disease, *Trends Endocrinol Metab,* 20(6) 295-302.
4. Burghardt K. et al. 2014 Endothelial nitric oxide synthetase genetic variants, metabolic syndrome and endothelial function in schizophrenia, *J Psychopharmacol,* 28(4) 349-356.

DISSOCIATION OF PROTEOLYTIC AND CA^{2+} CHANNEL ACTIVITIES OF PRESENILIN 1 *IN VITRO* AND RESCUE TEST IN *C. ELEGANS IN VIVO*

Grigorenko A.P.[1,2,3] , Moliaka Y.K.[1,2], Plotnikova O.V.[1], Smirnov A.[1], Nikishina V.A.[1], Goltsov A.Y.[2,3], Gusev F.[2,3], Nelson O.[4], Bezprozvanny I.[4], Rogaev E.I.[1,2,3]*

[1]Brudnick Neuropsychiatric Research Institute, University of Massachusetts Medical School, Worcester, USA; [2]Department of Genomics and Human Genetics, Institute of General Genetics, Russian Academy of Sciences, Moscow, Russia; [3]Center for Brain Neurobiology and Neurogenetics, Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia; [4]Department of Physiology, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA

** Corresponding author: evgeny.rogaev@umassmed.edu*

Key words: *Alzheimer's Disease, presenilin, intramembrane proteolysis, Ca2+ channel*

Motivation and Aim: The complete loss of function of presenilins (PSEN1 and PSEN2) leads to a lethal phenotype and severe development pathology [1]. The double conditional knockout of *PSEN1* and *PSEN2* genes in forebrain cause the impairment of hippocampus memory [2], and *PSEN1* only conditional knockout was associated with defects in neurogenesis in dental gyrus and enhanced fear memory [3]. The missense mutations in *PSEN* genes are causative factors for severe autosomal dominant forms of Alzheimer's disease (AD) [4-6]. Inhibition of γ-cleavage activity of *PSENs* producing Aβ, but not ε-like cleavage releasing physiologically essential transcription activators, would be an efficient approach in the development of rational therapy for AD. We designed the in vitro mammalian cellular models and in vivo *C. elegans* models to truck the effect of mutations in presenilins on proteolysis and development.

Methods and Algorithms: We created a series of constructs bearing mutations in the selected amino acids, focusing on ultra-conserved signatures and AD associated sites of PSEN1. Different mutations in the same aminoacid positions were incorporated to generate alterations in biochemical properties of the sites and were further tested in various intramembrane proteolysis assays. For the selected mutations we performed rescue experiments in transgenic C.elegans model and designed the endoplasmic reticulum (ER) Ca2+ leak assay [7] in mouse embryonic fibroblasts deficient for *PSEN1* and *PSEN2* genes.

Results: We confirmed that any mutations at functionally essential aspartates of *PSEN1* completely abolish the proteolytic activities of *PSEN1*. Mutations in other ultra-conserved sites reduce, but do not completely suppress, certain proteolytic activities. Substitutions to structurally distant amino-acids most dramatically change efficiency of proteolytic cleavage. We have demonstrated that *PSEN1* protein with a particular substitution of glycine near the conserved aspartic site retains functionally important APP ε- and Notch S3- protein cleavages, but inhibits APP γ-cleavage and Aβ production. We studied the selected PSEN1 mutations for the ability of the mutant proteins to restore the normal cellular ER Ca2+ leak in *PSEN1/PSEN2* double knockout MEF. In a series of experiments we observed that all tested mutations in the conserved glycine position were unable to reconstitute the normal ER Ca2+ leak. However, the substitution of glycine to the structurally similar aminoacid efficiently rescued the loss-of-function (Egl) phenotype of presenilin knockout in *C. elegans*.

Conclusion: Our data show that mutations near the active catalytic sites of *PSEN1* may have different consequences on the various protein functions and non-proteolytic functions of presenilins. We demonstrated the importance of the in vitro and vivo assay monitoring for identifying factors disassociating AD-related and physiological activities of presenilins.

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References

1. A.Herreman et al. (1999) Presenilin 2 deficiency causes a mild pulmonary phenotype and no changes in amyloid precursor protein processing but enhances the embryonic lethal phenotype of presenilin 1 deficiency, Proc Natl Acad Sci U S A, 96: 11872-11877.
2. C.A.Saura et al. (2004) Loss of presenilin function causes impairments of memory and synaptic plasticity followed by age-dependent neurodegeneration, Neuron, 42: 23-36.
3. S.E.McGuire, R.L.Davis. (2001) Presenilin-1 and memories of the forebrain, Neuron, 32: 763-765.
4. R.Sherrington, E.I.Rogaev et al. (1995) Cloning of a gene bearing missense mutations in early-onset familial Alzheimer's disease, Nature, 375: 754–760.
5. E.I.Rogaev, R. Sherrington, Rogaeva A. et al. (1995) Familial Alzheimer's disease in kindreds with missense mutations in a gene on chromosome 1 related to the Alzheimer's disease type 3 gene, Nature, 376: 775–778.
6. A.P.Grigorenko, E.I.Rogaev. (2007) Molecular basics of Alzheimer's disease, Mol Biol (Mosk), 41: 331–345.
7. H.Tu et al. (2006) Presenilins form ER Ca2+ leak channels, a function disrupted by familial Alzheimer's disease-linked mutations, Cell, 126: 981–993.

ANALYSIS OF NUCLEAR PORE COMPLEX GENES IN GLIOBLASTOMA BY TRANSCRIPTOME PROFILING

Gubanova N.V. [1]*, Bragin A.O.[1], Kovalev S.S.[1], Medvedeva I.V.[1], Babenko V.N.[1], Gaytan A.S.[3], Krivoshapkin A.L.[2], Orlov Y.L.[1]

[1]*Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia*
[2]*Meshalkin Research Institute of Circulation Pathology, Russia*
[3]*Novosibirsk State Medical University*

e-mail: nat@bionet.nsc.ru
[*]*Corresponding author*

Key words*: glioma, RNA-seq, cell culture, human brain, gene expression*

Motivation and Aim: The nuclear pore complex (NPC) is essential not only to regulating nuclear-cytoplasm transport but also to controlling genome organization and expression. Therefore, the NPC is linked with many diseases including cancers [1,2]. Nucleoporins have been directly implicated in cancers via three routes: chromosomal translocations generating fusion proteins; changes in protein expression levels; and single point mutations. The aim of present study was comparison of NPC genes expression in the cells of normal brain cultures and secondary glioblastoma (GBM).

Methods and Algorithms: Primary cell cultures from surgical samples of GBM and normal brain have been isolated and propagated in F12/DMEM medium supplemented by fetal bovine serum under standard conditions. The cell culture samples were processed for RNA extraction. This was followed by RNA-sequencing and filtration of reads. Cufflinks were used for assessment of gene expression level and finding differently expressed genes.

Results: We revealed set of differently expressed NPCs gene in normal brain and GBM cell cultures. Most of them are expressed higher in the GBM cells. The antisense RNA transcript of nucleoporin Nup50 (Nup50-AS1) is the only one among NPC-related genes that is expressed in tumor less than in normal brain. At the same time expression of Nup50 gene is not distinguished in tumor and normal brain cell cultures. It has been suggested that there is a higher level of Nup50 protein in tumor cells and it is regulated by antisense RNA transcript.

Conclusion: The RNA-seq analysis of the cells cultures of normal brain and GBM confirmed association of some NPCs genes with tumor progression. The protein Nup50 is a member of the FG-repeat containing nucleoporins and functions as a soluble cofactor in importin-alpha:beta-mediated nuclear protein import. It has been recently reported that Nup50 is required for cell differentiation and exhibits nuclear dynamics which is dependent on active transcription by RNA polymerase II. The expression of gene Nup50-As1 increases in the human neocortex during development period spanning infancy to adulthood [2]. Our finding demonstrates the complicated role of nuclear pore complex proteins in tumor progression.

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References:

1. Seidel S., Garvalov B.K., Acker T. (2015) Isolation and culture of primary glioblastoma cells from human tumor specimens, *Methods Mol Biol*., 1235:263-75.
2. Lipovich L. et al. (2014) Developmental changes in the transcriptome of human cerebral cortex tissue: long noncoding RNA transcripts, *Cereb Cortex*, 24(6):1451-1459.

EPIGENOME LANDSCAPE ANALYSIS OF BRAIN CELLS IDENTIFIES PUTATIVE NOVEL GENES ACTIVE IN CORTICAL NEURONS

Gusev F.E.[1-3], Reshetov D.A.[2,3], Mitchell A.[4], Andreeva T.V.[2,3], Dincer A.[4], Solovyev V.[5], Grigorenko A.[1,2], Akbarian S.[1,4], Rogaev E.I.[1,2,3]*

[1]Brudnick Neuropsychiatric Research Institute, Department of Psychiatry, University of Massachusetts Medical School, Worcester, MA, USA [2] Department of Human Genetics and Genomics, International Center For Genetics and Epigenetics Research, Vavilov Institute of General Genetics of Russian Academy of Science, Moscow, Russia [3] Center of Brain Neurobiology and Neurogenetics, Institute of Cytology and Genetics of Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russia [4] Department of Psychiatry and Department of Neuroscience, Friedman Brain Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [5] Bioinformatics Division, Softberry Inc., Mount Kisco, NY, USA

** Corresponding author: evgeny.rogaev@umassmed.edu*

Key words: *reference genome, gene, annotation*

Motivation and aim: The near-complete human reference genome and corresponding gene annotation maps are widely used for medical genetic and population studies. The majority of disease-associated variants identified by genome-wide association studies (GWASes) are located outside of gene exons [1], suggesting a greater role for regulatory elements and non-coding RNA (ncRNA) genes. We suggested that, potentially, unannotated yet genes, especially ncRNA genes can be identified by scanning of open chromatin signals marked by modified histones located at active gene promoters. Here, we apply epigenetic mapping to predict yet unknown genes that are active in human cortial neurons.

Methods and algorithms: To robustly identify genes active in human cortical neurons, we combined two independent sources of experimental data: transcriptome profiling (RNA-seq, which provide deep analysis of gene transcripts) and chromatin modification profiling (H3K4me3 ChIP-seq, which marks gene promoters poised for activation) for multiple individuals. In addition, human genome sequences were determined for some individuals.

Results: We identified over a thousand potential genes that have not been yet annotated to human reference genomes in widely used databases Ensembl [2], UCSC [3]. While most of these genes are non-coding RNAs, some were predicted to have a notable protein coding potential and we validated status for one of them based on evolutionary history and expression pattern.

Conclusion: A comprehensive genomic map of human genes has yet to be completed. Novel human ncRNA genes and even putative protein-coding genes are predicted in this study. Furthermore, genetic variants in unannotated previously genes missed in common bioinformatic analysis may, in part, represent the "missed heritability" that could contribute to phenotype/disease status.

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References:

1. Welter D, MacArthur J, Morales J, Burdett T, Hall P, Junkins H *et al*. The NHGRI GWAS Catalog, a curated resource of SNP-trait associations. *Nucleic Acids Research* 2014; 42: D1001–1006.
2. Flicek P, Amode MR, Barrell D, Beal K, Billis K, Brent S et al. Ensembl 2014. *Nucleic Acids Research* 2014; 42: D749–D755.
3. Rosenbloom KR, Armstrong J, Barber GP, Casper J, Clawson H, Diekhans M et al. The UCSC Genome Browser database: 2015 update. *Nucleic Acids Research* 2015; 43: D670–D681.

SYSTEMS BIOLOGY, CONTROL THEORY AND ORIGIN OF AGING

Khalyavkin A.V.*, Krut'ko V.N.
Institute of Biochemical Physics of RAS and FRC CSC RAS, Moscow, Russia
e-mail: antisenesc@mail.ru
**Corresponding author*

Key words: *origin of aging, systems approach, self-maintenance, environmental influence*

The central question of aging just now is why after complicate morphogenesis of multicellular organism it cannot solve a much simpler task – just to keep what has been already formed. Despite the fact that the pursuit of cellular-molecular and genetic causes of aging receives substantial attention and financial support today, the efforts were insufficient yet to distinctly clarify the picture. Because, when interconnected, cross-talking, and cooperating components of such large system as an whole organism function like a single unit, they have rather new characteristics that are not detected in the study of these parts separately (phenomenon of emergence). For this reason, our understanding of the primary cause and control of aging is still limited. A brief overview of our current knowledge of this problem can help us better understand some general peculiarities of macro-systems in different environment and might lead us to the development of useful approaches to the origin of aging and its control [1-6]. Indeed, an aging is perceived as an enigma not because its main initiator has not yet been discovered, but because it exists despite the fact that all the components of a complex organism are theoretically capable of complete self-renewal. If we take into account the fact that withstandability of really sustainable systems and modes is possible only in certain limited range of ambient condition, then the control theory and systems approach are sufficient both to discover the root cause of aging and to understand the underlying mechanisms of its implementation. Outside adequate functioning modes determined by the environment even ageless hydras and immortalized cells start aging.

References:

1. A.V.Khalyavkin. (2001) Influence of environment on the mortality pattern of potentially non-senescent organisms. General approach and comparison with real populations, Adv. Gerontol., 2: 46-49.
2. A.V.Khalyavkin, A.I.Yashin. (2007) Nonpathological senescence arises from unsuitable external influences, Ann. N.Y. Acad. Sci., 1119: 306-309.
3. A.V.Khalyavkin, A.I.Yashin. (2007) Aging: the role of the control signals, In: Gerontology In Silico: The Emergence of a New Discipline. Mathematical Models, Analysis of Data and Numerical Experiments, G.I.Marchuk et al. (Eds.), 114-147 (BINOM).
4. A.V.Khalyavkin. (2012) From macro- to nano-systems and back in search of the primary cause and control of aging, In: Proceedings of International Conference "Instabilities and Control of Excitable Networks: From Macro- to Nano-Systems", Dolgoprudny, 69-76.
5. A.V.Khalyavkin. (2013) Phenoptosis as genetically determined aging influenced by signals from the environment, Biochemistry (Moscow), 78: 1001-1005.
6. A.V.Khalyavkin, V.N.Krut'ko. (2014) Aging is a simple deprivation syndrome driven by a quasi-programmed preventable and reversible drift of control system set points due to inappropriate organism-environment interaction, Biochemistry (Moscow), 79: 1133-1135.

THE ROLE OF B CELLS IN PATHOGENESIS OF ALZHEIMER'S DISEASE

Kim K.[1], Bodogai M.[1], Aliseychik M.[2], Baljinnyam T.[1], Rogaev E.[2,3,4*], Biragyn A.[1*]
[1]Immunoregulation section, National Institute on Aging, Baltimore, USA; [2]Department of Genomics and Human Genetics, Institute of General Genetics, Russian Academy of Sciences, Moscow, Russia, [3]Brudnick Neuropsychiatric Research Institute, University of Massachusetts Medical School, Worcester, USA; [4]Center for Brain Neurobiology and Neurogenetics, Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia
e-mail: evgeny.rogaev@umassmed.edu; biraarya@yahoo.com
** Corresponding author*

The immune cells play important role in maintenance and thereby proper function of the central neural system (CNS). Although a risk for a progressive neurodegenerative disorder, dementia and Alzheimer's disease (AD) increases together with the chronic inflammation and dysregulation of immune cells in the elderly, the role of immune cells remains poorly understood. Our recent data suggest that B cells can alleviate AD symptoms via generation of Aβ-neutralizing antibody 1. However, upon aging B-cell function appears to change, as their ability to generate humoral response is impaired while induction of CD4+ T cells expressing IL-17, a cytokine potentially harmful for integrity of blood-brain barrier, is increased 2. Our recent data also indicate that innate B cells lose their suppressive function and instead acquire potentially pathogenic activity, such as they induce the generation of autoimmune CD8+ T cells, upon aging of humans, macaques and mice 3,4. Thus, B cells and T cells may have both protective and pathogenic roles in the CNS and thereby modulate pathogenesis of Alzheimer's disease (AD). Although AD is caused by the accumulation of Aβ plaques and neurofibrillary tangles of aggregated hyperphosphorylated tau, the disease can be exacerbated due to dysregulation of B cells and T cells upon aging. To test this idea, we crossed triple transgenic AD mice (3xTg-AD), which develop AD at older age, with congenic B-cell deficient mice. While memory responses become impaired in 3xTg-AD mice by 14-15 month of age, we detected no memory dysfunctions in age-matched B-cell deficient 3xTg-AD mice. We found that the B-cell loss in 3xTg-AD mice results in a marked reduction of Aβ plaques and loss of activated microglia in hippocampus. Overall, our results for the first time suggest that B cells can play pathogenic role in AD, revealing a new insight in the role of adaptive immune cells in memory loss and dementia.

