JOURNAL OF CLINICAL MEDICINE OF KAZAKHSTAN

Шолу Мақала / Обзорная Статья / Review Article *DOI: 10.23950/1812-2892-2016-4/jcmk-00364*

Orienting reflex is the key to autistic brain: fMRI study

Rodion Konovalov[1], Vladimir Matvievskiy[2], Saule Mukhametzhanova[3]

[1]Department of Radiology, Scientific Center of Neurology, Moscow, Russian Federation
[2] Department of Human Resource, Innovative educational center, Moscow, Russian Federation
[3]Department of Radiology, Republican Diagnostic Center, Astana, Kazakhstan

This work is licensed under a **Creative Commons Attribution 4.0 International License**

Received: 24-08-2016
Accepted: 31-10-2016
UDC: 616.8-089

J Clin Med Kaz 2016; 4(42):6-11

Corresponding author: Мухаметжанова С.В. Республиканский диагностический центр, отделения радиологии, Астана, Казахстан, ул. Сыганак д.2, Астана, Казахстан, Телефон: +7(7172)702070 Факс: +7(7172)701550, e-mail: dokray@bk.ru

Abstract

Recent researches show that the neural emulators in sensorimotor apparatus determine the keeping and modulation of existing repertoire of efferent copies. Consciousness helps people to break out of the vicious circle of the former perceptual experience, but more and more often we face with a situation where a child in the pre-speech period is a prisoner of its own adaptive memory. Care inward becomes a biological necessity of his autistic pervasive disorders. Our functional Magnetic Resonance Imaging (fMRI) studies show that in case of the reflexive affective vestibular-proprioceptive presence in the 3D space doesn't cause sense differentiation in sensorimotor apparatus does not form efferent copies. Such presence arouses affective perception in a child, "What is this?" The child literally absorbs with 3D scenes Pavlovian spatial orienting reflex "What is it?". Besides, "what is it?" reflexive affective efferent state in the actual 3D space contributes into the neural organization of the subcortical and cortical structures, contributes into General Adaptation Syndrome.

Keywords: autism spectrum disorders - orienting reflex "What is it?"; efferent copies - General Adaptation Syndrome.

БАҒДАРЛАМАЛЫ РЕФЛЕКС - АУТИСТТІК МИҒА КІЛІТ: ФМРТ ЗЕРТТЕУІ

Коновалов Р. Н.[1], Матвиевский В. Я.[2], Мухаметжанова С. В.[3],
[1]РМҒА Неврология Ғылыми орталығы, радиология бөлімшесі, Мәскеу, Ресей федерациясы
[2]Инновациялық білім беру орталығы, кадрлар бөлімі, Мәскеу, Ресей федерациясы
[3]Республикалық диагностикалық орталығы, радиология бөлімшесі Астана, Казахстан

ТҰЖЫРЫМДАМА

Болжамды, түсінікті аутист баланы шығару үшін, мидың нейронды желілердің қалыпты жұмыс істеуі ең маңызды болып табылады. Зерттеу мақсаты – нақты 3D кеңістікте кеңістіктік болжамды "бұл Не?" рефлексті қолдану арқылы ми жұмысының қалпына келуін және оның басқару белсенділігін, мидың нейронды желілерінің жағымды өзгерістері мен функцияның дамуын бақылау. Бұл рефлекс туа біткен және сөзсіз рефлекс ретінде, И.П.Павловпен алғаш ашылды. Бірақ аутизм жағдайы бар балада ол тежелген, басылып калған куйде болады, бұл жағдай қыртыс және қыртысасты құрылымдарының нейронды желілерінің қалыпты жұмыс істеуінің бұзылуына әкеледі. Зерттеуге қатысушылар ретінде аутизмді жеңген балалар және де қазір сол аутизмнен шығу жолындағы балалар мен осы балалардың аналары, сондай-ақ ана-тьютор бағдарламасы бойынша арнайы дайындықтан өткен аналар болды. Мақсатты іске асыру кезінде, нақты 3D кеңістікте осы рефлексті қою арқасында, мидың функционалдық желілерде біртұтас құрылымдық өзгерістер, кеңістікті меңгеру тиісті өзекті парадигмаға сәйкес екеніне көзіміз жетті. Біздің практикалық жұмыс және функционалды магнитті-резонансты томография (фМРТ) зерттеу осындай парадигма арқылы құрылды.

