Гендерные различия проявляются также в привычках, связанных с риском для здоровья. Сообщается о лучших привычках, связанных со здоровьем, у студенток, в сравнении со студентами.

რეზიუმე

ავადობის შეფასება ქართველ სტუდენტებში გენდერული ნიშნის გათვალისწინებით

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სტუდენტებში აღინიშნება მნიშვნელოვანი გენდერული განსხვავებები ავადობის, სტრესის აღქმის, ფიზიკური აქტივობისა და კვების მიხედვით.

კვლევის მიზანს წარმოადგენდა სტუდენტების ავადობისა და ჯანმთელობისათვის სარისკო ქცევითი ფაქტორების სტრუქტურის განაწილება სქესის გათვალისწინებით.

გამოიკითხა 15-დან 35 წლამდე (საშუალო ასაკი 20,7±2,4 წ.) 766 ქართველი სტუდენტი, მათ შორის 347 მამაკაცი და 419 ქალი. ჩატარდა ჯვარედინი კვლევა.

კვლევამ აჩვენა, რომ მამრობითი სქესის სტუდენტებს აქვთ წონის მომატების და სქესობრივი გზით გადამდები დაავადებების უფრო მაღალი ფარდობითი შანსი, ვიდრე გოგონებს - OR=1.70 (95%CI: 1.16-2.50) და OR=9.86(95%CI:1.23-79.26), ასევე რესპირატო-რული ავადობის და წონის მნიშვნელოვანი კლების ფარდობითი შანსი - OR=0.35(95%CI:0.23-0.53) და OR=0.38 (95%CI:0.25-0.60), შესაბამისად. გამოცდების პერიოდში ქალებში სარწმუნოდ უფრო მაღალი იყო თავის ტკივილი, ვიდრე მამაკაცებში - 96 (22.91%) და 57 (16.43%), (p=0.0254) და მადის დაქვეითება - 103 (24.58%) და 62 (17.87%), შესაბამისად, (p=0.0244).

ქართველ სტუდენტთა შორის აღინიშნება გენდერული განსხვავება ავადობასა და ჯანმრთელობასთან დაკავშირებულ სარისკო ქცევებში. ვაჟ სტუდენტებთან შედარებით, ჯანმრთელობასთან დაკავშირებული უკეთესი ჩვევები დაფიქსირდა გოგონებში.

THE ROLE OF BURSTS IN SENSORY DISCRIMINATION AND RETENTION OF FAVORED INPUTS IN THE CULTURED NEURAL NETWORKS

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The ability of neural tissue to distinguish sensory impulses dictates how we identify world diversity. Burst responses are widely accepted as an additional synaptic tool in the brain tissue for successful information coding mechanisms. Different nature, origin and functions are descovered in burst discharges. In spite of the variety of views reserchers of the computational neuroscience agree that single spikes and bursts create the parallel mechanisms for synaptic transmission, but bursts have even more effectiveness to strengthen weak synapsis compared to single action potentials [10,16]. One of the most significant goals of neuroscience nowadays is to determine the mechanisms underpinning information coding in brain tissues on the one hand, and to decode information encoded in neural circuits on the other [9]. In humans and higher vertebrates, sophisticated nervous system functions like memory, sensory processing and perception necessitate the engagement of the high order brain structures. However, whether sensory processing and memory, characteristic feature of high order nervous system functions are present and interrelated at the level of local neural circuits and how bursting mechanisms help to realize these complicated processes is a fascinating question in neuroscience.

Dissociated cortical culture (DCC) homed in a multielectrode array (MEA60) allows mimicking neural networks of the brain and use it for investigation of neural computation processes [7]. This system becomes an effective scientific tool for modeling brain to body feedback systems [12,14] and even prototyping neuro-prosthetic or brain to machine cyborg systems using complicated algorithms, advancing a topic of great medical significance [3,13]. As a result, they're frequently referred to as *in vivo like in vitro* system [1,6,15,]. Suitable arrangement of multiple electrodes capable of both stimulation and recording allows to simulate a variety of sensory inputs and to investigate the processing of sensory information in the developing neural circuits of DCC.

In this work we were interested in whether the neural networks of DCC was capable of sensory discrimination and especially, to determine the particular role of bursts in the information processing needed for that. By this reason, we attempted to register newly established bursts in DCCs and investigate its role in the "sensory acquisition" processes when preferred stimuli were perceived. Our previous work helped us in approaching the topic and provided a more conducive environment for research. Over time, the population of about 100000 neuronal and glial cells in our experimental setting formed a simplified but realistic brain structure and could live on MEA for two months. This allowed us to track and assess the structural and functional refinement of freshly formed neural circuits, as well as their capacity for information collection, processing and coding.

