КЛИНИЧЕСКАЯ МЕДИЦИНА

НЕРВНЫЕ БОЛЕЗНИ

POTENTIAL OF NEUROENERGY MAPPING IN DIAGNOSIS OF PATHOPHYSIOLOGICAL CHANGES IN THE CENTRAL NERVOUS SYSTEM IN PATIENTS WITH DEVELOPMENTAL DISORDERS

Alexandra Al. Maximova
(ORCID 0000-0002-2149-9256)
Chief Researcher, "Miraculum" Medical Center (Tbilisi, Georgia)
3-5, G. Tabidze Street, Tbilisi, 0105, Georgia;
E-mail: aleksandra-krasn@mail.ru

Andrey Al. Maximov
(ORCID 0000-0002-9839-8701)
CEO, "Miraculum" Medical Center (Tbilisi, Georgia)
3-5, G. Tabidze Street, Tbilisi, 0105, Georgia;
E-mail: am@maximov.com

Yulia M. Silina
"Miraculum" Medical Center (Tbilisi, Georgia)
3-5, G. Tabidze Street, Tbilisi, 0105, Georgia;
E-mail: yullia.silina@gmail.com

Arkadiy Al. Yasashniy
Technical Director, "Miraculum" Medical Center (Tbilisi, Georgia)
3-5, G. Tabidze Street, Tbilisi, 0105, Georgia;
E-mail: bankiru@gmail.com

ABSTRACT

The possibilities and advantages of neuroenergy mapping (NEM) in the diagnosis of pathologies of the central nervous system (CNS) in 78 children with developmental disorders are described. NEM evaluates the intensity of the patient’s cerebral energy exchange by comparing levels of Direct current potentials (DC-potentials) in various brain areas with reference values. Computer visualization of these deviations from the norm was helpful in suggesting the presence of gross pathologies in the CNS.

Its simplicity and convenience make NEM a tool applicable for examining children with severe and complex negative behavior, which sets it apart from other modern, instrumental brain studies. This can solve fundamentally important problems when diagnosing medical causes of negative behavior in children with developmental disabilities.

In this study, NEM first identified children with no dominant CNS pathologies (36 or 46%), and categorized remaining children into their primary type of obvious neurological pathologies (42 or 54%):

- cerebrospinal fluid disorders (24 or 31%);
- central circulatory disorders (9 or 12%);
- cortical ischemia (6 or 7%);
- rare combinations of pathologies of the skeletal, endocrine, and nervous systems (3 or 4%).

Classification of patients into groups of disorders, thanks to NEM data, allowed clinicians to:

- develop and implement protocols for "point-based" follow-up research,
- suggest successful therapeutic strategies based on a final diagnosis, and
- correct pharmacological interventions.

Legitimate therapeutic and pharmacological interventions led to the stabilization and improvement of patients' conditions, up to and including the disappearance of negative behavior.

The approach described in this article is important for children with autism and other developmental disorders. When prescribing medications for these children, many doctors focus on diagnostic criteria such as negative and antisocial behavior (in accordance with official guidelines). However, the causes of negative behavior shown by NEM (for example, brain overexcitation versus cortical ischemia) are quite different, as are subsequent treatment protocols. We recommend that doctors who work with children with similar diagnoses, before prescribing neuroleptics and other medications, pay attention to possible medical causes of negative behavior.

АННОТАЦИЯ

Показаны возможности и преимущества нейроэнергокартирования (НЭК) при диагностике патологий центральной нервной системы (ЦНС) у 78 детей с нарушениями развития. НЭК оценивает интенсивность церебрального энергетического обмена пациента за счет сравнения уровней постоянных потенциалов (УПП) различных зон его головного мозга (ГМ) с эталонными значениями. А компьютерная визуализация отклонений от нормы позволяет предположить наличие грубых патологий в работе ЦНС.

Простота и удобство делает НЭК инструментом, доступным для обследования детей с самым сложным поведением, что выгодно отличает его от других современных инструментальных исследований ГМ. При этом оно может решать принципиально важные задачи диагностики медицинских причин негативного поведения детей с нарушениями развития.

В данном исследовании НЭК позволил сначала выделить детей с отсутствием доминирующих патологических состояний ЦНС (36 детей или 46%), а затем разделить оставшихся по основным типам очевидных неврологических патологий (42 / 54%):

- ликвородинамические нарушения (24 / 31%);
- перевозбуждение коры ГМ (9 / 12%);
- нарушения центрального кровообращения / корковая ишемия ГМ (6 / 7%);
- редкие комбинации патологий костной, эндокринной и нервной систем (3 / 4%).

Классификация пациентов по группам нарушений благодаря данным НЭК позволила:

- разработать и выполнить Протоколы "точечного" дообследования
- предложить на основе окончательного диагноза успешные терапевтические стратегии,
- скорректировать фармакологические вмешательства.

Правомерные терапевтическое и фармакологическое вмешательства привели к стабилизации и улучшению состояния пациентов, вплоть до уменьшения или исчезновения негативного поведения.