Маңызды сөздер: аутичті аумақтын бұзылымдары - бағдарлы "бұл Не?" рефлексі - эфферентті көшірмелер - Жалпы Бейімделу Синдромы.

ОРИЕНТИРОВОЧНЫЙ РЕФЛЕКС – КЛЮЧ К МОЗГУ АУТИСТА: ФМРТ-ИССЛЕДОВАНИЕ

Коновалов Р.Н.[1], Матвиевский В.Я.[2], Мухаметжанова С.В.[3]
[1]Научный центр неврологии РАМН, отделения радиологии, Москва, Российская федерация
[2]Инновационный образовательный центр, отдел человеческих ресурсов, Москва, Российская федерация
[3]Республиканский диагностический центр, отделения радиологии, Астана, Казахстан

РЕЗЮМЕ

Восстановление нормального функционирования нейронных сетей мозга аутиста имеет фундаментальное значение для прогнозируемого вывода детей из аутизма. Целью данного исследования было изучение позитивных контролируемых изменений и развитие функционирования нейронных сетей мозга в процессе актуального восстановления и управления активностью пространственным ориентировочным рефлексом "Что это?" в реальном 3D пространстве. Данный рефлекс был открыт И. П. Павловым как врождённый и безусловный рефлекс. Но в аутичном состоянии ребенка он оказывается подавленным, что приводит к нарушению нормального функционирования нейронных сетей подкорковых и корковых структур. В качестве участников исследования мы привлекли детей, преодолевших и преодолевающих аутизм, а также мам этих детей, которые прошли специальную подготовку по программе мама-тьютор. В процессе реализации цели мы убедились, что благодаря целенаправленной постановки данного рефлексав реальном 3D пространстве, в функциональных сетях мозга происходят целостные структурные изменения, соответствующие актуальным парадигмам овладения этим пространством. На подобных парадигмах и строилась и наша практическая работа, и функциональная магнитно-резонансная томографическая (фМРТ) исследования.

Ключевые слова: аутичный спектр нарушений - ориентировочный рефлекс "Что это?" - эфферентные копии - Общий Адаптационный Синдром.

Introduction

The orienting reflex (OR) is widely interpreted referring to I. P. Pavlov as "an aspect responding to any environmental stimuli attending in which an organism's initial response to a change or novel stimulus makes the organism more sensitive to the stimulation, as when the pupil of the eye dilates in response to dim light" [1]. Let us return to Pavlov's definition.

While studying salivary conditioning, I. P. Pavlov noted that a novel extraneous stimulus would elicit head and body movements toward the new stimulus. He used the terms "what is it?" or "orientation reflex" (OR) in referring to this phenomenon. He observed that the presentation of a novel, neutral stimulus will result in its eliciting what he termed an investigatory reflex that "brings about the immediate response in man and animal to the slightest changes in the world around them so that they immediately orientate their appropriate receptor organ in accordance with the perceptible quality in the agent bringing about the change; making the full investigation of it" [1]. It is important to stress "that the immediate response in man and animals" takes place "to the slightest changes in the world around them", i.e., in spatial scene around them, and "they immediately orientate their appropriate receptor organ in accordance with…" that spatial scene, where the changes take place. Those spatial changes bringing by way of "the perceptible quality in the agent" may take under control the spatial scene of the man or animals and in that way to seizure their space. For them that is the concrete question of their living space, but not the abstract question of any agent in that space. Orienting reflex protects that living space and from this point of view it seems like the defense reflex. Pavlov also mentions not ordinary repetitive for an organism stimulus (liked in light to the pupil of the eye), not any new stimulus (when there is no seizing of the living space) but unexpected novel extraneous stimulus which causes the orienting reflex to control the organism's living space. It is not a stimulus which "makes the organism more sensitive to the stimulation". After all an organism loses the control of the living space and organism generates defensive, fight or flight response relatively to that threat. This response is recognized as the first stage of the General Adaptation Syndrome that regulates stress responses. General Adaptation Syndrome, developed by Hans Selye [2], is a profile of how organisms respond to stress; adaptation is characterized by three phases: a nonspecific mobilization phase, which promotes sympathetic nervous system activity; a resistance phase, during which the organism makes efforts to cope with the threat; and an exhaustion phase, which occurs if the organism fails to overcome the threat and depletes its physiological resources. In the case of spatial orienting reflex predomination, a nonspecific mobilization phase, promotes "full investigation" of the safety of the living space by way of immediate response of vestibular, proprioceptive, tactile organs via spinocerebellar and spinoreticular pathways [3]. Those pathways activate bottom-upreticular formation faster (80-150 milliseconds) as compared with top-down brain calculations (300 and more milliseconds). The descending reticular formation immediately affects posture and autonomic nervous system. Thus, spatial orienting reflex in conjunction with defensive reflex causes strong inhibitory effect over spinal cord interneurons and, therefore, over all other reflexes and sensorimotor efference copies. It also causes strong autonomic/homeostatic effect: the appearance of galvanic skin response, cardiovascular reactions, the change of breath, finally, the emergence of phenomena "desynchronization" bioelectrical reactions in the brain, expressed in the depression "alpha rhythm" (electrical oscillations in 10-12 seconds, typical for the work of the cerebral cortex at rest). In fact, such kind of orienting/defensive reflex makes a man or animals to overcome their local sensation of the space (local vestibular-proprioceptive, tactile, as well as local auditory and visual efference copies are suppressed for the moment) and organism may perceive for the moment global space, as his living space. Along with such mobilizing, the level of excitability of brain regions is raised substantially; dishabituation of its repetitious stimulation takes place, and "desynchronization" of the brain habitual connectivity create favorable conditions for the formation new neural networks corresponding to the global spatial orientation. 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" [4].

