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AND STRUCTURE\SYSTEMS BIOLOGY (BGRS\SB-2018)

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Contents

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The long-term consequences of early-life dexamethasone treatment on the cognitive ability of male mice and gene expression in the hippocampus

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Key words: neonatal dexamethasone, transcriptome, hippocampus

Motivation and Aim: Dexamethasone (DEX) treatment in early life can activate HPA axis and lead to different negative consequences in adult ages.

Methods and Algorithms: DEX was injected on postnatal day 1–3 once a day with decreasing dose (0.5, 0.3, 0.1 mg/kg, s.c.). Manifestation of neonatal reflexes and delayed effects on adult behavior were investigated. RNA-seq analysis in hippocampus was done on adult animals after neonatal treatment with DEX or saline.

Results: The DEX treatment in early life leads to delay in manifestation of neonatal reflexes and decrease in the weight of male mice. Adult mice that had received neonatal treatment with dexamethasone, showed a decreased anxiety and impaired spatial memory and learning in Morris water maze. To reveal the transcriptomic events in hippocampus accompanying the long-term behavioral effects of neonatal DEX treatment, an RNA-seq study was performed in adult mice. The expression of 12 genes was altered in DEX-treated mice compared to saline-treated animals. Among them, *Arc* gene seem to be the most appropriate to describe the observed cognitive disturbances, since it is tightly connected with formation of long-term memory as well as with regulation of synaptic plasticity.

Conclusion: Our data clearly demonstrated that neonatal treatment with DEX has adverse effects on cognitive abilities of adult mice. The transcriptomic study proposes only a few genes that may be involved in hippocampus malfunction, resulting in the observed cognitive impairments.

Acknowledgements: The work was supported by Russian Science Foundation project 16-15-10131.

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Consequences of early life stress in mice: transcriptional and epigenetic hallmarks in frontal cortex and hippocampus

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Key words: early life stress, maternal separation, transcriptome, H3K4me3 ChIP-seq

Motivation and Aim: Stressing events in early postnatal period cause disturbances in neural connections and networks which lead to both direct and delayed effects on brain development.
Methods and Algorithms: We have investigated the influence of different types of early life stress – prolonged repeated separation of pups from their mothers for 3h per day or short-term repeated separation (15 min per day) during the first 2 weeks of life, and 24 h single maternal separation on 9th day of life.
Results: Short-term repeated separation led to some positive effects on behavior of mice, enhancing the social behavior and decreasing anxiety. Single separation resulted in decreased locomotor activity. Prolonged maternal separation led not only to changes of individual behaviors but also to deterioration of spatial memory and learning in Morris water maze and to impaired ability to recognize novel object. We detected the direct effects (on 15th day of life) of maternal separation on transcriptome in two brain regions – hippocampus and frontal cortex. In the frontal cortex, the stress negatively affected the axon ensheathment and myelination. In the hippocampus, downregulated genes were associated with NCAM interaction and signaling for neurite outgrowth. The analysis of distribution of H3K4me3 (ChIP-seq) in frontal cortex showed only some subtle changes in adult male mice with a history of early life stress.
Conclusion: Summing up, our data indicated that disturbances in expression of developmental genes may be mediated by alterations of epigenetic landscape which in turn may provide a basis for observed long-term effects of stress.
Acknowledgements: The work was supported by Russian Science Foundation project 16-15-10131.

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Plasmon-activated water is an effective agent in suppressing the progression of dental, metabolic, and neurodegenerative disorders

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Key words: periodontitis, diabetes mellitus, Alzheimer's disease, Parkinson's disease, oxidative stress

Motivation and Aim: With the coming of the aging society, more and more people are suffered from chronic metabolic and neurodegenerative disorders in which oxidative stress and systemic inflammation may underlie the molecular mechanism of these deficiencies. During the past few decades, a variety of drugs have been developed to depress or counteract the progression of such dysfunction. However, none of these drugs can persistently maintain their function. Moreover, their modest benefits are often offset by severe side effects. With regard to this viewpoint, developing a natural agent with no cytotoxicity, high biocompatibility, and significant anti-oxidative and anti-inflammatory properties will be of great help in rescuing the metabolic and neuronal function disrupted by related sequelae.
Methods and Algorithms: By letting the deionized water (DIW) flow through supported gold nanoparticles (Au NPs) under resonant illumination, we have developed the plasmon-activated water (PAW) with small water clusters that are more active in various chemical and physical reactions [1]. Adult rats subjected to periodontitis, diabetes mellitus, sleep deprivation, Alzheimer's disease, and Parkinson's disease were daily drunk of PAW, and the potential effects of PAW on protecting the cell function were comprehensively assessed by oxidative status, morphological profiles, molecular signaling in biochemical reaction, bio-energetic level as well as the metabolic and cognitive expressions.
Results: Significant improvement including decreased oxidative stress, depressed inflammatory responses, enhanced anti-oxidative enzymes expression, increased bio-energetic level, as well as successful recovery of metabolic and cognitive functions were all clearly detected in diseased animals daily drunk of PAW as compared to that of rats received DIW treatment along.
Conclusion: As PAW could effectively suppress the progression of numerous dental, metabolic and neurodegenerative disorders, daily drinking of PAW may serve as a valuable strategy to improve the cellular function with a healthier, cheaper, more natural, and more convenient way.
Acknowledgements: Supported by the Ministry of Science and Technology (MOST 106-2314-B038-003).

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Innovatively therapeutic strategy on Alzheimer's disease by daily drinking plasmon-activated water

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Key words: Alzheimer's disease, plasmon-activated water, anti-inflammation, amyloid, prevention

Motivation and Aim: Alzheimer's disease (AD) is the most common cause of dementia and AD is characterized by memory impairment followed by decline of many cognitive domains, including executive and visuospatial, resulting in dysfunction of activities of daily life. Amyloid accumulation in the brain which occurs before clinical presentation is the first and key step for development of AD. Many clinical trials are aiming to remove amyloid from the brain of AD patients but none is successful till now. Plasmon-activated water (PAW) is produced by gold (Au) nanoparticles (NPs) reducing the hydrogen-bonded (HB) structure of water [1]. PAW has been found to contain anti-oxidation and anti-inflammation effects [1, 2]. Here, we analyze the function of PAW in eliminating the progression of AD. The APPswe/PS1dE9 transgenic mice are treated with PAW or regular water for 9 months from 5-month-old.
Methods and Algorithms: The mice were kept in individually ventilated cages with feeding racks and water bottles were attached to the front panel of the cage which allows animals to reach food and water. Mice were maintained in a 12-hour light/ 12-hour dark cycle (12L/12D; light on 7:00, light off 19:00). The food and deionized water (DIW) or PAW were freely available and change the water every day. Six (APP/PS1) mice for each group were fed with PAW or DIW for 9 months from 5-month-old.
Results: The mice treated with PAW present the better memory performance, little amyloid and phosphorylated Tau burden in hippocampus. Collectively, our findings support the function of PAW on conferring effects of amyloid reduction and memory improvement in AD mouse model. We propose that the effect of PAW on reduction formation of senile plaque was not in synthesis of amyloid-beta protein but in prevention aggregation of amyloid-beta protein.
Conclusion: In conclusion, PAW confers the effects on reduction of amyloid accumulation and deceleration of memory decline. These new findings indicate the potential of PAW as an effective antioxidant without side effects for therapy on neuro-related diseases.
Acknowledgements: This work was supported by Taipei Medical University and Shuang Ho Hospital (105TMU-SHH-01-1).

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Vitamin D_3, affective-related disorders and perimenopause

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Key words: cholecalciferol, vitamin D_3, affective-related disorders, estrogens, perimenopausal period, women

Motivation and Aim: Mood disorders in perimenopausal period are common and considered as a public health issue. A strategy to alleviate the mood disorders associated with perimenopause is menopausal hormonal replacement therapy (MHT) [1]. However, controversial results related to the effectiveness of such treatment have been frequently reported. There has been longstanding interest in the role of «natural» treatments for depression and mood disorders, such as nutritional and dietary products. Among other nutraceuticals, one of such «natural» substances for treatment of affective-related state could be vitamin D [2].

Methods and Algorithms: This study evaluated the effect of cholecalciferol supplementations in high doses (60000-100000 IU, per os) alone or in a combination with standard MRT on anxiety/depression scores and hormonal status for perimenopausal women. The women treated with cholecalciferol in 80000 and 100000 IU doses alone or in a combination with MHT had greater reduction in anxiety scores than the control group. The cholecalciferol-treated groups of perimenopausal women had significantly higher 25-hydroxyvitamin D_3 concentrations and gonadal hormones levels in the blood serum in comparison to the control group.

Results: In 3 months, a combined administration of cholecalciferol in different doses and MHT resulted in summarization of positive effects of both treatments. It means that affective-related profile was lower in women given with such combined therapy. In 6 months, affective-related profile in perimenopausal women treated with combination of cholecalciferol at different doses and MHT has been completely eliminated. Simultaneously, we found that combined administration of cholecalciferol in different doses and MHT also improved hormonal state in perimenopausal women.

Conclusion: The present trial showed that consuming high doses of vitamin D_3 daily was effective in decreasing depression and anxiety levels in perimenopausal women. Furthermore, this is the first clinical study to show a beneficial effect of chronic Vitamin D_3 in high doses administration on anxiety/depression scores in perimenopausal women. This work promotes more effective creating of the novel therapeutic targets and strategies for affective-related state treatment in perimenopausal women.

Acknowledgements: This work was supported by Russian Science Foundation (RSF) accordingly to the research project № 16-15-10053.

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Sleep disorders and gene NPAS2 polymorphism in male population in Russia/Siberia: MONICA-psychosocial study

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Key words: NPAS2, gene polymorphism, sleep disorders

Motivation and Aim: To study the prevalence and NPAS2 gene association with sleep disorders as cardiovascular risk factor in male population in Russia/Siberia.

Methods and Algorithms: In 2014–2016 a random representative sample of the male population 25–44 years of one of the districts of Novosibirsk was examined. A random method was used to select 200 men (mean age = 35.5 years) who underwent psychosocial testing using the C.D. Jenkins scale "4-item Jenkins Sleep Questionnaire". In men, included in the study, the frequency distribution of genotypes rs4851377 of the NPAS2 gene was studied. Approved by Ethical Board. Differences in the frequency distribution of the rs4851377 of the NPAS2 gene between the groups were evaluated by the Chi square test (X2).

Results: Most of men needed 7 hours of sleep per day – 46.7 %. The rates of those with an 8-hour sleep were 24.4 %. Genotype C/C of gene NPAS2 rs4851377 is more common in those who slept in the day at least 8 hours (33.3 %) and 9 hours (33.3 %). Genotype C/T and T/T were in persons with 7-hour sleep (50 and 53.3 %, respectively). Allele T carriers in 4.5-fold higher had 6 hours of sleep compared to the C allele carriers whose sleep was 9 hours. Allele T carriers had lower sleep duration (7 instead of 9 hours of sleep) in 4 times compared with allele C.

Conclusion: The findings suggest that site rs4851377 of gene-candidate NPAS2 determines need for sleep in men.