Описанный в статье подход имеет для детей с аутизмом и другими нарушениями развития огромное значение. При назначении им фармепаратов многие врачи ориентируются на такие диагностические критерии, как негативное и асоциальное поведение (в соответствии с официальными руководствами). Однако причины негативного поведения, показанные благодаря НЭК (например, перевозбуждение или ишемия ГМ), совершенно разные, также, как и протоколы лечения. Рекомендуем врачам, работающим с детьми с подобными диагнозами, до назначения нейролептиков и других препаратов, обратить внимание на возможные медицинские причины негативного поведения.
**Keywords:** autism, brain hypoxia, developmental disorders, cortical ischemia, cerebrospinal fluid disorders, central circulatory disorders, cerebrospinal fluid disorders, neuroleptics, neuroenergy mapping, ASD, ADHD, epilepsy, episindrome.

**Abstract:**

Purpose of the study:

Develop a technique for using neuroenergy mapping (NEM) for the diagnosis of various pathophysiological conditions in children with diagnoses of autism spectrum disorder (ASD) and other developmental disorders.

Show the effectiveness of NEM in diagnosing:

- cerebrospinal fluid disorders,
- central circulatory disorders,
- cortical cerebral ischemia as one of the of triggering mechanisms for symptomatic epilepsy or, in its short form, episindrome,
- rare (non-obvious) complex combined pathologies of the skeletal, endocrine, and nervous systems.

Describe successful therapeutic strategies and demonstrate the use of NEM in selecting appropriate pharmacological interventions in this study.

Research objectives:

1. Describe the possibilities of NEM as a new tool for diagnosing various pathophysiological conditions in patients with ASD and other developmental disorders.
2. Identify possible correlations between:
   - high Direct current potentials (DC-potentials) in brain ventricular projection and cerebrospinal fluid disorders,
   - significantly increased DC-potentials, especially in the frontal lobe of the brain’s cortex and the relation of its overexcitation with a subsequent psychotic clinical condition.
   - a low DC-potentials and cortical ischemia of the frontal divisions of the brain that increase sharply in tests of fine motor skills and epileptic syndrome.
3. Describe possible uses of NEM in diagnosing rare (non-obvious) combined pathologies of the skeletal, endocrine, and nervous systems as seen in 3 clinical cases diagnosed with:
   - spina bifida of the cervical spine,
   - pituitary adenoma,
   - a combination of Naffziger syndrome (anterior scalen e syndrome), muscular-tonic syndrome, and vertebral artery syndrome.
4. Suggest successful therapeutic strategies for each of the pathophysiological conditions discussed in the article.
5. Explain the rationale for:
   - not prescribing neuroleptics at a low DC-potentials level.
   - prescribing neuroleptics for a high DC-potentials, especially when in the frontal lobe of the brain’s cortex.

- prescribing anti-seizure pharmacological therapy for low DC-potentials and cortical ischemia of the frontal parts (with mandatory verification of the presence of epilepsy or episindrome using EEG monitoring at night).
6. Show that:
   - negative behavior can depend on neurological disorders, and
   - correction of neurological disorders can lead to a reduction or disappearance of negative behavior.

**Research materials:**

This study was conducted at the Center for Integrative Medicine, Miraculum; Tbilisi, Georgia (Integrative Medicine Center Miraculum LLC, State Registry Identification Number #405298244; www.facebook.com/autism.ge); as part of a general research on the dependence of negative behavior and emotional disorders in children and adolescents on various pathological conditions [1; 2; 3].

Within the framework of this project, NEM studies were performed for 78 patients, aged 3 to 19 years, over a period of 4 months from June to September 2020. Diagnoses included childhood autism (F. 84) and atypical autism (F. 84.1) - 59 patients; anxiety personality disorders (F. 41) - 9 patients; hyperkinetic disorders (F. 90) - 6 patients; dissocial personality disorder (F. 60.2) - 4 patients.

At the time of the NEM, 16 out of 78 children were taking neuroleptics (aripiprazole, risperidone, and/or Truxal). Antidepressants, in particular Zoloft and/or sertraline, were given to 5 more patients.

**Research methods:**

1. study of the disease’s history and patient’s life;
2. assessment of physical development;
3. examination by a pediatrician, neurologist, psychiatrist, neurophysiologist, psychologist, oculist, and otolaryngologist;
4. neuroenergy mapping of the brain: study of the intensity of the cerebral energy exchange in the brain through analysis of DC-potentials as determined by changes in the acid-base balance of brain tissues.

Appointment of additional examinations for primary NEM indications:

- Doppler ultrasound (DUS) of the brain and neck blood vessels (intra / extracranial),
- radiography of the cervical spine in three projections,
- EEG monitoring at night,
- additional consultation with an oculist to check the condition of the fundus and visual fields.
5. Basic research protocol, mandatory for all patients at Miraculum, to determine possible pathological disorders in systems other than the CNS:

- feces analysis for dysbacteriosis,
5.2. coprological analysis of feces,
5.3. bacteriological culture of feces with sensitivity to bacteriophages and antibiotics,
5.4. bacteriological culture from the nasopharynx and oropharynx with determination of sensitivity to bacteriophages and antibiotics,
5.5. general analysis of urine,
5.6. bacteriological culture of urine with determination of sensitivity to bacteriophages and antibiotics,
5.7. general blood test,
5.8. tests for: ASLO, lactate, homocysteine; IgG / IgM to Epstein-Barr viruses, cytomegalovirus, herpes type 6; TSH, cortisol.