In the 1970s, O'Keefe had discovered neurons called place cells in the hippocampi of rats [5]. 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 [6]. 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 simultaneously at several other forwarding places too, as if a rat went globally. Due to reflexive persisting in global spatial orientation a rat can, through particular local places, overcome a maze.

Now we know that grid cells exist and work also in human brain and they have firing fields dispersed over the external 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 in response to orienting reflex "what is it?" not only of where we are, but of global intention as well. Besides entorhinal cortex some other brain regions (prefrontal cortex, hippocampus, basal ganglia, etc.) contribute into the global organization of the brain connectivity. The orienting reflex "what is it?" plays the crucial role in child's development since birth [7]. The body of the child emerging from the womb of the mother is radically changing living space. And the first unconditional homeostatic responses of the body (the rhythm of breathing, heartbeat, body tone, visceral- motor reflex, facial perception) are immediately captured completely with that absolutely novel living space.

The primary sensations of his body-muscle, skin, of his tactile, auditory and visual organs on the mother's breast are imbued with the completely novel for the organism unconditional homeostatic response, with the response-generating innate unconditional

spatial orientating reflex, "what is it?" reflex [7]. Mother, in a state of euphoria, feeling of a newborn on her chest, experiences also homeostatic reactions similar to the reflex state "what is it?" She is full of real physical sense of a completely novel living space with the child. Her eyes, hands, chest, body are literally permeated with this novel reflexive spatial sense of stimulating the child's unconditional homeostatic responses. Thus, the child finds himself in a completely real physical living space, which causes so called the sixth proprioceptive sensation, sensation of actual spatial orienting as "what is it?" reflex. Studies show that within ten minutes after the birth a child can schematically differentiate mother's face. The striking fact, with totally immature perception, a newborn has an actual sense of presence in real 3D space and perceives its features. Moreover, that proprioceptive sense of space develops so rapidly that, as shown by studies, by the third - the fourth week of his life the neural formation of the entorhinal cortex completes which is responsible for mapping the space for the global positioning of the body in space and plays a critical role in spatial reflexive development. Spatial orienting reflex plays the specific function to a child's period of awareness and speech development [8]. The human organism, as we know, while perceiving a stimulus simultaneously forms a sensory efference copy of its motor perception. It refers to any sensorimotor perception: visual, auditory, tactile, motor, etc. In such a way habituation takes place which is absolutely necessary for adaptation. But as the result of such habituation the perception of new stimulus is more and more determined with matrix of efference copies strengthening habituation which in return strengthens a matrix of efference copies, etc. Congenital unconditional spatial orienting reflex enables a child in the pre-speech period to overcome that vicious circle. Later communication, awareness, speech enables to persist on a new stimulus (conscious re-afferentation) and to elicit "what is it?" reflex to some extent. A child in pre-speech period doesn't have such re-afferentation; his organism cannot use awareness to overcome the vicious circle. At the confluence of a number of adverse factors (stress, genetic load, etc.) the orienting reflex might be suppressed and that circle starts playing a leading role in biological mechanism of child's perception protecting in such a way his homeostasis. Spatially oriented/defensive reflex gives a way to defensive reflex per se.