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Reference

1. Olkhanud PB, Mughal M, Ayukawa K, et al. DNA immunization with HBsAg-based particles expressing a B cell epitope of amyloid beta-peptide attenuates disease progression and prolongs survival in a mouse model of Alzheimer's disease. Vaccine. 2012;30:1650-1658.
2. Tomihara K, Shin T, Hurez VJ, et al. Aging-associated B7-DC+ B cells enhance anti-tumor immunity via Th1 and Th17 induction. Aging cell. 2012;11:128-138.
3. Lee-Chang C, Bodogai M, Moritoh K, et al. Accumulation of 4-1BBL+ B cells in the elderly induces the generation of granzyme-B+ CD8+ T cells with potential antitumor activity. Blood. 2014;191:4141-4151.
4. Lee-Chang C, Bodogai M, Moritoh K, et al. Aging Converts Innate B1a Cells into Potent CD8+ T Cell Inducers. J Immunol. 2016;196:3385-3397.

APPROACHES TO THE STUDY OF OSCILLATORY RESTING-STATE NETWORKS

Knyazev G.G.
Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia
e-mail: knyazev@physiol.ru

Key words*: resting-state networks, fMRI, EEG, oscillations*

Motivation and Aim: It would not be an overstatement to say that fMRI is now the leading method for the investigation of human brain function. In fMRI research, the most popular theme now is the study of resting-state networks (RSN). Avalanche-like increase of the number of publications on RSN is evident in the last ten years. However, a number of disputable and unresolved questions still exist in this field.

Methods and Algorithms: RSN structure and function has been predominantly investigated using fMRI. However, the fMRI BOLD signal only indirectly relates to neuronal events [2]. Therefore, a reproduction of fMRI findings in electrophysiological domain is vitally important. This way is hindered by a number of methodological difficulties arising from the nature of EEG/MEG data [7]. Recent studies have developed approaches to EEG/MEG data analysis, which partly overcome these difficulties [1, 3, 4, 5]. Seed-based oscillatory power envelope correlation analysis in conjunction with beamformer spatial filtering allows to reconstruct RSNs spatial features as they have been described in fMRI research.

Results: Two examples of application of this approach to real data will be presented. Firstly, we show that depressive symptoms are associated with a predominance of the default mode network (DMN) over the task-positive network. Secondly, increasing integration within DMN and segregation between this and other networks during development is shown in a longitudinal study of 8 to 10 year old children.

Conclusion: In spite of low spatial resolution and a number of other methodological problems inherent to EEG method, contemporary approaches to data analysis allow to use it for the study of resting-state networks, thus providing an alternative to fMRI source of information about their functional correlates.

Availability: The pipeline of EEG data analysis that was used in these studies has been described in published papers [6].

References:

1. Brookes MJ et al. 2011 Investigating the electrophysiological basis of resting state networks using magnetoencephalography Proc. Natl Acad. Sci. USA 108 16783–88.
2. Debener S et al., Single-trial EEG/fMRI reveals the dynamics of cognitive function. Trends Cogn Sci 2006 10 558-563.
3. de Pasquale F et al. 2010 Temporal dynamics of spontaneous MEG activity in brain networks Proc. Natl Acad. Sci. USA 107 6040–6045.
4. Hall EL et al. 2014 The relationship between MEG and fMRI Neuroimage 102 80–91.
5. Hipp JF et al. 2012 Large-scale cortical correlation structure of spontaneous oscillatory activity Nat. Neurosci. 15 884–90.
6. Knyazev GG et al. 2016 Task-positive and task-negative networks and their relation to depression: EEG beamformer analysis. Behav. Brain Research 306 160–169.
7. O'Neill G.C. et al. 2015 Measuring electrophysiological connectivity by power envelope correlation: a technical review on MEG methods. Phys. Med. Biol. 60 R271–R295.

A MULTIDIMENSIONAL APPROACH TO PERRSONALITY TRAITS ASSESSMENT FOR PSYCHOMETRIC EXAMINATIONS

Kolomenskii N.Yu.
Republican Psychiatric Hospital, Republic of Karelia, Russia
e-mail: n.c@nm.ru

Key words: *multidimensional approach, multiaxial approach, psychodiagnostics, psychometry test, MMPI, personality traits, personality disorders*

Motivation and Aim: The Diagnostic and Statistical Manual of Mental Disorders (DSM) uses multiaxial or multidimensional approach to psychiatric diagnostics. However, personality disorders historically are viewed in a categorical classification. The most widely used phychodiagnostic test, MMPI (Minnesota Multiphasic Personality Inventory), is based on clinical scales in accordance to a "single-dimension" model. In the recent, fifth edition of the DSM, an alternative hybrid categorical-dimensional model for personality disorders is included to stimulate further research. On practice, personality traits assessment plays a significant role in psychiatry diagnostics, but present methods lack exactness. For example, in forensic psychiatry patient's fate may depend on the result of such method. This work proposes a new approach to process data, received from psychometric examination. I.e., the aim is to improve existing methods of psychometrics and to elaborate new ones.

Methods and Algorithms: In this work human personality is presented as a figure in a multidimensional space, one dimension representing one personality trait. Each subtest of psychodiagnostic examination estimates the expression of some trait. In MMPI test human personality is figured as a broken line in 2-dimensional space, and accentuation is diagnosed if the line goes beyond some level of "normality". For certain reasons this approach lacks accuracy. In multidimensional space the level of "normality" becomes a multidimensional sphere, and certain personality disorders are pictured as areas in the space beyond this sphere. The multidimensional figure that depicts patient's personality may situate within one or more of those areas, which represents accentuation of some traits. Meanwhile the surface area of that figure is the combined index representing total "harmonicity" of patient's psyche. This representation solves some theoretical difficulties concerning advantages and disadvantages of use of clinical-based scales in the MMPI-2 vs use of "atheoretical" scales in the old MMPI.

Results: The work proposes a new approach to assess personality traits which resolves some theoretical problems and may make the diagnostics of personality disorders more precise. The reliability of this method is being implemented and tested on virtual models.

ADAPTIVE EXPERIENTIAL LEARNING FOR BUSINESS INTELLIGENCE AGENTS

Kolonin A.G.
Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia
Aigents Group, Novosibirsk, Russia
e-mail: akolonin@gmail.com

Key words*: business intelligence, experiential learning, software agents, web navigation*

Motivation and Aim: We are creating portable semantic web crawling and indexing engine, available for personal computational devices, including laptops, tablets and smartphones. It makes possible for end users to perform business intelligence (for businesses) and consumer intelligence (for customers) research in respect to specific web segments of their interest.

Methods and Algorithms: We state the problem as follows: given set of patterns identifying goal (target) web pages and set of starting web pages eventually leading to the specified goals, let evolve universal navigation graph (directed and acyclic) labeled with textual contexts identifying web links, expecting these graphs to be traversed consuming the least computational resources. To address the problem, we propose and implement adaptive web link navigation component which schemata comprised with two complementary algorithms – rigid (for familiar situations) and adaptive (for novel situations) [1-6].

Results: For practical example of application of the schema described above, we considered the task of getting leadership information from official web sites of 10 most innovative companies in robotics. Application of our technique has shown significant (times to tens of times) reduction of time and CPU power needed to perform targeted crawling of the sites given specific targets identified by respective patterns.

Conclusion: Described approach and implementation appear useful for minimizing response times and spending of computational resources in cases when only particular fragments of entire web space are being monitored for business intelligence purposes, targeting specific topics of interest identified by their textual contexts.

Availability: The described solution available as web service at https://aigents.com/ or Android application “Aigents” for smartphones and tablets. Standalone applications for Windows, Linux and Mac OS/X servers and desktops are available as well.

References:

1. Kolonin A. 2015 Aigents: Adaptive Personal Agents for Social Intelligence, Knowledge Engineering and Semantic Web, 6th International Conference Proceedings, ISSN 1865-0929, Moscow, Russia, 2015, 283-290.
2. Goertzel B. 2012 CogPrime: An Integrative Architecture for Embodied Artificial General Intelligence, October 2.
3. Nandagaonkar S., Hanchate D., Deshmukh S. 2012 Survey on Event tracking and Event Evolution, Int.J.Comp.Tech.Appl, Vol 3 (1), 1-4.
4. Ulasen S. 2014 Organizing dialogue in the system of communication in natural language (Eugene Goostman), AINL-2014 Conference.
5. Nixon B., Clark P., Hajishirzi H. 2015 Learning Knowledge Graphs for Question Answering through Conversational Dialog, NAACL 2015 Conference.
6. Kolonin A. 2015 Automatic text classification and property extraction, SIBIRCON /SibMedInfo Conference Proceedings, ISBN 987-1-4673-9109-2, 27-31.

STUDUING HUMAN SOCIAL ENVIRONMENT AND STATE WITH SOCIAL NETWORK DATA

Kolonin A.G.
Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia
Aigents Group, Novosibirsk, Russia
e-mail: akolonin@gmail.com

Key words*: collective consciousness, mental state, personal awareness, social network*

Motivation and Aim: Tight connectivity of humans in world-wide social networks is getting close to the one of human brain. Importance of the latter transition for evolution and humanity could not be underestimated because of amount of nodes and links in modern computer networks is exponentially growing with addition of artificial agents being involved in "hybrid" human-computer networks. It becomes critically important to understand phenomena of social interactions, so that effects of social behavior based on collective consciousness could be well understood, predictable and manageable – from perspective of humans exposed to modern information networks.

Methods and Algorithms: We consider approach for building computational model encompassing knowledge acquired by entire society by means of evidence supplied by each of it members, called "social evidence-based knowledge representation". In this work we focus on the nearest social surrounding of a person interacting with social networks – in attempt to build personal model of the collective consciousness and let person identify their state within this model, by means of extraction of social network data for given user and applying clustering and graph analysis techniques to it.

Results: For studied users, we have discovered patterns not obvious for conventional interactions with social networks, which has turned useful for a person to re-evaluate their state in social environment and possibly correct their mental state.

Conclusion: Described approach is considered practical for people who desire to increase their level of self-awareness while interacting with social networks and can help them to improve their social performance and comfort.

Availability: The described functionality is being made available as web service at https://aigents.com/. Future support for Android application "Aigents" for smartphones and tablets and standalone applications for Windows, Linux and Mac OS/X servers and desktops is expected in the future.

References:

1. Kolonin A. 2015 Aigents: Adaptive Personal Agents for Social Intelligence, *Knowledge Engineering and Semantic Web, 6th International Conference Proceedings*, ISSN 1865-0929, Moscow, Russia, pp.283-290.
2. Muchnik L. et al. 2013 Social Influence Bias: A Randomized Experiment, *Science 341*, 647, DOI: 10.1126/science.1240466.
3. Vityaev E. 2015 Unified formalization of «natural» classification, «natural» concepts, and consciousness as integrated information by Giulio Tononi. The Sixth international conference on Biologically Inspired Cognitive Architectures (BICA 2015, November 6-8, Lyon, France), Procedia Computer Science, v.71, Elsevier, 2015. 169-177.

THE STUDY OF THE PHARMACOLOGICAL EFFECT OF LITHIUM – CONTAINING COMPOSITION ON MICE IN CASE OF BEHAVIORAL DISORDERS DUE TO SUBCHRONIC ALCOHOL INTOXICATION

Kotlyarova A.A.[1*], Letyagin A.Yu.[1], Tolstikova T.G.[2], Rachkovskaya L.N.[1]
[1]*Federal state budgetary scientific institution "Scientific Institute of clinical and experimental lymphology", Novosibirsk, Russia*
[2]*N.N. Vorozhtsov Institute of Organic Chemistry of the Siberian Branch of Russian Academy of Science, Novosibirsk, Russia*
e-mail: kotlyarova.anastasiya@yandex.ru
[*]*Corresponding author*

Key words*: lithium, subchronic alcohol intoxication, ethanol, behavioral despair test (Porsolt Forced Swim Test), conditioned passive avoidance reflex*

Rationale and Purpose: Today there are actual medical, social and economic problems associated with alcoholism and related nervous system disorders. Lithium preparations are widely used for stabilize mood in case of bipolar affective disorder. Currently neuroprotective and neuroregenerative effects of lithium show the effectiveness as for acute brain injury, also in chronic neurodegenerative diseases such as dementia, alcoholism, Alzheimer disease, etc. [1, 2]. In clinical practice use of lithium preparations is limited due to difficult adjustment of drug dosage, necessity of monitoring its concentration in blood, side effects development as a result of accumulation of lithium in a body. For improvement of pharmacologic properties lithium is combined with other agents (for example modifying sorbent) thus it can produce longer-term and more harmless (less side reactions) effect in the long view [3, 4]. Lithium immobilization on sorption basis will allow to use sorbent as detoxicant and carrying agent of drugs to body. The purpose of the work is studying the effect of the lithium – containing composition on terms of behavioral reactions under subchronic alcohol intoxication model.

Methods and Algorithms: During the work we used nonlinear mice- males weighing 25-30 g (180 animals). Alcohol intoxication was caused through intragastric administration of a 40% aqueous ethanol solution (3 g per 1 kg of body weight) in combination with 5% - ethanol solution as drink ad libitum for 5 weeks. Control animals were inserted 0,9% salin solution. After two weeks of alcoholization groups were formed on the basic of preparations introduction: lithium carbonate, lithium citrate, sorbent - carrier and sorbent modified lithium citrate. Emotional state of animals was assessed through behavioral despair test (Porsolt Forced Swim Test), short – term memory assessment was performed through conditioned passive avoidance reflex (CRPA). The parameters of conditioned reflex activity were determined on 7th, 14th and 21 days after the start of the test substances. The results were processed using STATISTICA 8.0 statistical program.

Results: Subchronic alcoholism of mice, caused through daily intragastric administration of a subtoxic dose of ethanol for 5 weeks leads to behavioral and neurological disorders, which are occurred in the form of a depression of psychomotor activity, violations of the processes of learning and memory. In the course of the treatment by lithium-containing composition in the behavioral despair test on 21 day time before the first immobility increase by 41.5%. In passive avoidance conditioning on 7thday

after the start of the test composition memorization skill consolidation improve of 44% in compare with the negative control, on 21 day memorizing decline by 29.7 %.

Conclusion: The proposed dosage form of lithium (immobilized on a sorbent carrier) has a complex neurotropic action showing antitoxic properties against a background of long-term administration of ethanol.

References:

1. Chi-Tso Chiu, De-Maw Chuang. 2010 Molecular actions and therapeutic potential of lithium in preclinical and clinical studies of CNS disorders Pharmacol. Ther. V.128, № 2. P. 281–304.
2. Chuang D.M. et al. 2002 Neuroprotective effects of lithium in cultured cells and animal models of diseases Bipolar. Disord. V.4, № 2. P. 129–136.
3. Rachkovskaya L.N. et al. 2015 Modified sorbents for practical health, Bull. East. Sib. Sci. Cent. Sib. Branch Russ. Acad. Med. Sci. V.35 P. 47–54.
4. Borodin Y.I. et al. 2006 For Physical and Psychological Rehabilitation, Owl, Novosibirsk.

DYSFUNCTION OF AUTISTIC GENES EXPRESSION IN THE HIPPOCAMPUS OF MALE MICE WITH THE DISTURBANCES OF SOCIAL BEHAVIOR INDUCED BY CHRONIC SOCIAL DEFEAT STRESS

Kovalenko I.L.*, Galyamina A.G., Smagin D.A., Karpushina A.A., Kudryavtseva N.N.
Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia
**Corresponding author, e-mail: koir@bionet.nsc.ru*

Key words*: social defeats, depression, abnormal social interactions, low communication, repetitive behaviors, autistic genes*

Motivation and Aim: Ability of people to communicate with each other is a necessary component of social behavior and normal development of individuals living in community. Apparent decline in sociability can be the result of negative social environment, development of affective and neurological disorders including depression and autism. In this work we studied expression of genes that are involved into autistic spectrum disorders in the hippocampus of male mice with long chronic social defeat stress (CSDS) which accompanied by disturbances in social behaviors. Methods: Chronic social defeat stress was generated in male mice by exposure to CSDS in daily agonistic interactions [1]. The hippocampus was dissected according to the map presented in the Allen Mouse Brain Atlas. The collected samples were sequenced at JSC Genoanalytica (http://genoanalytica.ru/, Moscow, Russia). The Cufflinks program was used to estimate the gene expression levels in FPKM. Genes were considered to be differentially expressed at the level of statistical significance $p < 0.05$ and $q < 0.05$.