Research results:
The LCP indications obtained in NEM studies identified the following groups in a total sample of 78:
- children and adolescents with a mix of unstable (reversible) changes and invisible dominant pathophysiological processes - 36;
- patients with high DC- potentials in brain ventricular projection, indicating cerebrospinal fluid disorders - 24;
- patients with a significant increase in DC- potentials, especially in the frontal lobe of the brain’s cortex, indicating an overexcitation;
- patients with a sharp DC- potentials decrease in all areas of the brain’s cortex, with elements of cortical ischemia in frontal areas of the brain that significantly increase during the stimulation of a fine motor skills test;
- patients with persistent cerebrospinal fluid disorders in combination with severe hyperexcitation and ischemia of the brain’s cortex during stimulation tests, including: (1) high DC- potentials in the occipital lobe when diagnosed with spina bifida, (2) high DC- potentials across the entire surface in pituitary adenoma, and (3) low DC- potentials in most of the brain’s cortex with elements of gross cortical ischemia from vertebral artery syndrome.

There were 36 patients with no obvious pathologies. Recommendations for these children included focusing on neurorehabilitation, stimulation of the brain’s cortex, and cognitive development. Analysis of DC- potentials indicators during stimulation tests enabled drawing up of recommendations to parents for rehabilitation and training protocols for their child, taking into account identified features of his or her perception (visual, auditory, tactile, taste, smell, and proprioception). Unfortunately, in the context of the pandemic and current restrictions on the operation of rehabilitation centers in Georgia, it has not, to date, been possible to evaluate the effectiveness of these recommendations.

Depending on the general condition of the child, parents were advised to have medical examinations following the basic protocol for all Miraculum patients (see paragraph 5 in Research Methods). This will identify possible violations that the child might have in major bodily systems, primarily in the gastrointestinal tract and hormonal sphere.

Based on the type of neurological disorder detected, the other 42 patients were assigned additional examinations to confirm or correct preliminary diagnoses (based on the results of NEM). With a final diagnosis, all groups were offered therapeutic strategies as described in this article.

In several cases, NEM made it possible to reasonably correct an existing pharmacological intervention or prescribe a new one. These corrections were based on:
- inappropriately prescribing neuroleptics for brain ischemia (low DC- potentials),
- appropriately prescribing neuroleptics for brain overexcitation (high DC- potentials),
- appropriately prescribing anticonvulsants after EEG confirmation of epilepsy or episyndrome (low DC- potentials / ischemia of the brain’s frontal zones).

After successfully correcting identified neurological disorders, negative behavior disappeared or decreased. For several patients, the degree of reduction depended on whether disorders were present in other major bodily systems. Improvements in condition and behavior were observed in all patients without exception.

Conclusions.
The NEM study itself is not sufficient for a definitive diagnosis, especially in complex clinical cases. However, interpreting obtained data on the level of an acid-base balance - its shift in one direction or another - enables setting the search direction and significantly reduces time, resources, and the necessity for additional surveys. With NEM, it is possible to assume that the causes of disorders of the CNS, whether it is cerebrospinal fluid disorders (and, as a consequence, benign intracranial hypertension), ischemia, or overexcitation of the cerebral cortex. The clinical manifestations of these disorders are largely the same, but the causes and, accordingly, protocols for therapeutic and pharmacological interventions are quite different. In these conditions, NEM significantly reduces the likelihood of gross medical error because it is an instrumental study that does not depend on the human factor.

Dividing patients into 5 groups that referenced the main indications of DC- potentials classifications made it possible to develop and implement standard protocols for a targeted point follow-up examinations of patients, confirm a final diagnosis, and offer a successful therapeutic strategy. In some cases, this included correcting a pharmaceutical intervention.

In the near future (after curtailing or at least reducing restrictions related to the pandemic), a significant expansion of the patient sample and evidence-based clinical practice will lead to an expansion of the various classifications of options and combinations of DC- potentials indications. Accordingly, the classification of groups and subgroups of patients will also become more diverse, especially in terms of cerebrospinal fluid disorders and/or their combinations with overexcitation and ischemia of the brain.

In this article, the possibilities of NEM are analyzed for children with developmental disabilities. This patient
cohort initially assumes a high probability of pathophysiological changes in the central nervous system, so here NEM is expected to show a particularly high diagnostic efficiency. In the future, however, neuroenergy mapping might be quite applicable and also necessary for neurotypical children and adults whose condition and/or symptoms are suspected to be neurological disorders (chronic headaches, insomnia, depression, anxiety).

**Introduction**

Current diagnostic guidelines classify autism and other developmental disorders as mental illnesses. These diagnoses have different national characteristics, but most medical communities focus on the DSM-5 [8] and/or ICD-10 [9] or 11 [10]. With each new revision of the manuals, guidelines, and classifications; the number and variety of developmental disorders grow. Regardless, the basis for their formulation is still the external manifestations of negative, antisocial, stereotypical, and repetitive behavior; with a large, constantly growing, variety of other external signs that include phobias, aggression and self-aggression, toile and sleep disorders, and nutritional disorders. Psychiatrists, psychologists, and other specializations are not encouraged to search for alternative medical causes for negative behavior. In fact, they are often encouraged to ignore the complaints of parents and to refuse to conduct additional examinations that would, in neurotypical children, be carried out without a quibble.