Our electrophysiological data revealed that tiny neural networks of DCC have high selectivity to physical nature and spatial position of the sensory inputs and produces prolonged memorised responses after training that facilitate future perception. The disposition of burst elements in sensory discrimination and learning processes could indicate their true meaning for information coding.

Material and methods. Experiments were carried out in accordance with the guidelines of the International Animal Care and Use Committee (IACUC) and the Free University of Tbilisi's bioethics committee.

Preparation of DCC. Our experimental procedures were largely based on Potter and colleagues' [7] protocols for DCC preparation, care, and electrophysiological registration on a multielectrode array, with considerable modifications to match our experimental objectives. In short, embryos were removed from pregnant rats after 18 days of gestation under the influence of ether. Cortical slices were derived from a fetus brain (total number 15 from the 6 litters). The usage of a biosafety cabinet class 2 and 70% alcohol provided sterility. Cortical tissue pieces were transferred to cold Hank's balanced salt solution (HBSS), where blood and arachnoid remnants were removed. AP5 (0.025 mM final concentration), a selective antagonist of NMDA receptors, and Kynurenic acid (final concentration 1 mM), an antagonist of ionotropic excitatory amino acids, were added to solution to reduce the risk of seizures, excitotoxicity, and apoptosis in neural tissue. Enzymatic digestion of tissue was performed for 20 minutes using a mixture of active papain (15 units) and DNase (50 M). The digested tissue fragments were washed away using Thermofisher's CO2 independent hibernation medium with B27 plus supplement (2%) and fetal bovine serum (10%). The suspension was passed through a 40 μm Cell Strainer to form a colony of dissociated cells (neurons and glial cells combined). Bovine serum albumin was added to the solution and following that, it was centrifuged at 200x speed and washed with a final medium to remove toxins produced during the tissue digesting process. A hemocytometer and microscope were used to determine the cell concentration, which was approximately 5000-6000 cells per 1 μL. To avoid deviations from estimated concentration, Dilution or centrifugation were used. Because glial cells help neurons survive, there was no attempt to separate them. For 30 seconds, 15-20 μl of cell suspension was kept poured over the surface of MEA electrodes that had been pre-coated with polyethilen imine (0.05%) and laminin (0.001%). After 30 minutes of incubation, the cells adhered to the surface, and the final medium was added to the MEA basin. HEPES (hydroxy-ethil-hyperazin-ethan-solphonic acid) solution (0.01 M final concentration) was added to the media as a buffering agent. The incubator's temperature was 36°C, with a humidity level of 65%. Half of the medium was usually refreshed twice a week. The other half was left to ensure a sufficient level of intrinsic cell survival factors. To maintain sterile conditions with the ability to transfer surrounding CO_2 (5 %) in the incubator, a suitable cover with teflon milliphore membrane (from multichannelsystems Co.) was enclosed to the ring of MEA (Fig. 1 A). DCC was kept alive in those conditions for two months to ensure that the tissue was healthy and capable of generating action potentials.

Morphological control. An inverted digital microscope with a magnification of 200-400X was used to observe the morphological state of DCC cells for electrophysiological study. The first morphological control was carried out during the cytometric adjustment of the cell concentration on the day of preparation of the culture and then, twice a week before sessions of electrophysiological recording. The photos were captured using the AMCAP software that comes with the digital camera. Cell concentration, region cleanliness, cell distance from electrodes, and neural fiber growth degree were all determined using microscopy. Pictures from the same two places were taken during the whole experiments for better juxtaposition. The length of neural fibers was determined by comparing it to the diameter of electrodes (30 μm) using fundamental geometric approaches.

Electrophysiological recording. Setup of 60 channel electrophysiological systems The MEA1060-UP-BC preamplifier is developed for 60 electrode MEA recordings and has incorporated blanking circuitry that allows the stimulating electrodes to be registered with the rest of the electrodes. To ensure the system's coordinated operation, the preamplifier, stimulator STG4002, and computer (with the supplied cardboard) were all synced. Registration, stimulation, and selection of the sets of stimulating and grounding electrodes were accomplished using the free software MC_Rack, MC_Stimulus, and MEA_Select (Multichannelsystems Co., Germany).