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A system for remote recognition of emotions from a facial expression

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Key words: facial expression, arousal, valence, psychophysiology, machine learning, data streams

Motivation and Aim: Nowadays social networks are a commonplace platform for communication of many people. Users create web content, check out the content of others and send private messages. Network communication enables people to control their actions carefully, while anonymity allows them to act without reservations about getting unclosed. Therefore, it is interesting to find the relation between the real psychophysiological state of users and their various actions. This paper describes a method for collecting information of user's emotional state based on its facial expressions and linking the data acquired to the user's actions in a time.
Methods and Algorithms: At client side, we use reactive programming model implemented by RxJS library to manage data streams. Our client library includes logic to combining events from different sources such as MediaStream APIs, classic DOM event API. We have developed our own neural network architecture that allows us to map the facial expressions of people into a continuous space of arousal/valence [1]. The same architecture for classification of emotions was used. We used inception and residual blocks and batch normalization layers to achieve higher accuracy. In addition, we augment train data by adding pose variations using 3D face reconstruction [2].
Results: We have developed a system that allows us to collect various data such as video stream and events of user interaction with the webpage. We also trained a neural network that shows high accuracy. One part of the system is a client library that does not require the user to install any special software and can be easily integrated into the website. The other part is a server application that enables the site owner to analyze the data collected.
Conclusion: The developed system allows us to collect the necessary data about users remotely and in settings familiar for people. The next steps in our study are to collect a large amount of data and compare the actions of users with their psychophysiological state. Besides, we aim to try to extract other user characteristics such as heart rate and sentiment from deleted text messages.

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Effect of 5-HTTLPR on connectivity and topological properties of resting state EEG networks

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Key words: serotonin transporter gene, promoter, genetic variants, magnetic resonance imaging, brain networks

Serotonin transporter is one of the most widely investigated genetic markers of individual variation in serotoninergic function. The promoter region of the serotonin transporter gene (5-HTTLPR) contains long (L) and short (S) variants with the latter one having reduced transcriptional efficiency. S allele has been found to increase the risk of depression and other mental health problems, but some evidence suggests that S-allele carriers outperform subjects carrying the long allele in an array of cognitive tasks. Functional magnetic resonance imaging studies demonstrate a heightened amygdala response to negative emotional stimuli and diminished connectivity among key areas involved in emotion regulation in S allele carriers. However, evidence linking this polymorphism with individual variation in electrophysiological properties of resting state brain networks is still very limited. This study investigated the effect of 5-HTTLPR polymorphism on EEG current source density, connectivity, and topological properties of resting state networks. As compared to L homozygotes, S-allele carriers showed lower current source density and connectivity in most frequency bands in areas overlapping with the default mode and emotion regulation regions. The analysis of graph-theoretical measures showed that as compared to L homozygotes, S-allele carriers have less optimal topological properties of brain networks in theta, but more optimal in alpha band. This dissociation may reflect predisposition to emotional disorders, which is inherent to S allele carriers, and, on the other hand, their superior functioning in some cognitive domains.
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Cystatin C as regulator of autophagy in the brain of transgenic murine model of Parkinson's disease

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Key words: cystatin C, autophagy, transgenic mice, Parkinson's disease, overexpression of alpha-synuclein

Motivation and Aim: Cystatin C is one of the potent regulators of autophagy. Changes in the expression and secretion of cystatin C in the brain have been found in amyotrophic lateral sclerosis, Alzheimer's and Parkinson's diseases and in some animal models of neurodegeneration, demonstrating its protective role. Cystatin C is regarded to play an important role in amyloidogenesis and be promising approach for treatment of neurodegenerative diseases. In Parkinson's disease, serum cystatin C levels may predict disease severity and cognitive dysfunction, although the exact role of cystatin C remains unclear. The aim: to evaluate expression of cystatin C in transgenic mouse model of Parkinson' disease at early stage of disease development (5 m.o.) and estimate results as related to mechanism of autophagy activation.

Methods and Algorithms: 5-month-old male mice of B6.Cg-Tg(Prnp-SNCA*A53T) 23Mkle/J) (further – B6.Cg-Tg) and control C57Bl/6J strain were used. Total RNA was isolated from mouse brain areas (striatum, amygdala, hypothalamus, hippocampus). Gene expression levels were detected using qPCR-RT. LC3-II levels were evaluated in brain cryosections with immunohistochemical analysis. Cystatin C levels in plasma were determined by specific ELISA kits.

Results: Analysis of cystatin C (*Cst3*) gene expression in the striatum and, especially, in amygdala revealed a significant decrease in B6.Cg-Tg mice compared to controls. Low levels of *Cst3* expression were associated with suppression of autophagy: a marker of autophagy activation LC3-II was reduced in the striatum and s. nigra while expression of *Becn1* encoding another marker of autophagy activation was significantly decreased in the frontal cortex. Cystatin C concentration in plasma of transgenic mice was not changed vs. controls.

Conclusion: The results obtained provide further evidence of association between cystatin C and autophagy activity. Cystatin C may play a protective role in multiple neurodegenerative disorders including Parkinson's disease.

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Psychophysiological predictors of effective adaptation to the allostatic load of the mountain climbers

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Key words: mountain climbers, allostasis, go/no-go, hypoxia, heart rhythm, handedness, orthostasis

Motivation and Aim: A study of phenotypic characteristics of human adaptation to extreme factors of the external environment (such as, for example, hypoxia) represents the actual task and allows identifying the predictors of the organism's successful functioning [1]. It was found that the result of adaptation depends not only on the functional abilities of the organism and allostatic changes [2], but also on the volitional and personal characteristics of the subjects. Of particular interest is the study of human cognitive functions in the course of such adaptations [3]. It is shown that due to strong-willed qualities people can overcome physiological ailments [4] or to carry out excessive physical loading, in particular, at high-mountain ascents. The authors investigated the handedness, the reserves of the cardiovascular system and the features of sensorimotor integration in mountain climbers as possible predictors of adaptation to extreme factors of the external environment.
Methods and Algorithms: At qualified mountain climbers taking into account proficiency and age difficult sensorimotor reaction (go/no-go at normoxia and normobaric hypoxia) was studied, assessment of handedness and indicators of orthostatic test (A. Riftin's technique) were carried out.
Results: Stability of sensorimotor integration in climbers under hypoxia is higher than in normoxia. The correlation between the results of the shoulder test (handedness test) and the assessment of the cardiovascular system's reserves obtained on the basis of orthotest indicators (reserves higher for left-side preferences) is shown.
Conclusion: The relation of the regulation of the autonomic nervous system with left-handers, resulting in more effective adaptation to the high altitude and the possibility of using handedness as a phenotypic predictor of the level of reserves of the climbers' cardiovascular system. It is suggested that the factor of hypoxia in climbers in certain conditions has a stimulating effect on the processes of sensorimotor integration.
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Cognitive activity and students' coping strategies

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Key words: allostasis, coping, cognitive activity, educational activity, first year students

Motivation and Aim: Various aspects of the allostatic load of students in educational activities have been studied as factors in the effectiveness of the educational process for a long time [1]. The study of behavioral strategies and cognitive features of first year students is essential [2]. Characteristic features of students majoring in psychology are manifested both in coping with the stress of the educational process [3] and in their professional skills [4].
Methods and Algorithms: There studied mistakes in the course of nonspecific cognitive activity (an analogue of educational activity) and in coping strategies of first year students majoring in psychology (group 1) and of first year students who study psychology majoring in nonpsychological subjects (group 2).
Results: It is shown that both groups do not differ statistically in intelligence, however, students from group 1 while performing cognitive activity make more mistakes than students from group 2 ($p < 0.05$). 37.5 % of group 1 have tiredness and 62.5 % of group 1 have different types of fatigue. 31.1 % of group 2 have work stress, 43.2 % of group 2 have tiredness and 25.7 % of group 2 have different types of fatigue. Group 2 uses all copying strategies except the emotionally-oriented strategy of "self-control" (<40T-score). Group 1 also uses all copying strategies but the most preferred (>60T-score) are the search for social support (problem-oriented) and positive re-evaluation (emotionally-oriented).
Conclusion: Coping strategies of small efficiency (emotionally-oriented ones) of the first year students go along with many their mistakes in cognitive activity. There is no one among the first year students majoring in psychology who has work stress (minimum state that is suitable for effective cognitive activity) – all students from group 1 have tiredness or different types of fatigue. Students majoring in psychology need additional courses to develop skills for effective coping with stress during the first year study.

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Impact of early life stress on susceptibility to chronic social stress in adult mice

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Key words: maternal separation, social defeat stress, behavioural tests

Motivation and Aim: Despite the growing population of depressed patients and development of new antidepressants, fewer than half achieve full remission and many are not responsive with currently available treatments, including antidepressant medications and psychotherapies. One of the possible reasons for this situation is our incomplete understanding of the mechanisms of the depression and the wide individual variations seen in response to prolonged stress, an important risk factor for depression. A significant contribution to the individual diversities in response to stress can be caused due to previous stress experience, in particular, the adverse experience in childhood. The aim of this study is investigation of early life stress influence on susceptibility to social stress in adulthood.
Methods and Algorithms: As a model of early life stress we used prolonged repeated maternal separation (MS) for two first weeks of life. Further, in adult life chronic social defeat stress paradigm (SS) during 10 days was used. Thus, the following groups of mice were formed: group with MS in early life and SS in adult life, group with only SS in adult life and control group, which was not exposed to any type of stress. For estimation of susceptibility to social stress we evaluated levels of anxiety in elevated plus-maze test, exploratory, communicative and locomotor activity in social interactions test and depressive-like behavior in forced swim test.
Results: Group of mice with MS in early life and SS in adult life demonstrated more depressive-like traits in forced swim test: they had significantly decreased time of the first immobility in comparison with group subjected to only SS in adult life. All experimental groups exposed to social stress both maternal separated in early life, and without such separation, showed significant behavioral alterations in comparison with control group. Thus, they demonstrated less time spent in open arms and significantly increased time spent in closed arms in elevated plus-maze test, which indicated increased level of anxiety in comparison with control group. Moreover, all groups with SS showed decreased moved distance and communicative features in social interactions test compared with control group.
Conclusion: Repeated maternal separation in early life leads to increased sensibility for social stress in adult life. Thus, early life stress is a potential risk factor for development of various mood diseases.
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Ionic imaging and bio-energetic analysis of club drug-induced cognitive deficiency by time-of-flight secondary ion mass spectrometry (TOF-SIMS)

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Key words: gamma-hydroxybutyric acid (GHB), cognitive dysfunction, hippocampal, TOF-SIMS

Motivation and Aim: Excessive exposure to club drug gamma-hydroxybutyric acid (GHB) would cause cognitive dysfunction in which impaired hippocampal Ca^{2+}-mediated neuroplasticity may correlate with this deficiency. However, the potential changes of *in vivo* Ca^{2+} together with molecular machinery engaged in GHB-induced cognitive dysfunction have never been reported. This study aims to determine these changes in bio-energetic level through ionic imaging, spectrometric, biochemical, morphological, as well as behavioral approaches.

Methods and Algorithms: Adolescent rats subjected to GHB were processed for TOF-SIMS, immunohistochemistry, biochemical assay, together with Morris water maze to detect the ionic, molecular, neurochemical, and behavioral changes of GHB-induced cognitive dysfunction, respectively. Extent of oxidative stress and bioenergetics were assessed by levels of lipid peroxidation, Na^+/K^+ ATPase, cytochrome oxidase, and [^{14}C]-2-deoxyglucose activity.