In spite of the fact that both reflexes are protective their spatial frameworks are different. The dominating orienting reflex of the normal child, as we stressed above, protects organism's homeostasis in the world around. The real 3D scenes are the actual living space of an organism's homeostasis and they keep General Adaptation Syndrome (GAS) on the spatial orienting alert relative to the living space [9]. Nonspecific mobilization phase of GAS generates adaptation energy for promotion control of the living space by way of immediate response of vestibular, proprioceptive, tactile receptors, affects posture and autonomic nervous system and causes "desynchronization" of the brain habitual connectivity. Due to such generation adaptation energy, a normal child (sliding down a hill on sleds) may overcome efference copies of his local sensation and may perceive for the moment the global space, as his longed living space. His autonomic/homeostatic affect applies to that living space and during the second, resistance phase of the GAS, distribution adaptation energy takes place along the resisting functional systems, i.e., systems coping with the real 3D scenes (coping with the sliding down per se). Actual coping with such kind of 3D spatial scenes causes affect. An organism gets positive experience to overcome its own efference copies, to strengthen corresponding resisting functional systems, to generate and distribute adaptation energy for that purpose. An organism doesn't deplete its physiological resources; it enriches ability to acquire the living space. No wonder, that a normal child experiences the first stressful phase of AGS as eustress. It is impossible to force an autistic child sliding down a hill on sleds. The defense reflex of the autistic child protects matrix of efference copies as homeostatic balance. The real 3D scene is the threat to that balance and keeps GAS on the defense alert relative to the space [10]. First nonspecific stressful mobilization phase of the ADS generates adaptation energy for safety of the matrix of efference copies and, in fact, is closely intertwined with the second, resistance phase. A homeostatic negative affect of an autistic child applies to that matrix and by way of immediate response of sympathetic nervous system activity distribute adaptation energy along the corresponding resisting functional system not to cope with the sliding down per se. Such kind of resistance doesn't eliminate negative affect. An organism gets negative stressful experience to resist its own efference copies; it fails to overcome the threat and depletes its physiological resources. As the result, an autistic child experiences negative exhaustion as distress. He mostly spends his adaptation energy than it produces. We assume that suppression of the orienting reflex and eliciting defensive reflex plays the key role in General Adaptation Syndrome of an autistic child in pre-speech period which prevents normal development and critically contributes into pervasive brain-body degradation. We argue that the actual treatment in the real 3D scenes may lead to recovery of the orienting reflex and on its basis further developing appropriate brain functional configurations. In our work with autistic children we explore treatment of the GAS in the actual 3D scenes and it brings visible, predictable, and positive results [11].

1. Blocking matrix efferent copies and homeostatic imbalances:

PreSMA/IFG - Basal Ganglia – Cerebellum

Efferent copies are formed in response to the GO command generated by the basal ganglia. These commands are generated by any spontaneous muscle activity of sensory-motor apparatus (visual, audio, skin- tactile, motor, sound, speech motor), for any somatic or visceral suspense.

The basal ganglia are not only generating the GO command, memorize and reproduce it as an efferent copy, preventing afferent information, but it is also causes corresponding neural networks in sensorimotor apparatus of vision, hearing, skin tactile system, motor system. Such neural process is called emulation process which forms neural emulator systems. In fact, it determines the direction and efferent modulation of attention with respect to the matrix of the efference copies. Thus, the basal ganglia are the most important organ of involuntary attention in the midbrain [12].

Blocking begins with control of the prefrontal pre-supplementary motor area (pre-SMA) [13]. Though this field and is a part of the supplementary motor area, but in fact, it is independent. It is not located in the motor area but in the prefrontal area. Its cellular structures are not susceptible to motor signals coming from the muscular-motor system, but the structure associates global spatial incentives eye movements, facial, body, gestures as visual-motor stimuli in the actual 3D scene.

This feature of the area gives a donor chance to influence the visual perception of autistic child exactly with that kind of incentives to generate actual 3D visual-motor association in pre-SMA. It should be emphasized that the result of the association in not visual image of the eyes or the face of the donor in the visual cortex per se, but the spatial orientation.