Proper electric stimuli protocols were designed in the MC_Stimulus program, which is meant to give synchronized electric stimulations for MC_Rack recordings, before beginning experimental recordings. Various types of electric stimuli were employed to replicate distinct sensory inputs to DCC and to train the particular neural networks. Two-phase rectangular pulses with a duration of 100 μs and a voltage of 300 mV were used for single, paired pulses (PP, with an ISI of 20 ms) and various stimulation frequencies of 1, 5, 10, 20 and 100 Hz. stimuli lasting for 1 sec. A pair of electrodes delivered certain types of stimulations at random time interval (>10 sec). The length of the stimulation sessions, which were eventually divided into training and testing phases, varied depending on the experimental settings and responses.

A baseline level of spontaneous multi-neuronal activity was observed before stimulation sessions. A Butterworth 2nd order high-pass filter was used to filter the signals, which were captured at a sample rate of 25 kHz (>200). After that, stimulation sessions were carried out, followed by registration for the appropriate amount of time. The multichannel structure of the registering software, as well as the electrode array, allowed for dimensional dispersion of signal processing.

Data analyzes. For neural data analyses, MC_Rack, the data collecting software, offers limited capabilities. The Python programming language was used to create a data analysis application pack (NeuroSpace) that allowed to move data to appropriate graphical and numerical datafiles before being analyzed in the SPSS statistical program. The presentation of real-time signals from a single channel, the separation of stimulus-induced evoked frequencies, the processing of specified partitions, the separation of single-units, the detection of neuronal and network bursts, and the generation of appropriate datafiles were all possible with NeuroSpace. For burst detection, standard methods were employed, with four spikes occurring in 20 msec and a minimum gap between bursts up to 10 msec. This approaches were used to investigate up to 27 MC_Rack electrophysiological recordings in total.

Electrophysiological data was obtained from matured DCCs aged 30 to 50 days in vitro (DIV). The key categorization criteria related to the stimuli used for certain training session were: 300 mV single, PP, and varied frequencies of 1, 5, 10, 20 and 100 Hz for 1 sec. Each of them was used for a prolonged period and the recorded data was examined at three different levels: 1. the baseline level of activity obtained from the phase of recording be-

fore stimulations began, 2. the training phase during stimulation when neuronal activity was gradually increasing, and 3. the testing phase after stimulus evoked activity reached its maximum level. Spike frequencies of multi-unit and single-unit activity, which were determined before and after the applied stimulus paradigms, were the parameters of interest for evaluation. Three distinct methods were used to make these comparisons: Instant response (up to 300 ms) intervals; longer-term (up to 2000 ms) periods; and general activity levels elicited by specific stimuli. For analyzing the effect of specific stimuli patterns the percentage of probability of evoked responses were used as well.

Statistics. IBM SPSS statistics software was used to conduct the statistical analyses. Univariate ANOVA analysis with Bonferroni post-hoc tests were used to assess activity at different phases within the different stimulation groups. For phase and pre- vs. post-stimulus (for 2 sec) comparisons, the same two-factor test was used; two-way ANOVA analyses were required to assess the impact of stimuli on the phases within the groups; multi-factorial ANOVA tests with the same Bonferroni post-hoc analysis were used to investigate the impact of different stimuli types on pre- vs. post-stimulus conditions (for 2 sec) in different phases.

Results and discussion. *Morphology.* After adjusting the cell concentration to the appropriate range of 5000-6000 cells in 1 µl, morphological monitoring of neuronal culture began on 0 DIV. Cells were bare oval/round-shaped white bodies with no fiber descendants at the time. This demonstrated that enzymatic digestion of neural tissue resulted in the loss of the characteristics that bind cells together to form neural tissue, and we acquired dissociated healthy cells (Fig. 1, A). Morphological control was done twice a week before electrophysiological sessions during the experiments. At 3-4 DIV, differentiated cell bodies were visible, and axo-dendritic fibers reached about 40±15 µm after 7 DIV (n=30). Following weeks of cultivation, there was a gradual increase in cell fibers: 65±13 at 14 DIV, 75±25 at 21 DIV, which did not change significantly later (Fig. 1, B, C). Although some cells demonstrated fiber expansion after 3-4 weeks, there was a consistent reduction in cell number across the counted region.

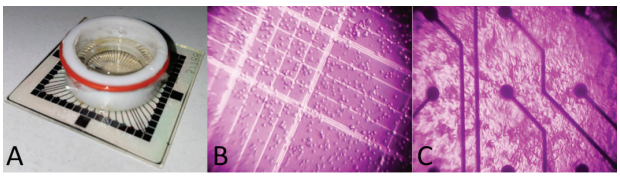

Fig. 1. A, Multielectrode array (MEA) with Teflon Millipore cover; B, DCC on the hemocytometer at 0 DIV, exhibiting adequate dispersion of healthy cells; C, DCC attached to the MEA surface at the day 30 DIV, revealing developed neuronal network with axonal and dendritic fibers

Electrophysiology. We were interested to determine the par1nsory processing due to their reduced but realistic structure.