Results: The study indicated that in GHB intoxicated rats, decreased Ca^{2+} imaging and reduced NMDAR1, nNOS, and p-CREB reactivities were detected in hippocampus. Depressed Ca^{2+}-mediated signaling corresponded well with intense oxidative stress, diminished Na^+/K^+ ATPase, reduced COX, and decreased 2-DG activity, which all contributes to the development of cognitive deficiency. As impaired Ca^{2+}-mediated signaling and oxidative stress significantly contribute to GHBinduced cognitive dysfunction, delivering agent(s) that improves hippocampal bio-energetics may thus serve as a promising strategy to counteract the club drug-induced cognitive dysfunction emerging in our society nowadays.

Conclusion: In summary, with the assistance of advanced spectrometric, ionic imaging, biochemical, morphological as well as behavioral approaches, the present study addressed for the first time that chronic and excessive exposure to GHB would cause cognitive dysfunction in which impaired hippocampal bio-energetics may contribute to the pathogenesis of this deficiency.

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Temporo-parietal junction as a mediator of reactive social behavior: the role of agreeableness

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Key words: social interactions; agreeableness; multilevel mediation analysis; reactive behavior; EEG

Motivation and Aim: Human behavior in social situations has two distinct components – reactive and nonreactive. Reactive behavior is largely driven by the perceived behavioral manifestation of the opponent and is indispensable for successful social interactions. The ability and willingness to pay attention and correctly interpret verbal and nonverbal signs from the opponent and to tune his or her own behavior accordingly should depend on personality, but little is known about brain underpinning of this behavior and the impact of personality. In this study, we used a model of virtual social interactions, which allows to manipulate the emotional display of the 'opponent' and to register actor's responses to these manipulations.
Methods and Algorithms: High-density EEG was recorded throughout the experiment and participants additionally filled in the IPIP Big-Five Factor Markers [1]. The emotional stimulus category was used as a predictor, behavioral response as outcome, and source-level event-related oscillatory power was used as a mediator in the multilevel mediation analysis [2].
Results: Significant mediation effects were revealed only in the theta frequency band. For the reactive response, a positive mediation effect was found in the Brodmann area 39. Event-related theta activity in this cluster increases as stimuli characteristics change from happy to neutral and from neutral to angry facial expressions and this increase is associated with increased probability of a more-aggressive/less-friendly behavioral response. Fisher z-transformed mediation coefficients (path AB) correlated with agreeableness ($r = 0.50$, $p = 0.001$), but not with other personality variables. For the nonreactive response, a positive mediation effect effect did not correlate with personality variables.
Conclusion: The association between the predictor and the outcome was mediated by event-related theta activity in the right temporo-parietal junction and the strength of mediation was moderately positively associated with agreeableness, suggesting that the brain mechanism underlying reactive social behavior is more active in agreeable individuals.
Acknowledgements: Supported by the Russian Science Foundation (RSF) under Grant No. 17-18-01019.

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Revealing the basis of energy metabolic deficiency common to neurodegenerative diseases with differential expression meta-analysis

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Key words: neurodegenerative diseases, differential expression, meta-analysis

Motivation and Aim: "Hypometabolism, characterized by decreased brain glucose consumption, is a common feature of many neurodegenerative diseases. Initial hypometabolic brain state, created by characteristic risk factors, may predispose the brain to acquired epilepsy and sporadic Alzheimer's and Parkinson's diseases. Deficient glucose metabolism is likely a primary initiating factor for these diseases, and resulting neuronal dysfunction further promotes the metabolic imbalance, establishing an effective positive feedback loop and a downward spiral of disease progression. Therefore, metabolic correction leading to the normalization of abnormalities in glucose metabolism may be an efficient tool to treat the neurological disorders by counteracting their primary pathological mechanisms" [1].
Methods and Algorithms: Differential expression meta-analysis.
Results: Differential expression meta-analysis reveal the proteins whose expression profiles match under all neurodegenerative diseases and differ both from that in the normal healthy stage as well as under specific diseases such as epilepsy or Alzheimer's disease. This filter out the particulars of specific neuropathologies and bring ahead the coherent groups of genes underlying the characteristics of the problem of the vicious circle of hypometabolism in neurodegenerative diseases and the consequent neuropathology itself. Future planned addition to the analysis of the expression profiles from the individuals treated with the energy supply metabolites (i. e. pyruvate) under the normal and pathological conditions will help to reveal the gene basis of the neuroprotective effects of energy metabolic correction and further elaborate the patients treatment strategy.
Another planned direction of the research is to include into the analysis the information of the individual viability to the pathological factors that may reveal the weak and strong parts of the system and the potential targets to individual treatment as well as possible common though not total resisting and labile mechanisms.
Conclusion: Here we propose a method that can be used to reveal the genetic basis of energy metabolic deficiency common to neurodegenerative diseases.
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Effects of the endothelial nitric oxide synthase gene polymorphisms on the risk of metabolic syndrome in subjects with schizophrenia

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

Motivation and Aim: The frequency of metabolic syndrome (MetS) is significantly higher in schizophrenia (SCH) patients, when 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]. The aim of this study was to evaluate whether genetic variants in NOS3 gene could be associated with the risk of MetS in SCH patients from Russian population.
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 ($\chi^2 = 6.80$; $p = 0.009$, OR = 0.59; 95%CI: 0.40–0.88), rs2070744 C allele ($\chi^2 = 6.80$; $p = 0.009$, 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: Based on these results, we can conclude that the promoter T-786C variant of NOS3 gene may be considered as a potential genetic marker of increased risk of MS in patients with schizophrenia and may serve as a prognostic biomarker for MetS among Russian schizophrenic subjects.
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Arranging the high-confidence microRNA binding regions into web tool for analyzing variants in diagnostic next generation sequencing

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Key words: Regulation of gene expression, microRNA-mRNA interactions, microRNA, miRNA, nucleotide variants

Motivation and Aim: It is well-known that microRNA plays a key role in the gene expression regulation. Today it is known more than 2'500 human microRNAs, while a majority of microRNA-mRNA interactions remain unidentified. A common method for determining the microRNA-mRNA interactions is the use of prediction programs that show a small intersection of the results and are poorly consistent with known experimental data [1]. Therefore, using experimentally obtained data of the microRNA binding regions should be the most promising approach in order to identify new molecular mechanisms for the etiopathogenesis of hereditary diseases.
Methods and Algorithms: We collected results of 79 AGO2-CLIP-seq data (18 PAR-CLIP and 61 HITS-CLIP) from 9 different cell lines. We also took data from two modified CLIP-seq studies (CLASH, CLEAR-CLIP) [2, 3] that straightforwardly detect microRNA–mRNA pairs as chimeric reads. We developed the algorithm for analyzing the microRNA binding regions.
Results: Totally, we revealed 156 thousand microRNA binding regions and formed a subset of 46.8 thousand high-confidence regions that were identified in at least two different experiments. The analysis of high-confidence microRNA binding sites revealed tissue-specific interactions for two predominate cells: HEK293 and Huh7.5. On the other hand, we obtained a group of "house-keeping" microRNA binding regions that were identified in predominant cells. The identified high-confidence microRNA binding regions have been formed in web-tool. This tool analyzing nucleotide variants from patients with an inherited disease which could be caused by breaking in the microRNA–mRNA interactions.
Conclusion: We identified the subset of 46.8 thousand high-confident human microRNA binding regions that were arranged in the tool (available online: http://score.generesearch.ru/services/mirna/). Hence, it will be a valuable resource that should provide additional insights into the identification new molecular mechanisms of hereditary diseases caused by breaking in the microRNA-mRNA interactions.

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Neurophysiological features of verbal divergent thinking in elderly scientists

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Key words: alpha, divergent thinking, elderly, interhemispheric asymmetry, verbal memory

Motivation and Aim: Cognitive training and rich information environment can contribute to high productivity of divergent problem solving in aging via specific reorganization of brain activity. We investigated scientific activity and originality-related differences in EEG activity during verbal divergent problem solving. Alpha power varies as a function of originality of ideas and creativity-related task demands [1], so, we have considered alpha1, 2 frequency bands. Since alpha synchronization is associated with access to long-term memory [2], we explored its relation with parameters of verbal memory.
Methods and Algorithms: Elderly adults participated in the study: 43 were engaged in professional scientific activity (SA, M = 65.2 years, SE = 0.97) and 41 were continuing their professional non-scientific activities (non-SA, M = 62.4, SE = 0.99). EEG data were recorded from 52 electrodes during divergent test "Alternate Uses Task" implementation. Alpha 1, 2 power was calculated using FFT; power reactivity was calculated as log(test)–log(prestimulus). Verbal memory was assessed by dichotic test. ANOVA, regression and correlation analysis were used.
Results: SA outperformed non-SA elderly in originality and amount of ideas, speed of divergent problem solving. Interhemispheric asymmetry of alpha power reactivity with larger values in the right then in the left hemisphere was significant in low original SA subjects only ($p = 0.008$). For all subjects, dominance of right lateralized verbal memory (over left lateralized one) made positive impact in that interhemispheric alpha power asymmetry ($p < 0.004$). High number of successfully retrieved words presented in the right hemisphere was accompanied by lower originality of creative ideas in SA subjects only ($r = –0.46$, $p = 0.003$).
Conclusion: Interhemispheric alpha power reactivity asymmetry with larger values in the right then in the left hemisphere during verbal divergent problem solving is associated with the predominance of right hemispheric strategies of verbal memory. This effect is related to low creative originality in SA elderly. The possibility that different information processing strategies contribute to creative originality in SA and non-SA elderly is discussed.
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The effect of 5-HTTLPR polymorphism on EEG current source density

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Key words: 5-HTTLPR; EEG; sLORETA; current source density

Motivation and Aim: The S allele of the promoter region of the serotonin transporter gene (5-HTTLPR) is associated with increased risk of depression and other mental disorders. Evidence linking this polymorphism with individual variation in electrophysiological properties of resting state brain networks is still very limited. We aimed to explore the effect of 5-HTTLPR polymorphism on source-level EEG activity in eyes-closed and eyes-open resting condition.

Methods and Algorithms: EEG recordings were performed using 100 electrodes positioned in an elastic cap according to the International 10-10 system with a Cz as the reference. The fronto-central electrode was used as the ground. The signals were amplified using 'Neuroscan (USA)' amplifiers, with a 0.1–100 Hz analog bandpass filter and continuously digitized at 1000 Hz. Electrode impedances were kept at or below 5 kilo-ohms. Artifacts were corrected using independent component analysis in the EEGlab toolbox (http://www.sccn.ucsd.edu/eeglab/) and EEG data were recomputed to the average reference and down-sampled to 250 Hz. The standardized Low Resolution Brain Electromagnetic Tomography method [1] (sLORETA) was used to localize the sources of scalp-recorded EEG data. Current source density data were analyzed using second-level full factorial design in the SPM 12 toolbox (http://www.fil.ion.ucl.ac.uk/spm). There were three factors – the between-subject group factor (L/L vs. other two genotypes) and two within-subject factors, i. e., condition (eyes closed vs. eyes open) and frequency band (seven levels). Of primary interest was the main effect of the group factor and its interactions with the two other factors.

Results: As compared to L homozygotes, S-allele carriers showed lower current source density, with this effect being most pronounced in alpha2 and beta bands in areas overlapping with the default mode regions, the orbitofrontal, temporal cortices, and in the insula.

Conclusion: The effect of genotype was significant in brain regions that are involved in self-referential and emotional processing. We can assume that this effect may reflect the predisposition to emotional disorders inherent to S allele carriers.