Results: Male mice with experience of social defeats displayed avoidance of social contacts with conspecific, immobility and low communication. Exploratory activity (rearing) and approaching behavior time towards partner were decreased and number of episodes of repetitive self-grooming behavior was increased in the defeated mice in comparison with the control. These symptoms were similar to those that are used in animal models of autistic spectrum disorders. Analyzing of RNA-seq database of whole transcriptome of the hippocampus we found in the defeated mice increased expression of genes which are associated with autistic spectrum disorders in humans: *Shank2, Reln, Nlgn2, Pcdh10, Arx, Vegfa, Ep300*. Conclusion: Chronic social defeat stress induces the development of depression-like state in male mice under CSDS which is accompanied by disturbances in social behaviors and changes in the expression of genes that are involved in autistic spectrum disorders.

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Reference:

1. Kudryavtseva NN, Smagin DA, Kovalenko IL, Vishnivetskaya GB 2014 Repeated positive fighting experience in male inbred mice, *Nat. Prot.* 9:11: 2705 – 2717.

APPLICATION NEUROELECTROSTIMULATION OF A PERIPHERAL NERVOUS SYSTEM FOR CORRECTION OF COGNITIVE CHARACTERISTICS IN A PROBLEM OF LEARNING ABILITY

Kublanov V.S.*, Petrenko A.A.
Research Medical and Biological Engineering Centre of High Technologies
Ural Federal University, URFU, Yekaterinburg, Russian Federation
e-mail: kublanov@mail.ru
**Corresponding author*

Key words: *neuroelectrostimulation, cognitive characteristics, attention, learning ability, neuroplasticity, neuroscience of learning*

Motivation and Aim: Neuroscience of learning is rather young direction which is crossed with neurology, psychology, pedagogy, neurophysiology, etc. Interest in a problem of cognitive disturbances was increased at the end of the 20th century. On the one hand, relevance of a problem is caused by opening of pathogenetic mechanisms of disturbance of cognitive functions and advancement of new approaches on restoration of brain neurones, on the other hand — augmentation of a share of older people in the population and sharp increasing of the survival of patients with a myocardial infarction and a stroke [1]. The concept of neuroplasticity becomes key concept of the neurosciences field. According to the rule of Hebba [2], the change in synaptic activity based on learning and memory. Thus, development of cognitive skills is associated to emergence of new patterns of neuroways where neuroplasticity plays an important role [3].

Cognitive characteristics and, first of all, indicators of attention and memory, are one of the main parameters, impact on which can increase result of training [4]. The method of a neuroelectrostimulation [5] can become one of perspective methods for improvement and recovery of cognitive characteristics in a problem of learning ability. The neuroelectrostimulation allows to reorganize neuronal networks by means of modulation of their communications and is capable to modulate the highest cortical functions to facilitate training, a recognition of visual images, to improve memory, analog thinking and decision-making, and also can be used for neuro and cognitive rehabilitation [6].

The purpose of this work is to investigate influence of one of the methods of a neuroelectrostimulation of a peripheral nervous system on attention parameters as one of the main characteristics of training process.

Methods and Algorithms: The study involved 15 subjects between the ages of 18-25 years who gave their informed consent to voluntary participate in the study.

The «SYMPATHOCOR-01» device was selected as neuroelectrostimulation of a peripheral nervous system. The device provides multichannel percutaneous non-invasive impact on the pathways of nerve formations and neck ganglia with the help of spatially distributed field of current pulses. The «SYMPATHOCOR-01» device is permitted for use in medical institutions of the Russian Federation and is included in the register of medical equipment (registration certificate № FSR 2007/00757 at 27.09.2007).

Methodology «Bourdon test» was used for the study of attention parameters [8]. At Bourdon test performance subjects was presented a table filled with symbols formed

randomly. Looking through the table row by row, the subject must locate and highlight certain characters. Bourdon test is designed to assess the stability of the volume and switching of attention. The quality of the test was assessed by the speed of browsing, the number of errors, the number of passes, the number of odd symbols, the number of scanned characters and productivity index.

To assess the mental fatigue was used adapted subjective questionnaire of acute mental fatigue by A.B. Leonova [9]. The questionnaire contains 18 statements describing different degrees of mental fatigue. Index of mental fatigue (IMF). was calculated based on these data. Mental fatigue is the most important factor that limits human performance in the workplace, especially learning activities [4].

The characteristics of heart rate variability (HRV) were analyzed as a physiological indicator of changes of the subject functional state during the study. Encephalan - EEGR-19/26 was used to register the HRV signal. It is known that the spectral components of HRV reflect the physiological changes in the body and allow to find patterns in the regulation of physiological and mental (psycho-emotional) condition of the person: HF component reflects the activity of the parasympathetic part of the autonomic nervous system, in particular vagus activity and the power of respiratory waves; LF index characterizes the state of the sympathetic division of the autonomic nervous system, in particular, the system of regulation of vascular tone; VLF spectral component is closely related to psycho-emotional stress and the functional state of the cerebral cortex [10]. Analysis of the spectral components of HRV data was performed using the program implemented in MATLAB. ANOVA implemented in the package application "STATISTICA 10.0 was carried out to process the data obtained in the course of study for groups "before" and "after" correction.

Results: The results are shown in Table I-II.

Table I. Average values of the Bourdon test parameters and IMF in the groups "before" and "after" correction

Group	IMF	Number of scanned characters	Number of errors	Number of passes	Number of odd symbols	Speed of browsing	Productivity
before	13	1561	26	24	9	167	1,3
after	5	1971	24	19	5	197	1,53
standard deviation	2	108	6	6	5	7	0,05

Table II. Average relative values of the HRV spectral components in the groups «before» and «after» correction

Group	HF	LF	VLF
before	0,16	0,29	0,48
after	0,15	0,35	0,42
standard deviation	0,02	0,02	0,03

Analysis of the results presented in Table I-II showed the following:

Significant between-group changes were obtained in terms of the speed of browsing, productivity rate and the number of scanned characters. An average of speed browsing and productivity increased up 18%, and the number of characters scanned up 26%.

IMF increased at Bourdon test performance but after the correction procedure using

«SIMPATHOCOR-01» IMF dropped and returned to the original background values.

Significant between-group differences were obtained on LF and VLF components. No significant differences were observed in the HF component. VLF component increased and LF reduced at the Bourdon test performance. After the correction procedure VLF and LF components returned to the original background values.

Discussion: Thus, during the course of this study it was showed that the method neuroelectrostimulation of a peripheral nervous system allows to enhance and activate the attention parameters, namely speed of browsing and productivity, and reduce index of mental fatigue. At the same time indicators of subject efficiency changes are changes of some characteristics of an autonomic nervous system, in particular LF and VLF spectral components. VLF spectral component increases at performing the Bourdon test that indicating the psycho-emotional stress, and LF reduces that indicating the decrease in vascular tone, but after the correction the indices of spectral components normalize.

Conclusion: The received data showed that the application «SYMPATHOCOR-01» device for neuroelectrostimulation of a peripheral nervous system allows to improve attention parameters, namely speed of browsing and productivity. It demonstrates activation of the mechanisms underlying human cognitive activity. Thus, realization of the neuroplasticity principle allows to control development of a nervous system and to intensify process of training and restoration of a cognitive reserve.

Availability: Knowledge of the pathophysiological mechanisms underlying neuroplasticity, will optimize therapeutic approaches to development of science-based correction techniques to restore and improve cognitive abilities [11]. The results of research can be applied in the design programs to improve the learning efficiency and the development of techniques for the cognitive abilities correction. Also a follow-up work will involve clinical trials in patients with various diseases associated with impaired attention parameters.

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References:

1. Damulin I.V. 2004 Mild cognitive impairment*, Consilium Medicum*, 2:138-141.
2. Hebb D. 1949 *The Organization of Behaviour*, 34-46 (New York: Wiley)
3. Slanevskaia N.M. 2012 *BRAIN, MIND and SOCIETY. Part II,* (RIKON, St.Petersburg).
4. Karpenko M.P. 2008 *Teleobuchenie* (MUH).
5. Kublanov V.S. et al. 2015 Multi-Electrode Neurostimulation System for Treatment of Cognitive Impairments, *37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society.*
6. Rossi S., Rossini P. 2004 TMS in cognitive plasticity and the potential for rehabilitation, *Trends in Cognitive Sciences,*8: 273-279.
7. Kublanov V.S. et al. 2010 About innovative possibilities of the device SYMPATOCOR in management of functional disorders of autonomic and central nervous system in neurology, *Kremljovskaya Medicina J.*, 4: 60–64
8. Brunner E. 2006 *Better than attention. Methods of diagnostics and psychological correction* (Fenix, Rostov-on-Don).
9. Leonova A.B., Velichkovskaia S.B. 2002 Differentsialnaya diagnostika sostoyaniy snizhennoy rabotosposobnosti, *Psychology mental states*, 4: 326-343.
10. Baevsky R. et al. 2001 HRV Analysis under the usage of different electrocardiography systems (Methodical recommendations), *Journal of arrhythmology*, 24: 65-87.
11. Zhivolupov S.A. et al. 2013 Contemporary conception of neuroplasticity (theoretical aspects and practical significance) *The Korsakov's Journal of Neurology and Psychiatry*, 10: 102-108.

PROSPECTS OF DEVELOPMENT OF NEUROIMAGING TECHNOLOGIES IN MODERN MEDICINE

Letyagin A.Yu.
Institute of Clinical and Experimental Lymphology, Novosibirsk, Russia
Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia
e-mail: letyagin-andrey@yandex.ru

Key words*: magnetic resonance imaging (MRI), 3.0 Tesla MRI scanner, neuroimaging MRI technologies*

Motivation and Aim: The market of diagnostic neuroimaging is associated with the MRI scanners, which sub-segmenting into 7T MRI and 3T MRI (ultra high field), 1.5T MRI (high field), Low Field MRI, and others.

Methods and Algorithms: Review of activity in the developing, research and clinical using of new technologies in neuroimaging for ultra high field MRI.

Results and conclusions: 3.0 T MRI can achieve linear (spatial) resolution up to 500-1000 mkm and the ability to produce images with a cubic voxel (~1 mm2), suitable for postprocessing multiplanar reformatting and morphometry. 3.0 Tesla 3D-FLAIR sequence with 1 mm2 isovoxels is the most sensitive for the detection of dysplasia in small CNS structures. Sequence MPRAGE, which gives a high contrast between gray and white matter of the brain used for voxel-based morphometry (VBM). There are same morphometric analysis programmes (MAP), which generate a parameter map, highlighting the difference in cortical thickness, cortical heterotopia towards white matter and basal ganglia volume - as compared to healthy individuals base.

Cerebral microbleeds (CMBs) are detected by MRI techniques T2*-WI (GRE) and SWI sensitive to paramagnetic products of blood' degradation, after stroke, in hypertensive encephalopathy, as well as in neurodegenerative diseases. Tissue-selective MRI technologies T2-STIR and T2-DIR give excellent results in visualization of the oedematic paravasal micro loci and micro foci in neurodegenerative conditions.

MR fingerprinting technology based on the relaxation parameters of voxels of T1 and T2 WI that are very stable in healthy volunteers, but vary in the course of treatment, or even be able to provides early diagnosis of brain cancer and metastasis.

MR-angiography at 3,0 T MRI systems provides superb high-resolution results. MRI technology FIESTA reliably identifies the angio-neural microanatomical "conflict" of the cranial nerves and cerebral vessels.

"Diffusion" technology (DWI, DTI, DKI) provide new insights into the functional neuroanatomy to identify micro lesions and to analyze the structure of the neural tracts of the central nervous system and peripheral nerves, especially for the preoperative planning of neurosurgical intervention in order to minimize postoperative deficits.

Functional MRI of the central nervous system (fMRI) provides visual information of the brain tissue activity in the pathology, in the psychological stress, at rest (rs-fMRI) and functional tests, etc.; that could eventually create vulnerability and treatment markers for psychiatry and psychoneurology.

DISC1 INTERACTOME AND MENTAL DISORDERS: INPUT OF ANIMAL MODELS

Lipina T.V.
Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk State University, Novosibirsk, Russia
e-mail: lipina@physiol.ru

Key words: *Disrupted-In-Schizophrenia-1 (Disc1), protein-protein interactions, gene, brain, behavior, mice*

Motivation and Aim: Nearly a quarter of the world's population report problems, at some point of their life, which meet the criteria for the diagnosis of mental disorders [1]. Hence, significant efforts have been put into understanding the causes of psychiatric disorders to improve their early diagnosis and treatments. Disrupted-In-Schizophrenia-1 (DISC1) gene emerged as genetic factor predisposing individuals to a wide range of mental disorders detected by genetic, clinical association studies and emerging biology [2,3]. Notably, a number of genes encoding proteins interacting with DISC1 are also considered as risk factors of mental disorders. Hence, it is reasonable to suggest that understanding of mental disorders in the context of DISC1 network principles (DISC1 interactome, protein-protein interactions) may help to untangle complex molecular mechanisms of certain psychiatric disorders and address fundamental features of DISC1 as disease gene.

Methods and Algorithms: First, functional role of DISC1 and its molecular complexes in the brain will be described. Secondly, DISC1-associated mental disorders will be reviewed in the context of DISC1 and its interactome. Next, I will focus on behavioral phenotypes of DISC1 lines and genetic mouse lines with altered expression of proteins interacting with DISC1 to assess the impact of individual DISC1 interacting proteins into DISC1-associated mental disorders.

Results: The most comprehensive list of DISC1 interacting proteins was identified by yeast two-hybrid screen [4], which consists of 127 proteins and 158 interactions (DISC1158 network), suggesting that DISC1 acts as a scaffolding protein in the cell. DISC1 ties together several functional pathways such as: Akt/mTOR, dopaminergic pathway coupled with GSK-3, D2R, PDE4/cAMP and GSK-3/β-catenin. Generally, these pathways play important roles in neurodevelopment and such subcellular functions as synapse formation, synaptic plasticity, intracellular signaling, gene expression, mitochondrial functions and microtubule-based intracellular transport. Around 10% of human genes are known as disease associated [5]. Moreover, the linkage of one gene to different diseases indicates that these diseases have a common genetic origin. Indeed, a human disease network was recently developed [6], where 68% of the estimated diseases were connected to at least one other disease. There is a strong interconnectivity among most of the DISC1-associated psychopathologies, and perhaps, DISC1 interactome may help to better understand the molecular base of comorbidity of brain disorders. The biggest proportion of DISC1-interactors [PDE4B, GSK-3, PCM1, TNIK, KIF5A, Kal-7, Dysbindin, FEZ1, 14-3-3, PCNT, MIPT3, SRR, DIXDC1, ATF4/ATF5, LIS1, NDE1/NDEL1 and Grb2] is involved in schizophrenia. A large part of DISC1 interactors is also associated with bipolar disorder [IP3R1, PDE4, GSK-3, Dysbindin, PCNT, SRR, DIXDC1, ATF4]. Then, some amount of DISC1 interactors is linked with Alzheimer's

disorder [GSK-3, APP, KLC-1/KLC2/DIC, Kal-7, PCNT, SRR] and mental retardation [KLC1/KLC2/DIC, BBS4, PCNT, MIPT3, ATF4/5, LIS1, NDE/NDEL1]. Fewer DISC1-interactors are associated with Huntington's disease [PCM1, FEZ1, Grb1, N-CoR], major depression [Dysbindin, FEZ1, 14-3-3], addiction [Dysbindin], autism [Grb2], ADHD [Kal-7], epilepsy and developmental delay [LIS1, NDE1/NDEL1] [7]. Analysis of behavioral phenotypes on 18 DISC1 models and 30 genetic mouse lines with modified DISC1 interacting proteins [7] showed that a large proportion of genetic mouse lines without gross abnormalities of sensory-motor functions demonstrated alterations in emotional, cognitive and social behaviors, supporting the DISC1 interactome in range of psychiatric disorders.