Before each session of stimulation, spontaneous responses were recorded for roughly 10 minutes to establish a baseline level of activity. This activity was characterized by a wide spectrum of responses, ranging from rare spikes to intense bursts that became stronger with age implying that the network structure is essential for bursting. The channel had to be active for long enough to register for both spontaneous and stimulation sessions, which was a necessary prerequisite for registration (at least 30 min). Random pair of electrodes were utilized to induce a range of electric shock sessions using random time intervals (>10 sec) after a spontaneous activity registration sessions.

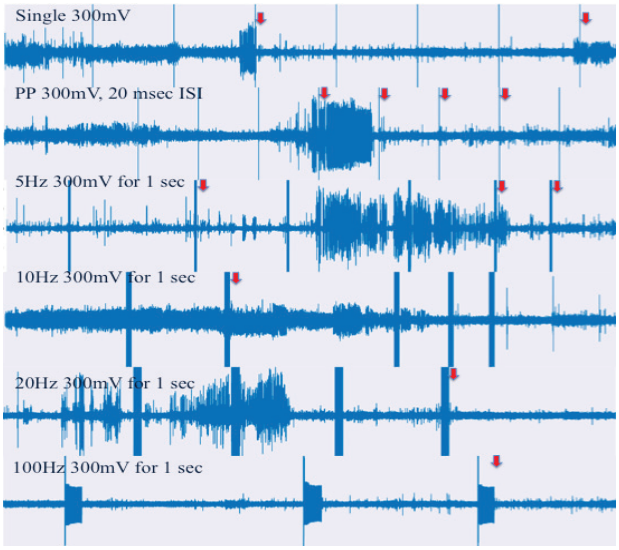

Fig. 2. Discrimination of multi-unit neuronal evoked responses to a variety of electric stimuli. Above the recordings applied paradigms are indicated. Red arrows show location of evoked responses generated in a short duration (<=300 ms) of applied stimulation. There is a high probability of evoked responses and change of quantity of activity in response to low frequency stimuli and especially to PP stimuli

For this research, we applied the previously used protocol: 300 mV single, PP with 20 ms ISI, and varied frequencies of 1, 5, 10, 20 and 100 Hz for 1 s. Stimulation sessions revealed that a variety of electric stimuli elicited particular tonic and burst responses in DCC and that in most cases they displayed preferred responsiveness to low frequency and specifically, to PP stimuli, when other forms of electric stimuli were neglected or decreased level of activity (Fig. 2). However, in rarely occuring conditions, greater responsiveness to other types of stimuli, even with higher frequencies was also observed. Many of our recordings revealed that a specific DCC's preference for certain stimuli types was strongly dependent on the stimuli utilized in training sessions. Despite a few prior discoveries [2,5,10] indicating that neural networks in DCC prefer low frequency stimuli, our work was the first to offer a clear proof of the discriminate ability of these tiny networks.

In independent studies, DCCs have been demonstrated to be responsive to some generated low frequency stimuli and blocked by high frequency stimuli [2,10]. High frequency bursts, such as 20 Hz, were employed in certain studies to induce neuronal plasticity in DCC networks [5]. The most plasticity changes in our experimental setup were caused by PP activation. In our case, 20 Hz training did not yield the best results for increasing plasticity, whereas PP stimuli did. There is no disagreement in our perspective, however it depends on the specificity of the neural network employed in the study. We noticed a difference in the nature of DCCs in our situation, which we thought was useful to this investigation.

Despite a clear preference for low frequency and PP stimuli in our research, several versions of our findings indicate that neural networks of individual DCCs or even within the same culture have the specific structural and functional basics that determine preference to certain types of sensory stimuli. Surely, specific

