ДРУГИЕ ВОПРОСЫ ОБЩЕСТВЕННОГО ЗДРАВООХРАНЕНИЯ И КЛИНИЧЕСКОЙ МЕДИЦИНЫ
ҚОҒАМДЫҚ ДЕНСАУЛЫҚ САҚТАУ ЖӘНЕ КЛИНИКАЛЫҚ МЕДИЦИНАНЫҢ БАСҚА ДА МӘСЕЛЕЛЕРІ
OTHER PUBLIC HEALTH AND CLINICAL MEDICINE ISSUES

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BREAKING INTO THE AUTISTIC BRAIN THROUGH THE ACTUAL 3D SPACE: FMRI STUDY

It is well-known that babies are born with a primitive sense of where they are in 3D space. This sense develops rather intensively and contributes immensely into developing appropriate brain functional configurations in the brainstem, in the subcortical and cortical areas. FMRI studies suggest that, for example, the grid system (system which provides global mapping and actual spatial positioning) is fully established at around three or four weeks after birth.

An autistic child misses the chance of such normal 3D spatial grasping the world. As the result, the crucial brain functional configurations turn to be undeveloped causing pervasive autism spectrum disorders.

We hypothesize that the actual motion in the real 3D scenes may serve as the egocentric reference frame for developing appropriate brain functional configurations and contribute into overcoming an autistic state.

Keywords: autism spectrum disorders; actual motion in the real 3D scenes; brain functional configuration, brain images analysis.

INTRODUCTION

A) FROM LOCOMOTION TO CEREBELLUM

It is generally accepted that human locomotion depends on neuronal circuits (networks of interneurons) in the spinal cord (the central pattern generator, or CPG). Afferent information influences the central (spinal) pattern and, conversely, the CPG, under control of cerebellum, selects appropriate afferent information according to external requirements. To break into autistic locomotion and autistic cerebellum we explore 3D special scenes as the external requirements.

Participant A, the former autistic child, learned locomotion procedures to cope with the actual 3D spatial motion. She learned spatial manner of walking “from local stance to global 3D space”. That is the way to induce proprioceptive, vestibular-gravitational information and to provide the basis for adequate conscious brain representations of body in 3D scene.

She also learned how to interact voluntary spatial kinesthetic motor commands with reflex system and the CPG to evoke the proper gait “from local stance to global 3D space” and to avoid her habitual autistic manner of walking.

The conscious control of such locomotion involves the use of actual 3D spatial afferent information from a variety of sources in the visual, vestibular and proprioceptive systems and CPG integrates these inputs on the basis of polysynaptic reflexes.

The polysynaptic pathway allows integrating 3D spatial inputs from muscle, joint and cutaneous afferents and converge them with commands from supra-spinal centers to common spinal interneurons. In addition, this reflex system has excitatory and inhibitory connections to both extensors and flexors.

Two main sources of afferent input are integrated in the polysynaptic pathway while participant A walking "from local stance to global 3D space": vestibular-load-related and proprioceptive joint-position-related information.

Load receptors, or graviceptors in conjunction with vestibular system signal the influence of gravity, the inertial force of gravity on participant's A body and opposing forwarding force, which is represented in her body thanks to the proprioceptive information, signals of her joint-position, parts of the body forwarding in the actual 3D space.

Gravitational inertial reference frame firmly controls via vestibular system a local stance and it cannot be ignored while taking step forward along the global linear perspective of the actual 3D scene. Opposing forwarding force is created due to the proprioceptive joint-position in the actual 3D space. Interplay between these two forces causes global inertial linear acceleration as driving force.

Thus, while walking "from local stance to global 3D space" participant A experiences both forces simultaneously, learns how to interplay between them, and voluntary experiences global inertial linear acceleration as motivational driving force.

The sensory proprioceptive joint/limbs-position information is conveyed bottom up from the body via the dorsal spinocerebellar tract to the "Clarke's column" in the brainstem (a major relay center for unconscious proprioception), further to the inferior cerebellar peduncle which leads, in turn, to the vestibulocerebellum.