This approach guarantees that, in many countries around the world, the variety of pathophysiological conditions and disorders of children diagnosed with autism and other developmental disorders remains deeply under-researched. For three years, the Center for Integrative Medicine, Miraculum (Thilisi, Georgia), has conducted a series of clinical studies that indicate, first, that children’s negative behavior depends on a variety of pathological conditions, and, second, that this same negative behavior reduces or disappears when successfully corrected. Since June 2020, the results of these studies have been published in Russian and international medical journals. This research focused on such areas as the dependence of negative behavior on general pathological conditions [1], on violations of intestinal microbiocenosis [2], and on hormonal disorders [3]. This article continues the series with an examination into the correlation of negative behavior with pathophysiological changes in the central nervous system.

In this area, the general under-examination of children with ASD and other developmental disorders is compounded by objective difficulties in conducting instrumental studies of the brain and CNS in such patients. Many children, especially in severe cases (most of Miraculum’s patients), are not able to wear an electrode cap or will not allow anyone to install several dozen sensors for an EEG, nor are they able to maintain the immobility necessary for an MRI. Anesthesia is also contraindicated for many, as well as the special contrast mediums necessary for spectroscopy and other functional diagnostics of the brain.

In contrast to, for example, disorders of the gastrointestinal tract, there are significantly fewer or no studies in world science that search for mechanisms that trigger such pathophysiological conditions as cerebrospinal fluid disorders, including increased intracranial pressure (ICP), central circulatory disorders, and overexcitation of the brain’s cortex or its ischemia. Complaints or suspicions of persistent headaches in children diagnosed with ASD are also extremely common. However, according to Miraculum’s parent surveys, doctors ignore these complaints and simply ascribe them to autism in most cases. Often, the level of ICP is not checked, and the possibility of benign intracranial hypertension is not considered.

There are similar reports in the field of ADHD. In a few studies, this developmental disorder is not associated with a possible violation of the central circulation, and a high level of anxiety is not associated with a possible benign intracranial hypertension. In the few studies that focus on high ICP and increased levels of anxiety associated with headaches, attention was mainly paid to children with hydrocephalus [14]. There is a single study showing that ADHD children have impaired cerebral blood flow [7]. However, this conclusion was not reflected in the appropriate use of vascular drugs in the mass diagnosis of vascular pathologies and microcirculatory disorders for children diagnosed with ADHD.

To solve the above-mentioned problems, Miraculum adapted and applied a non-invasive, simple, convenient, and acceptable method of neuroenergy mapping for its children with special needs. It is based on long-known technologies for measuring the intensity of cerebral energy exchange in the brain using DC-potentials (more details later). For the use of NEM in Miraculum’s clinical cases, the authors developed a method of interpreting results. It confirms that in many children with developmental disorders, there are persistent cerebrospinal fluid disorders and/or central circulatory disorders up to and including cortical ischemia of the brain.

When diagnostic guidelines ignore medical reasons for negative and antisocial behavior in children, it has another unpleasant consequence. This is because, in some cases, there is no choice when selecting pharmacological interventions. Currently; neuroleptics, central-acting sympathomimetics, antidepressants, and sedatives are first-line medications for correcting negative behavior in ASD, ADHD, dissociative personality disorder, and other diagnoses associated with developmental disorders. The problem is that seemingly identical manifestations of negative behavior can have different medical causes. Thus, a uniform pharmacological protocol prescribed by official guidelines can lead to counterproductive consequences. In some cases, it aggravates the pathological condition of the child, which is the root cause of negative behavior.

Not surprisingly, many studies in recent years have focused on the side effects of neuroleptics, especially in children:

- the appearance of excess weight,
- extrapyramidal disorders,
- increased blood pressure,
- impaired liver function [11].
The appropriateness of these prescriptions, as well as the diagnostic criteria under which they are prescribed, needs to be examined. Today, unfortunately, a high level of anxious, hyperactive, negative, and antisocial behavior are considered violations. Guidelines dictate that they be corrected using only certain classes of medications, without first searching for medical causes. In other studies, recommendations say not to limit the use of neuroleptics but to also pay attention to other drug classes [13].

A recent study was conducted on the use of baclofen in combination with a neuroleptic to reduce negative behavior in children with ASD. Baclofen showed an excellent effect, but the mechanism of its influence was described through gamma-aminobutyric acid (GABA), the most important inhibitory neurotransmitter of the human central nervous system [12]. However, Miraculum’s clinicians found that the use of baclofen as a central muscle relaxant led to improved behavior in children with ASD for another reason. It stabilized the central circulatory system, primarily blood circulation in the cervical-collar zone.

Selective serotonin reuptake inhibitors are also considered as drugs that can reduce repetitive behavior in children with ASD [15]. In Miraculum’s clinical practice, however, repetitive behavior may be associated with increased ICP and cerebrospinal fluid disorders and/or central circulatory disorders rather than with depression and low serotonin levels.

Another study focused on reducing hyperactivity by using risperidone and propentofylline combined as an activator of presynaptic alpha1 receptors. The decrease in hyperactivity led to a decrease in irritability because, with improved concentration, children became calmer. In other words, improved concentration naturally led to a reduction in negative behavior; in this case, to a decrease in irritability [6].