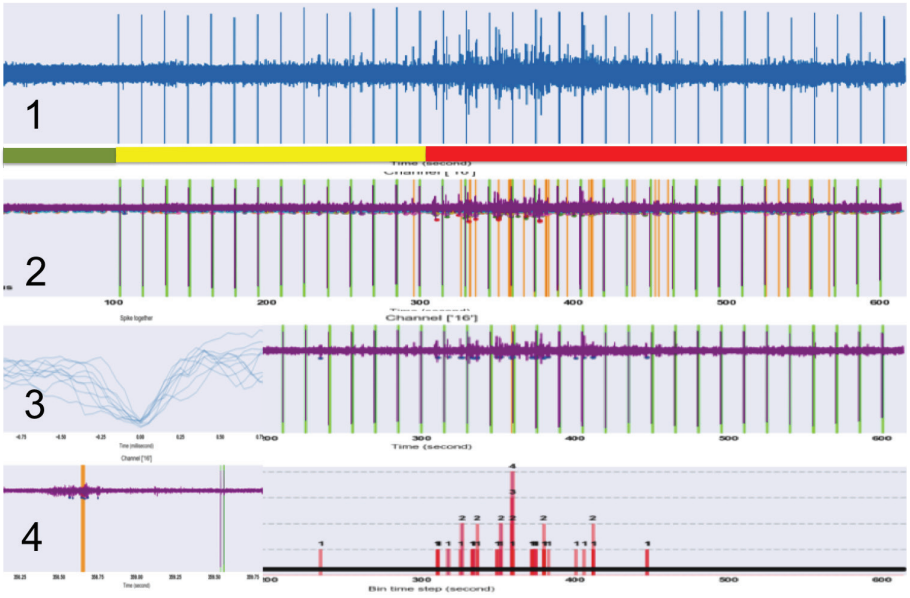

Fig. 3. Neural plasticity-dependent modifications in multi-unit neuronal responses to the favored PP continuous electric stimulation. Green, yellow, and red colored underlines show the background, training, and testing phases of the recorded activity. 1 – Spontaneous activity followed by 34 PP stimuli, which elicited steadily rising responses during training and stable evoked responses during testing. 2 — The same recording with vertical orange lines showing network-bursting responses. 3 – The incidence of a single-neuronal burst was demonstrated by separated neuronal responses; the location of the bursting response is shown on the recording. 4. A close view of the burst response. On the right, a frequency diagram of a same single neuron's activity is depicted

selectivity to various electric stimuli can reveal information about the given neural network's individual features. Despite the current trend in cortical culture research to regard them as a homogeneous structures [6,7,15], the results of our study reveal their more complex and brain-like features, in our opinion. The reason for this could be due to the less synchronized network in our case, which was observed in general activity across the entire DCC surface.

In most cases, a rise in activity did not occur immediately, and training sessions were required before the network was engaged. Unexpectedly, network activity started before occurrence of evoked responses, which only became prevalent after training sessions (Fig. 3, A, B). As a result, trained networks still showed different probability of the evoked responses with the spiking and bursting components that reached approximately 60 % of cases for PP stimuli ($P<0.001$, n=14), 35-40 % for single or 5 Hz stimuli ($P<0.01$, n=12 and 14), about 15-20 % for 10 Hz stimuli, up to 10 % for 20 Hz and as low as 5 % for 100 Hz stimuli ($P<0.05$, n=12, 12, 10, 9 correspondingly). Also, significant difference was found in between the groups analyses, showing a signifficantly higher effect with PP stimuli compared to all others ($P<0.05$, 0.05, 0.01, 0.01, 0.001, 0.001; correspondingly for single, 5 Hz, 10 Hz, 20 Hz and 100 Hz stimuli).

We suggest that the structural and physical nature of the neural networks in DCC, which clearly determines preference for distinct types of stimuli [2,5,10] should be the source of this processes. There should be a mutually supportive relationship between two related phenomena: Because the physical nature of specific neuronal circuits gives them a selective preference for certain electric patterns, different patterns of persistent electric stimulation might improve their efficiency.

During the PP stimulations, which was the most effective paradigm to elicite responses, the probability of evoked responses was around 42 % at the training phase, from which as few as 20% of subsequent activation of the network followed. As a result, the comparison of pre-stimulus vs post-stimulus frequencies rarely reached significant difference in particular cases, when general comparison of 12 recordings showed significant difference ($P<0.001$). However, probability of evoked responses with the dominance of bursts reached about 60% during the testing phase, from which 85% showed subsequent increase of activity level showing significant difference ($P<0.01$) at individual recordings and showing absolute effect in general comparisons ($P<0.0001$, n=12). At the same time, around 20 % did not change activity level. significant difference was found in comparisons between the training and testing phases ($P<0.001$, in single recordings; $P<0.0001$, in summarized comparisons) (Fig. 3, E, F). Interestingly, responses that were seldom created during training were delayed and occurred at later stimulus timepoints (>300 ms), but after attaining the maximum level of bursting, both bursting and tonic responses became steady and often generated after stimulus at shorter timepoints. This clearly demonstrate that training with favored stimuli leads to changes in DCC neural plasticity and, as a result, changes in related responses.