Conclusion: There is a need to build a comprehensive DISC1 disease network, integrating several levels of research: 1) interactions among genes, proteins and intracellular biochemical processes; 2) communication between distinct neuronal and glial cellular populations; 3) behavioral endophenotypes, with altogether will offer a basis for future network medicine.

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References:

1. WHO International Consortium in Psychiatric Epidemiology 2000. Cross-national comparisons of the prevalences and correlates of mental disorders, *Bulletin of the World Health Organization,* 78.
2. Chubb J.E. et al. 2008 The DISC1 locus in psychiatric illness, *Mol. Psychiatry* 13 36-64.
3. Brandon N.J., Sawa A. 2011 Linking neurodevelopmental and synaptic theories of mental illness through DISC1, *Nat. Rev. Neurosci,* 12 707-722.
4. Camargo L.M. et al. 2007 Disrupted in Schizophrenia 1 Interactome: evidence for the close connectivity of risk genes and a potential synaptic basis for schizophrenia, *Mol. Psychiatry* 12 74-86.
5. Amberger J. et al. 2009 McKusick's Online Mendelian Inheritance in Man (OMIM), *Nucleic Acids Res* 37 D793–D796.
6. Barabási A.L. et al. 2011 Network medicine: a network-based approach to human disease, *Nat. Rev. Genet.* 12 56-68.
7. Lipina T.V., Roder J.C. 2014 Disrupted-In-Schizophrenia-1 (DISC1) interactome and mental disorders: impact of mouse models, *Neurosci Biobehav Rev*. 45 271-294.

CIRCULAR RNA (CIRCRNA) CIRS-7 IN ALZHEIMER'S DISEASE (AD) AFFECTS MICRORNA-7 (MIRNA-7) TRAFFICKING

Lukiw W.J., Zhao Y., Rogaev E.I.*, Bhattacharjee S., Percy M., Pogue A., Dua P.
*Neuroscience Center, Louisiana State University School Medicine, New Orleans, LA USA; Neurogenetics, University of Toronto, Toronto, ON, Canada; Alchem Biotek, Toronto, ON, Canada; *Vavilov Institute of General Genetics, Russian Academy of Sciences, Moscow, Russia; *Center for Brain Neurobiology and Neurogenetics, Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences, 630090 Novosibirsk, Russia; *Department of Psychiatry, Brudnick Neuropsychiatric Research Institute, University of Massachusetts Medical School, Worcester, Massachusetts, USA; *School of Bioengineering and Bioinformatics, Lomonosov Moscow State University, Moscow, Russia; Bioinformatics and Health Science Management, Ruston, LA USA*
** Corresponding author: evgeny.rogaev@umassmed.edu*

Circular RNAs (circRNAs) are a naturally occurring family of small noncoding RNAs (sncRNAs) highly represented in the eukaryotic transcriptome. Recently characterized, traditional methods of RNA detection and analysis requiring a free 5′ or 3′ ribonucleotide terminus may have significantly underestimated circRNA abundance and significance. Intrinsically resistant to exonucleolytic RNA decay, circRNAs appear to be enriched in mammalian brain tissues. Interestingly, specific sncRNAs such as the evolutionary ancient homo sapien microRNA-7 (hsa miRNA-7; chr 9q21.32; ~23 nt; http://www.mirbase.org/cgi-bin/mirnaentry.pl?acc= MI00 00263;a known, important post-transcriptional regulator of phagocytosis), are not only very abundant in the human CNS, but are also associated with a circRNA for miRNA-7 (ciRS-7) in the same tissues. ciRS-7 contains about ~70 tandem anti-miRNA-7 sequences; ciRS-7 (~1400 nt) thereby acts as a kind of endogenous, competing, anti-complementary miRNA "sponge" to adsorb, and hence quench, normal miRNA-7 function. Using miRNA arrays, enhanced Northern blot hybridization and the circularity-sensitive probe RNaseR we here provide initial evidence of a mis-regulated ciRS-7-miRNA-7 system in sporadic Alzheimer's disease (AD). Deficits in ciRS-7, and ciRS-7"sponging activities" might be expected to increase ambient miRNA-7 levels in AD-affected brain cells, as is observed, to ultimately contribute to the down-regulation of selective miRNA-7-sensitive messenger RNA (mRNA) targets. The presence of up-regulated miRNA-7, due to a deficiency in ciRS-7 "sponging" effects, was shown to down-regulate AD-relevant targets, such as, for example, the ubiquitin conjugating enzyme E2A (UBE2A; miRNA-7-UBE2A mRNA energy of association, EA = −22.86 kcal/mol). UBE2A, an autophagic, phagocytic protein essential in the proteasome-mediated clearance of amyloid peptides is depleted in AD brain. Such circRNA-miRNA-mRNA regulatory systems appear to represent another important layer of epigenetic control over gene expression in the CNS. Indeed, our ideas on sncRNAs in the CNS continue to evolve, and technological advancement, refinement and recent discoveries continue to challenge the basic doctrines of nucleic acid biochemistry and evolutionary neurobiology in both health and disease.

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TRANSCRIPTOME PROFILING IN RAT BRAIN AREAS TO STUDY GENETIC BASIS OF AGGRESSIVE AND TOLERANT BEHAVIOR

Orlov Y.L.[1], Bragin A.O.[1,2]*, Medvedeva I.V.[1,2], Chadaeva I.V.[1], Markel A.L.[1]
[1]*Institute of Cytology of Genetics SB RAS, Novosibirsk, Russia*
[2]*Novosibirsk State University, Novosibirsk, Russia*
e-mail: ibragim@bionet.nsc.ru
[*]*Corresponding author*

Key words*: behavior, aggression, RNA-Seq, differential gene expression, rat, animal models, molecular mechanisms.*

Motivation and Aim: Aggressive behavior is a complex behavior phenomenon having genetics and physiological roots. Basic studies have shown that the frequency and severity of aggression depends on the hereditary predispositions, previous experience of aggressive behavior and social context [1].

Methods and Algorithms: To study genetic component of aggressive behavior we used published data on genes expression (RNA-seq and microarrays) related to aggressive behavior in mouse and rat as well as in-house experimental data [2]. The research was intended to study the molecular and genetic mechanisms of enhanced aggressiveness in comparison with tolerant behavior using two unique experimental models which were developed at the Institute of Cytology and Genetics SB RAS. Grey rats (*Rattus norvegicus*) have been subjected to selection during several generations in two directions - friendly, tolerant behavior towards man (tame gray rats) and increased aggressive behavior ("aggressors"). The latter rats demonstrated reinforced enhanced not only towards man (in the glove test) but also towards conspecifics in intermale agonistic interactions.

Results: After RNA-sequencing of the rat brain tissues samples, constructing differentially expressed gene lists we used set of tools for coexpression analysis to found characteristic features of gene network related to aggressive behavior. The use of computer technologies such as GeneNet and ANDVisio gives the possibility of reconstructing genetic networks - assemblies of coordinately functioning genes controlling biochemical, molecular-genetic, and physiological processes - based on the published data. There was a significant difference between the aggressive and tame rats in proportions of alternative transcripts in a number of the synapse genes.

Conclusion: RNA-seq analysis of differentially expressed genes in rat confirmed presence of genes known as related to aggressive behavior, such as MaoA. We continue work on gene network reconstruction using RNA-seq experiments on additional mouse brain structures in contrast groups of laboratory animals using digital atlas of such structures.

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References:

1. Kudryavtseva N.N., Markel A.L., Orlov Y.L. 2014 Aggressive behavior: genetic and physiological mechanisms, *Vavilov journal of genetics and breeding*, 18(4/3):1133–1155. (In Russian)
2. Heyne H.O. et al. 2014 Genetic influences on brain gene expression in rats selected for tameness and aggression, Genetics, 198(3):1277-90.

TRANSCRIPTOMICS ANALYSIS OF DIFFERENTIAL EXPRESSION IN HELIX LUCORUM STATOCYSTS

Osypov A.A.[1,2]*, Kolosov P.[1], Aceyev N.[1], Chesnokova E.[1], Roshchin M.[1], Bal N.[1], Balaban P.[1]

[1]*Institute of Higher Nervous Activity and Neurophysiology of RAS, Moscow, Russia,*
[2]*Institute of Cell Biophysics of RAS, Pushchino, Russia*
e-mail: aosypov@gmail.com
[*]*Corresponding author*

Key words*: Helix lucorum, statocysts, gravity reception, transcriptomics, differential expression*

Motivation and Aim: *Helix lucorum* snail is a classical model object for studies of the nervous system functions. In order to understand the genome mechanisms of the gravity reception in the snail nervous system we performed a near single-cell transcriptomics analysis of space flight induced differential expression in *Helix* statocysts.

Methods and Algorithms: There were 8 animals in two equal groups of snails - that flied into space (n=4) and remained on Earth (n=4), some 13 cells were used per every sample. We performed a full novel transcriptome assembly based on the total mRNA sequenced by means of Ion Proton System.

Results: Near 60% of reads per sample were mapped to the assembly, yielding more than 40 significantly differentially expressed (i.e. downregulated by space flight) genes of high accuracy. Most of them relate to the cell reception and different stages of intracellular signaling pathways, including gene expression regulation. Interestingly they were no significantly differently expressed genes if transcripts were mapped to the whole nervous system transcriptome assembly provided by our colleagues, and the overall portion of the mapped reads was less by nearly 20%.

Conclusion: The data obtained indicates that genes that are differently expressed are specific to the statocysts themselves and are probably related to gravity reception.

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TOWARDS A NEUROBIOLOGICALLY REASONABLE C. ELEGANS NERVOUS SYSTEM SIMULATION: NEURON, MUSCLE AND SIGNAL PROPAGATION MODELLING

Palyanov A.Yu.[1,2]*, Samoilova Kh.V.[2], Palyanova N.V.[3]
[1]*A.P. Ershov Institute of Informatics Systems, Novosibirsk, Russia*
[2]*Novosibirsk State University, Novosibirsk, Russia*
[3]*Institute of Molecular Biology and Biophysics, Novosibirsk, Russia*
e-mail: palyanov@iis.nsk.su
[*]*Corresponding author*

Key words*: computational modeling, computational neurobiology, electrophysiology, simulation, nervous system, muscle cell, ion channels modeling, C. elegans*

Motivation and Aim: The reverse-engineering and reproduction of *Caenorhabditis elegans* (*C. elegans*) as its computer simulation is one of the grand challenges at the interface between neuroscience, biophysics and computational modeling. Participating in the international open science OpenWorm Project, we share the aim of developing the computational models and techniques for solving this problem. Reproduction of ion channels, neurophysiologic parameters and morphology is required for a neurobiologically reasonable simulation of a typical *C. elegans* neuron (with passive signal propagation) and of a muscular cell (capable of firing slow long-lasting Ca2+ driven action potentials).

Methods and Algorithms: The models and algorithms proposed in this work were created within the NEURON simulation environment [1], which includes a built-in programming language HOC and an ability for construction of custom models of ion channels and other cellular mechanisms via Neuron Model Description Language (NMODL) expanding NEURON's standard repertoire.

Results: We have proposed a model of a typical *C. elegans* neuron (based on our recent investigations [2]) and of a pharyngeal muscle cell, taking into account their morphologic and electrophysiologic properties. On the basis of the available experimental data and models of related ion channels we have constructed and optimized EGL-19 Ca2+ and EXP-2 K+ ion channels [3]. Then we introduced them into the model of a muscle cell, to make it correctly shape the action potential time profile. The model of a neuron reproduces quite accurately the mechanism of neural signal transmission based on passive propagation.

Conclusion: Obtained models are in a good accordance with known facts about simulated objects and reproduce their properties really well. They allow enhancement with more sophisticated mechanisms in order to represent the specifics of various cell classes and and to construct the networks of the elements involved.

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References:

1. N.T. Carnevale and M.L. Hines (2006) The NEURON Book, Cambridge, UK: Cambridge University Press.
2. A.Yu. Palyanov, A.S. Ratushnyak (2015) Some Details of Signal Propagation in the Nervous System of C. elegans. Russian Journal of Genetics: Applied Research, 5(6): 642-649.
3. B. Shtonda, L. Avery. (2005) CCA-1, EGL-19 and EXP-2 currents shape action potentials in the C. elegans pharynx. J. Exp. Biol. 208: 2177–2190

APPLICATION OF THE DYNAMIC CORRECTION OF THE SYMPATHETIC NERVOUS SYSTEM IN TREATMENT OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER

Petrenko T.S.[1,2]*, Kublanov V.S.[1], Retyunskiy K.Ju.[2]
[1]*Research Medical and Biological Engineering Center of High Technologies, Institute of Radio Engineering and Information Technology, Ural Federal University, Yekaterinburg, Russia*
[2]*Ural State Medical University, Yekaterinburg, Russia*
e-mail: psy66@narod.ru
[*]*Corresponding author*

Key words*: attention deficit hyperactivity disorder, neuroelectrostimulation, autonomic nervous system, executive functions*

Motivation and Aim: Attention deficit hyperactivity disorder (ADHD) in childhood is one of the most actual problems in medicine today due to its high prevalence, insufficient amount of pathogenetic mechanism's knowledge, and, consequently, low efficiency of therapy [1]. Actuality verifying the effectiveness of the dynamic correction of the sympathetic nervous system (DCASNS) to restore executive functions in children with attention deficit hyperactivity disorder

Methods and Algorithms: Objectives: 35 children with clinical signs of ADHD (pursuant to ICD-10 – F90), age 6-9 years old, intellectual indicants not below the average according to the Wechsler Scale held specific treatment for at least 6 months without a significantly improvement. All patients received medication approved for use in pediatric practice facilities, including a nootropic, cardiovascular drugs, anticonvulsants, and course of neuroelectrostimulation by SIMPATOKOR-01 device, realized DCASNS method. Its method implemented using an electrical pulse generator that delivers the spatially-distributed field of the carefully-controlled current pulses in the nervous structures of the neck [2]. This allow to control of autonomic regulation activity (by stellatis ganglion) and stimulate stem neural centers. Patients were assessed using the psychometric method - Attention deficit hyperactivity disorder – Rating scale IV [3], psychophysiological methods – the test of variability of attention (TOVA) [4], electrophysiological method – 21-chanel electroencephalography (EEG).

Results: The initial clinical state of the patients was clinical severe, and low rates of neuropsychological tests. As a result of ten DCASNS procedures improved significantly psychometric assessments by ADHD scale (tabl. 1) and psychophysiological assessments by TOVA test (tabl. 2).

Table 1. The dynamics of ADHD RS-IV in children with ADHD before and after treatment

ADHD-RS-IV score	Before treatment	After DCASNS
Inattention	1,99±	1,15±
Hyperactivity / impulsivity	2,17±	1,28±
Total	2,08±	1,22±

Table 2. The dynamics of the TOVA before and after treatment in children with ADHD

Data	Before treatment	After DCASNS
Omission errors, %	32,5 ±	8,1 ±
Commission errors, %	23,2 ±	19,9 ±
Response time, msec.	681 ±	656 ±

* $p<0,05$ – significance of differences compared before treatment.

The data from Tables 1 and Table 2 shows that after the course of the DCASNS for the children with ADHD changed psychophysiology parameters to the direction of normalization, and decrease the severity of symptoms of this disorder.

The brain activity in children with ADHD was characterized by increased theta and delta activity in the anterior cortical areas and reduction of level of the beta rhythm in the area. The EEG analysis at 6 and 12 months after beginning the treatment allows one to establish reduction of the high-amplitude slow-wave activity in all investigated children, and change of the ratio between theta and beta rhythms. Moreover, an increase of resistance with respect to loads was observed, i.e., raising the seizure threshold.

Conclusion: During this twelvemonth trial of DCASNS method's effectiveness in children with ADHD, we achieved significant clinical improvement with significant optimization of attention's quality indicants. We also observed reduction of hyperactivity and impetuosity. Clinical efficiency was proven with positive dynamics of ADHD psychometric indicants on the scale ADHD-RS-IV and psychophysiological ones according to TOVA-test.