**Neuroenergy mapping: concept and principles of its work**

NEM evaluates the intensity of cerebral energy metabolism by analyzing the DC-potentials indicators associated with the acid-base balance of brain tissues. DC-potentials refer to a stable difference in the millivolt range potentials recorded between the brain (or extracerebral structures) and reference areas using direct current amplifiers. In a stable functional state, this difference of potentials is stable within 1 mV for tens of seconds. The NEM actually registers slow brain activity. The DC-potentials level correlates with a variety of biochemical parameters of the brain and main bodily systems, allowing resulting data to be used for diagnosing pathophysiological conditions. NEM shows the patient’s DC-potentials in 5 zones of the brain:

- frontal zone,
- central zone,
- occipital zone,
- right temporal zone,
- left temporal zone.

NEM results are compared to the standards of brain activity in these areas. The comparison is based on actual physical indicators, which deviate from the norm in one direction or another and is visualized by the software in a particular color scheme (see Snapshot 1).

**Snapshot 1. Example of NEM survey element**
"The method of registration and analysis of brain DC-potentials, Neuroenergy mapping” (official name), was developed by a doctor of biological sciences, Professor V. F. Fokin, in the Neurophysiology laboratory of the Scientific center of neurology of the Soviet and later Russian Academy of Medical Sciences [5]. In searching for a convenient tool for brain research, NEM was chosen because it can be used for children with complex negative behavior. It is simple to use and non-invasive: Five sensors are attached to the head, with one sensor on the child’s hand; a full-fledged electrode cap is not required. In a difficult situation, you can receive basic information in a few minutes. If possible, we also take samples from stimulation tests. This is the authors’ method developed at Miraculum and a topic for a future independent article. Unfortunately, NEM is currently used to diagnose medical causes of developmental disorders only at Miraculum. The NEM method is either little known or unknown outside of Russia and, accordingly, is not generally used in clinical practice [3; 4].

Research results

The 78 patients who took part in the study were divided into 5 groups according to the classification of DC-potentials indicators. First, patients with no pathologies (Group 1) were separated from patients with obvious neurological pathologies (Groups 2 to 5).

The variety of combinations and indications of DC-potentials do not allow for classification. However, all brain zones reflect close to normal usage, at least in comparison with other patient cohorts. When evaluating processes based on DC-potentials, the following needs attention:

• absence of strong overexcitation of the cortex or parts of the brain’s cortex (absence of brown and, in particular, dark brown color),
• absence of cerebrospinal fluid disorders (no lilac color in the brain’s ventricular projection area),
• absence of severe cerebral cortex ischemia (lilac, bright blue, blue tones),
• smooth (without sharp jumps) excitation of the brain’s cortex during stimulation tests (a predominance of green and yellow-brown colors reflecting the norm for brain operation).

Behavioral assessment of this group of patients using the Vineland scale of adaptive behavior on average showed quite high scores. The average score in the socialization and household skills block was 16 out of a possible 20 points. In motor skills, the average was 18, and in communication and cognitive development, it was 15.

When NEM was administered, this group had no experience in using neurological and psychotropic drugs, and the choice of drug classes used depended on the individual characteristics of the patient. As a rule, drugs that improve the microcirculation of the brain, nootropics and/or antioxidants, were chosen. The goal was to improve and accelerate both the learning process and the effectiveness of correctional therapies. The result was that children learned and assimilated everything faster, memorized faster, concentrated better, and so on.

1 Each brain snapshot is signed with a code. For example, "AA.m.3" stands for the patient’s initials, gender, and age. This makes their medical history and/or complete record of their NEM study easily available.
Due to the absence of dominant pathophysiological changes in the central nervous system, this group belongs to a cohort of patients with relatively mild symptoms. Their condition is close to normal; pathologies are possible but not catastrophic. In these cases, parents and specialists can focus on the children’s rehabilitation and cognitive development. They need competent rehabilitation intervention based on ABA, speech therapy, neurocorrection, audio and music therapy, and sensory therapy.

The above does not mean that patient group 1 does not require medical monitoring and examination. It does mean that medical correction should be designed to stabilize the work of the autonomic nervous system, not the CNS. The latter should provide a reliable basis for introducing pharmacological interventions necessary for the brain to successfully make up deficit cognitive development. From a medical perspective, parents and specialists should focus on stabilizing the gastrointestinal tract by identifying and removing possible foci of chronic infection, while correcting the balance in vitamins and trace elements. In the future, regular monitoring of these indicators is required to verify that pharmaceutical products are activating the brain for maximum positive effect.


In this group, NEM showed a high DC-potentials through outmost of the brain’s cortex (dark brown and/or red), but, in the brain’s ventricular projection area, the already high DC-potentials began to literally “go off the scale” (lilac color). It is the dominance of lilac that is the main diagnostic criterion for the diagnosis of cerebrospinal fluid disorders.

For the most part, even patients who were verbal did not call what they were feeling a headache. In the case of Miraculum’s non-verbal ASD patients, they are even less likely to describe symptoms that a doctor might suspect are cerebrospinal fluid disorders (typically, a blinding headache).

This patient cohort (Group 2) was generally similar in behavior to the others, but they were more likely to show high levels of anxiety, emotional lability, and aggression. These were often manifestations of anxiety and depressive disorder with episodes of low concentration. Some verbal patients described them in words, such as: “I can’t concentrate for some reason;” or “I can’t control my own anger that suddenly appeared out of nowhere.”