Close observation of bursting elements revealed that most of them originated from the network population of neurons (Fig. 3. 1, 2) and a few percent (up to 5%) belonged to the single-units (Fig. 3. 3, 4) that may correspond to the well-known pacemakers of bursts [16]. In cases, bursts occurred mostly in the later stages of responses after the stimulus was applied, but appeared in evoked responses after training stage was executed. Generation of bursting activity mostly associated with the network activation to the preferred stimuli and dominated while many circuits of neurons were involved in responses. That corresponds well to the supposed role of bursts in the coding processing of information [9].

Many of our recordings revealed progressively increasing spiking and especially bursting responses to the favored stimuli, indicating gradual degrees of neural circuit involvement in information processing. Training aids the formation of synapses

[8], which is an important part of the proper development of brain tissue. Simultaneously, as established in our study, it enhances the likelihood of evoked responses in the presence of favorable stimuli.

Instant and delayed evoked responses should reflect immediate and delayed information processing, with the likelihood of rapid responses increasing at training sessions with preferred stimuli. It shows how synaptic plasticity affects memory formation in response to positive sensory input. At the same time, it emphasizes how information is processed in a sequential manner in order to be memorized. Our findings suggest that subsequent responses, specifically bursts, are important for stimulus discrimination, which could be a reflection of the long-term neuroplasticity processes that could aid information coding, particularly in developing neural circuits. The generation of later responses is likewise dependent on stimulus specificity, and they are not existent before they are administered, according to the data. There are few findings in the literature for those reactions, with the focus being on evoked responses with a short latency. However, few studies have highlighted the importance of delayed reactions in brain plasticity processes [4].

Furthermore, our findings support Nieus and colleagues' recent findings in hippocampal neural cultures [11] regarding state-dependent representation of stimulus-evoked activity. In our recordings, it was frequently noted that when stimulus occurrence corresponded with elevated activity levels, particularly bursts, subsequent evoked responses were blocked. These cases certainly needed to be looked at independently from the cases of evoked responses in order to make sense of them and avoid losing their meaning. From a medical aspect, it could play a significant role in seizure disorder care in the near future.

The study's main finding is that DCC's tiny neural networks are capable of retaining knowledge from discriminating sensory stimuli that served as a training element, allowing them to retain that information and respond more efficiently the following time the same stimuli are presented, and the bursting responses strengten at the critical stage when these alterations occur. Typically, that function is linked to high nervous system capabilities in terms of how memory affects sensory processing and perception. Simple DCC neural networks, on the other hand, offer a large potential for achieving essentially the same functional mechanisms, where stored information can impact the acquisition of the same inputs. This also demonstrates that despite the well-known fact that the entire brain is often engaged in the realization of cognitive processes, some local circuits may provide a rather complicated support for those mechanisms and bursts play a crucial role in these alterations.

Conclusions.

1. Neural networks of DCC are equipped with enough mechanisms for the "first steps" of sensory discrimination.

2. Both population and neuronal bursts play crucial role in generation of the particular responses to the preferred stimuli.

3. The presence of bursting elements in responses to favored stimuli shows that bursts play a critical role in the learning of perceived information.

This work was supported by the Shota Rustaveli National Grant Foundation (FR17-506).

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SUMMARY

THE ROLE OF BURSTS IN SENSORY DISCRIMINATION AND RETENTION OF FAVORED INPUTS IN THE CULTURED NEURAL NETWORKS

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The capacity of neural tissue to discriminiate the sensory signals determines how we recognise the world diversity. Dissociated cortical culture (DCC) homed in a multielectrode array allows mimicking neural networks of the brain and using it for investigation of neural computation processes. This *in vivo-like in vitro* system allows tracking and assessing structural and functional refinement, as well as the ability for information acquisition, processing, and coding in neural networks. We had an increased interest to the burst phenomenon as it represents one of the strongest tools for information coding. We were interested in whether the neural circuitry of DCC was capable of sensory discrimination and memorization of the preferred electric stimuli and to determine the role of bursts in these processes.

Matured DCC from the 30th to 50th day of *in vitro* cultivation were used for the study. In order to simulate a variety of sensory inputs, 300 mV of single, paired-pulse (20 ms interstimulus interval), 1, 5, 10, 20 and 100 Hz stimuli for 1 sec were repeated at random time interval (>10 secs) from effective pairs of electrodes; Activity was registered from all active channels.

The data revealed that during the variety of electric stimulations neurons increased activity in response to one of the stimulus types while responding less effectively to others. Single, 5Hz, and notably PP stimuli were the favored paradigms. The training phase frequently showed a progressive increase in activity level, with short burst prevalence. However, repetition of the preferred stimuli enhanced the occurrence of both tonic and burst evoked responses with prolonged duration throughout the testing phase.