References:

1. Barkley R.A. ADHD (handbook). – 3-ed. – New York, The Guilford Press. 2006.
2. Kublanov V.S., Shmirev V.I., Shershever A.S., etc. On the innovative possibilities of the device SIMPATOKOR-01 in neurology in functional disorders of the central and autonomic nervous system. Kremljovscaya Medicina. Clinichesky Vestnik 2010 V.4. P.60-64.
3. DuPaul G.J., Power T.J., Anastopoulos A.D., et al. ADHD Rating Scale-IV: Checklists, Norms, and Clinical Interpretation. New York, NY: Guilford Press; 1998.
4. Greenberg L.M., Waldman I.D. Developmental normative data on the test of variables of attention (T.O.V.A.). J Child Psychol Psychiatry. 1993 Sep;34(6):1019-30.

THE NON-INVASIVE ADAPTIVE NEUROELECTROSTIMULATION FOR RECOVERY OF THE COGNITIVE FUNCTIONS IN PATIENTS WITH AMNESTIC SYNDROME

Petrenko T.S.[1,2]*, Kublanov V.S.[1], Retyunskiy K.Ju.[2]
[1] *Research Medical and Biological Engineering Center of High Technologies, Institute of Radio Engineering and Information Technology, Ural Federal University, Yekaterinburg, Russia*
[2] *Ural State Medical University, Yekaterinburg, Russia*
e-mail: psy66@narod.ru
[*]*Corresponding author*

Key words*: neuroelectrostimulation, cognitive functions, amnestic syndrome*

Motivation and Aim: Actuality verifying the effectiveness of the dynamic correction of the sympathetic nervous system (DCASNS) using a non-invasive multichannel neurostimulation device "SYMPATHOCOR-01". The task is to restore cognitive function in patients with organic amnestic syndrome.

Methods and Algorithms: Objectives: Three patients with clinical organic amnestic syndrome resulting of brain damage (poisoning, alcohol and trauma) held inpatient treatment for at least 12 months in the neurology or psychiatry department without a significantly improvement. Methods: DCASNS method implemented using an electrical pulse generator that delivers the spatially-distributed field of the carefully-controlled current pulses in the nervous structures of the neck [1]. This allow to control of autonomic regulation activity (by stellatis ganglion) and stimulate stem neural centers. Patients were assessed using the clinical method, neuropsychological scales: Frontal Assessment Battery (FAB) [2], Montreal Cognitive Assessment (MoCA) [3], Mini-Mental State (MMSE) [4], magnetic resonance imaging (MRI), electroencephalography (EEG), heart rate variability (HRV).

Results: The initial clinical state of the patients was severe, with structural damage on MRI and low rates of neuropsychological tests. As a result of seven DCASNS procedures improved significantly neuropsychological assessments: FAB (from 5,7±3,1 to 12±4,0); MCA (from 11,3±3,0 to 16,3±4,0); MMSE (from 15,3±6,2 to 21,3±8,3). EEG comparison analysis showed an increase in power of Alpha waves and power reduction of Delta waves on all leads. HRV comparison analysis showed an increase total power and the change in autonomic balance.

Conclusion: The DCASNS method able to recover in the short working memory and other cognitive functions in patients with organic amnestic syndrome.

Availability: The DCASNS method can be used for the effectiveness treatment of cognitive dysfunctions resulting organic lesions of the central nervous system.

References:

1. Kublanov V.S. 2008 A hardware-software system for diagnosis and correction of autonomic dysfunctions. *Biomedical Engineering*. V.42(4) P. 206-212.
2. Dubois B., Litvan I. 2000 The FAB: A frontal assessment battery at bedside. *Neurology*. 55(11) P. 1621-1626.
3. Julayanont P. et al. 2015 The Montreal Cognitive Assessment—Basic: A Screening Tool for Mild Cognitive Impairment in Illiterate and Low-Educated Elderly Adults. *Journal of the American Geriatrics Society*. V. 63(12) P. 2550–2554.
4. Folstein M.F. et al. 1975 "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician". *Journal of Psychiatric Research* 12(3) P. 189-198.

THE FUNCTIONAL ASYMMETRY FEATURES IN PATIENTS WITH COGNITIVE IMPAIRMENT AS RESULT OF ORGANIC BRAIN DAMAGE

Petrenko T.S.[1,2]*, Kublanov V.S.[1], Retyunskiy K.Ju.[2], Koshurnikov R.V.[2]
[1]*Research Medical and Biological Engineering Center of High Technologies, Institute of Radio Engineering and Information Technology, Ural Federal University, Yekaterinburg, Russia*
[2]*Ural State Medical University, Yekaterinburg, Russia*
e-mail: psy66@narod.ru
[*]*Corresponding author*

Key words*: functional asymmetry, cognitive impairment, electroencephalography*

Motivation and Aim: Cognitive deficit is the result of the organic brain damage. The task of early cognitive impairment diagnostic is urgent for designing of the effective clinical programs. One of the perspective directions, is the electrophysiological study of the functional brain asymmetry (FBA) [1]. The goal of the present work is to study features of the functional asymmetry patients with cognitive impairment as result of organic brain damage.

Methods and Algorithms: Objectives: Four patients with clinical signs of cognitive impairment after organic damage and one healthy volunteer. Subjects performed cognitive tasks (dynamic praxis, reciprocus coordination, auditory motor coordination). During task performance, record of the 21-channel electroencephalography (EEG) was carried. The recorded biosignals were analyzed by the software package "FBA" Medicom Ltd (Taganrog).

Results: The features of the cross-correlation and cross-spectrum were the most informative for the alpha waves (8-13 Hz). Signals of patients, compared to signals of the healthy volunteer, showed significant decrease of the alpha waves power during performance of the cognitive tasks. The features of the coherent analysis were the most informative for beta waves (13-24 Hz). For patients with the organic brain damage dissociation of the intra- interhemispheric connections was noted. The dissonance was stronger expressed when patient had difficulties during the task performance. For healthy volunteer the formation of the powerful connections between different areas of the brain cortex mostly in the reight hemisphere.

Conclusion: The common feature for all patients was the decrease of the intra- and interhemispheric connections effectiveness. These connections are required in normal state for the cognitive task solution. For patients with the organic brain damage the significant decrease of the general energetic processes in the brain was noted. Results of the EEG signal coherent analysis allows one to quantify interaction of different areas of the cortex during performance of the cognitive tasks.

Availability: Results of the pioneer work allows us to formulate task of the in-depth research of the FBA patterns in order to develop methods of the early diagnostics of the organic brain damage and methods of the forecasting of its consequences.

References:

1. Zenkov L.R. 1996 Clinical Electroencephalography with elements Epileptology. Taganrog: TRTU 358 p.

ARTIFICIAL NEURAL NETWORK FOR DIAGNOSIS OF COGNITIVE IMPAIRMENT IN CHILDREN WITH DIFFERENT CLINICAL FORMS OF PERINATAL LESIONS OF THE CENTRAL NERVOUS SYSTEM

Pijanzin A.I.[1,2,3*], Ashkinadze A.V.[2], Shaidurov A.A.[1], Ivchenko E.V.[3]
[1]*Altai State University, Barnaul, Russia*
[2]*Altai State Medical University, Barnaul, Russia*
[3]*Altai Region Clinical Children's Hospital, Barnaul, Russia*
e-mail: bio7777777@mail.ru
[*]*Corresponding author*

Key words*: Artificial neural networks, central nervous system, children, cognitive impairment*

Motivation and Aim: Develop basic approaches of artificial neural network for diagnosing cognitive impairment in children undergoing various clinical forms of lesion of the central nervous system.

Methods and Algorithms: Children with a history of different clinical forms of perinatal lesions of the central nervous system: 1-lesion of hypoxic-ischemic perinatal genesis; 2-hypoxic-gemorragic lesion; 3-natal spinal injury; 4-kraniospinal trauma; 5- control group without perinatal lesions. The neuropsychological screening study included analysis of parameters of memory, attention, gnosis, praxis and intelligence. The diagnosis of mental disorders was based on the international classification of diseases (ICD-10). Mathematical methods included calculation of Spearman correlation coefficients, principal component analysis, artificial neural networks and classical statistical methods.

Results: Study of children between groups of correlation analysis method for psychologically showed some significant differences. The number of coefficients with high correlation depending on the form of perinatal lesions differed and was from 12 to 28. The method of principal component analysis based on the results of psychological testing, the children were divided into several classes. Assessment of the statistical significance of differences between groups of children was used to build artificial neural network.

Conclusion: Preliminary statistical selection of indicators of psychological testing is allowed to choose the most important options for constructing artificial neural network that can be used for diagnosing cognitive impairment in children with perinatal lesions of the central nervous system.

TATA-BOX AND BRAIN GENES NORM OF REACTION

Ponomarenko M.P.[1,2]*, Suslov V.V.[1], Gunbin K.V.[1,2], Ponomarenko P.M.[3], Vishnevsky O.V.[1,2]
[1]*Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia*
[2]*Novosibirsk State University, Novosibirsk, Russia*
[3]*Children's Hospital Los Angeles, Los Angeles, CA, USA*
e-mail: pon@bionet.nsc.ru
**Corresponding author*

Key words: *TATA-box, norm of reaction, gene expression, brain, evolution*

Motivation: In 2014, we demonstrated that the TATA-box is a molecular regulator of gene expression norm of reaction (NR). Pearson's coefficient of variation (Cv, the ratio of the standard deviation to the mean) is the measure of variations in gene expression. Hence it used as measure of the NR of the gene's expressional level. Sequences -70 to -20 bp. are proximal promoters (PP) that carry out of TATA-boxes or its analogues. This study is conducted to find correlation between the TBP/TATA affinity ($-ln[K_{D,TATA}(S)]$) of PPs for genes with brain's expression and Cv of the expression of these genes [1].

Methods. Maximum of the ($-ln[K_{D,TATA}(S)]$) in 26 bp. sliding window for PP was found by the equilibrium equation for the four steps of TBP/TATA-box binding. As brain expressed were sampled 35609 mRNAs in 946 human brain segments of Allen Brain Atlas [2] and 12931 mouse genes taken from the its brain transcriptome [3]. The human PPs were extracted from the hg19 human reference genome in the RefSeq database, release 52, and the mouse PPs from the reference mouse genome, release 69 of the Ensembl database. Cv value (%) of the expressional level for each gene were characterized according data [2, 3]. Pairs of Cv value and ($-ln[K_{D,TATA}(S)]$) for human and separately mouse genes were scaled to a (0; 1) scale of relative units and clustered by Statistica. Gene functional annotation provided by ten Gene Ontology (GO) terms with the highest confidence estimations with Bonferroni corrections.

Results: 1) Human genes divided on minor (8375 genes = 24%) and major (27234 genes = 76%) clusters. The minor cluster with high mean Cv values (36±9%) that is expression of these genes are variable. Cv values of these genes show a significant correlation with the ($-ln[K_{D,TATA}(S)]$) of their PPs: r=0.48 ($p<10^{-20}$). Hence, TBP affinity to PPs of these genes contribute to their wide expressional NR within human brain. GO annotation in good agreement with these data. These 8375 genes encode signaling pathway receptors on outer membranes of human brain cells as well as reception, sensory and cognition processes in brain. The major cluster with low both mean Cv values (10±6%) and correlation with ($-ln[K_{D,TATA}(S)]$) (r=0.16, $p<10^{-20}$), and with steady expression include genes of basic (intra)cellular metabolism. 2) Mouse genes divided on two clusters too: 1126 genes = 9% with high both mean Cv value (551±166%) and significant correlation (r=0.41, $p<10^{-20}$); 11805 genes = 91% with low both mean Cv value (189±98%) and correlation (r=0.26, $p<10^{-20}$). It was not shown reliable GO terms for certain cluster, but for all sample [3] most of GO terms matched by human major cluster only.

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References:

1. Ponomarenko P.M. et al. 2014, *Rus. Journ. of Gen.: Appl. Res*., 18 1219-1230.
2. Jones A. et al. 2009, *Nat. Rev. Neurosci*., 10(11) 821–828.
3. Lein E.S. et al. 2007, *Nature*, 445 168–176.

INTERHEMISPHERIC FUNCTIONAL DISCONNECTION IN AGING: INFLUENCE OF GENDER AND CLUSTRIN GENOTYPE

Ponomareva N.V.[1*], Andreeva T.V.[2,3], Protasova M.[2], Kunizheva S.S.[2], Shagam L.I.[2], Malina D.D.[1], Goltsov A.[2] , Fokin V.F.[1], Rogaev E.I.[2,3,4*]

[1]*Research Center of Neurology RAMS, Moscow, Russia*

[2]*Vavilov Institute of General Genetics, RAS, Moscow, Russia*

[3]*Center of Brain Neurobiology and Neurogenetics, Institute of Cytogenetics and Genetics RAMS, Novosibirsk, Russia*

[4]*University of Massachusetts Medical School, BNRI, Massachusetts, US*

ponomare@yandex.ru, Evgeny.Rogaev@umassmed.edu

Key words*: Brain functional connectivity, memory, EEG, Clusterin, Aging.*

Motivation and Aim: Genetic predisposition and aging are the greatest known risk factors for Alzheimer's disease (AD). *Clusterin (CLU)* gene was identified to be associated with AD in different populations, including Russian population (Harold et al., 2009; Lambert et al., 2009; Golenkina et al., 2010). The prevalence of AD is higher in women, but the mechanisms of the gender-related differences are not completely understood. The normal brain undergoes a substantial decrease of functional connections within resting-state networks during aging, but gender- and *CLU*-related differences in functional connectivity remain unknown.

The present study aimed to determine the possible gender-related differences of the alterations of brain functional connectivity in normal aging and to define the effect of *CLU* genotype on theses alterations.

Methods and Algorithms: We examined age-related differences in resting state functional connectivity assessed by interhemispheric EEG coherence in 157 non-demented volunteers (age range 20-80 years), subdivided into subgroups of those younger and older than 50 years of age and stratified by gender and *CLU rs11136000* genotype. Informed written consent was obtained from all participants. All subjects underwent a neurological examination and cognitive screening. The significance of the differences between the log-transformed EEG and parameters in different groups was estimated using ANOVA in the general linear model (GLM). The analysis was adjusted for *ApoE* genotype.

Results: The older women showed decreased interhemispheric coherence values compared to the younger women, while in the man age-dependent decrease of the EEG coherence was significant only for beta coherence. In the women older than 50 years of age the presence of AD risk variant *CLU CC* was associated with lower alpha1 coherence. The reduction of alpha and beta interhemispheric coherence correlated with the worse performance in Luria verbal memory test.

Conclusion: The results indicate that altered functional connectivity in normal aging is associated with gender and *CLU* genotype. Progressive decline in interhemispheric connectivity contributes to memory decrement and suggests the impact of age-related disconnection process in pathogenesis of AD in women carrying AD risk variant *CLU CC*. The results suggest that the neurophysiological markers may be important in monitoring preclinical disease progression in at-risk elderly.

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TARGETS FOR HUNTIGTIN PATHOGENIC FORM IN PROTEIN-PROTEIN NETWORKS OF THE HIPPOCAMPAL DENDRITIC SPINES INTERACTOM

Proskura A.L.*, Zapara T.A., Ratushnyak A.S.
Design Technological Institute of Digital Techniques, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia
e-mail: annleop@mail.ru
**Corresponding author*

Motivation and Aim: Huntington's disease (HD) is a hereditary neurodegenerative disease at which early stage the violation of cognitive disorders, problems with spatial orientation and training is noted. HD caused by a pathological expansion of a CAG repeat in the first exon of the gene coding the huntingtin (HTT), resulting in an abnormally long polyglutamine stretch. The alteration of molecular structure of HTT leads to toxic gain-of-function effect possibly through the aberrant protein interactions. In normal HTT interacts with the wide range of proteins, having SH3 (Src homology 3 domain), WW (regions containing two tryptophans (W)), EVH1 (Enabled, VASP, Homology 1) domains [1]. The database GeneNet (ROSPATENT № 990006 from 02.15.1999) accumulated and structured the information on the key proteins that provide the structural and functional plasticity in the CA1 hippocampal region [2]. The aim was to study the huntingtin contribution to the changing the synaptic plasticity in the hippocampus and identify potential targets for pathogenic form of huntingtin.