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Reconstruction of leptin and dopamin molecular counter-regulation in glutamatergic hippocampal synapses

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Key words: synaptic receptors density, AMPA receptors, leptin, dopamin, dendritic spine, exciting synapses, hippocampus

Motivation and Aim: Long-term potentiation increase density of AMPARs (The α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor) at synaptic contact. In addition the receptors of various hormones, in particular leptin, growth and neurotrophic factors, as well as the receptors of other mediator systems, in particular, dopamine receptors, are present in the synaptic contacts zone. The hormone leptin crosses the blood brain barrier and regulates numerous neuronal functions, including hippocampal synaptic plasticity. The role of dopamine in the hippocampus remains poorly defined.
Results: The interactome of hippocampal dendritic spines was reconstructed (technology GeneNet was used (ROSPATENT No. 990006 from 15/02/1999)). After Long-term potentiation (LTP) a key event is the groundwork of second messenger's pools. P4 → PIP2 (PtdIns(4,5)P2) catalyzed Phosphoinositide 5-kinase (PI5K); PIP2 → PIP3 (PtdIns(3,4,5)P3) – Phosphoinositide 3-kinase (PI3K). PtdIns(4,5)P2 is hydrolyzed at inositol 1,4,5-trisphosphate (InsP3; IP3) and diacylglycerol (DAG) by phospholipase C (PLC). DAG activates protein kinase C (PKC), that phosphorylates GluR2- and GluR1-AMPAR. After that GluR2-AMPARs move from and GluR1-AMPARs incorporate at the synaptic contacts. Note GluR1-AMPAR have to be phosphorylate of protein kinase A (PKA).
The activity of PKC is mediated by protein kinase PDK1 (3-phosphoinositide-dependent protein kinase 1) which binds to PtdIns(3,4,5)P3. Thus, PIP3 mediated a positive regulatory contour increasing the GluR1-AMPAR synaptic density: PIP2 → PIP3 → PDK1 → PKC → GluR1-AMPARs incorporation. This counteracted by PTEN, which is observed when the basic synaptic activity takes place. After LTP induction leptin promotes the removal of PTEN and, thus, support the expression of GluR1-AMPARs at the synapses. Dopamine trigger the cascade generation of cAMP that needed for activation of PKA. PKA phosphorylates of GluR1-AMPAR too that critical for anchoring them on the plasma membrane of spines and for forming the pool of AMPAR, which increases the density of synaptic AMPAR after LTP induction.
Conclusion: A model in which the synaptic contact is represented not as a passive receiver of an input signal, but as a complexly organized multicomponent molecular system has been suggested. Leptin mediates the anchoring of AMPAR at synapses. Dopamine is probably involved in the formation of a receptors pool that there may be rapid introduction to synapses after LTP induction.
Availability: http://wwwmgs.bionet.nsc.ru/mgs/gnw/genenet/viewer/AMPA.html
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How have our clocks evolved? Adaptive and demographic history of the out-of-African dispersal told by the genetic markers of morning-evening preference

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Key words: SNP, 1000 Genomes Project, latitudinal cline, morning-evening preference, polygenic selection, skin pigmentation, Neanderthal's genome, migration out of Africa

Motivation and Aim: The natural cycles of night and day, and their length, remain stable in near-equatorial African regions but they vary with latitude and season in Eurasia. Therefore, this new environmental factor seemed to shape the adaptation of the circadian rhythms of Eurasians after the out-of-African dispersal of their African ancestors [1]. We tried to identify the genetic-based signatures of this latitude-dependent adaptation.
Methods and Algorithms: Geographic variation in allele frequencies of more than 28 hundred genetic variants was analyzed using data from 5 African and 11 Eurasian populations sampled for the 1000 Genomes Project Phase 3 (1594 individuals).
Results: As we expected, the genetic signatures of latitude-dependent polygenic selection were found more frequently within non-coding DNA regions associated with morning-evening preference in 4 genome-wide association studies (GWASs). These signatures were identified less frequently among polymorphisms hinted by GWASs of other traits/diseases and among polymorphisms sampled from pseudogenes and from protein-coding regions in either circadian clock genes or reference genes. The frequencies were also high for loci associated with those traits that, like morning-evening preference, were shaped by latitude-dependent adaptations (e. g. skin pigmentation). Some of these genetic variants were located within the introgressions of the Neanderthal's genome into the genomes of Eurasians.
Conclusion: A promising approach to prioritization of genetic markers of morning-evening preference would be to aim future candidate gene studies on examination of the strength of association of this trait with a set of loci harboring latitude-dependent adaptations.
Availability: The statistics on the analyzed loci are available from the authors upon request.
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Interference reconditioning after visual memory training in older adults

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Key words: aging, memory, interference, inhibition, computerized cognitive training

Motivation and Aim: Decrease in inhibitory control is considered as the basis for the age-related impairment of different cognitive functions [1]. It is known the phenomenon of retrieval-induced forgetting as the function of release inhibition. The analysis of cognitive training in the domains of executive function and working memory detected nonconvergent effects [2, 3]. The age-related changes in brain structure and function are not uniform, and mechanisms underlying the individual changes are yet not fully discovered. The aim of our study is to find interference changes due to memory training in older vs. young adults.
Methods and Algorithms: The inhibitory function in retrieval-induced forgetting (RIF) in older age (65 years, $n = 60$) (GR_O) and in young group (22 years, $n = 50$) (GR_Y) have been studied using memory training program. The computer-based platform was created to analyze different forms of memory including an assessment of proactive interference in visual memory retrieval [4].
Results: It was found that 74 % participants in GR_O performed the task no more than 20 times, 18 % continued training to 80 sessions, and 8 % – up to 180 times whereas only 15 % in GR_Y had memory training more than 10 sessions. In connection with this variability of training intensity, the mean scores of memory retrieval calculated for the first 18 sessions were compared to analyze age differences. The results revealed that the memory indices improved in GR_Y by 29 % compared to the baseline level, and in GR_O only by 13 % (while the values in GR_Y remained significantly higher than in GR_O, however, with greater variability of learning effectiveness for different sessions). RIF index was calculated as difference in the memory measure between final and initial probes in each test while training session. Age-associated difference of RIF dynamic was revealed, i. e. training induced comparable inhibitory efficiency in two groups due to reduced the inhibition-deficit in older adults.
Conclusion: The inhibition reconditioning in older group was found that pointing to the restructuring of the neural systems due to the visual memory training
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The potential impact of periodontitis on the pathogenesis of Parkinson's disease and cognitive deficits

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Key words: periodontitis, systemic inflammation, neuroinflammation, Parkinson's disease

Motivation and Aim: Previous studies have highlighted the importance of inflammatory reaction in the initiation and progression of neurodegenerative disorders. Periodontitis is one of the most prevalent chronic inflammatory diseases, which increased inflammatory burden that forms the basis for the proposed link to various systemic diseases such as cardiac diseases, diabetes, renal diseases, low birth weight as well as Alzheimer disease. However, although chronic inflammation is consistently associated with the pathophysiology of Parkinson's disease, so far, there is no direct evidence interlinking the detrimental effects of periodontitis on the pathogenesis of Parkinson's disease. In this regard, it is important to clarify the potential impact of periodontitis on the induction or development of Parkinson's disease.
Methods and Algorithms: Both *in vitro* and *in vivo* approaches were utilized to clarify the potential impact of periodontitis on the development of Parkinson's disease. For the *in vitro* study, both LUHMES cell and BV2 cell, representing the midbrain dopaminergic neuron and microglia, respectively, were exposed to periodontal pathogen-derived lipopolysaccharide (*P.g.* LPS) to demonstrate the cellular responses and the potential signaling pathway involved in the pathogenesis of Parkinson's disease induced by periodontitis. For the *in vivo* study, the pathological changes as well as the related neurochemical expressions in the substantia nigra and hippocampus were extensively examined by the use of two animal models: (1) directly infecting the periodontal tissue with periodontal pathogens, and (2) tightly encompassing the periodontal tissue with cotton threads.
Results: *In vitro* studies showed that although *P.g.* LPS did not affect the cell viability of both LUHMES and BV2 cells, it actually induced the oxidative stress and up-regulated the cytokine levels that may ultimately contribute to neuroinflammation. *In vivo* studies showed that decreased tyrosine hydroxylase, increased glial fibrillary acidic protein, and enhanced α-synuclein immuno-expressions were all detected in the SN of rats subjecdted to periodontitis.
Conclusion: As periodontitis significantly depressed TH expression and induced the expression of α-synuclein, one of the most important pathological features of Parkinson's disease, these evdiences thus support the close interaction between periodontitis and the development of Parkinson's disease.
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Previous mother's experience and early life stress: impact on aggression and cognition in adult mice

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Key words: previous mother's stress, early life stress, social behavior, aggression,cognition

Motivation and Aim: The early postnatal period is important for nervous system development and programming future behaviors. Both a decreased level of maternal care as well as stress in early life are risk factors for various psychiatric disorders. Here, we hypothesized that early life stress can lead to a change in the level of maternal care in adult female offspring. Thus, the objective this study is estimation effects of previous mother stress, early life stress or both on behavior in adult mice
Methods and Algorithms: The mothers of the mice in the current study were either allowed to raise their pups without exposure to stress (normal rearing condition, NC) or with maternal separation (3h/day, maternal separation, MS) on lactation days 2–14. Adult female F0 with a history in early life stress (mother's stress experience, ME) and undisturbed females (UM) were used for creating F1 offspring. We evaluated anxiety-like behavior, levels of exploratory, locomotor activity (open field test), aggression (resident-intruder test) and cognition (Morris water maze) in 4 groups of adult males F1 offspring (UM+NC, UM+MS, ME+NC, ME+MS).
Results: We found that males ME+MS group were more aggressive to compare other groups. Moreover, winner males ME+MS group demonstrated tendency to improve the memory. In contrast, winner males ME+NC group demonstrated learning impairment. We did not find any significant differences in the parameters of anxiety-like behavior, levels of exploratory and locomotor activity.
Conclusion: We found that the previous mother's stress experience in early life can have a pronounced contribution to adult offspring behavior than their own stress in early life. However, a combination of these conditions can even lead to some advantages, at least in some situations.
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Reconstruction of gene networks associated with autism and related to mTOR signaling pathway using ANDSystem

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Key words: autism spectrum disorder (ASD), ANDSystem, associative gene networks, mTOR pathway

Motivation and Aim: According to epidemiological studies it is known, that autism spectrum disorder (ASD) can affect near 1% of the world's population. The symptoms of ASD includes the presence of limited interests, problems in social communication, stereotyped and repetitive behavior. It is postulated that one of the mechanisms involved in ASD pathogenesis is disruption in mTOR signaling pathway [1]. The aim of this work was reconstruction and analysis of gene networks associated with ASD, related to the mTOR signaling pathway, by ANDSystem [2] in order to identify potential gene-targets that are promising for drug development studies.
Methods and Algorithms: The list of genes associated with ASD was created based on the information from Malacards database (https://www.malacards.org/) and ANDSystem [2]. Genes involved in mTOR signaling pathway were taken from KEGG database. Reconstruction and analysis of gene networks was performed using ANDSystem. Gene Ontology enrichment analysis was made by DAVID 6.8.
Results: Analysis of information from Malacards and ANDSystem revealed 452 genes associated with ASD. The reconstructed gene network contains 12147 interactions between these proteins and genes. There were 271 expression regulation relations in the reconstructed gene network. According to KEGG database 151 genes are involved in mTOR signaling pathway and it was found that eight (EIF4E, HRAS, IGF1, PRKCB, PTEN, TSC1, TSC2, WNT2) are related with ASD. Among them PTEN had the highest value of betweenness centrality (16214) and it was in the top 20 most central genes of ASD gene network. Using ANDSystem it was found that 82 genes/proteins from 151 involved in mTOR signaling pathway were directly linked with 193 genes/proteins associated with ASD. This 193 genes/proteins associated with ASD and interacting with mTOR signaling pathway were enriched with the following Gene Ontology biological processes: positive regulation of B cell proliferation, antigen processing and presentation, immune response, response to drug, protein localization to synapse.
Conclusion: The results obtained in this work suggest that genes/proteins from the mTOR signaling pathway have central role in the gene network associated with ASD. The mTOR signaling pathway is highly connected to ASD gene network. Among them PTEN could be the most perspective for further investigation as potential drug target.
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The psychological and EEG effects of 5-HTTLPR gene polymorphism among people from different ethnic groups in Siberia