The pre-SMA in interplay with right Inferior Frontal Gyrus

and Subthalamic Nucleus can inhibit afferent motor cortex (SMA), as well as motor commands of the basal ganglia [14]. Such kind of inhibition (stopping actions) a donor can use, by way visual-motor stimulation within on-line regime of an autistic child's visual perception in the actual 3D scene, to tune the neural network "Pre-SMA/IFG - Basal Ganglia – Cerebellum". Here are brain images of two autistic childs after donor's tuning of that neural network: child A and child R (Figure 1A and 1B).

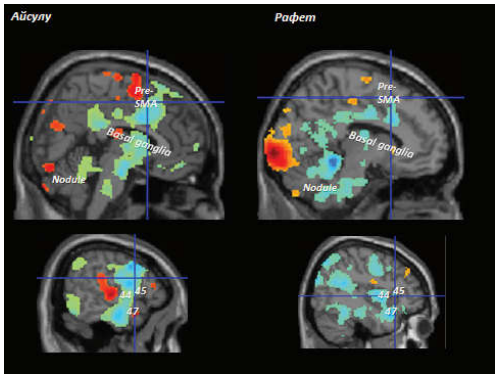

Figure 1A **Figure 1B**

Figure 1A - Brain images of two autistic childs after donor's tuning of that neural network.

Child A is advanced in a donor training **(Figure 1A),** and as we see he demonstrates during functional Magnetic-Resonance Imaging (fMRI) study rather developed Pre-SMA, right Inferior Frontal Gyrus and Subthalamic Nucleus as well as response of vestibular cerebellum (Nodule).

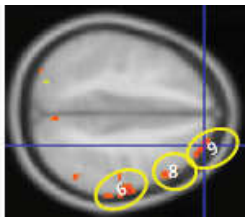

Figure 2

It is significant that at this level of a donor training in the cerebral cortex begins to form the dorsal system of space-based attention **(Figure 2),** as well as an integrated activity of the brain sensorimotor apparatus corresponding to the system of attention **(Figure 3).**

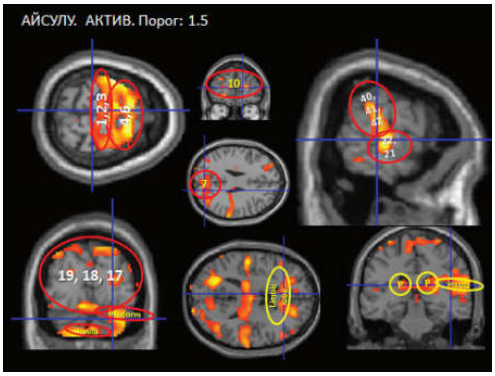

Figure 3 - Image of integrated activity of the brain

Child R is a beginner in a donor training **(Figure 1B)** but nevertheless he also demonstrates the starting point of the same neural pattern formation.

2. Mastering stressors: FEF/SC - Pulvinar – Amygdala

Disintegration and stereotyping of the central or peripheral vision closes for an autistic child normal development of the spatial orienting reflex "What's that?". Preliminary functional vision correction in this case is absolutely necessary. Saccades output is under control of the Frontal Eye Field (FEF) [15]. Tuning of the PreSMA/IFG - Basal Ganglia – Cerebellum functional neural network contributes in vision correction and proper functioning of the Superior Colliculus.

The main function of the Superior Colliculus is the direct body alignment in space relative to the sudden visual-motor stimulation [16]. In this primary function Colliculus is a natural subcortical structure to keep on-line the orienting reflex "What is it?". Therefore, a donor should control a child's 'pursuit - saccades' pattern, or "Global directions staircase of saccades - axis depth tracking of visual-motor association".

Superior colliculus translates the pattern in the same coordinates in Pulvinar. The pattern generates reflexes as the basis of salient attention and the Pulvinar plays in that processing a significant role.

Due to such retinotopic stimulation Pulvinar, its nuclei directly record global orientation and axis depth in the same coordinates as the retina, and the top layer of the Superior Colliculus. Thus, Pulvinar integrates a global vision and a local reflexive orienting "What is it?".

Pulvinar plays a key role in the selection of appropriate incentives, ignoring noise. It plays also a fundamental role in the modulation of the considered stimulation here to generate a corresponding top-down (global) and bottom-up (local) attention reflexive orienting "What is it?". It also stimulates the BA 7 and medial prefrontal areas, modifying actual body motion, actual body state in general in correspondence with the real 3D space [17].