Results: Normally HTT acts as a scaffold molecule providing the order of events when endocytosis of glutamate receptors takes place, and also is involved in the process of moving the vesicles with receptors along the tubulin dendritic cytoskeleton. The domain composition of the protein group involved in maintaining the neurotransmission in the hippocampus [3] was analyzed. It has been found that pathogenic HTT interacts with SH3 domains of SH3GL3 and PACSIN1 with higher affinity [1]. The high level of similarity between sequences of SH3 domains this proteins and proteins of GeneNet Data Bank was identified (using the Smith-Waterman algorithm (http://www.ebi.ac.uk/Tools/psa/emboss_water/)).

Conclusion: The key proteins of postsynaptic density, regulators of endocytosis and remodeling the actin network can appear as a targets of the Htt pathogenic form that may underlie the structural and functional disorders in the hippocampus and may mediate the cognitive disorders on early presimptomatic stage.

Availability: http://wwwmgs.bionet.nsc.ru/mgs/gnw/genenet/viewer/AMPA.html

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References:

1. Gao Y.G. et al. 2006 Structural insights into the specific binding of huntingtin proline-rich region with the SH3 and WW domains, *Structure*, 14 1755-1765.
2. Proskura A.L. et al. 2014 The Protein-Protein Interaction Networks of Dendritic Spines in the Early Phase of Long-Term Potentiation, *J Comput Sci Syst Biol*, 7 040-044.
3. Proskura A.L. et al. 2013 Inter-molecular interactions in functional neuron systems, *Vavilov journal of selection and breeding B*, 17 620-628. (In Russian)

MOLECULAR MECHANISMS UNDERLYING THE COGNITIVE FUNCTIONS OF THE NEURON

Ratushnyak A.S.*, Zapara T.A., Proskura A.L., Sorokoumov E.D.
Institute of Computational Technologies of SB RAS, Novosibirsk, Russia
e-mail: ratushniak.alex@gmail.com
**Corresponding author*

Motivation and Aim: To solve the key problems of neurobiology it is important to integrate the knowledge about the molecular mechanisms of realizing the main functions of all living systems - maintaining the vital functions on the base of prognostics. At the molecular and the cellular levels those properties were evolutionally formed and later became the basis of higher information functions of brain. At this level, biologically active substances, pharmacological drugs and exposures are acting to restore, preserve and increase the brain resources. Therefore, the most urgent task at this stage of brain research is to integrate the existing knowledge about molecular organization and neuron functional architecture dynamics. This will create the prerequisites for the formation of a generalized theory of functioned of the neuronal systems as a physical phenomenon of decreasing the entropy on the base of informational and forecasting processes in the complexes of molecular assemblies.

The ability to create such a theory based on the negentropic principle seems now problematic because it is unreal to integrate a huge amount of research results in the field of neuroscience which have appeared in recent years. However, it is hoped that this problem can be solved on the basis of the limited range of conceptual studies. Preconditions for its implementation are the subject of this work which is focused on the theoretical and experimental analysis of the molecular architecture characteristics, information properties and molecular structures of basic functional systems oriented on performance of prediction tasks.

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AGING-INDUCED REORGANIZATION OF COGNITIVE FUNCTIONS

Razumnikova O.M.[1,2*], Volf N.V.[1], Savinykh M.A.[2]
[1]*Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia*
[2]*Novosibirsk State Technical University, Russia*
**e-mail: razum@physiol.ru*

Key words*: aging, intelligence, attention systems, memory, computerized cognitive test battery*

Motivation and Aim: It is known that the basic cognitive functions most affected by age are attention and memory. However, the age-related changes in brain structure and function are not uniform, and mechanisms underlying the individual changes will be discovered. The complexity of neural organization of cognitive functions makes relations between brain and behavior extraordinarily difficult, although ultimately testable [1]. Establishing such links between intelligence, attention, and memory and their changes that occur in normal human aging is the aim of our study.

Methods and Algorithms: The relationships between intelligence and indicators of attention systems functions, retrieval of verbal and figural stimuli, as well as the lateral characteristics of verbal memory in older age (65 years, n = 83; 43 women) and in young group (22 years, n = 133; 83 women) have been studied. The computer-based cognitive measuring and training platforms were created using Pascal and C++. One part of programs was designed to analyze selection processes, others – for different forms of memory [2]. Lateral characteristics of verbal memory were measured by dichotic testing [3]. General intelligence (IQ) was assessed using the Eysenck's test.

Results: It was found that the rate of information selection in conflict conditions is a predictor of the level of intelligence, regardless of age. In old age a higher level of intelligence corresponds to shorter time of executive control system while in the young people significant relations between intelligence and functions of attention systems are not found. In the analysis of memory, aging-independent a positive contribution to the intelligence have the words addressed to the left hemisphere; additionally, in the young age the contribution of verbal memory when words addressing the right hemisphere, and in the elderly - the retrieval of verbal and figural stimuli. Gender specificity in age-associated reorganization of attention and memory as predictors of intelligence was revealed, i.e. age-related changes were more pronounced in men.

Conclusion: The different relationships between cognitive functions in old and young groups were found pointing to the restructuring of the neural systems due to the age or sex factors. Acknowledgements: This work was partially supported by a grant of the Russian Foundation for Humanitarian Research, project No 15-06-10052.

References:

1. Park D.C., Reuter-Lorenz P. 2009 The adaptive brain: Aging and neurocognitive scaffolding. Annu Rev Psychol. 60 173–196.
2. Razumnikova O. et al. 2016 A computerized cognitive test battery. Individual differences in cognitive characteristics: Measuring and dynamic of training, Proc. 11th Intern. Forum on Strategic Technology (IFOST), Novosibirsk, 256-258.
3. Volf N.V. 1994 Sex differences in memotizing dichotic represemtation of words, Zh. Vyssh. Nerv. Deiat. 3: 18-24.

CONNECTION OF GENETIC AND ENDOPHENOTYPIC INDEXES WITH PERSONALITY PROPERTIES OF THE HEALTHY PARTICIPANTS AND THE PATIENTS WITH AFFECTIVE PATHOLOGIES

Savostyanov A.N.[1,2,3]*, Bocharov A.V.[1,2], Bazovkina D.V.[3], Naumenko V.S.[3], Karpova A.G.[4], Borisova A.G.[4], Kavai-ool U.N.[5], Knyazev G.G.[1]
[1]*Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia*
[2]*Novosibirsk State University, Novosibirsk, Russia*
[3]*Institute of Cytology and Genetics of SB RAS, Novosibirsk, Russia*
[4]*North-Eastern Federal University, Yakutsk, Russia*
[5]*Tuvan State University, Kyzyl, Tyva Republic, Russia*
E-mail: Alexander.Savostyanov@gmail.com
**Corresponding author*

The study was aimed to revealing of the connections between of the genetic markers, the behavioral features and the endophenotypic indexes of brain activity (EEG) with the risk of development of the affective pathologies in the healthy participants and the clinical patients with depression. The research was organized in the several ethnic groups (Russians, Tuvinians, Yakuts and Mongols) and in the city and rural environmental conditions. In addition, comparison of the healthy people with different inclination to affective pathology and the clinical patients before and after treatment was carried out. The recognition of facial emotionality, the recognition of emotional speech and the motor control task were applied as the experimental methods. Interaction of the effects of various genetic polymorphisms, related with functions of serotonin's system, and socio-cultural features of participants was monitored by means of the behavioral, psychometric and electrophysiological methods.

As a result of research, the complex interactions of the biological and social factors determining inclination to affective pathology in different climatic and social living conditions were revealed. It was shown that endophenotypic indexes of brain activity could be applied for more detailed analysis of dependence between the biological and social reasons of pathology and for control over efficiency of therapy.

DATA MINING TECHNIQUE IN DETECTION OF PERINATAL AFFECTION OF THE CENTRAL NERVOUS SYSTEM OF NEWBORNS ON THE BASIS OF CLINICAL SYMPTOMS OF GESTATION COURSE

Shaidurov A.[1]*, Pijanzin A.[1,2,3]
[1]*Altai State University, Barnaul, Russia*
[2]*Altai State Medical University, Barnaul, Russia*
[3]*Altai Region Clinical Children's Hospital, Barnaul, Russia*
e-mail: shaidurov@phys.asu.ru
[*]*Corresponding author*

Key words*: Artificial neural networks, central nervous system*

Motivation and Aim: The detection of perinatal affection of the central nervous system is a complex problem demanding a just analysis of large amounts of constantly changing information.

Methods and Algorithms: Statistics from Altai Region Clinical Children's Hospital and maternity hospitals of the Altai Territory has been used. Diagnoses of newborns: hypoxic-ischemic lesion of the CNS – 384 newborns; hypoxic-hemorrhagic lesion of the CNS – 82 newborns; natal spinal cord damage – 357 newborns; natal craniospinal damage – 147 newborns; the absence of the diagnoses mentioned above – 1294 newborns. 20 clinical symptoms of gestation course have been included in the data pool. At the first stage when detecting the list of discriminating symptoms for each diagnosis of perinatal affection of the CNS, discriminative analysis has been used. At the second stage artificial neural networks (ANN) on the basis of neuro paradigm "Back Propagation" has been applied.

Results: The statistical processing based on the discriminative analysis shows pre-delivery symptoms which play an important role in detection of perinatal affection of the CNS. When detecting hypoxic-ischemic lesion of the CNS the number of discriminating symptoms includes 18, hypoxic-hemorrhagic lesion of the CNS -14, natal spinal cord damage – 9, natal craniospinal damage – 13. Obtained curtailed samples have been studied with artificial neural networks. In the course of numerical experiment artificial neural network architectures, detecting hypoxic-ischemic lesion of the CNS within the accuracy of 72%, hypoxic-hemorrhagic lesion of the CNS – 96%, natal spinal cord damage – 79%, natal craniospinal damage- 91%, have been obtained. The specificity of detection has ranged from 85% to 98%. The sensitivity of detection of normal patients - 90%. The study outcome is the creation of diagnostic system included joint use of neural networks with different architecture and functional areas.

Conclusion: In such a way, using data mining technique provides more accurate detection of perinatal affection of the central nervous system of newborns and adequate treatment when planning the act of delivery.

ENGINEERING AND NEUROCOGNITIVE ASPECTS IN THE DEVELOPMENT OF NON-INVASIVE BRAIN-COMPUTER INTERFACES

Shishkin S.L.
e-mail: sergshishkin@mail.ru
National Research Centre "Kurchatov Institute", Moscow, Russia

Key words*: brain-computer interfaces, hybrid BCI, EBCI*

Development of the brain-computer interfaces (BCIs) is a multidisciplinary area that involves many engineering, neurophysiological, psychological and medical aspects. Between them, a certain imbalance exists: while many efforts were made to improve the classifiers of brain signals, more impressive progress seems to be achieved with the introduction of new neurocognitive approaches or new areas of application. We will review a number of significant improvements recently made to the non-invasive BCI technology and discuss implications from the experience of our group in designing new types of BCIs. In particular, this experience includes the use of single-stimulus paradigm known from psychophysiology (a variant of the oddball paradigm) for calibration [2] and for online control [1], and the development of a fully fluent hybrid BCI that detects short gaze fixations intentionally used for interaction with a computer using a specific variant of fixation-related brain potentials possibly not yet known in psychophysiology (Eye-Brain-Computer Interface, EBCI; [3]). Together with the neurocognitive studies, however, serious engineering efforts, especially in creating new tools that support programming for online joint analysis of multimodal signals, were crucial for making the development of these new BCIs possible. It follows that all aspects of the multidisciplinary task of BCI development require high attention. Among the possible future directions of these and other non-invasive BCI technologies, an interesting perspective is associated with modern machine learning approaches, such as deep learning, that could be applied to the EEG and eye tracking data considered in the context of various situations of the EBCI-mediated interaction with computer GUIs.

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References:

1. Fedorova A.A., Shishkin S.L., Nuzhdin Y.O. et al. 2014 A fast "single-stimulus" brain switch. Proc. 6th Int. Brain-Computer Interface Conf. 2014. Article ID 052. DOI:10.3217/978-3-85125-378-8-52
2. Shishkin S.L., Nikolaev A.A., Nuzhdin Y.O. et al. 2011 Calibration of the P300 BCI with the single-stimulus protocol Proc. 5th Int. Brain-Computer Interface Conf. 2011. P. 256-259.
3. Shishkin S.L., Nuzhdin Y.O., Trofimov A.G. et al. 2016 Fixation-based eye-brain-computer interfaces: approaching a better human-computer symbiosis. Opera Medica et Physiologica S2: 83-84 (Proc. of Volga Neuroscience Meeting, July 24-30, 2016).

COMPARATIVE PROTEOMIC ANALYSIS OF SERUM FROM PATIENTS WITH BIPOLAR DISORDER AND HEALTHY INDIVIDUALS

Smirnova L.P.[1]*, Seregin A.A.[1], Loginova L.V.[1], Simutkin G.G.[1], Zgoda V.G.[2], Ivanova S.A.[1]
[1]*Mental Health Research Institute, Tomsk, Russia*
[2]*Institute of Biomedical Chemistry, Moscow, Russia*
e-mail: lpsmirnova@yandex.ru
[*]*Corresponding author*

Key words*: proteomics, bipolar affective disorder, biomarkers*

Motivation and Aim: In clinical practice, bipolar affective disorder often have similar clinical picture with other mental disorders. Laboratory criteria for the differential diagnosis of bipolar disorder are not available. We have done a comparative proteomic analysis of blood serum of healthy individuals and patients with bipolar disorder.

Methods: Diagnostics was carried out in accordance with the current classification ICD-10. Preparation of samples included: purification from serum major proteins by affinity chromatography, separation of proteins by 1-D electrophoresis, the proteins in the gel trypsin digestion followed by extraction.

Results: During the study, we identified proteins, which do not occur in healthy people: ankyrin repeat domain-containing protein 12; glutamate NMDA-receptor subunit zeta-1. Was identified ankyrin repeat domain-containing protein 12 is a protein with a molecular weight of 235 kDa. Domains containing ankyrin repeats mediate a variety of protein-protein interactions. Mutations in genes encoding ankyrin like proteins may cause defects in gene expression that lead to various diseases, for example, a gene ankyrin G, performing many different functions in the CNS associated with bipolar disorder, although this connection with pathogenic mechanism remains unknown. Another protein with a molecular weight of 105 kDa – glutamate NMDA-receptor subunit zeta-1. It is known that in the manic phase of bipolar disorder observed an elevated level of glutamate in the left dorsolateral prefrontal cortex against decrease density of NMDA-glutamate receptor. Perhaps due to the expressed excitotoxicity are damaged synapses, which leads to the appearance in serum of NMDA receptor subunits. The appearance in the blood contributes to receptor subunits damage the blood-brain barer.

Conclusion: By increasing the amount of probands, it is possible to assume the use of the detected proteins as biological markers of bipolar disorder

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APPLICATION OF GENETIC MODELS FOR EXPERIMENTAL STUDY OF COGNITIVE FUNCTIONS AND NEUROPROTECTION

Tikhonova M.A.[1,2]*, Amstislavskaya T.G.[1,2]
[1]*Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia*
[2]*Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia*
e-mail: tikhonovama@physiol.ru
[*]*Corresponding author*

Key words*: animal models, cognitive functions, neurodegeneration, Parkinson's Disease, accelerated aging, behavioral phenotyping, neuroprotection, ceftriaxone*

Motivation and Aim: Modern research tools of advanced behavioral phenotyping allows accurate monitoring the behavioral impairments in rodent models of different neurologic and psychiatric disorders. We will present the methods for evaluation of cognitive functions in mice and rats and discuss the criteria for models of cognitive decline. Original results that were obtained using a genetic model of Parkinson's Disease (B6.Cg-Tg(Prnp-SNCA*A53T)23Mkle/J mouse strain) and a genetic selected model of accelerated senescence (OXYS rat strain) will be introduced. The aim of the study was to compare cognitive characteristics and their neuromorphological correlates in models of cognitive decline associated with neurodegenerative disturbances and to assess the neuroprotective effects of ceftriaxone (CEF).

Methods and Algorithms: We conducted the behavioral testing including open-field test, novel object recognition test, Barnes test, T-maze, and IntelliCage as well as neuromorphological study of neuron density and autophagy levels in the frontal cortex and hippocampus. To evaluate the effects of CEF, the animals of experimental groups were treated daily with the drug (100 mg/kg/day, i.p., 36 days).