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Key words: 5-HTTLPR, EEG, Ethnic differences

Motivation and Aim: Serotonin transporter is one of the most widely investigated genetic markers of individual variation in serotonergic function. The promoter region of the serotonin transporter gene (5-HTTLPR) contains long (L) and short (S) variants. The 5-HTTLPR allele polymorphism of serotonin transporter (5-HTT) is associated with inclination to anxiety-related psychopathology, including depression. However, the effect of 5-HTTLPR to the risk of depression and anxiety disorder is highly variable in different ethnic groups. According to the most of reports, an S- allele has been found to increase the risk of mental health problems in the Caucasoids, but also the same allele has an opposite effect or no effect on the different Mongoloid groups. This study comparatively investigated the effects of 5-HTTLPR polymorphism on psychological measures, EEG current source density, connectivity, and topological properties of resting state networks, and the ERSP indexes under recognition of emotional-related stimuli in the groups of Caucasoid Russians (210 persons) and Siberian Mongoloids – Tuvinians, Yakuts and Evenks (183 persons).

Methods: The trait anxiety level, the neuroticism scores and the emotional intelligence scores were measured in all participants by means of different self-report inventories. EEG was recorded in the Russians by means of the 128-channel and in Mongoloids by means of 64-channel Brain Products amplifier, Germany. EEG was recorded during the resting state, during execution of experimental tasks, which were related with recognition of facial and speech emotionality.

Results: SS homozygotes showed higher scores of anxiety and neuroticism and lower scores of the emotional intelligence in comparison with the L-allele carriers among all ethnic groups. The ERSP indexes of theta synchronization in the people with L-genotype showed the amplitude difference for recognition of stimuli with different emotional modalities, whereas there were not detected such differences in the SS homozygotes for all ethnic groups. As compared to L-carriers, S homozygotes from the Caucasoid group showed lower current source density and connectivity in most frequency bands in areas overlapping with the default mode and emotion regulation regions. However, the opposite effect of the S allele was revealed in the Mongoloid group, i.e. the Mongoloid S homozygotes showed higher current source density and connectivity in the same brain areas and frequency bands in comparison with the Mongoloid L-carriers. In addition, the associations between resting-state EEG and these psychological measures were different among ethnic groups.

Conclusion: The effect of 5-HTTLPR polymorphism on EEG and on association of resting-state EEG networks with psychometric measures looks unstable and depends on many additional climatic and cultural parameters.

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Cystatin C as regulator of autophagy in brain of transgenic mice with model of Parkinson's disease

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Key words: Cystatin C, autophagy, transgenic model of Parkinson's disease

Motivation and Aim: Autophagy was shown to be suppressed in striatum of transgenic mice with model of Parkinson's disease [1]. Cystatin C is one of the potent regulators of autophagy [2]. Changes in the expression and secretion of Cystatin C in the brain have been shown in amyotrophic lateral sclerosis, Alzheimer's and Parkinson's diseases and in some animal models of neurodegeneration, demonstrating protective role of Cystatin C [3]. It was suggested that Cystatin C plays the primary role in amyloidogenesis and perspective as treatment of neurodegenerative diseases. Cystatin C colocalizes with amyloid beta-protein in brain in Alzhemer's disease. Controlled expression of a cystatin C-peptide was suggested as a new approach to therapy for Alzheimer's disease. In Parkinson's disease serum Cystatin C levels can predict disease severity and cognitive dysfunction, although the exact role of Cystatin C remains unclear. The aim: to evaluate expression of Cystatin C in transgenic mice with model of Parkinson' disease in early pathological state of disease (5 months) and evaluate results as related to mechanism of development of autophagy.
Methods and Algorithms: 5-month-old male mice of B6.Cg-Tg(Prnp-SNCA*A53T)23Mkle/J) (further – B6.Cg-Tg) and control C57Bl/6J strain were used. Total RNA was purified from mouse brain areas (striatum, amygdaloid complex, hypothalamus, hippocampus) using RNeasy Plus mini kit (Qiagen). qPCR was performed in a CFX96 Real-Time PCR Detection System (Bio-Rad, USA) using HS-qPCR Mix SYBR Green (2x) (Biolabmix, Russia), 200 nM real-time PCR primers (Forward Primer (5′→3′) AGGAGGCAGATGCCAATGAG; Reverse Primer (5′→3′) GGGCTGGTCATGGAAAGGA), 5 µl template (1:50 diluted cDNA).
Results: Cystatin C (*Cst3*) gene expression analysis in *striatum and*, especially in *amygdaloid complex*, in mice with transgenic model of Parkinson's disease (5 months) revealed statistically significant ($p = 0.0168$) decrease vs control; there was a correlation between the *Cst3* expression and marker of autophagy *LC32* level (immunohistochemistry). Cystatin C concentration in serum (ELISA) of transgenic mice was not changed *vs* control.
Conclusion: The data obtained confirms that *Cst3* expression in striatum correlates with autophagy. Cystatin C can play a protective role in multiple neurodegenerative disorders, including Parkinson's and Alzheimer's diseases.
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Disruption of D2R × DISC1 binding prevents conditioned place preference induced by morphine in mice

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Key words: conditioned place preference, morphine, dopamine receptor, DISC1

Motivation and Aim: Dopaminergic system plays an important role in the development of drug dependence. DISC1 (Disrupted-In-Schizophrenia-1) is a scaffold protein that interacts with numerous proteins in various cellular compartments. DISC1 is involved in the regulation of functions of dopaminergic system in brain [1]. Recently, direct binding of DISC1 to a type 2 dopamine receptor (D2R) has been shown, leading to inhibition of receptor internalization, which resulted in hyperactivation of dopaminergic system [2]. A peptide analogue of D2R binding site was synthesized, and a conjugate of this peptide with a peptide fragment from immunodeficiency virus envelope (TAT-D2pep) competitively inhibit D2 receptor interaction with DISC1 when administered systemically [2]. The aim of our work was to probe the effect of TAT-D2pep on the formation of conditioned place preference (CPP) in mice.
Methods and Algorithms: CPP to morphine was produced in C57BL/6J mice with an unbiased CPP procedure employing a three-compartment apparatus. The mice were divided into 4 groups. During the conditioning session, control animals received injections of saline (Sal), whereas experimental groups were treated by morphine/Sal, TAT-D2pep/Sal or TAT-D2pep injected in 15 minutes before morphine/Sal.
Results: Mice treated by TAT-D2pep/Sal did not differ from the control group in CPP, showing no preference to the compartment associated with TAT-D2pep, i. e. the peptide did not affect rewarding processes in mice. Mice treated by morphine/Sal spent significantly more time in the compartment associated with morphine, supporting the formation of CPP. Administration of morphine after the extinction session, recovered CPP in this experimental group of mice. Injection of TAT-D2pep prior to the administration of morphine, significantly reduced the time spent in morphine-associated compartment than in animals receiving only morphine and was not differ from the control group.
Conclusion: The peptide, which prevents the binding of D2R to the DISC1 protein, disrupted the CPP formation, induced by morphine. These data suggest the involvement of DISC1 in the development of opiate dependence.

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Neuroprotective effects of ceftriaxone: insights from *in vitro* and *in vivo* models

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Key words: cognitive deficits, neuroinflammation, mice, rats, Parkinson's disease, Alzheimer's disease, cortical neurons

Motivation and Aim: Drug repurposing appeared to be quite effective strategy in psychopharmacology. Ceftriaxone (CEF) is a safe and multipotent agent that has been used for decades as an antimicrobial drug. Recently the data were obtained on its neuroprotective properties. We obtained promising results on its neuroprotective properties including the restoration of cognitive deficits in MPTP-induced rat model of Parkinson's disease. The aim of this study was to determine the potential effects of CEF to restore cognitive deficits in animal models of Alzheimer's disease (AD) as well as to reveal neuronal mechanisms in the effects.
Methods and Algorithms: Primary culture of rat cortical neurons was used to evaluate cell survival against H2O2 (50 μM) in MTT test after CEF treatment (100 μM, 1x, 5 days prior MTT test). Western-blotting was applied to estimate molecular changes. Mice of C57Bl/6J strain injected bilaterally i.c.v. with amyloid-beta fragment 25-35 were used as pharmacological AD model while rats of OXYS strain were used as a genetic model of sporadic AD. To evaluate the effects of CEF, the animals of experimental groups were treated with the drug (100 mg/kg/day, i.p., 36 days) and then underwent behavioral testing for cognitive function and their brains were assessed with Nissl staining and immunohistochemical analysis.
Results: CEF treatment exhibited beneficial effects on some of impaired cognitive features in OXYS rats and mice with deficits induced by amyloid-beta. Neuromorphologically, CEF increased the density of pyramidal neurons in the hippocampal CA1 area, decreased the number of degenerating neurons and edema of brain tissue in OXYS rats. It also decreased amyloid accumulation in mice. CEF significantly increased cell survival of cortical neurons *in vitro*. This effect was associated with a decrease in pAkt and pERK levels.
Conclusion: The results suggest CEF as a promising pharmacological tool for the prevention of cognitive decline at neurodegenerative disorders and gave new insights into mechanisms of its neuroprotective effects.
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Effect of ceftriaxone on cognitive deficits caused by amyloid-beta neurotoxicity in mice

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Key words: Alzheimer's disease, ceftriaxone, Aß 25-35, Barnes test