Amygdala is an important part of that processing. There is a short way from the bottom Pulvinar to the Amygdala. It is along this path flow orienting reflexes "What is it?". It comes from the immediate retinotopic registration in the retina and goes to Superior colliculus, and further to the pulvinar, and finally it reaches the Amygdala [18].

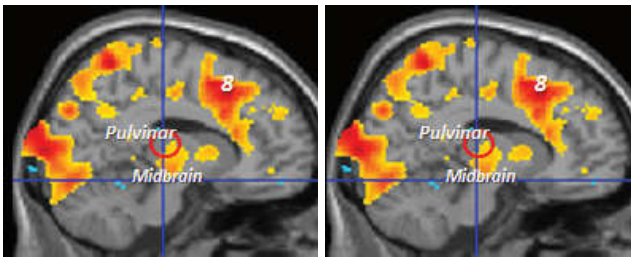

Figure 4 - FMRI study shows that child A, who is advanced in a donor training, demonstrates during donor ship procedure rather developed FEF (BA 8), active Superior Colliculus (Midbrain), Pulvinar, and Amygdala.

A flow of reflexes through Amygdala initiates the release of noradrenaline from the locus coeruleus (LC). It is known that the LC elicits corticotrophin releasing hormone (CRH), which leads to a mobilization HPA axis "fight or flight response". Such kind of homeostatic mobilization, in turn, elicits unconditional response of the body: the condition of skin and vascular reactions, respiratory condition, heart rate, visceral motility, flesh tone, facial expression state, etc.

The stressful energy is generated with homeostatic imbalance and unconditional responses. However, this energy is distributed in the bodily, subcortical and cortical brain networks involved in orienting reflex "What's that?". Thus, the stress becomes the source of the adopting energy to master the stress factors.

Such kind of stress is positive stress or eustress. It causes an affective state, in contrast to negative stress, distress, which inhibits affective state and reproduces an autistic matrix of efference copies. An autistic matrix might be initiated with any unexpected negative event or even with an unpleasant facial expression. A donor helps a child to cope with distress, to learn eustress procedure and in this way to overcome an autistic state.

3.Eustress episodic memory: IA/ACC – EntorhinalCortex – Hippocampus

We argue that spatial orienting affective state "What is it?" replaces autistic state. And consolidation of eustress episodic memory plays an important role in the replacement.

The primary afferent fibers (Ad and C) of small diameter innervate permeate all tissues of the body. They scan the affective condition of the muscles, joints, tendons and skin. Integrated affective afferent information via medulla, periaqueductalgray (PAG), amygdalareaches the cortex –anterior insula/anterior cingulate cortex.

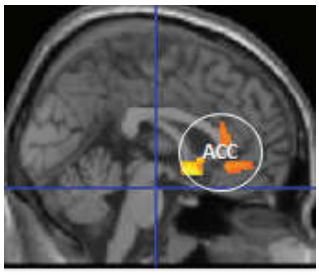

Figure 5A

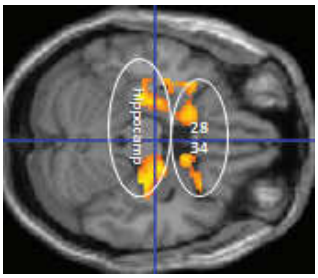

Figure 5B

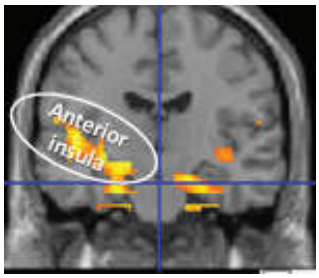

Figure 5C

Figure 5 - The dorsal part of the anterior insula **(Figure 5A)** translates affective corporal statevia spindle neurons to the anterior cingulate cortex **(Figure 5B)** and further to entorhinal – hippocampal system **(Figure 5C)** within a reflex act (80 - 150 milliseconds).

Navigation map of the entorhinal cortex reflects actual bodily stimuli within the 3D real spatial state. Actual global bodily navigation is transformed from entorhinal cortex(EC2) into hippocampal DG, CA3, and CA1 as a global bodily navigation, as well as from entorhinal cortex(EC3) by perfarant path (an opioid way) to CA1 as a local physical condition.

Global navigation plays the role of contextual priming of the hippocampus. During these periods spontaneous global spatial orientation "What is it?" takes place. Episodes are not local stressors per se, but their global interpretation within affective reflexive state "What is it?". The whole affective afferent pathway maintains and modulates "What is it?" reflexive state.