Data shows that neural circuits of DCC have high selectivity to physical properties and spatial position of the sensory inputs and produces early and late responses that include burst elements that may serve as the robust mechanism for reinforcement of the coding information needed for sensory discrimination and learning.

Keywords: In vivo-like in vitro, dissociated cortical culture, multielectrode array, neural plasticity, sensory discrimination, neural network.

РЕЗЮМЕ

РОЛЬ ВСПЫШЕК В СЕНСОРНОЙ ДИСКРИМИНАЦИИ И РЕТЕНЦИИ ПРЕДПОЧТИТЕЛЬНЫХ ВХОДОВ В КУЛЬТУРНЫХ НЕЙРОННЫХ СЕТЯХ

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Способность нервной ткани дискриминировать сенсорные сигналы определяет разнообразие распознования мира. Диссоциированная кортикальная культура (ДКК), расположенная в многоэлектродной матрице, позволяет имитировать нейронные сети мозга и использовать их для исследования процессов нейронных вычислений. Эта *in vivo*-подобная *in vitro* система позволяет отслеживать и оценивать структурное и функциональное развитие, а также возможность перцепции, обработки и кодирования информации в нейронных сетях. Особый интерес вызывает феномен вспышки нейронов, поскольку он является одним из самых сильных инструментов кодирования информации.

Целью исследования явилось определить возможность осуществления дискриминации сенсорных стимулов в нервных сетях диссоциированной кортикальной культуры, а также механизм кодирования информации и роль вспышек в этих процессах.

Для исследования использовались зрелые ДКК с 30 по 50 день культивирования *in vitro*. Для имитации различных сенсорных входов 300 мВ одиночных, парно-импульсных (ПИ, межстимулный интервал 20 мс), 1, 5, 10, 20 и 100 Гц стимулы в течение 1 сек воспроизводили в случайном временном интервале (>10 сек) от эффективных пар электродов. Активность регистрировалась со всех активных каналов. Результаты показали, что при различных электрических стимуляциях нейроны повышали активность в ответ на один из типов стимулов, в то время как менее эффективно реагировали на другие стимулы. Одиночные, 5 Гц и особенно ПИ стимулы были предпочтительными парадигмами. Фаза обучения часто демонстрировала прогрессивное повышение уровня активности с доминирующими короткими вспышками. Однако, повторение предпочтительных стимулов усиливало возникновение как тонических, так и вызванных вспышками реакций с продолжительностью на протяжении всей фазы тестирования.

Результаты показали, что нейронные сети ДКК обладают высокой селективностью к физическим свойствам и пространственному положению сенсорных входов и производят ранние и поздние ответы, включающие в себя элементы вспышек, которые могут служить надежным механизмом для подкрепления кодирующей информации, необходимой для сенсорной дискриминации и обучения.

რეზიუმე

ფეთქებადი აქტიურობის როლი სენსორულ დისკრიმინაციასა და შერჩეული ინფორმაციის შენახვაში ნერვული კულტურის ქსელებში

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ნერვული ქსოვილის უნარი - მოახდინოს სენსორული სიგნალების დისკრიმინცია, განსაზღვრავს ბუნების მრავალფეროვნების აღქმის შესაძლებლობას. მულტიელექტროდულ მესერზე გაზრდილი დისოცირებული ქერქული კულტურა წარმოადგენს ტვინის ნერვული ქსელების იმიტაციას, რომელიც შესაძლებელია გამოყენებული იყოს ნერვულ სისტემაში გამოთვლითი პროცესების საკვლევად. ეს *in vivo*-ს მსგავსი *in vitro* სისტემა საშუალებას იძლევა აღირიცხოს და განისაზღვროს ნერვული ქსელების სტრუქტურული

და ფუნქციური ცვლილებები, ინფორმაციის მიღების, დამუშავებისა და კოდირების მექანიზმები.

კვლევის მიზანს წარმოადგენდა გაგვერკვია,თუ რამდენად შესაძლებელია სენსორული სტიმულების დისკრიმინაციის განხორციელება დისოცირებული ქერქული კულტურის ნერვულ წრეებში, რა სახით ხორციელდება ამ ინფორმაციის კოდირება და რა როლი აკისრია ფეთქებად აქტიურობას ამ პროცესებში.

კვლევა ჩატარდა 30-50 დღის მომწიფებულ *in vitro* დისოცირებულ ქერქულ კულტურაზე. სხვადასხვა სენსორული შესავლის სტიმულაციისთვის გამოყენებული იყო 300 მვ ერთეული, წყვილადი (20 მს სტიმულთაშორისი ინტერვალით), 1, 5, 10, 20 და 100 ჰც-იანი 1 წმ ხანგრძლივობის სტიმულები, რომლებიც მეორდებოდა შემთხვევითი დროის ინტერვალით (>10 წმ). ნეირონული განმუხტვები ადირიცხებოდა ყველა აქტიური არხიდან.