Motivation and Aim: At the moment, there are no effective therapies that can stop or reverse the course of a serious and widely spread neurodegenerative disorder, Alzheimer's disease (AD). One of frequently used animal models of AD is based on the injection of amyloid beta (Aß) or its fragments into the brain that causes neurodegenerative changes and AD-like cognitive deficits. Recently, an antibiotic ceftriaxone that possesses neuroprotective properties was found to correct cognitive deficits in a genetic rat model of accelerated senescence and sporadic AD (OXYS rat strain) has been revealed. [1] The aim of this study was to study the effect of ceftriaxone on cognitive deficits caused by the amyloid-beta neurotoxicity in mice.
Methods and Algorithms: In the experiment, were used sexually mature male mice C57BL/6J. Animals were divided into 4 groups. Groups 1 and 2 received sterile water, and groups 3 and 4 received Aß fragment 25-35 (Aß 25-35) into the lateral ventricles of the brain. Groups 2 and 4 were chronically injected with ceftriaxone (100 mg/kg, i.p., 5 weeks) while groups 1 and 3 were given injections of saline. Open field test, Barnes test and T-maze were performed to assess the behavioral effects of ceftriaxone in mice.
Results: Mice injected with Aß 25-35 had a significant decrease in motor and exploratory activity in the open field test two weeks after the injections, whereas in the later these indicators recovered. Ceftriaxone had a positive effect on a number of parameters in the Barnes test. A significant decrease in the latency to find a target hole in the 4th session of the first day of training (short-term spatial memory index) and an increase in the percentage of goal hole nosepokes on the test day (long-term spatial memory index) were observed in mice of the 4th group. Ceftriaxone also significantly augmented percentage of correct choices (working memory index) in mice of the 4th group in the T-maze test.
Conclusion: The central injection of the fragment Aß 25-35 leads to a disruption in the learning ability and short-term spatial memory in the Barnes test. Chronic administration of ceftriaxone in mice injected with fragment Aß 25-35 caused an improvement in cognitive performance in the Barnes test. Moreover, ceftriaxone administration influenced various indicators in other behavioral tests. Those alterations are apparently related to the neuroprotective properties of ceftriaxone, based on the restoration of glutamate transport in astrocytes and the reduction of excitotoxicity, which plays an important role in the pathogenesis of AD.
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The effects of 5-HTTLPR gene polymorphism on the behavioral reactions under emotional speech recognition among Mongolians

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Key words: 5-HTTLPR, Speech Recognition task, Emotional intelligent

Motivation and Aim: 5-HTTLPR serotonin transporter gene polymorphism is associated with individual features in regulation of human emotional behavior. The expression of this gene was detected in the limbic structures of brain, such as amygdala. According to the most of report, SS genotype of this polymorphism is usually associated with lower level of emotional intelligent in comparison with LL and LS genotypes. However, such effects can be modulated by many other factors, including gender, age and cultural properties of people. This study comparatively investigated the effects of 5-HTTLPR polymorphism on psychological measures and behavioral reactions under recognition of emotional written sentences in the groups of Caucasoid Russians (154 persons) from Novosibirsk and Mongolian students from Khovd (54 persons).
Methods: The trait anxiety level, the neuroticism scores and the emotional intelligence scores were measured in all participants by means of different self-report inventories. Under experiments, the participants executed the error recognition task in Russian or Mongolian. 200 sentences were selected for the experiment. Half of the sentence list for each language contained a syntax error. Correct and incorrect samples were presented randomly with inter-trial interval varying between 4 and 7 s. The subjects were instructed to judge whether a presented sample contains an error by pressing one of two buttons by dominant hand. All sentences were related with one of emotional conditions. 20 % of sentences presented non-emotional description of unanimated objects, 20 % of sentences described the anxiety level of participant himself, 20 % of them described the anxiety level of some other persons, 20 % of sentences described the aggression of participant himself and 20 % described the aggression of some other persons. The participants were not instructed about emotional relation of sentences before the procedure. The speed of reaction and the quality of task execution separately for each emotional condition were used as the behavioral measures.
Results: Inter-ethnic differences were detected among the Russian and Mongolian groups by comparison of behavioral reactions on syntactically correct and incorrect sentences that reflects a gramma specificity of Mongolian language. Also, the behavioral measures under recognition of sentences with aggression had some ethnic specificity. SS homozygotes showed higher scores of anxiety and neuroticism and lower scores of the emotional intelligence in comparison with the L-allele carriers among the Russian, but not for Mongolian group. In addition, the associations between 5-HTTLPR genotype, behavioral reactions on the emotionally differing sentences and the psychological measures were different among ethnic groups.
Conclusion: The effect of 5-HTTLPR polymorphism on human emotional behavior depends on the cultural parameters of participants.
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Impact of the intellectual environment of professional activity on resting state EEG in older adults

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Key words: resting state EEG, old age, gender, mental activity

Motivation and Aim: Although there are clear common principles that can be demonstrated in cognitive aging, enormous variability exists across individuals. A question of great interest is what accounts for this variability. Among other factors inter-individual variability is attributable to involvement in mental activity. The purpose of this study is to outline the changes resting state EEG in aged men and women associated with difference in intellectual environment of their professional activity.
Methods and Algorithms: Elderly (age 63.8+0.5) scientists (N = 52, SA) and people unrelated to professional scientific activity (N = 63, NSA) participated in the study. All subjects were employed full time. EEG was recorded from 26 symmetrical regions of the hemispheres in a states with closed and with open eyes. Power spectral density was calculated in delta, theta, alpha 1, 2, 3, beta 1, 2 and gamma frequency ranges. The bandwidths for the frequency bands were defined using individual alpha peak frequency as the anchor point. The mean power spectral density values were calculated for frontal (Fp1/Fp2, AF3/AF4, F7/F8, F5/F6, F3/F4, F1/F2), central (FC3/FC4, FC1/FC2, C3/C4, C1/C2, CP3/CP4, CP1/CP2), central-temporal (FT7/FT8, FC5/FC6, T7/T8, C5/C6, TP7/TP8, CP5/CP6) and parietal-occipital (P7/P8, P5/P6, P3/P4, P1/P2, PO7/PO8, PO5/PO6, PO3/PO4, O1/O2/) cortical regions separately for the right and the left hemispheres.
Results: In condition with closed eyes, ANOVA revealed significant gender × frequency band × region × group (SA, NSA) interaction. Testing of interaction demonstrated effects in alpha 2, 3, rhythms power density, characterized by opposite changes of antero-posterior spectral power gradients in SA and NSA groups of men and women. There was no difference between SF and NSA groups in frontal power density. Among women members of ND group had lower posterior power than those of NND group. Conversely, among men, members of ND had greater posterior spectral power in comparison with NND. In eyes open condition, significant asymmetry due to higher power values in right in comparison with left hemisphere in frontal and temporal regions was found in SA group. Asymmetry of power values was not revealed in NSA.
Conclusion: This result of the study confirmed dividing the mentally healthy older population into two subgroups according to levels of intellectual loads during the course of professional activity: significant differences exist in terms of resting state antero-posterior network organization and in hemispheric asymmetry measures.
Acknowledgements: Supported by the RFBR (No. 17-46-540705).

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Association of *PIP5K2A* gene polymorphisms with the effectiveness of the therapy of current depressive episode

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Key words: PIP5K2A kinase, depressive disorders, genotyping, polymorphic variants

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. Modern studies indicate the involvement of PIP5K2A kinase in the pathogenesis of depressive disorders and schizophrenia spectrum disorders. 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. 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 306 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 to assess 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 micro technique. 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 a 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 a 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 PIP5K2A kinases in the mechanisms underlying the therapeutic effect of antidepressants.
Acknowledgements: Supported by the RFBR No. 17-29-0205.

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MicroRNA-210 mediates the hippocampal neurogenesis following traumatic brain injury

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Key words: Mir-210, hippocampus, neurogenesis, traumatic brain injury

Motivation and Aim: Adult neurogenesis is a crucial process for brain tissue repair and remodeling after traumatic brain injury (TBI). MiR-210, a unique and pleiotropic microRNA, has been known to be upregulated in various tissues under hypoxic condition. This study is aimed to investigate the role of miR-210 in TBI-induced neurogenesis and the implicated mechanism.
Methods and Algorithms: TBI was induced by weight-drop device. Immunofluorescence staining of BrdU- and DCX-labeled neurons were used to qualify neurogenesis among different groups after TBI. The expression of miR-210 was evaluated by real-time PCR and the expression of ERK/MEK/Raf cascade was detected by Western blot.
Results: In this study, we found the level of MiR-210 significantly increased within 1 hour after TBI and reached a peak 4 hours after TBI. Administration of a shRNA against miR-210 not only reversed the TBI-associated upregulation of miR-210, but also attenuated the TBI-induced neurogenesis. The upregulation of miR-210 after TBI was found to be mediated by HIF-1α and regulated the phosphorylation of ERK/MEK/Raf cascade, a signal pathway also involved in adult neurogenesis. TBI triggered an approximate 3.0–3.5 fold stimulation in ERK/MEK/Raf phosphorylation, and the administration of miR-210 shRNA effectively dampened the TBI-induced activation of ERK/MEK/Raf cascade.
Conclusions: These results strongly suggest that the increase in miR-210, conferred by TBI, is mediated by HIF-1a expression and might have led to the stimulation of ERK/MEK/Raf cascade, which in turn promotes the TBI-induced neurogenesis.

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Using drift diffusion model to understand age-related differences in inhibitory control

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Key words: emotional inhibition, emotional stop signal paradigm, drift-diffusion model, ICA, fMRI

Many situations require one to inhibit the impulse to react to others' emotional facial displays. Considerable evidence, however, points to age-related changes in response inhibition in older adults. In addition, evidence also shows more automatic regulation of affect in older compared to younger adults. How these two opposing processes operate in young and older adults remains unclear. In this study, a drift diffusion model was used to each participant's behavioral data to extract components of psychological processing, including measures of caution, motor execution time, and stimulus processing speed. The individual differences in the resulting components were further examined in relation to fMRI activation to evaluate the underlying neural correlates and the emotional modulation in young and older adults. Thirty-two young and 32 older normal adults underwent an emotional stop signal paradigm (ESSP) in an fMRI experiment with disgusted and neutral emotional faces. Participants were instructed to make a target response (Go) as quickly as possible to face stimuli unless a red border appeared (between 40 to 400 ms of face onset), in which case they were to withhold their response (Stop). Young adults made more Stop than Go errors to neutral faces. Disgusted faces increased Stop false alarms, decreased Go hits, and also reduced reaction times compared to neutral faces. Older adults made more Go than Stop errors to neutral faces. Disgusted faces increased Stop false alarms, increased Go Hits, and also reduced reaction times compared to neutral faces. Two-sample t-tests are used to delineate the role of aging in emotional inhibition tasks. The results show that older adults tend to engage more neural circuits than young adults including striatum and hippocampus regions. Younger adults show more focal activations in right inferior frontal cortex, inferior parietal lobule and postcentral gyrus for inhibition contrasts. Using drift-diffusion modeling principles, our findings suggest whereas negative affect increases the rate of evidence accumulation for target and stop feature decisions in younger adults, negative affect lowers the decision criterion in older adults.

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International expertise on education programs and Neuronet inititaive

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Key words: bioinformatics, neurobiology, education, Neuronet initiative, international science exchanges

National technological initiatives assume development of novel educational programs on modern perspective technologies – neurobiology, neuroinformatics, bioinformatics, analysis of big data in genomics. The BGRS (Bioinformatics of Genome Regulation and Structure) biannual conference series in Novosibirsk became a kernel of international cooperation and student exchange programs, presentation of novel software in interdisciplinary fields of biology, informatics and Life Sciences overall.

National "Neuronet" initiative in Russia [1, 2] presents novel type of strategic science and commercial projects establishing leading positions in world research. Several regional Neuronet-centers in the format of non-commercial partnerships will be created in Russia. Among them, the Pacific Center in partnership with the Far Eastern Federal University, the Volga Region Center in partnership with the Samara State Medical University and the company "BiTronics", the Novosibirsk Center in partnership with the Research Institute of Physiology and Basic Medicine of SB RAS, as well as the Neuronet-center "St. Petersburg" in partnership with the company "MDG-Innovation". In addition, the centers will be created in partnership with the Moscow Institute of Physics and Technology (MIPT) and the Skolkovo Institute of Science and Technology (SkTech). The Center in St. Petersburg will specialize in projects related to artificial intelligence. Far Eastern University is interested in developing and promoting technologies of augmented and virtual reality. Specific interest of MIPT Center will also be artificial intelligence, and the Novosibirsk Neuronet-Center will focus on pharmaceuticals and medicine.