When evaluated using the Vineland scale, the lowest average score was in the communication and cognitive development block (9 points), due to a lack of communication skills. Most of these patients avoid normal communication with others due to their uncontrolled outbursts of aggression and anxiety. The average in motor skills was 12. In socialization and household skills, the average was 17, reflecting their higher skills in navigating everyday life.

Prior to NEM, patients in this group took neuroleptics, sedatives, and/or anti-depressants. Verbal patients or parents ascribed no significant effect to this prescribed therapy. There were isolated cases when antidepressants led to some reduction in anxiety, but aggression and other negative manifestations remained.

Customary follow-up examinations for this group included patient referrals to:
- an optometrist to assess the condition of the fundus, and
- a Doppler ultrasonography (DUS) of the vessels of the brain and neck (samples with mandatory rotation).
The samples with rotation detected (but not always!) circulatory disorders. Specifically, it detected the violation of venous outflow and/or the dilation of retinal veins during an optometric examination, indirectly confirming increased ICP. Most cases had similar conclusions, but sometimes the results of the ultrasound Dopplerography and the conclusion of the oculist contained records of possible violations. However, the therapy prescribed to patients in Group 2 to correct ICP led, without exception, to a positive result with an improvement in the condition and behavior of children.

According to NEM and subsequent follow-up examinations of this patient group, a high level of DC-potentials in the brain’s ventricular projection area indicates cerebrospinal fluid disorders with confirmation of benign intracranial hypertension and venous outflow disorders. Unfortunately, in current clinical practice and in most cases, specialists pay little attention to such pathological changes.

It should be noted that in patients with cerebrospinal fluid disorders, a large number of disorders from all systems were recorded. These were mostly in the gastrointestinal tract and reflected the state of intestinal microbiocenosis. Primarily, they included:

- chronic infections in the large intestine,
- enzymatic insufficiency of the digestive system, and
- high bacterial and viral loads (chronic viral and bacterial infections caused by various types of bacteria and herpes viruses).

Therapeutic strategy for Group 2 patients included medications and diuretics to reduce ICP. After administering the prescribed course, symptoms were reduced or disappeared.

In some cases, the existing pharmacological intervention had to be corrected. Depending on the patient's condition, a combination of drugs or monotherapy was given:

- neuroleptics discontinued, and/or
- supplemented with a diuretic, or
- combined with other, more suitable, drugs.

When the strategy for pharmacological intervention was changed, a patient's clinical symptoms were stabilized or significantly improved.


In this group, a sharp increase in DC-potentials is noteworthy, especially in the frontal lobe of the brain’s cortex, indicating a pronounced overexcitation of this zone (red-lilac color). At the same time, the remaining surface of the brain’s cortex is either overexcited (dark brown) or working stably (green).

On the Vineland adaptive behavior scale, these patients had the lowest scores in the area of socialization and household skills and in communication and cognitive development, ranging from 6 to 9 points. Negative behavior included outbreaks of aggression/self-aggression and pronounced emotional lability, in which the child quickly passed from a state of euphoria to one of irritability/depression and back several times a day. Motor skills were at a fairly high level, with an average score of 15 out of a possible 20.

Before NEM, none of the patients were administered neuroleptics. Their main medications were tranquilizers and/or antidepressants. These did not appear to have a positive effect, as parents reported an increase in aggression/self-aggression in some cases, along with increasing obsessive and delusional states, and did not report a decrease in aggression.

The call for additional examinations in this group was based, first, on the basic research protocol for determining possible pathological disorders in other bodily systems (paragraphs 5.1.-5.8. in Research methods). They showed that these patients were dominated by gastrointestinal problems, primarily a variety of infectious processes and enzymatic insufficiency in the digestive system. Bacterial and viral loads were relatively rare and in small amounts. All patients followed an anti-inflammatory nutritional program aimed at increasing the effectiveness of prescribed medications. Individual therapeutic interventions were administered to reduce viral and bacterial loads, if any.

After successful correction of the above-mentioned pathological conditions, a neurologist and a psychiatrist decided with clinicians whether to give neuroleptics. Doses were selected individually, and, after 8 to 10 days, a sharp improvement in the child's condition was generally noted, and behavior stabilized.
Snapshot 5. Level of the brain’s acid-base balance in 6 patients in Group 4
(a sharp decrease in LCP in all parts of the brain’s cortex, with elements of cortical ischemia of the brain’s frontal area)

NEM examinations in 6 patients recorded a sharp decrease in DC-potentials in all parts of the brain’s cortex with a sharp ischemia of the frontal lobe (Snapshot 5-blue and purple). DC-potentials ranged from -17.473 to -21.779 MV (with an average norm of 8.300 MV), indicating a strong imbalance toward acidification in the acid-base balance. In Miraculum’s practice, this violation occurred against a background of pronounced musculoskeletal pathologies in the cervical spine and associated vertebral artery syndrome. An additional diagnostic criterion was an increase in the brain’s ischemia during a stimulation test for fine motor skills (see Snapshot 6).

Snapshot 6. A sharp increase in cerebral ischemia
in conducting trial stimulation of fine motor skills
(left - recording at rest: 200th second of examination; right - test for fine motor skills: 306th second of examination)

In this patient cohort, the focus of cortical ischemia in the brain’s frontal cortex, when conducting a test for fine motor skills, increased sharply and moved to the brain’s parietal cortex area. A significant drop in DC-potentials continued to be recorded in the brain’s frontal cortex. The images clearly show that, within a minute and a half when performing a test for fine motor skills, the child’s brain went into cortical ischemia.