Results: Mutant B6.Cg-Tg(Prnp-SNCA*A53T)23Mkle/J mice showed higher horizontal locomotor activity and a tendency to increase in vertical locomotor activity in the open-field test. Moreover, both 5- and 10-month old mutant mice displayed certain impairments in the performance of the Barnes test including decreased exploratory motivation and retarded learning. At the age of 5 month old OXYS rats demonstrated the disturbed performance of the novel object recognition test and a lowered neuronal density in the hippocampal CA1 area (but not in the CA3 area or frontal cortex) and a tendency to dopaminergic attenuation in the nigrostriatal system. CEF exhibited beneficial effects on cognitive features and neuromorphological disturbances in both models.

Conclusion: Application of the genetic models in combination with the modern research tools of advanced behavioral phenotyping for experimental study of cognitive functions and neuroprotection appeared to be an established approach in cognitive neuroscience and neuropharmacology. We revealed cognitive disturbances in two genetic models of neurodegenerative disorders. Neuroprotective drug CEF improved the impaired cognitive function in these models and restored neuronal disturbances. The data suggested CEF as a promising pharmacological tool for the prevention of cognitive decline at neurodegenerative disorders.

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RESEARCH OF PREFERENCES DEPENDENCE IN HIERARCHICAL TEXT MENUS OF USER INTERFACE FROM PERFORMANCE COGNITIVE PROCESSES

Varnavsky A.N.[1]*, Goubko M.V.[2]
[1]*Ryazan State Radio Engineering University, Ryazan, Russia*
[2]*V.A. Trapeznikov Institute of Control Sciences of Russian Academy of Sciences, Moscow, Russia*
e-mail: varnavsky_alex@rambler.ru
[*]*Corresponding author*

Key words: *user interface, hierarchical text menu, semantic parameters psychophysiological testing, cognitive processes, memory and attention performance, the level of logical thinking, evaluation of "like / dislike" logistic regression*

Motivation and Aim: Custom's text hierarchical menu is a key element in various programs. The convenience of the user experience with the product and the efficiency of interaction with the system depend on the menu organization. Therefore, the actual problem is the optimal organization of the menu structure.

Some works on the automated menu design appeared in recent years based on different optimization methods [1-5]. In these researches a variety of optimization techniques are offered, but the fundamental issue is the choice of optimization criterion. The criterion is a variation on the theme of the average navigation time in most researches, but the choice is always made quite speculative. If you do not set the task to create the "most rapid" menu but "menu, which was liked by most users," it should be possible to find out exactly what kind of menu aspects are important for the user to build the optimization criterion based on them. This problem is a challenge to identify the users' preferences. The necessity to research user preferences in selecting the hierarchical menu structure is not only connected with the aesthetic aspects, but also to the fact that the less the user like the work with the object (in this case with the menu), the more mental effort expended during handling [6-7], and thus fatigue occurs faster and higher the load on the system body. The aim is to investigate the influence of the structural parameters of the menu and the user's cognitive process indicators on the satisfaction of working with this menu.

Methods and Algorithms: The research was carried out experimentally.

1. The method of procedure

Participants. The participants of the experiment were 30 students of the 3-5 years from the Ryazan State Radio Engineering University. Number of men - 18, of women - 12. The participants' average age was 20,8±1,2.

Materials. 10 hierarchical user menus with different structure were created for the experiment. Raven's tests were used for evaluate the cognitive processes of the tested people and "Landolt Ring" was used for short-term memory capacity. Evaluation of menu preferences carried out on a scale of "like / dislike".

Procedure of investigation. Experiments were carried out in the morning for 3 days in groups of 8-12 people in a computer class in the same environmental conditions. After the briefing, explaining the meaning of the experiment and trial testing the record contains 10 two-digit numbers was showed to tested people, and test at the memory was performed. Then heard Landolt test forms and test for 8 minutes, the test is performed. After a 3-minute rest tested people worked in a pilot program with a variety of menus. Working with one menu takes 5 minutes, between working with neighboring menu there

was a 2-minute break to rest, during which the tested person assesses user experience and preferences menu. Upon completion of the program and longer rest the tested people performed Raven's test.

2. As a result of the experiment a set of test results and preference for 30 tested people were obtained. Indicators of cognitive processes were identified.

Results: Results of the experiment were processed in the statistical package R.

It's offered to construct a logistic regression, which will allow to predict whether the menu with preset parameters like specific user without cognitive processes. It was found that this logistic regression allows to classify 69% estimates the user experience the convenience of the menu correctly. The resulting model gives optimistic assessment concerning the fact whether the user like the menu. Logistic regression, which uses as predictors only selected indicators of cognitive processes without the options menu allows to classify 62% of the preference ratings correctly. Almost all assessments "Like" were classified correctly. However, a much larger part of the assessments "Dislike» were not classified correctly. This logistic model is too optimistic. It's offered to construct a logistic regression, which will allow to predict whether the menu with preset parameters like specific user with given parameters of cognitive processes. This regression allows to classify 78% estimates the user experience the convenience of the menu correctly. In this case the pairwise interaction of menu parameters and user was included the model. The interaction explains that the formation of menu preferences to a large extent depend on the state of cognitive processes and sensory systems of the body. These states will increasingly affected by the combination value of indicators and user menu. For example, if the user has as rate of short-term memory a small value, then with long menu items (in particular the component) an increased load will occur on the cognitive processes so discomfort will appear and evaluation of the menu will not high. A similar situation will be observed at low values of user's attention indicators when the load on the cognitive processes will provide not only the length of the menu item text but and the number of items in the menu bar and a number of composite panels. The level of logical thinking will influence on assessment of the menu is primarily due to the indicator "Combined menu", which by and large is specific.

Conclusion: The research showed that to build a menu that would be liked by users, it is necessary to take into account a combination of the values of the user's cognitive processes and menu options. The created logistic model allows to classify 78% assessments of the menu on the criterion of "like / dislike" correctly. To increase the percentage of correct classifications it's necessary to include in the model more factors and also consider the non-linear function.

References:

1. Fisher D.L., Yungkurth E.J., Moss S.M. 1990 Optimal menu hierarchy design: syntax and semantics Human Factors. V. 32(6) P. 665–683.
2. Matsui S., Yamada S. 2008 Genetic Algorithm Can Optimize Hierarchical Menus CHI'08, P. 1385-1388.
3. Goubko M.V., Danilenko A.I. 2010 An automated routine for menu structure optimization Proc. of the 2nd ACM SIGCHI Symposium P. 67–76.
4. Bailly G., Oulasvirta A., Koetzing T., Hoppe S. MenuOptimizer: Interactive Optimization of Menu Systems UIST'13, pp. 331-342.
5. Danilenko A.I., Goubko M.V. 2013 Semantic-aware optimization of user interface menus Automation and Remote Control, V. 74(8) P. 1399-1411.
6. Reber R. et al. Processing fluency and aesthetic pleasure: is beauty in the perceiver's processing experience? 2004 *Personal. Soc. Psychol. Rev.* 8(4) P. 364–382.
7. Leder H. A model of aesthetic appreciation and aesthetic judgments 2004 *Br. J. Psychol*. V. 95(4) P. 489–508.

RESEARCH OF PREFERENCE IN PLAYBACK SPEED OF LEARNING VIDEO MATERIAL DEPENDING ON INDICATORS OF COGNITIVE PROCESSES

Varnavsky A.N.
Ryazan State Radio Engineering University, Ryazan, Russia
e-mail: varnavsky_alex@rambler.ru

Key words*: video information, playback speed, cognitive processes, indicators of cognitive processes, adaptive processes, regression analysis, the personification of the display*

Motivation and Aim: Information perceiving depends on its presentation. In general case of people's consideration of different objects, connected with operations of certain rules of perception and attention, there can be certain mistakes and distortion [1]. Adverse conditions can increase time spent on perception of information flows and reduce information content that could have been assimilated.

In [2] peculiarities of perception of the most frequently used types are described. The results were based on electroencephalography and oculography. It was investigated that the types are remarkable for different graphic and psychophysiological characteristics that determine the quality of text perception, understanding and memorization of it. Whereas different types lead to different cognitive efforts and degree of tiredness. They also influence rate of text perception. According, performance and parameters of information flows must be optimized to maximize acquisition of information and to minimize negative influence on a user. However, the question on individual presentation of information is opened. Individual properties and showings of a person during displaying information flows must be taken into account as well, especially it concerns video information. It can be said that playback speed is the most important parameter of displaying video. Its quality will influence assimilation of information, time spent on viewing video and convenience of a user.

Hans Eysenck is one of the leaders in the biological trend in psychology. This British psychologist, the author of the popular IQ test, came to the conclusion that preferences are determined by amour of efforts spent on solving one or another problem. What is more, number of authors investigated preferences of an object or stimulus depended upon its characteristics and an observer's peculiarities.

These authors have come to the conclusion that aesthetic assessment and preference are not so conditioned by characteristics of stimulus or an observer's peculiarities, however, they depend upon the choice of a cognitive problem and its solving in the process of perception [3-6].

Accordingly, the more mental efforts are expended in the process of working with the object, the faster tiredness comes and the higher load of systems of human organism is. Thus, lower estimation of preferences of an object we get. Therefore, the researchers tried to investigate how cognitive processes during watching a learning video determine preferences of playback speed and the influence of nervous system. The strength of nervous system determines dynamics of efficiency and development of tiredness during the work. Registration of indicators concerning a user's adaptive processes is also of a great interest.

The aim of the work is to research preferences of video playback speed depending

on a learner's indicators of cognitive and adaptive processes and on strength of his nervous system. The importance of this research is conditioned by the fact that the lower evaluation and convenience of working with data entity, the more effort is expended during the work with the object, thus tiredness comes quicker and it increases load of systems of human organisms.

Methods and Algorithms:

1. The method of procedure

Participants. The participants of the experiment were 30 students of the 2-5 years from the Ryazan State Radio Engineering University. Number of men - 13, of women - 17. The participants' average age was 21,1±0,6;

Materials. The values of indicators concerning cognitive processes and strength of nervous system were resulted from psychophysiological test. The chosen tests can be used within the framework of e-learning in future. What is more, it was taken into account that memorizing and attention are the main processes that determine efficiency of the learning process. Thus, the Landolt C test (Brunner, 2006, 316 p.), which shows the ability of short-time memory (Karelin, 2007, 416 p.), and the tapping test (Karelin, 2007, 416 p.) were chosen. The indicators of adaptive processes were determined by the Poly-Spectrum-Rhythm. The player with regulated playback speed was used for displaying the video.

Procedure of investigation. The conditions of the experiments were equal for all participants. They were tested to investigate their memory and attention after briefing and explaining the gist of the experiment. The participants had to exclude the circles with a particular gap. This test was focused on their attention. Then they had to remember 12 two-digit numbers during 30 seconds and to reproduce them during 1 minute. After the participants had a minute rest. They were to be tested by the Landolt C test during 4 minutes, and then by tapping-test. After testing the Poly-Spectrum-Rhythm analyzed the electrocardiosignal during 5 minutes and generated estimates of the adaptive processes. To estimate preference of playback speed each of the participants was shown 30 seconds videos with different average playback speed from s1 = 62 words/min to s8 = 118 words/min with the pace of 8 words/min. The participant had to estimate his or her convenience of watching Ui video with different playback speed si (i = 1...8) on the basis of the 10-point system.

2. Results obtained

On the basis of the actuarial data gathered the following parameters for each participant were calculated according the formulas:

- memory coefficient x1;
- coefficient of efficiency x2 = N;
- accuracy figure of attention x3;
- data point x4 of dynamic type of efficiency in the tapping-test which characterises strength or weakness of nervous system and gets the values 1, 2, 3, 4;
- index of vegetative balance x5;
- stress-index x6;
- playback speed y which has provided the experiment with the supreme estimate from u1, ..., u8.

Results: The regression analysis resulted into such a multiple linear regression:

$$y = a0 + a1 \cdot x1 + a2 \cdot x2 + a3 \cdot x3 + a4 \cdot x4 + a5 \cdot x5 + a6 \cdot x6$$

with R2 = 0,78 (F(9, 20) = 8,074, p < 0,001)

The most successful model in the context of index R2 is the multiple linear regression with intercommunions:

$$y = b0 + x4 \cdot (b1 \cdot x1 + b2 \cdot x2 + b3 \cdot x3) + b5 \cdot x5 + b6 \cdot x6$$

with R2 = 0,89 (F(15, 14) = 7,295, p < 0,001).

The regression analysis indicates that preferences of playback speed are explained by the process of attention. What is more, the strength of nervous system also influences preferences of playback speed, as it also affects the process if tiredness.

Consequently, we get the model that explains mobility in preferable playback speed by almost 90%. Such a model allows to predict the best video playback speed from the point of view of perception and preference, based on indices of cognitive processes, efficiency and adaptive processes. Fig. 1 shows the indices of playback speed gained through the experiments in the coordinate axes y(x3) with the help of the circles, and the triangles mark projected indices by regression.

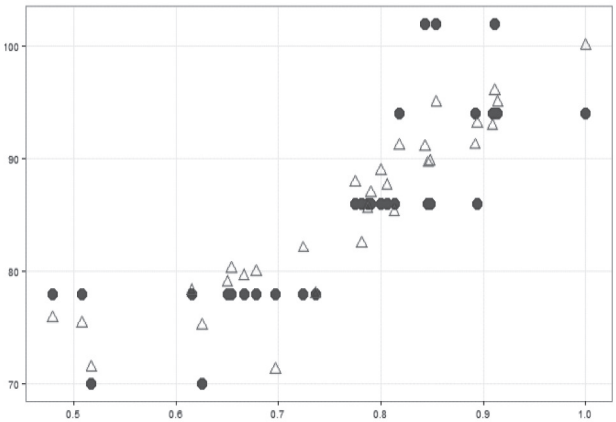

Fig. 1. Experimental and projected indices of preferable video playback speed

Conclusion: A lot of factors influence efficiency of information perception, that include its presentation and psychophysiological state of a user. The research has shown the influence of indices of the adaptive processes, memory, attention and strength of nervous system on preference of video playback speed. In the basis of the gained data the personified model of dependence between the best playback speed and marked indices was created. The accuracy of forecasting can be improved by specification of coefficients of the model during various experiments including the usage of smaller paces in playback speed between two videos.

References:

1. Beloskova K.V., Artemenkov S.L. 2010 Experimental research about the perception of textual information on the display Experimental Psychology in Russia: traditions and perspectives P. 230-234.
2. Morozova L.V., Murin I.N. 2013 Psychophysiological specifics of perception of the printed text Bulletin of the Northern (Arctic) Federal University. Series: Natural sciences. №3 P. 76-85.
3. Reber R., Schwarz N., Winkielman P. 2004 Processing fluency and aesthetic pleasure: is beauty in the perceiver's processing experience? *Personal. Soc. Psychol. Rev*. V. 8(4) P. 364-382.
4. Leder H. 2004 A model of aesthetic appreciation and aesthetic judgments *Br. J. Psychol.* V. 95(4) P. 489-508.
5. Allakhverdov V.M. 2001 Psychology of Art. Essay on secret emotional impact of art. DNA SPb.
6. Chetverikov A.A. 2014 The impact on the efficiency of visual search affective evaluation of pictures Experimental Psychology.V.7(2) P. 37-48.

GENOTYPE 5-HTTLPR OF SEROTONIN TRANSPORTER GENE IN REGULATION OF COGNITIVE FUNCTIONS: INTERACTION WITH GENDER, AGE, AND INTELLECTUAL ACTIVITY

Volf N.V.[1,2]*, Bazovkina D.V.[3]
[1]*Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia*
[2]*Novosibirsk State University, Novosibirsk, Russia*
[3]*Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia*
e-mail: volf@physiol.ru
**Corresponding author*

Key words*: 5-HTTLPR, cognitive functions, sex, age, intellectual activity*

Motivation and Aim: The observed association of polymorphism 5-HTTLPR gene serotonin transporter with cognitive processes and "adaptive" nature of one of its genotype, as well as data on gender differences in the serotonergic system of the brain served as a basis for studying the association of this polymorphism with the efficiency of cognitive functioning in men and women depending on the age and intellectual activity.

Methods and Algorithms: Scientific activity has been selected as high-intensity intellectual activity. Young and old, employed at the time of the study, scientists (scientific activity - SA, N = 126) and people not associated with science (NSA, N = 144). IQ was measured using the Eysenck test. In computerized experiments 3 forms of attention were studied in the Attention Network Test, lateral characteristics of the motor component of the orienting reaction were studied in a modified version of odd-ball test. The study of memory was based on dichotic listening task memorization of syllables and shapes. Genotypes of 5-HTTLPR (S / S, S / L and L/L) was determined using polymerase chain reaction.

Results: Regardless of the other factors S/S genotype carries 5-HTTLPR of polymorphism demonstrated higher intelligence in comparison with L allele carries having higher transcriptional activity. Association of 5-HTTLPR polymorphism with characteristics of vigilance and orientation differed in SA and NSA groups: among S/S genotype carries vigilance was significantly higher in the SA than NSA and the orienting effect was more pronounced in NSA group compared to SA in carriers of L/L genotype. High Intellectual activity was a factor preventing age-related verbal memory decline. It has been found that only in women S/S genotype carries, demonstrated better memory for syllables and shapes.

Conclusion. The results indicate that associations 5-HTTLPR polymorphism with cognitive functions are modulated by sex and intellectual activity. It may be hypothesized that positive qualities of S/S genotype which were found in our study are possible evolutionary advantage to conserve the S allele in human population, which may counterbalance its disadvantage of vulnerability to mood disorders.

ASSOCIATION OF *PIP5K2A* GENE POLYMORPHISMS WITH THE EFFECTIVENESS OF THE THERAPY OF CURRENT DEPRESSIVE EPISODE

Vyalova N.M.*, Simutkin G.G., Ivanova S.A.
Mental Health Research Institute, Tomsk, Russia
e-mail: Natarakitina@yandex.ru
**Corresponding author*

Key words*: depressive disorders, PIP5K2A gene, current depressive episode, effectiveness of the therapy*

Motivation and Aim: The search for genetic markers associated with the development and course of depressive disorders, will allow developing effective methods of diagnosis and treatment of the disease [1, 2]. Modern studies indicate the involvement of *PIP5K2A* kinase in the pathogenesis of depressive disorders and schizophrenia spectrum disorders [3]. The mechanisms underlying the therapeutic effect in chronic lithium treatment for bipolar affective disorders, is associated with differential expression of genes associated with phosphoinositide metabolism, including *PIP5K2A* [4].

The aim of our study was to assess the effectiveness of therapy current depressive episode based on the definition of polymorphic variants rs10828317 and rs10430590 *PIP5K2A* gene, previously studied by us both associated with depressive disorders.

Methods and Algorithms: We examined 218 patients with depressive disorders were diagnosed as having current depressive episodes of varying severity within F31-F32, aged 20 to 60 years who were treated at the Department of Affective States clinics of Mental Health Research Institute. Assessment of the severity of the current depressive episode was performed using the scales SIGH-SAD, CGI-S, CGI-I, allowing assessing the severity of the disease before, on the 14th and 28th days of therapy. The control group consisted of 147 mentally and somatically healthy donors Russian population of the Siberian region of Tomsk and Tomsk region) aged 20 to 60 years. As the material for the study was used venous blood. DNA was isolated by standard phenol-chloroform microtechnique. Genotyping for polymorphic variants *PIP5K2A* gene was performed by polymerase-chain reaction (PCR) in real time using fluorescence on the amplifier "Step One Plus" company Applied Biosystems (USA). Statistical processing of results was performed using the program SPSS 20.0.

Results: For studying the link between severity of depression and the assessment of the effectiveness of the therapy with the *PIP5K2A* gene polymorphism and the study of dependence of average aggregate scores in CGI-I, CGI-S and SIGH-SAD from the studied genotypes in patients with depressive disorders before therapy and on the 14th and on 28th day of treatment. Before the treatment, all patients had significantly high scores on the scale SIGH-SAD, CGI-I, CGI-S, and on the 14th and 28th days of therapy was observed significant decrease in scores on all scales investigated, which indicates an improvement in the clinical condition of patients. Our results revealed the association of the polymorphic variants rs10828317 *PIP5K2A* gene with the score for typical depressive symptoms on a scale SIGH-SAD to initiation of therapy and with the score on a scale CGI-S at day 28 of therapy, and rs10430590 *PIP5K2A* gene shows a statistically significant association with the score on a scale CGI-S at day 28 of therapy.

Conclusion: Association of polymorphic variants of the gene *PIP5K2A* with the

amount of points for typical depressive symptoms on a scale SIGH-SAD with initiation of therapy and with an average amount of points on a scale CGI-S at day 28 of therapy on the background of clinical improvement proves the involvement of kinases in *PIP5K2A* the mechanisms underlying the therapeutic effect of antidepressants.

Acknowledgements: The study was performed with the support of the scholarship of the President of the Russian Federation №SP-1786.2015.4

References:

1. Fedorenko O. et al. 2008 A schizophrenia-linked mutation in PIP5K2A fails to activate neuronal M channel, Psychopharmacology, 199(1) 47-54.
2. Losenkov I.S. et al. 2014 Proteins of Akt1/GSK-3β-signaling pathway in peripheral blood mononuclear cells of patients with affective disorders, Neurochemical Journal, 8(3) 208-213.
3. Vyalova N.M. et al. 2013 Study of PIP5K2A gene polymorphism association with depressive disorders, Fundamental Research,1(2) 299-303.
4. Stopkova P. et al. 2003 Polymorphism screening of PIP5K2A: a candidate gene for chromosome 10p-linked psychiatric disorders, Am. J. Med. Genet. B. Neuropsychiatr. Genet., 123B (1) 50-58.

HISTONE H3 ACETILATION PARTICIPATES IN MEMORY FORMATION IN THE HONEYBEE

Zachepilo T.G.*, Lopatina N.G.
Pavlov Institute of Physiology of RAS, Saint-Petersburg, Russia
e-mail: polosataya2@mail.ru
**Corresponding author*

Key words*: acetylation of histone H3, memory, formation, honeybee*

Motivation and Aim: The posttranslational modifications of histone H3 are important for regulation of gene expression during memory formation in mammals. We studied activating modification – histone H3 K9/K14 acetylation – in the honeybee brain 1 hour after conditioning trials.

Methods and Algorithms: The PER (proboscis extended reflex) paradigm was applied for honeybee learning. Through 1 hour after the conditioning trials. Brains were dissected, fixed and mounted in paraffin. Paraffin sections were stained with antibody against histone H3 K9/K14 acetylation. It had elevated number of stained neurons of mushroom bodies (associative areas of insect brain) after training.

Results: It was shown that increased levels of histone H3 K9/K14 acetylation in mushroom bodies' neurons of the trained bees at 1 hours after conditioning trials.

Conclusion: Thus, data obtained show the involvement acetylation of histones into the epigenetic mechanisms of memory formation in the honeybee.

ABDUCTIVE REASONING IN PSYCHOTHERAPY

Zavyalov V.Yu.
Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia
e-mail: zavidi60@gmail.com

Key words*: psychotherapy, abductive reasoning, therapeutic ideas, change in cognition*

Motivation and Aim: A specific effect of psychotherapy can be presented as some positive possible inner event in the life of the patient, planned and designed by the therapist. This positive event occurs due to the best explanation of some important facts for the patient. Numerous other effects of psychotherapy such as placebo, spontaneous remission, self-regulation, environmental influence are considered to be non-specific and cannot be planned and regulated by the therapist. Traditionally, the art of interpreting the symptom is practiced as the main method (intervention) in psychotherapy. The author believes such interpreting is based on deductive reasoning. The aim of this work is to reveal the art of speech influence of successful therapists in the practice of using abductive conclusion abiding the rules of logic abduction [1]. To achieve this, the author uses formalization of the process of generating effective hypotheses and conjectures, leading to positive changes in the thinking and behavior of the patient.

Methods and Algorithms: The author has created the model for the best explanation of the facts based on abductive reasoning described in classical works of Ch.Pierce that can motivate patients to change their understanding of the problem situation and their behavior in it. In the author's early works Dianalysis [2] had been worked out, based on the phenomenological dialectics by A.F. Losev. In Dianalysis therapeutic hypothesis were called "therapeutic ideas". Now the author prefers getting such hypothesis with the help of abductive reasoning. Abduction is the process of picking out some explanation of an important fact from the patient experience, which leads to a change in his cognition and behavior. Criteria for picking out a member representing "the best" explanation include the simplicity, the prior probability, or the explanatory power of the explanation and so-called Peirce's own maxim. The author uses the terminology of Peirce (Case, Rule, Result) in the construction of the general schemes of the generating hypothesis that best explains the motive of change in cognitive errors and misconceptions in the patient.

Results: The scheme worked out for abductive reasoning allows to receive non-trivial hypotheses for explaining the meaning of the symptom and the solution of the problem. The data obtained allow to formalize the process of «micro-interventions» search in the psychotherapeutic process [3].

Conclusion: Such approach to generating therapeutic hypotheses-explanations lets formal scientific methods of work in psychotherapy practice.

Availability: The method has been tested in teaching of psychotherapy and supervision practice and it can be used for constructing personal agent in computer applications.

References:

1. Flach P.A., Hadjiantonis A. M. 2013 Abduction and Induction: Essays on their Relation and Integration. Springer Science & Business Media. 309 p.
2. Zavyalov V. Yu. 2015 Dianalysis as integrative psychotherapy and counseling. *Applied Psychology and Psychotherapy*. №1. P. 24-35.
3. Zavyalov V.Yu. 2015 The experiment in psychotherapy/Theory and Practice of Psychotherapy 2.10, October. P. 2-13 (in Russian).

REGULATION OF TREM2 EXPRESSION BY AN INDUCIBLE, NF-KB-SENSITIVE MIRNA-34A

Zhao Y.[1], Bhattacharjee S.[1], Jones B.M.[1], Dua P.[2], Hill J.M.[1,3], Andreeva T.[4,5], Aliseychik M.[4,5], Rogaev E.I.[4-6], Lukiw W.J.[1,7]*

[1]LSU Neuroscience Center, Louisiana State University Health Sciences Center, New Orleans LA, USA; [2]Deptartment of Health Information Management, Louisiana State Technical University, Ruston LA, USA; [3]Department of Pharmacology, Louisiana State University Health Sciences Center, New Orleans LA, USA [4]Vavilov Institute of General Genetics, Russian Academy of Sciences, Moscow, Russia; [5]Lomonosov Moscow State University, Moscow, Russia; [6]Department of Psychiatry, Brudnick Neuropsychiatric Research Institute, University of Massachusetts Medical School, Worcester, Massachusetts, USA; [7]Department of Ophthalmology, Louisiana State University Health Sciences Center, New Orleans LA, USA
e-mail: WLukiw@lsuhsc.edu
**Corresponding author*

Aging is a common risk factor for cognitive and memory dysfunction and variety of degenerative processes and cancer. Genetic deficits and loss-of-function for the triggering receptor expressed in myeloid cells 2 (TREM2; encoded at chr6p21.1), a transmembrane spanning, stimulatory receptor of the immunoglobulin/lectin-like gene superfamily, have been associated with deficiencies in phagocytosis and the innate-immune system in Alzheimer's disease (AD), and in other progressive neurodegenerations of the central nervous system (CNS). In this report we provide evidence that TREM2 is down-regulated in sporadic AD hippocampal CA1 compared to age-matched controls. TREM2 expression was also found to be down-regulated in age-related macular degeneration (AMD), a common, progressive deterioration of the human retina associated with amyloidogenesis. An NF-κB-sensitive and inducible miRNA-34a (encoded at chr1p36.22), up-regulated in AD, was found to target the 299 nucleotide human TREM2 mRNA 3'-UTR, and down-regulate the expression of a TREM2-3'-UTR reporter vector. A stabilized anti-miRNA-34a (AM34a) effectively quenched this pathogenic response. The results suggest that an epigenetic mechanism involving an NF-κB-mediated, miRNA-34a-regulated down-regulation of TREM2 expression may shape innate-immune and phagocytic responses that contribute to progressive inflammatory neurodegeneration.

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PROBLEM OF PHYLOGENETIC POSITION OF DICYEMIDS

Zverkov O.*, Rusin L., Lyubetsky V., Aleoshin V.
Institute for Information Transmission Problems of the Russian Academy of Sciences (Kharkevich Institute), Moscow, Russia
e-mail: zverkov@iitp.ru
** Corresponding author*

Key words: *Dicyemida, Orthonectida, Spiralia, Gastrotricha, Plathelminthes, Gnathostomulida, Rotifera, transcriptome assembly, ortholog groups, multiple sequence allignment, phylogeny reconstruction*

Motivation and Aim: The continuing challenge of the identification of the phyla Dicyemida and Orthonectida on the phylogenetic tree of Spiralia was addressed.

Methods and Algorithms: We considered 93 species from 16 spiralian phyla. Four ecdysozoan species were used as the outgroup. The 102 proteomes of 97 species were in part extracted from public sources and in part (33 proteomes) assembled from the Sequence Read Archive or own sequencing data. The proteome assembly included cleaning (using the Sequence Cleaner program and the UniVec and rRNA databases), transcript assembly (Trinity), and ORF predictions (the TransDecoder program and the Pfam and UniProtKB/Swiss-Prot databases). Orthologous families were identified by OrthoMCL-DB. The results presented in [1] were used as the basis. Alignments of amino acid sequences were generated by the MUSCLE program.

Results: The phylogeny reconstructed using the maximum likelihood method suggested that dicyemids are close to the phyla Gastrotricha and Plathelminthes. Our data allow that Dicyemida can neighbor Gnathostomulida and Syndermata (rotifers and acanthocephalans) but reject the position of the phylum within or adjacent to the clade Lophotrochozoa. According to our data, dicyemids are not regressed annelids, mollusks, flatworms, rotifers, or other extant phyla. It was also confirmed that Micrognathozoa, the newest-described animal phylum, is the sister group of Rotifera. Low support of certain clades and long branch effects suggest finer phylogenetic reconstruction methods to be applied, and this work is currently in progress.

Conclusion: Data on the taxonomic position of dicyemids have been obtained.

Availability: Currently obtained results are presented on the following Web page: http://lab6.iitp.ru/en/dicyemida/.

Acknowledgements: The research was supported by the Russian Science Foundation, project 14-50-00150.

References:

1. T.H. Struck, A.R. Wey-Fabrizius, A. Golombek, L. Hering, A. Weigert et al. (2014) Platyzoan Paraphyly Based on Phylogenomic Data Supports a Noncoelomate Ancestry of Spiralia, Mol Biol Evol, 31(7):1833–1849.

РЕШЕНИЯ ДЛЯ АНАЛИЗА NGS-ДАННЫХ ОТ КОМПАНИИ ILLUMINA

Gazizova D. (Газизова Д.)
ООО "Альбиоген"
e-mail: d.gazizova@albiogen.ru

Ключевые слова: *Illumina, Альбиоген, NGS, MiniSeq, MiSeq, NextSeq, HiSeq, BaseSpace*

Компания Альбиоген – официальный дистрибьютор продукции компании Illumina на территории РФ, Беларуси и Казахстана. Портфолио компании Illumina представлено секвенаторами нового поколения (MiniSeq, MiSeq, NextSeq и HiSeq), сканером биочипов iScan и широким ассортиментом наборов для приготовления библиотек. В основе работы секвенаторов Illumina лежит самая надежная и точная на данный момент технология секвенирования путём синтеза (SBS, sequencing by synthesis).

Помимо продуктов для получения высококачественных геномных данных, Illumina предлагает и решения для их обработки. BaseSpace – масштабный, не имеющий аналогов сервис Illumina для анализа, хранения и обмена полученными данными, располагающий широким ассортиментом интуитивно-понятных приложений, позволяющий пользователям, не имеющим биоинформатических навыков, качественно обработать свои данные.

Секвенаторы MiSeq и MiniSeq оснащены программным обеспечением, позволяющим в автоматическом режиме, сразу по окончании запуска, проводить выравнивание полученных последовательностей на референс и осуществлять определение вариантов (инсерции, делеции, SNP). Пользователи клинических панелей серии TruSight могут аннотировать и фильтровать обнаруженные варианты в VariantStudio, а исследователям в области HLA-типирования и преимплантационного генетического скрининга предоставляется доступ к специально разработанному для этих целей ПО.

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