The international seminar on the discussion of scientific perspectives in the field of neurotechnologies will be held in the frames First Russian-Chinese Workshop on Bioinformatics and System Biology in the form of a round table with open discussion. It will present the development of methodological recommendations for the selection and involvement of the expert community of the scientific and technical sphere for the discussion and evaluation of roadmap projects of the National Technological Initiative in Russia. Foreign experts will share their experience in international education programs on bioinformatics and National education initiatives.

The authors will present their vision of the existing projects of road maps of the National Technological Initiative in the field of neurotechnologies, fundamental medicine and bioinformatics in the format of open discussion.

Russian and international experts in the field of bioinformatics and neurobiology will include several science groups from Europe and Asia.

Three delegations from largest Chinese Universities (Shanghai Jiao Tong University, Zhejiang University and Huazhong Agricultural University) will take part in the scientific seminar: Prof. Xiaodong Zhao, Prof Ming Chen, Dr Yan Li, Prof. Hong-Yu Zhang. The

neurobiology experts from Academia Sinica, Taiwan, will share their expertise – Profs Arthur C. Tsai, Hung-Ming Chang, Ya-Ling Yang.

The European group will be presented by Spain, the Netherlands, Italy, Germany, Finland, Austria and Norway. The participants are: Dr Rubén V. Rial, University of the Balearic Islands, Palma de Mallorca; Prof. Hans V. Westerhoff, and Dr. Matteo Barberis, University of Amsterdam, Amsterdam, Holland; Prof. Gianluca Tell, University of Udine, Italy; Dr. Olga Krebs, Heidelberg Institute for Theoretical Research, Heidelberg, Germany; Prof. Juha Kantanen, Institute of Natural Resources of Finland, Jokiainen, Finland; Dr. Fyodor Kondrashov, Institute of Science and Technology, Klosterneuburg, Austria; Dr. Maxim Zakharsev, Norwegian University of Natural Sciences, Oslo.

The invited speakers - medical doctors and bioinformaticians from Russia will continue the discussion about national programs in neurobiology: Irina M. Larina, Institute of Mathematical Problems of Biology RAS (IMPB RAS), Alexey A. Lagunin, Russian National Research Medical University named after N.I.Pirogov, Moscow; Maria G. Samsonova, Saint-Petersburg Polytechnic University, Saint-Petersburg.

The seminar presentations on national international education programs will be started by Prof. Ralf Hofestädt, Bielefeld University, Germany. He will discuss German-Chinese network on bioinformatics and education in bioinformatics. Dr. Marko Đorđević, Belgrade University, Serbia, will tell about Integrating computational systems biology and bioinformatics in research and education. Drs. Tatiana Tatarinova and Cecile Ben (University of La Verne, USA, and University of Toulouse, France) will give educational program review “Bioinformatics: science of a toolbox?”

Bioinformatics, as an interdisciplinary field, is a case example for analysis of science history perspectives. Thus, Prof. M.Chen, Zhejiang University, Hangzhou, China will present professional initiatives in bioinformatics in China. There are more than 30 bioinformatics related societies/organizations are set up to promote the bioinformatics development. Scientists from European countries are attracted to work in China by the improved research and funding environment. Thus, International cooperation research institutes/centers are established, e.g. the Max Planck–Chinese Academy of Science Partners Institute in Computational Biology in Shanghai, which employs a number of European scientists and plays key roles in facilitating international collaborations [3].

During the seminar the analytical materials on increasing the effectiveness of the implementation of the activities of the roadmap projects of the National Technological Initiative will be discussed. We aim develop methodological recommendations, including on the use of educational process starting from the example of the Department of Medicine and Psychology and the Humanitarian Institute of Novosibirsk State University.

Acknowledgements: The participation of the incited speakers at the BGRS conference and the workshop has been supported by Russian Ministry of Science project 28.12487.2018/12.1.

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Author index

Компания Huawei является ведущим мировым поставщиком ИКТ-решений. Благодаря установлению взаимовыгодных отношений с нашими партнерами и заказчиками компании Huawei удалось добиться существенных преимуществ в сфере операторских сетей, корпоративного и потребительского бизнеса, а также в сфере облачных технологий. Мы стремимся создавать максимальные преимущества для операторов связи, предприятий и потребителей путем разработки конкурентных ИКТ-решений и услуг. Оборудование и решения Huawei используются в более чем 170 странах мира. Компания обслуживает более трети населения земного шара.

Имея богатый опыт и технические знания в области НИОКР, Huawei придерживается стратегии тесного сотрудничества и интеграции с корпоративными заказчиками и предоставляет им широкий спектр высокоэффективных клиентоориентированных ИКТ-решений и услуг, на базе глубокого понимания их потребностей. Согласно этой стратегии Huawei предлагает широкий выбор передовых ИКТ-решений в сфере государственного управления, общественного сектора, финансов, транспорта, электроэнергетики, крупных предприятий, а также малых и средних предприятий (SME). Эти решения охватывают корпоративные сети, универсальные системы связи и взаимодействия (UC&C), системы облачных вычислений и центры данных, системы корпоративной беспроводной связи, сетевого электропитания, а также инфраструктурные услуги.

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Huawei is a leading global ICT solutions provider. Through our dedication to customer-centric innovation and strong partnerships, we have established end-to-end capabilities and strengths across the carrier networks, enterprise, consumer, and cloud computing fields. We are committed to creating maximum value for telecom carriers, enterprises and consumers by providing competitive ICT solutions and services. Our products and solutions have been deployed in over 170 countries, serving more than one third of the world's population.

By leveraging our strong R&D capabilities and comprehensive technical expertise, Huawei's strategy in the enterprise domain focuses on close cooperation and integration with partners to deliver a wide range of highly efficient customer-centric ICT solutions and services that are based on a deep understanding of customer needs. In line with our strategy, we offer a broad portfolio of innovative ICT solutions that cater to global vertical industry and enterprise customers across government and public sector, finance, transportation, energy, large enterprises and small and midsize enterprises (SMEs). Our portfolio covers enterprise networking, unified communications & collaboration (UC&C), cloud computing & data center, enterprise wireless, network energy and infrastructure services.

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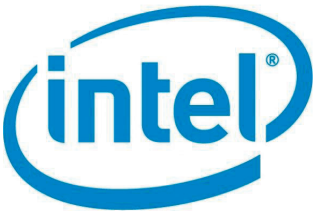

Корпорация Intel

Корпорация Intel была основана в 1968 году Робертом Нойсом и Гордоном Муром. На протяжении 50 лет Intel создает инновационные технологии, открывающие новые возможности для людей.

Корпорация Intel является мировым лидером в области микроэлектроники и информационных технологий. Intel создает технологии для умного мира эпохи больших данных. Основное внимание корпорация уделяет созданию интеллектуальных решений для умного мира, от устройств Интернета вещей и пользовательских ПК до коммуникационной инфраструктуры, технологий для центров обработки данных и суперкомпьютеров.

Штаб-квартира корпорации расположена в г. Санта-Клара, шт. Калифорния. Общий штат Intel насчитывает более 100 тыс. сотрудников в более, чем 60 странах по всему миру. Главным исполнительным директором корпорации является Роберт Свон (Robert Swan).

Intel в России

Первое представительство Intel в России было открыто в 1991 году в Москве. Сегодня в российских офисах Intel в Москве и Нижнем Новгороде работают более 800 человек.

В московском офисе компании представлены отделы маркетинга и развития бизнеса, группы по разработке программного обеспечения, юридический отдел.

В НИОКР центре Intel в Нижнем Новгороде создаются новые и инновационные продукты для разработки ПО. Сегодня он является одним из крупнейших центров исследований и разработок Intel в Европе. Более **700 специалистов и инженеров** разрабатывают программные инструменты и приложения для архитектур Intel. В Нижнем Новгороде также размещаются различные группы поддержки бизнеса (например, административно-хозяйственная часть, финансовый отдел, отдел ИТ, отдел кадров).

Центр исследований и разработок Intel в Нижнем Новгороде

Нижегородский офис Intel был является центром экспертизы корпорации в области высокопроизводительных вычислений, разработки программного обеспечения в области численных методов и беспроводной связи.

✉ MP Biomedicals
(ООО «МПБА диагностика»)
Адрес: 109147, г. Москва, ул. Марксистская, д. 3,
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Компания ООО «МПБА диагностика» является дочерней компанией MP Biomedicals, ранее известной как ICN Biomedicals, основанной в 1959 году, признанного лидера в области производства широкого спектра химических реактивов, оборудования для пробоподготовки (система для гомогенизации FastPrep) и наборов реагентов. Каталог продукции компании MP Biomedicals включает более 55000 наименований высококачественных продуктов для проведения биохимических исследований, фармацевтического и биотехнологического производства, для различных отраслей иммунологии и генетики.

ООО «Рош Диагностика Рус» – официальный импортер продукции Roche в России и лицензиат компании F.Hoffmann–La Roche Ltd.

Roche Sequencing Solutions, подразделение Roche, ориентированное на решения для NGS, а в частности на пробоподготовку к NGS, предлагает:

-**Наборы KAPA Biosystems для приготовления библиотек ДНК** (включают баркодированные адаптеры, частицы для очистки, наборы для оценки концентраций ДНК и библиотек методом ПЦР в реальном времени).

-**Наборы для направленного отбора генов перед NGS:**

NimbleGen SeqCap EZ –гибридизационное обогащение панелей генов, экзомов, транскриптомов и метиломов;

HEAT-seq - амплификационное обогащение панелей генов, в том числе и панелей онкогенов;

AVENIO –гибридизационное обогащение панелей онкогенов из внеклеточной опухолевой ДНК и анализ данных.

ООО «Рош Диагностика Рус» предлагает комплексные решения, включающие в себя не только оборудование и реагенты, но и технический сервис, обучение персонала и постоянную методическую поддержку.

Unlock the Potential of Every Sample

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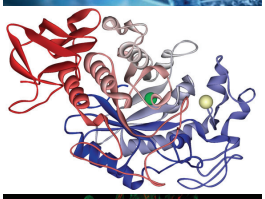
ООО «БиоЛайн» является официальным дистрибьютором компаний **BD Biosciences, Leica Microsystems, PerkinElmer, BioTek,** ведущих мировых производителей приборов и реагентов для биомедицинских исследований.

Благодаря уникальному портфолио продукции и опыту наших специалистов мы выполняем поставки и внедрение комплексных решений для разнообразных задач в области молекулярной и клеточной биологии.

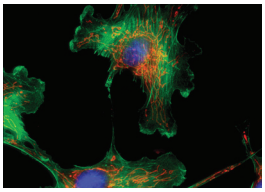
Молекулярно-генетические исследования

- Системы для выделения и молекулярного анализа одиночных клеток Becton Dickinson
- Станции для выделения ДНК, оборудование PerkinElmer для подготовки и контроля библиотек для NGS
- Наборы Nextflex для подготовки библиотек NGS PerkinElmer: полногеномное и таргетное секвенирование, транскриптомика, эпигенетика, метагеномика



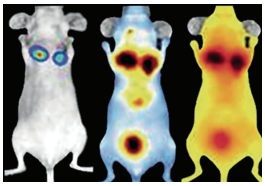
Протеомные исследования

- Передовые оптические технологии компании BioTek Instruments для биохимических исследований, идентификации и количественной оценки аналитов, исследования взаимодействия биомолекул
- Реагенты и расходные материалы PerkinElmer для протеомных исследований



Клеточные исследования

- Системы для проточной цитометрии и сортировки клеток компании BD Biosciences
- Оптическая визуализация клеток для моделирования процессов в клеточных культурах и на 3D сфероидах: решения PerkinElmer и BioTek Instruments
- Системы для конфокальной микроскопии Leica Microsystems



Исследования на животных

- Приборы для оптической визуализации ***in vivo*** Spectrum и Lumina, системы для КТ и ПЭТ компании PerkinElmer
- Оборудование для исследований на животных Leica Biosystems

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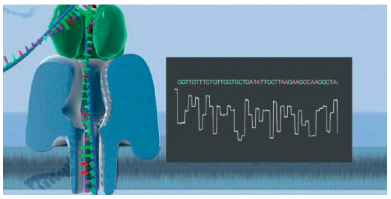
Компания Диаэм – крупнейший поставщик современного лабораторного оборудования на Российском рынке. Каталог компании насчитывает более 500 000 наименований приборов, реагентов и расходных материалов для медицинских и научно-исследовательских лабораторий.
В каталоге компании представлена продукция ведущих мировых производителей, как: Abcam, Applied Biosystems, Binder, Bio-Rad, Corning, Eppendorf, Illumina, Ion Torrent, Lexogen, Oxford Nanopore Technologies, Panasonic (Sanyo), Sage Sciences, Sigma-Aldrich, Thermo Fisher Scientific, Qiagen:

- Наборы для подготовки библиотек, для высокопроизводительного секвенирования NGS, для исследовательских работ и, в онкологии, репродуктивной медицине, в изучении наследственных заболеваний, реагенты и наборы для капиллярного секвенирования.
- Секвенаторы капиллярные и высокопроизводительные NGS, оборудование для анализа качества НК для NGS, роботизированные станции для подготовки библиотек и секвенирования.
- Все для ПЦР, реагенты,наборы, пластик, амплификаторы.
- Нанопоровые секвенаторы Oxford Nanopore Technologies, наборы для секвенирования ДНК и РНК.


Секвенирование теперь доступно каждому!

Диаэм сегодня представляет продукцию Oxford Nanopore Technologies – это секвенаторы третьего поколения – MinION, GridION, PromethION.
Технология секвенирования Oxford Nanopore Technologies позволяет делать прямое прочтение цепей ДНК или РНК в режиме онлайн, длина рида ограничена только длиной фрагмента, а портативность оборудования и быстрая подготовка библиотек дает возможность секвенировать даже в полевых условиях с минимальными требованиями к генетической лаборатории. С Oxford Nanopore Technologies секвенировать теперь может каждый, даже тот, кто ранее и не задумывался о секвенировании - это просто и доступно.
Секвенирование третьего поколения не заменяет и не отменяет применение капиллярных секвенаторов по Сэнгеру или платформ NGS второго поколения, наоборот, сочетание трех поколений генетического анализа открывает новые возможности получения ранее неизвестных данных.
Специалисты Диаэм прошли обучение в Oxford Nanopore Technologies, осуществляют профессиональное консультирование и техническую поддержку, помогут спланировать эксперимент и подобрать необходимые наборы реагентов для решения конкретной задачи независимо от бюджета лаборатории.
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Компания АЛЬБИОГЕН — официальный дистрибьютор illumina и Lucigen

Компания ООО «АЛЬБИОГЕН» с 2015 года является эксклюзивным (единственным) официальным торговым представителем и дистрибьютором компании illumina на территории Российской Федерации, Республики Беларусь, Республики Казахстан и Республики Узбекистан.

Нашей задачей является обеспечение полного доступа клиентов к передовым технологиям и сервисам illumina, включая современные системы NGS и анализа ДНК-биочипов, программное обеспечение для биоинформатики и весь спектр реактивов.

ООО «АЛЬБИОГЕН» предоставляет полный комплекс услуг, связанных с продажей, технической поддержкой и сервисным (гарантийным и постгарантийным) обслуживанием продукции компании Illumina, а также обучением пользователей работе на данном оборудовании.

Инновационная и стремительно развивающаяся компания illumina Inc., являющаяся мировым лидером в области геномных технологий, заключила соглашение с компанией АЛЬБИОГЕН, специализирующейся на поставках оборудования и расходных материалов для секвенирования нового поколения (NGS) и анализа на ДНК-биочипах.

Новейшие продукты компании illumina, создаваемые совместно с ведущими мировыми учеными, позволяют изучать геном на очень глубоком уровне и дают возможность для новаторских достижений в науке, медицине, сельском хозяйстве и потребительской геномике. Более 90% научных статей, связанных с технологиями секвенирования нового поколения, сделаны при помощи оборудования Illumina.

Сотрудничество с компанией АЛЬБИОГЕН направлено на то, чтобы сделать технологии NGS и анализа ДНК-биочипов более доступными на территории Российской Федерации и в странах СНГ.

Компания АЛЬБИОГЕН использует свой обширный опыт в области продаж и продвижения продукции, знания передовых технологий и сеть региональных представителей для обеспечения быстрой, эффективной и бесперебойной работы лабораторий клиентов illumina.

Компания АЛЬБИОГЕН также является официальным дистрибьютором компании Lucigen, основными продуктами которой являются ферменты и реагенты для секвенирования нового пколения и молекулярной диагностики.

Компания СкайДжин предлагает к поставке со склада в Москве и под заказ наборы реагентов, оборудование, расходные материалы, реактивы, а также специализируется на сервисном обслуживании и поверке дозаторов, лабораторных весов различных производителей. Мы предлагаем гибкие условия работы и очень большой ассортимент продукции.

Поставляемая нашей компанией продукция широко используется в научно-исследовательских лабораториях и R&D центрах, лабораториях секвенирования, при решении практически любых молекулярно-биологических задач.

Большая часть производителей в нашем портфолио - это прямые, эксклюзивные поставки. Мы являемся первым звеном в поставках для таких компаний как New England Biolabs, Agilent Technologies, Oxford Nanopore Technologies, QIAGEN, 10x Genomics, NIMAGEN, Integrated DNA Technologies, Thermo Fisher Scientific, SIGMA-ALDRICH, BioSan, Gilson.

К флагманским продуктам наших линеек относятся:

- Набор для пробоподготовки образцов от New England Biolabs ULTRA II FS с интегрированной системой фрагментации и другие наборы серии ULTRA для образцов ДНК, РНК и микроРНК;
- Digital NGS: готовые панели и наборы для обогащения на основе ПЦР от QIAGEN с мономолекулярным баркодированием;
- Специализированные наборы для работы с микроРНК и анализа экспрессии от QIAGEN-Exiqon;
- Нанопоровые секвенаторы третьего поколения: портативный секвенатор MinION, высокопроизводительный секвенатор GridION;
- Уникальная система Chromium производства 10x Genomics для автоматической пробоподготовки геномов и транскриптомов единичных клеток.

За дополнительной информацией о производителях, товарах, ценах и условиях поставки обращайтесь к нашим квалифицированным специалистам.

Будем рады ответить на Ваши вопросы и помочь выбрать качественное и недорогое решение для Ваших задач!

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ХИМЭКСПЕРТ

Агентство Химэксперт

Информация о компании:

Компания Химэксперт существует 16 лет и давно зарекомендовала себя, как надежный поставщик приборов, реактивов и расходных материалов для молекулярной биологии. Мы собрали для своих клиентов самые интересные и перспективные бренды, большинство из которых в России можно приобрести только у нас.

Химэксперт предлагает оборудование для анализа ДНК и РНК, в том числе и методами NGS, фундаментальных протеомных и цитологических исследований, фармацевтики и биотехнологий, прикладного тестирования, включая идентификацию личности и установление родства в криминалистике и судебно-медицинской экспертизе.

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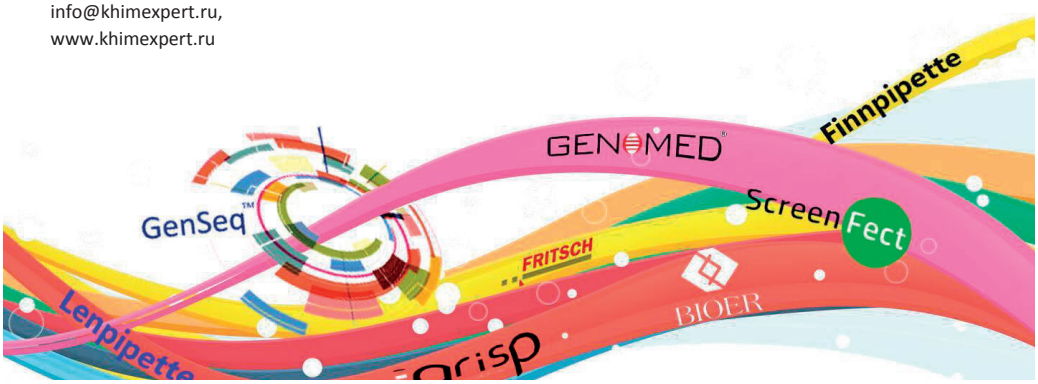

www.genexplain.com

The geneXplain GmbH is glad to welcome you at the BGRS/SB'2018 conference and is proud to introduce you the following software and database solutions for the needs of bioinformatics, systems biology and systems medicine:

geneXplain platform – is a high-performance tool for multi-omics data analysis, which allows identification of new therapeutic targets and biomarkers. A unique feature of the geneXplain platform is its Upstream Analysis. You can register and immediately receive access to a free account.

TRANSFAC database – is a unique collection of transcription factors, their experimentally validated binding sites (TFBS) and a widely known library of positional weight matrices (PWMs). The database has its own integrated methods for TFBS search. It can also be used as an integral part of the geneXplain platform. TRANSFAC is available online or can be downloaded as a set of flat files.

TRANSPATH database – is one of the biggest and most famous collections of signaling and metabolic pathways, which counts over 489000 reactions. The database can be applied for master-regulators search within the geneXplain platform. TRANSPATH is also available online in one package with HumanPSD database or can be downloaded as a set of flat files.

HumanPSD database – is a collection of genes, proteins and micro-RNAs, which includes information about disease biomarkers and clinical trials for various diseases. Besides the detailed biomarkers data, the database contains information about drugs.

BRENDA database – is a comprehensive enzyme and enzyme-ligand information system. Its manually derived core contains over 3 million data points about 77,000 enzymes annotated from 135,000 literature references.

PASS – is a software tool for evaluating the general biological potential of organic compounds based on their structural formula. This program predicts main and side pharmacological effects, molecular mechanisms of action, specific toxicities, and antitargets, actions associated with the metabolism and transport of pharmaceutical substances and their influence on gene expression.

PharmaExpert – is a software tool for analysis of the biological activity spectra of substances predicted by PASS and selecting compounds with the desirable set of biological activity, for analyzing the relationships between biological activities, drug-drug interactions and for multiple targeting of chemical compounds.

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COGNITIVE SCIENCES,
GENOMICS AND BIOINFORMATICS (CSGB-2018)

Symposium

Abstracts

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БИОИНФОРМАТИКА РЕГУЛЯЦИИ И СТРУКТУРЫ
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КОГНИТИВНЫЕ НАУКИ,
ГЕНОМИКА И БИОИНФОРМАТИКА (CSGB-2018)

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