The integrative motor vestibular-gravitational information (visual tracking and oculomotor control, inputs of the otolith organs which reflect gravity and linear accelerations of the head, as well as control of axial muscles for balance) is conveyed top-down via vestibular nerve to the vestibular nucleus, medulla oblongata/olivary nucleus, and further via climbing fibers, inferior cerebellar peduncle also to the vestibulocerebellum.

The way to the vestibulocerebellum (olivary nucleus, climbing fibers, and inferior cerebellar peduncle) strictly concerns with integrating proprioceptive sensory input with motor vestibular-gravitational functions such as balance and posture maintenance. And the vestibulocerebellum (nodulus) isolates and encodes such integration, due to specific features of Purkinje cells in this part of cerebellum, as global inertial linear acceleration.

Thus, vestibulocerebellum plays a forwarding role; it contributes into on-line interplay of vestibular-gravitational and proprioceptive joint/limbs-position forces by way of convergence passive gravitational inertial force into active drive force of the global inertial linear acceleration.

B) FROM RETINAL VISUAL PERCEPTION TO THE SUBCORTICAL RETINOTECTAL PATHWAY

Global-in-local locomotion in the linear perspective of the pine opening demands from Participant A persistent visual tracking and oculomotor control of the global inertial linear acceleration. The vestibulocerebellum, at that, subliminally uses on-line vestibular-gravitational inputs to keep the eye tracking proper proprioceptive joints/limbs-position in the actual 3D scenes.

Such forwarding on-line functioning of the vestibulocerebellum triggers the orienting visual reflex-like response, an immediate visual response to a change in 3D scene. In each step "from local stance to global 3D space" participant A faces novel and significant stimulus: what is it?

The Superior Colliculus or tectum by way of visual and auditory reflexes is in charge to direct behavioral responses toward specific local-in-global body-centered positioning in the actual 3D scenes.

And as far as participant A permanently encounters novel stimuli she pays visual attention to them even before identifying them. She focuses her attention on global inertial linear acceleration, but not on the pine opening per se.

There is distinction between cortical visual pathways which goes via LGN in thalamus to cortical visual areas (V1, V2, etc.,) and subcortical reflexive orienting vision which goes directly to the Superior Colliculus and further to the Pulvinar and Amygdala. Pulvinar is considered to play a role in generating global inertial linear acceleration attention.

As it was mentioned above in each step "from local stance to global 3D space" participant A faces novel stimuli. They cause unconditional responses of the medulla in conjunction with the Amygdala: changes in muscle tone, heart rate, rhythm of breathing, visceral-motor reflex, facial response, etc. In that case participant A experiences the unconditional responses as modulatory drive force strongly associated with the orienting visual reflex in response to novel stimuli. FMRI data show the positive activation of the Amygdala and its involvement into subcortical visual pathway.

In our fMRI study participant A we hypothesize to reproduce the described feedforward subcortical route of the subliminal visual orienting reflex via Superior Colliculus, Pulvinar, and Amygdala.

C) FROM ACTUAL LOCOMOTION IN 3D SCENE TO THE GLOBAL POSITIONING MAPPING

In 2014 year the Nobel Prize for physiology has been awarded to three scientists (John O'Keefe, May-Britt Moser and Edvard Moser) who discovered the brain's "Global positioning system, GPS system".

In the 1970s, O'Keefe had discovered neurons called place cells in the hippocampi of rats. These cells fire only when an animal is in a particular local place. In 2005, husband and wife team, May-Britt and Edvard, discovered a different part of the brain, entorhinal cortex, which acts more like a nautical chart.

The researchers saw that some of entorhinal neurons, grid cells, fired when the rats moved onto or through a particular local place in the box, just like hippocampal place cells. But the neurons went on to fire at several other forwarding places too, as if a rat went globally.

Now we know that grid cells exist and work also in human brain and they have firing fields dispersed over the global environment in contrast to place cells which are restricted to certain specific regions of the environment. Thus, these cells in human brain can unconsciously keep mapping not only of where we are but global intention as well.

The grid cells are anchored to external landmarks, but persist in darkness, suggesting that grid cells may be part of a self-motion based map of the spatial environment. Unlike the visual cortex, whose coding will be influenced by light falling onto the retina, the entorhinal cortex creates the global-in-local pattern internally, by integrating body-internal information.

We consider that described above the body reflexive global inertial linear acceleration in the actual 3D scenes may cause the vestibular-proprioceptive body-internal information as the source of global-in-local positioning in the entorhinal cortex.

Besides grid cells, entorhinal cortex and some other brain regions (thalamus, hippocampus, striatum, etc.) which contribute into the body reflexive global inertial linear acceleration, contain head direction (HD) cells. HD cells are mostly orientation-specific and location-invariant. They strongly depend on the vestibular system, and the firing is independent of the position of the animal's body relative to its head. Their compass is inertial: it continues to operate even in the absence of light. The HD system integrates the vestibular output to maintain a signal of cumulative rotation.

Thus, we can hypothesize that entorhinal cortex in conjunction with other brain regions encode on-line information about dynamic global-in-local positioning (grid cells) and globally directional invariant inertial linear acceleration (head direction cells and conjunctive position-by-direction cells) while locomotion takes place in the actual 3D scene.

PARTICIPANTS AND DATA ACQUISITION

As participants of our fMRI study we recruited 9 year girl (participant A) who overcame an autistic state. Visual perception, learning and talking in the actual 3D scenes were critical for her treatment. The treatment of participant A was based on the self-regulation learning in the actual 3D scenes. V. Matvievskiy in his e-book shows quite observable, predictable and measurable way of such treatment (Matvievskiy, 2014).

For the purpose of comparison we involved a normal child of the same age (participant B) who didn't have such experience. Besides for the same purpose of comparison we recruited one untrained and 8 trained mothers' of autistic children and 2 practitioners, their trainers.

PARADIGMS

During one session of scanning each participant of research performed a task which was mastered by it in advance. The visual presentation of incentives was used: videos for each task through a projector in the console it was output to the translucent screen installed in the patient's feet, from where through mirror system of the image were directly available to perception of the participant of research. Each paradigm had the block structure consisting of 4 alternating blocks of the period of activation and a dormant period lasting 21 about everyone (the general duration of each paradigm – 2,48 min.). The task began with a dormant period during which the look of the participant was fixed on the white cross displayed. Then the activation period consisting of display of the video followed (for example, the avenue going to depth in pine forest). Display was followed by speech instructions. In general research consisted of seven paradigms. Three of them allowed to investigate activation of spatial structures, and four paradigms on activation of speech ways.

SCANNING PROTOCOL

MRT-data were received on the MR-tomograph with intensity of a magnetic field of 3 T of Magnetom Verio of Siemens, Germany. Research began with the standard T2 mode a gradient echo in an axial projection for an exception of pathological changes of substance of a brain. For obtaining anatomic data research in the mode 3D-T1 a gradient echo (T1-mpr) with receiving a set from 176 sagittal cuts covering all volume of substance of a brain was carried out (time of repetition (TR) - 1940 ms, time an echo (TE) - 3,1 ms, a tilt angle – the 15th hail, a matrix – 256 x 256 mm, cut thickness – 1,0 mm, the voxel size – 1 x 1 x 1 mm).

Then 7 sets of functional data (for each of paradigms) in the T2*-gradient mode an echo in an axial projection were consistently received (time of repetition (TR) – 3000 ms, time an echo (TE) - 30 ms, a tilt angle – the 90th hail, a matrix – 64 x 64 mm, cut thickness – 3,0 mm, the voxel size – 3 x 3 x 3 mm). Each T2 * the mode included the 56 measurements of all volume of substance of a brain.

ANALYSIS OF DATA

Functional MRI data were then analyzed using SPM8 analysis software. Imageswere realigned to correct for motion, corrected for errors in slice timing, after that thefirst for correction, then the average functional file coregistered linearly with the corresponding anatomic file with the subsequent spatial normalization of the first (3 x 3 x 3 mm) and the second (1 x 1 x 1 mm) spatially transformed to standard stereotaxic space (based on the Montreal Neurological Institute coordinate system). Before thestatistical analysis the transformed functional data were washed away by means of Gaussian kernel size (10 x 10 x 10 mm) to decrease spatial noise (due to weakening of high-frequency noise) and compensations of variability of a structure of crinkles between subjects. Statistical parametrical cards were generated on the voxel-basis of comparison by means of the general linear model. For decrease in artifacts from the movement of the patient parameters of rigid transformation at alignment were entered as regressors at statistical processing of the first level (for each examinee).

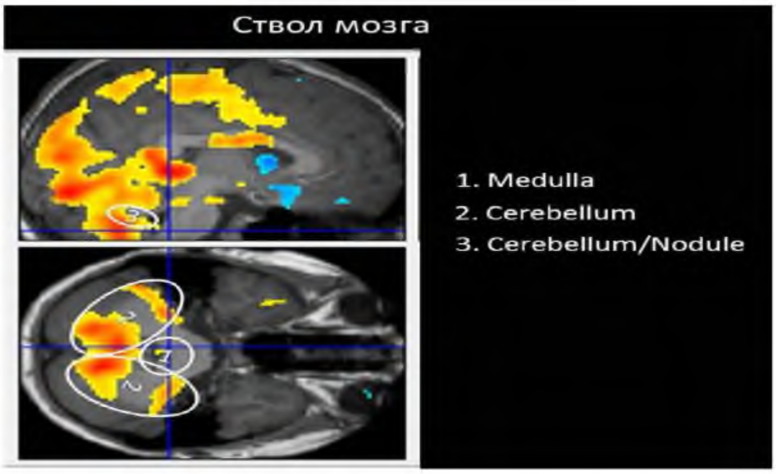
BRAIN IMAGING

Paradigm 1 - "Global-in-local locomotion in the linear perspective of the pine opening"

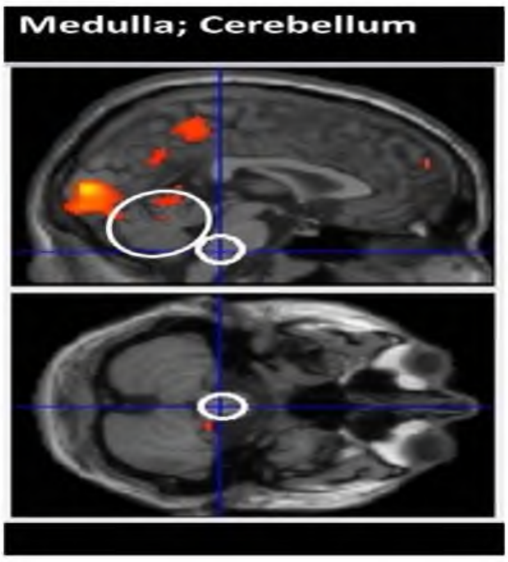
Image 1

Participants were instructed to persist in walking along the video-moving linear perspective as along the depth axis of the pine opening (see image 1). At that, each local step should cross the global edge of the depth axis. In such away each step should be step "from local stance to global 3D space". Naturally, participants experience simultaneously on-line vestibular global gravitational inertial force and opposing proprioceptive forwarding antigravity muscle and joint-position force in the actual 3D space.

The correct interplay between these two forces causes global inertial linear acceleration as driving force, which should be coded in vestibulocerebellum (nodulus) in conjunction with medulla oblongata activation.



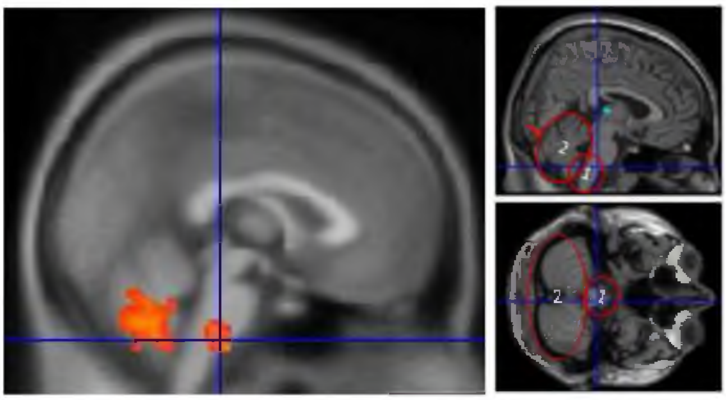
Participant A



Participant B

As we can see, the results of the brain imaging are quite different. Participant A, a former autistic child, learned the actual motion in the real 3D scenes as the egocentric reference frame and could properly control her walking. That is the reason why her medulla and nodulus are in the state of active functioning.

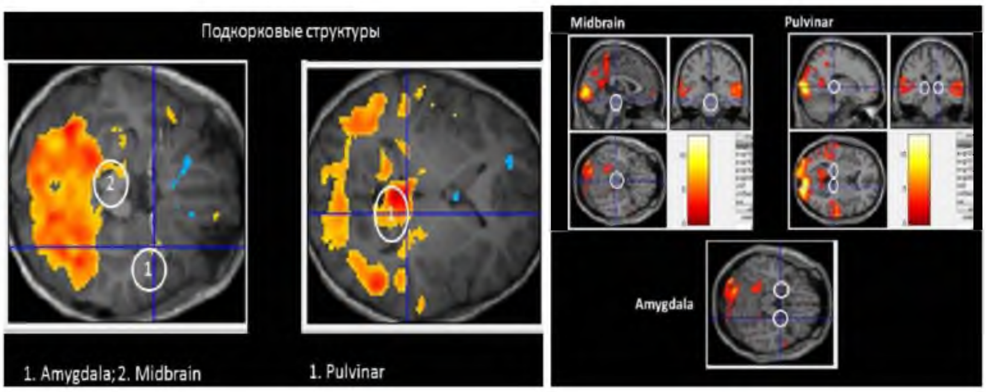
Participant B, was not an autist, but didn't learn how to control his actual presence in the real 3D space. He demonstrates total lack of vestibulocerebellum (nodulus) and medulla functional activation. We got absolutely identical results with adult participants (group: 8 mothers of autistic children who are trained in the actual 3D space plus 2 practitioners, and one who wasn't trained).



1O Trained adult participants (group imaging) Untrained adult participant

Paradigm 2 - "Focusing attention on liner perspective as on the global inertial linear acceleration"

Participants were instructed while walking "from local stance to global 3D space" to persist in focusing attention on liner perspective of the pine opening as on the global inertial linear acceleration, but not on the pine opening (trees, grass, etc.) per se. The target was to activate subcortical retinotectal visual pathway: midbrain/Superior Colliculus, Pulvinar, Amygdala



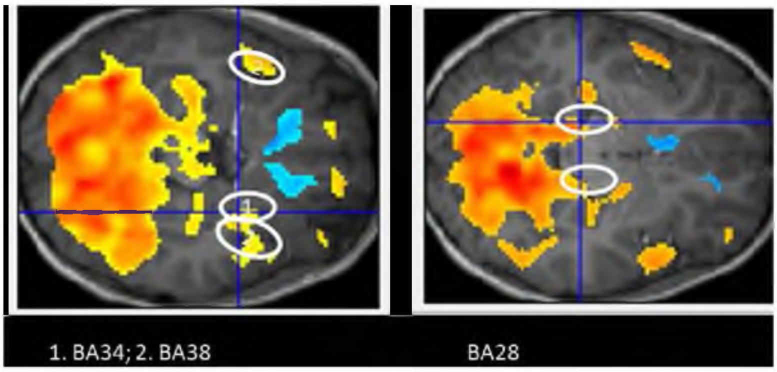
Participant A Participant B

Again, we can see that participant A demonstrates all three structures in active functioning state. She is able to persist in visual tracking and oculomotor control of the global inertial linear acceleration, to trigger the immediate visual response to novel stimuli in 3D scene, and to experience, at that, the unconditional responses as affective modulatory drive force.

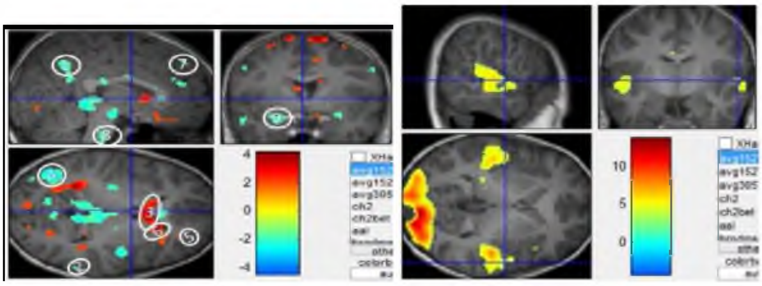
Participant B demonstrates the total lack of these functional activities. The subcortical retinotectal pathway (midbrain/Superior Colliculus, Pulvinar, Amygdala) is silent.

Paradigm 3 - "Transformation of the global inertial linear acceleration in the actual 3D scene into Global Cortical Positioning Mapping"

In the last paradigm participants were instructed to keep mapping the global inertial linear acceleration along the globally-directed edges of the linear perspective (see image 1, pine-tree shadows as natural landmarks of the mapping).



Participant A: entorhinal areas



Participants A Participant B.

The brain image of Participant B is rather poor. He sees the pine-opening (trees, grass, etc.) per se and hears the voice of instructor and that is why visual, auditory inputs are mapped in the corresponding brain areas (BA 17, 18, 19 – visual inputs; BA 41, 42, 22-auditory inputs). There is no in the brain image neither global presence in the actual 3D scene, no cortical mapping.

Quite opposite cortical brain image demonstrates Participant A. The first image shows the wide-spread and intensive functioning of the entorhinal area (BA 34, 28, 38). It demonstrates the Global Positioning of the participant A, while she follows the global inertial linear acceleration in the actual 3D scene.

The second image doesn't show the primary and secondary visual areas (BA 17, 18). In contrast, subcortical areas (Amygdala, Medulla, Striatum, and previously shown subcortical visual pathway) are functionally represented. In conjunction with Entorhinal Cortex they reveal transformation of the global inertial linear acceleration into subcortical reflexive pathway, into internal navigation mapping of the global-in-local positioning in the actual 3D space.

The cortical functional configuration: BA 39 (out-of-body experience), BA 40 (involved in global phonology), BA 10 (involved in strategic processes), BA 37/fusiform gyrus (face and body recognition in 3D space), BA 8 (saccadic and pursuit control of eye movements in the depth axis), Insula (controls homeostatic unconditional responses while grasping the global positioning). Thus, participant A demonstrates transformation of the global inertial linear acceleration into Global Cortical Positioning Mapping.

DISCUSSION

We assume that paradigms of participant A reveal developing brain functional configurations appropriate to the actual motion in the real 3D scenes and it proves our hypothesis.

Transformation of the global inertial linear acceleration in the actual 3D scene into Global Subcortical and Cortical Positioning Mapping might be reached by corresponding body, visual and cortical control.

Body control provides reproducing and appropriate interplay of the inertial gravitational and proprioceptive joint-position forces, and, eventually, mapping global inertial linear acceleration in the brainstem (medulla) and cerebellum (nodulus).

Appropriate visual orienting control of the global inertial linear acceleration provides corresponding subcortical mapping reflexive retinotectal pathway, and that plays crucial role in corresponding cortical mapping.

Cortical control of the global inertial linear acceleration based on the actual global-in-local directional allocentric landmarks. And in such a way cortical control integrates global-in-local position and actual direction in the real 3D scenes as position-in-direction mapping.

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Түйіндеме

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3D АЯДА МИДЫҢ АУТИСТІ КҮЙІН ЖЕҢУ

Бала дүниеге алғашқы 3D аяны сезіммен туатыны белгілі, сол аяда олар ары карай да болады. Осы сезім едәуір қарышты дамиды да, ми бағанасы, ми қыртысы және мидың қабық құрылымының қажетті дамуында маңызды рөлді атқарады.

ФМРТ деректерінің көрсетуі бойынша, тор жасуша жүйесі (grid cells), ғаламдық аянды топографиялық сканирлеуші энториальді қыртыс жүйесінің жасушалары, бала дүниеге келгеннен кейін үш - төрт аптадан кейін толықтай дамиды.

Аутисті күйдегі бала 3D аяда қалыпты әлемді сезу постижения мүмкіндігін жіберіп алады. Нәтижеде, мидың ең маңызды функциялық құрылымдары тежелген жағдайға ұшырайды, бұл аутисті бұзылыстар спектрінің кеңеюін туғызады.

Біздің жорамалымыз бойынша - ФМРТ зерттеу арқылы алынған мәліметтер бойынша аутизмді жеңуінің оң нәтижесін алуға бағытталған. Біз бекітеміз, шынайы 3D аяда көкейкесті қозғалыс мидың тежелген қызметінің дамуына себеп бола алады, бұл едәуір дәрежеде, болжаулы және нейрофизиологиялық түсіндіріле алатын аутизмнен шығару жағдайын туғызады.

Түйін сөздер: аутисті спектрлі бұзылыстар, фМРТ, 3D ая, функциялық нейронды мидың торы.

Аннотация

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ПРЕОДОЛЕНИЕ АУТИЧНОГО СОСТОЯНИЯ МОЗГА В АКТУАЛЬНОМ 3D ПРОСТРАНСТВЕ

Дети рождаются с первичным чувством 3D пространства оно развивается довольно интенсивно, играя при этом существенную роль в развитии должной функциональной связи ствола мозга, его подкорковых и корковых структур. Данные ФМРТ показывают, что, система сеточных клеток (grid cells), система клеток энториальной коры топографически сканирующие глобальное пространство, полностью оформляется уже к третьей – четвертой неделе после рождения. Аутичный ребенок упускает такой шанс нормального постижения окружающего его 3D мира. А в результате, важнейшие функциональные структуры мозга оказываются заторможенными, что порождает расширение спектра аутичных нарушений.

Наша гипотеза в настоящем ФМРТ исследовании нацелена на подтверждение уже полученных положительных результатов преодоления аутизма. Мы утверждаем, что актуальное движение в реальном 3D пространстве может служить основой для развития заторможенных функций мозга, и это в значительной степени предопределяет предсказуемый и нейрофизиологически объяснимый вывод из аутизма.

Ключевые слова: расстройства аутичного спектра, фМРТ, 3D пространство, функциональная нейронная сеть мозга.

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РЕЗУЛЬТАТЫ ДЕЯТЕЛЬНОСТИ МЕДИЦИНСКОГО ЦЕНТРА УПРАВЛЕНИЯ ДЕЛАМИ ПРЕЗИДЕНТА РЕСПУБЛИКИ КАЗАХСТАН ЗА 2014 ГОД

В статье отражены результаты работы подведомственных организациях Медицинского Центра Управления делами Президента Республики Казахстан, представлены количественные и качественные показатели деятельности, а также основные направления развития на среднесрочный период.

Ключевые слова: прикрепленный контингент, заболеваемость, структура заболеваемости, перспективы развития

Введение. В 2014 году деятельность Медицинского центра осуществлялась в рамках реализации Концепции развития и совершенствования деятельности Медицинского центра Управления делами Президента Республики Казахстан и его подведомственных организаций на 2012–2015 годы, утвержденная начальником Медицинского центра Управления делами Президента Республики Казахстан от 28 апреля 2012 года.

В декабре 2014 год утверждена приказом Руководителя МЦ Программа развития Медицинского центра Управления Делами на 2015-2020 годы.