In behavioral terms, this was the most complex patient group. On the Vineland scale, children scored the lowest number of points in all blocks, no more than 5 to 9. Negative behaviors; including sleep disorders, aggression/self-aggression, low concentration, and emotional lability; were observed. Unlike other patients, the fine motor skills block was relatively stable with no gross violations.

Three patients took a prescribed antipsychotic drug, but parents subsequently noted that sleep disorders sharply deteriorated and that the number and strength of aggressive outbursts increased.

Surprisingly, in patients with cortical ischemia, the health of other systems appeared to be unaffected. Recorded violations include minor problems with enzymatic insufficiency of the digestive system. The health of patients in this group appeared to be confined to neurological pathologies.

A low DC-potentials combined with cortical ischemia in the brain’s frontal area, which sharply increased during fine motor skills tests, suggesting the possibility of episyndrome. The protocol for additional examinations requires that EEG monitoring during the night be taken first. Results of this monitoring revealed that all patients had generalized epilepsy or episyndrome with uncontrolled foci of excitation.

After diagnosis, treatment was supplemented with anti-seizure therapy and low-dose medications that improve the brain’s microcirculation. All appointments were coordinated with the epileptologist who led the team for these patients. The children’s condition stabilized within a month. Sleep was normalized, and the number of aggressive outbursts and episodes of emotional lability decreased.

Possible causes of negative behavior in Groups 3 and 4.

Diagnoses of ASD and other developmental disorders are often made based on the same diagnostic criteria (at least within one specific diagnosis). However, the causes of negative and antisocial behavior, sleep disorders, aggression/self-aggression, low concentration, and emotional lability are different. In the first case, it is overexcitation of the brain’s cortex; in the second, it is cortical ischemia (see Snapshot 7). A doctor focusing on external behavioral signs has no reason to distinguish between these two groups of patients. Official diagnostic guidelines require uniform protocols be offered to parents and others. However, if the causes of negative behavior in children with a common diagnosis differ (see Snapshot 7), then the protocols for their correction should also differ. Regardless of a general diagnosis that has the same code and name, with the diagnostic criterion of, for example, negative behavior.
In the first case, the two patients on the left (Group 3, hyperexcitation of the brain’s cortex, especially the frontal lobe) needed neuroleptics and antioxidants. In the second set, the two patients on the right (Group 4, cortical ischemia), the treatment strategy was different. Here, the focus was on improving the perfusion of the brain’s cortex, supplemented by anticonvulsant therapy.

**Group 5. 3 patients with persistent cerebrospinal fluid disorders in combination with severe hyperexcitation or brain ischemia during stimulation tests**

In this group:
- In two cases, persistent cerebrospinal fluid disorders were detected in combination with pronounced overexcitation of the brain’s cortical area during stimulation tests.
- In one case, ischemia of the cortex spread and increased rapidly in all parts of the brain during stimulation tests.

The variety of NEM indications for these 3 patients could not be classified or even grouped. The high level of deviations from standard and the evidence of persistent cerebrospinal fluid disorders led the diagnostic team to search rare combined pathologies of the endocrine, skeletal, and nervous systems. After additional examinations, the following diagnoses were made:
- cervical spina bifida,
- pituitary adenoma,
- Naffziger syndrome (syndrome of the anterior scalene muscle) combined with muscular-tonic syndrome and vertebral artery syndrome.

A 5-year-old verbal child was diagnosed with mild mental retardation and episodes of motor and emotional overexcitation against a background of complete calm. No medications were used, but, based on a diagnosis of ASD, this child was prescribed various corrective and rehabilitation therapies. NEM recorded a highbiquitin-proteasome pathway (UPP) in all parts of the brain, especially in the cortex’s occipital lobe, suggesting the possibility of cerebrospinal fluid disorders. The patient was referred for further examinations and received:
- a DUS of brain and neck vessels (intra/extracranial),
- a radiography of the cervical spine in three projections.

Test results confirmed a diagnosis of spina bifida of the 3rd and 4th vertebrae of the cervical spine, with central circulation disrupted due to a sharp violation of venous outflow. Spina bifida is a birth defect that occurs when the spine and spinal cord don’t form properly, i.e. the spinal cord is factually exposed. It is a rare pathology, and, if not diagnosed in a timely manner, a fall or even a sharp turn of the head can cause a spinal cord fistula with consequences such as paralysis or death. In accordance with established procedure, the patient was referred to a neurosurgeon and an osteopath for consultations and transferred to the permanent supervision of a neurologist for conservative treatment.

This is a 7-year-old verbal child with delayed psychospeech development, flashes of motor arousal, and episodes of echolalia and logorrhea. Neuroleptics initially led to a small number of negative manifestations, but these gradually returned to their original state and continued to increase.
NEM recorded an increase in DC-potentials in all brain areas with a sharp violation of liquor flow. In Snapshot 9, the cortex is lilac, indicating that pressure prevents signals from passing normally and interferes with the brain’s normal blood supply. Stimulation tests led to increased disruption in blood flow.

The protocol for additional examinations included:
- consultation with an optometrist,
- brain MRI,
- hormone tests to check the condition of the pituitary gland.