In such a way the initial state of stress "What is this?" elicits the adaptation energy and spontaneously distributes it to those structural and functional systems of the body and the brain, which are directly involved in the actualization of this reflex and, as the result, causes the positive stress, or eustress.

Step by step mastering stressors as "What is this?" reflexive bodily state tunes integrated universal configuration of structural-functional systems of the body and brain turns to be a procedure of gradual displacement of an autistic child's condition, turns to be the non-specific basis for normal general adaptation syndrome.

Conclusion

"What is this?" spatial orienting reflex is unconditional, inborn reflex, but in case of autism it is totally suppressed. We demonstrate in our practice and fMRI study that it might be elicited and recovered through the actual procedures in the real 3D scenes. Moreover, it also leads to normal reorganization of the subcortical and cortical structures of the brain.

We also state that "What is this?" orienting reflex should be permanently reinforced with the corresponding unconditional affective response, in fact, twenty-four hours. Who can provide such reinforcement? From our point of view, it might be only mom.

But for any mom such reinforcement is terra incognito, and that is the terra of novel living space, with totally novel relations, regulations, reflections and control over the brain-body functioning preventing from all forms of alienation. It demands from a mom total transformation of her living space and brain- body activity.

References

1. Pavlov, I.P. *Conditioned reflexes.* London: Oxford, 1927
2. Selye H. The general adaptation syndrome and the diseases of adaptation. The journal of clinical endocrinology. 1946 Feb 1;6(2):117-230.
3. Dietz V. Proprioception and locomotor disorders. Nature Reviews Neuroscience. 2002;3(10):781-90.
4. Hampton T. Nobel Prize Winners' Research Relates to Brain Function and Neurodegenerative Diseases. Jama. 2014 Dec 17;312(23):2477-9.
5. O'Keefe J, Dostrovsky J. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. Brain research. 1971 Nov 12;34(1):171-5.
6. Hafting T, Fyhn M, Molden S, Moser MB, Moser EI. Microstructure of a spatial map in the entorhinal cortex. Nature. 2005 Aug 11;436(7052):801-6.
7. Bradley MM. Natural selective attention: Orienting and emotion. Psychophysiology. 2009 Jan 1;46(1):1-1.
8. Facoetti A, Paganoni P, Turatto M, Marzola V, Mascetti GG. Visual-spatial attention in developmental dyslexia. Cortex. 2000 Dec 31;36(1):109-23.
9. Campbell TS, Johnson JA, Zernicke KA. General adaptation syndrome. InEncyclopedia of behavioral medicine 2013 (pp. 842-844). Springer New York.
10. Epstein RA. Parahippocampal and retrosplenial contributions to human spatial navigation. Trends in cognitive sciences. 2008 Oct 31;12(10):388-96.
11. Matvievskiy V. Holistic functional approach to autism: a case study. USA: Author house; 2013., p 153
12. Mulckhuyse M, Theeuwes J. Unconscious attentional orienting to exogenous cues: A review of the literature. Acta psychologica. 2010 Jul 31;134(3):299-309.
13. Nachev P, Wydell H, O'Neill K, Husain M, Kennard C. The role of the pre-supplementary motor area in the control of action. Neuroimage. 2007 Dec 31;36:T155-63.
14. Hampshire A, Chamberlain SR, Monti MM, Duncan J, Owen AM. The role of the right inferior frontal gyrus: inhibition and attentional control. Neuroimage. 2010 Apr 15;50(3):1313-9.
15. Paus T. Location and function of the human frontal eye-field: a selective review. Neuropsychologia. 1996 Jun 30;34(6):475-83.
16. Jay MF, Sparks DL. Sensorimotor integration in the primate superior colliculus. II. Coordinates of auditory signals. Journal of Neurophysiology. 1987 Jan 1;57(1):35-55.
17. Robinson DL, Petersen SE. The pulvinar and visual salience. Trends in neurosciences. 1992 Apr 30;15(4):127-32.
18. Morris JS, Friston KJ, Büchel C, Frith CD, Young AW, Calder AJ, Dolan RJ. A neuromodulatory role for the human amygdala in processing emotional facial expressions. Brain: a journal of neurology. 1998 Jan 1;121(1):47-57.

How to cite this article: Konovalov R, Matvievskiy V, Mukhametzhanova S. Orienting reflex is the key to autistic brain: fMRI study. J Clin Med Kaz. 2016;4(42):6-11.