მიღებულმა მონაცემებმა აჩვენა, რომ სხვადასხვა ელექტრული სტიმულის გამოყენების დროს ნეირონული აქტიურობა იზრდებოდა გარკვეული სტიმულის პასუხად, მაშინ როდესაც სხვა სტიმულებზე პასუხი უმნიშვნელო იყო. ეფექტური აღმოჩნდა ერთეული, 5 ჰც და, განსაკუთრებით, წყვილადი სტიმულები. ტრენირების ფაზა ხშირად პროგრესულად ზრდიდა აქტიურობის დონეს ხანმოკლე ფეთქებადი აქტიურობის სიჭარბით. თუმცა, შერჩეული სტიმულების განმეორება აძლიერებდა როგორც ტონურ, ასევე ფეთქებად გამოწვეულ პასუხებს, რაც გამოვლინდა სტიმულებზე გახანგრძლივებულ პასუხებში მთელი სატესტო პერიოდის განმავლობაში.

შედეგებმა აჩვენა, რომ დისოცირებულ ქერქულ კულტურას აქვს სენსორული შესავლების ფიზიკური თვისებებისა და სივრცითი განაწილების მიმართ მაღალი სელექტიურობა და ვლინდება ადრეულ და მოგვიანო პასუხებში ფეთქებადი აქტიურობის ელემენტებით, რაც, თავის მხრივ, შესაძლოა წარმოადგენდეს მძლავრ მექანიზმს ინფორმაციის კოდირებისთვის სენსორული დისკრიმინაციისა და დასწავლის პროცესში.

ВЛИЯНИЕ ВАРУСНОЙ ДЕФОРМАЦИИ СРЕДНЕЙ ТРЕТИ БЕДРА НА СИЛУ МЫШЦ НИЖНЕЙ КОНЕЧНОСТИ

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Современные технологии остеосинтеза, при условии их адекватного применения и бережного отношения к мягким тканям, обеспечивают, в большинстве случаев, оптимальные биомеханические и биологические условия как для сращения диафизарных переломов бедра и голени, так и для восстановления функциональных характеристик повреждённой конечности. Однако, в ряде случаев результатом лечения этих переломов происходит сращение перелома с остаточным смещением фрагментов, иными словами, формируется посттравматическая деформация.

Лечение посттравматических деформаций является самостоятельной (отдельной) задачей ортопедии и травматологии, поскольку не может быть сведено только к нормализации взаимоотношений между фрагментами кости и их стабильной фиксации, как это делается при острой травме. Причиной этого отличия является функционирование поврежденного сегмента в измененных условиях, в результате чего развивается ряд вторичных изменений, часть которых носит адаптивный характер. Необходимость учета этого функционального влияния подчёркивалась еще в 1985 году G. Heirholzer, и K.H. Müller [10].

При анализе посттравматических деформаций большое внимание уделяется их влиянию на суставы. В частности, показано развитие изменений артрозного характера в прилегающих суставах после внесуставных переломов бедра и голени [7,15-17,23,25].

Нами на математической модели [1], и в эксперименте на животных [2], также оценено влияние посттравматических деформаций, и изучены изменения не только в суставах поврежденной, но контрлатеральной конечности.

Ортопедия-травматология, как отрасль медицины, имеет дело с опорно-двигательным аппаратом, иными словами, костно-мышечной системой. Следовательно, логично оценивать влияние деформации на весь опорно-двигательный аппарат. Но на текущий момент, недостаточно изучено влияние внесуставных деформаций нижних конечностей на работу мышц и всего пояса нижних конечностей. Кроме того, принятие решения о необходимости выполнения корригирующей операции основывается, большей частью, на детальном анализе рентгенограмм [9,10,14,20,22].

Функциональное состояние мышц повреждённого сегмента и конечности, в целом, чаще всего не анализируется и не учитывается при планировании лечебных мероприятий.

Цель исследования - определить влияние варусной деформации бедренной кости на уровне средней трети на силу мышц нижней конечности и минимально необходимую силу мышц для осуществления нормального шага.

Материал и методы. Анализ походки проводили в программе OpenSim 4.0 [5]. В основу моделирования взята модель gait2394 [3,6], позволяющей изучать 76 мышц нижних конечностей и туловища. Не масштабированная модель представляет собой объект ростом 1,8 м, массой 75,16 кг.