The oculist recorded significant dilation in fundus veins and a narrowing of visual fields, and, after performing an MRI and hormone tests, a diagnosis of pituitary adenoma was made. The patient was placed under the supervision of a neurosurgeon and endocrinologist.

This is a 6-year-old patient with cognitive development that is almost age-appropriate but with gross violations of fine motor skills and with episodes of emotional lability. No medications were given.

NEM recorded the strongest hypoxia in all parts of the brain’s cortex, with a lightning-fast increase in ischemic foci during all stimulation tests. However, the persistent focus of cortical ischemia on the right was significantly larger than on the left.

Because of these results, the patient received:
- an ultrasound of the brain’s and neck’s blood vessels (intra/extracranial),
- radiography of the cervical spine in three projections.

The additional procedures found:
- severe instability in the cervical spine,
- scalene muscle syndrome,
- vertebral artery syndrome,
- muscular- tonic syndrome,
- instability of the cervical vertebrae.

With these diagnoses, an unexpected and abrupt circulatory disorder may occur if certain steps are not taken. Children with this set of diagnoses should:
- wear a supporting cervical orthosis;
- participate in special gymnastics;
- receive pharmacological interventions throughout the year that include: (1) vascular medications, (2) medications that improve microcirculation, (3) muscle relaxants, and (4) antioxidants;
- be supervised by a neurologist.

This patient was therefore referred to a neurologist and received the following:
- drugs to improve the brain’s microcirculation,
- centrally-acting muscle relaxants,
- cervical orthosis for daytime wear, especially during training sessions,
- observation and classes with a rehabilitation specialist and physiotherapist.

After considering the clinical Snapshot, it was also recommended that a follow-up examination be conducted to detect possible motor neurone disease.

Conclusions

Its simplicity and convenience make NEM available for testing children with the most complex behaviors, which sets it apart from other procedures for modern brain studies. NEM can solve the fundamentally important task of diagnosing root causes of negative behavior in children with developmental disabilities. In this project, NEM facilitated the identification of children with an absence of dominant pathological conditions of the central nervous system and then enabled the remaining children to be categorized by their primary types of obvious neurological pathologies:
- cerebrospinal fluid disorders (high DC-potentials in the brain’s ventricular projection area);
- central circulatory disorders with a high probability of brain overexcitation (significantly increased DC-potentials, especially in the frontal lobe);
- cortical ischemia of the brain, with a high probability of episyndrome (low level of upper cortical ischemia of the frontal area, which increased sharply during tests for fine motor skills);
- rare combinations of skeletal, endocrine, and nervous system pathologies (a variety of non-classifiable DC-potentials indicators).

Classification of patients according to the types of disorders / patologies allowed us to refer children to targeted, on point follow examinations:
- for cerebrospinal fluid disorders: assessment of the fundus, DUS of the brain and neck blood vessels (samples with mandatory rotation), additional studies of the GI tract and Gut microbiocenosis, X-rays of the neck in 3 projections with functional tests, the Basic protocol (see item 5 in the Research methods);
- for brain cortex overexcitation: Basic protocol (see point 5);
- for cortical ischemia: nocturnal EEG monitoring; DUS of the brain and neck blood vessels (tests with rotation are also required), X-ray of the neck in 3 projections with functional tests;
- in rare combinations: assessment of the fundus and visual fields, DUS of the brain and neck vessels (intra/ extracranial), radiography of the cervical spine in three
projections. MRI of the brain and hormonal studies to check the condition of the pituitary gland. The last two are only for the patient with "pituitary adenoma".

In most cases, follow-up examinations confirmed Miraculum’s preliminary diagnoses and offered patients therapeutic strategies that significantly improved the patient's condition and reduced negative behavior. In some cases, NEM indicators indicated that pharmaceutical interventions needed correcting. In particular, the study showed that:

- when the DC-potentials is low, the use of neuroleptics is inappropriate.
- when the DC-potentials is high, especially in the brain’s frontal lobe, the use of neuroleptics is legitimate.
- with low DC-potentials and cortical ischemia, especially in the brain’s frontal area, prescribing anti-convulsive therapy is appropriate (with mandatory verification by EEG monitoring at night).

Finally, there are 3 more independent comments:

- First, an anti-inflammatory nutritional protocol was prescribed for all patients without exception. Diets in each group and for each patient had individual differences depending on the violations found. Therapeutic nutrition, however, was the foundation for successfully correcting disorders in any bodily system, including pathophysiological changes in the central nervous system.

- Second, future expansion of the patient sample and related evidence-based clinical practice is expected to lead to increased classification in the variety of options and combinations of DC-potentials indications. Accordingly, the classification of groups and subgroups of patients will also become more diverse, especially in terms of cerebrospinal fluid disorders and/or their combination with the brain’s overexcitation and/or ischemia.

- Third, NEM was expected to be highly effective in diagnosing children with a high probability of comorbid pathology. The benefits of NEM is also expected to be viable for neurotypical children and adults whose condition and/or symptoms indicate possible neurological disorders.

The main conclusion here, based on observations in this study, is that negative and antisocial behavior of children with the same diagnoses in the field of developmental disorders can have completely different root medical causes. Under these circumstances, external manifestations should not be the only and unconditional criteria for selecting therapeutic, pharmacological, and rehabilitation interventions. Specialists working with such children should use available diagnostic tools, including NEM reports, to determine medical causes of negative behavior and to decide whether an intervention is appropriate.

References:


