INTRAOPERATIVE NEUROPHYSIOLOGICAL MONITORING DURING SURGICAL TREATMENT. REAL-TIME NEUROMONITORING. THE VOICE OF NEUROSURGEON, NEUROPHYSIOLOGIST AND THE HEALTH CARE MANAGER

Jeremi Kościński, Juliusz Huber, Jakub Moskal, Przemysław Daroszewski
1Department of Neurosurgery, University of Medical Sciences, Poland
2Department of Pathophysiology of Locomotor Organs, University of Medical Sciences, Poland
3Department of Organization and Management in Health Care, Wiktor Dega Orthopaedic and Rehabilitation Hospital, University of Medical Sciences, Poznań, Poland

Neurosurgery is a branch of medicine dealing with the diagnosis and treatment of pathologies of the central and peripheral nervous system. Patient safety is paramount during the operation. Intraoperative neurophysiological monitoring plays an important role here. Intraoperative neuromonitoring is used for continuous monitoring of important functions of the nervous system, thus significantly reducing the risk of fatal neurological deficits. During the operation, the surgeon receives feedback on the functions in the operated area by means of neurostimulation and can adjust his further therapeutic strategy in the of emerging neurological changes. Neuromonitoring gives us versatile possibilities during resection of brain tumors with mapping of speech and movement center, in the case of pathologies of posteriori cranial fossa it is possible to control the functions of the cranial nerves and the brain stem, and in the spine it allows for the treatment of intramodullary pathologies and scoliosis.

Currently the most useful for neurophysiological intraoperative monitoring are the motor (MEPs) than somatosensory (SEPs) evoked potentials recordings. The non-invasive approach is preferred to modify MEPs recordings, in many cases criticizing the fundamentalism for neurophysiological research based on Evidence-Based Medicine. Recordings of MEPs with surface electrodes instead needle electrodes including muscles and nerves combinations during neurophysiological monitoring associated with surgical interventions to the spine begin to make sense because of anaesthesiological influences and pediatric purposes (surgeries of juvenile scoliosis). The use of non-invasive surface electrodes during neuromonitoring for MEPs recordings shortens the total time of surgical procedure. The quality of MEPs recordings during intraoperative neuromonitoring from muscles can be significantly influenced by the depths of anaesthesia or muscle relaxants administration, but not those recorded from nerves. The proposed definition of „real-time” neuromonitoring comprises the immediate warning from neurophysiologist about the changes of the patient neurological status during scoliosis surgery (especially during pedicle screws implantation, corrective rod implantation, distraction and derotation of spine) not after the subsequent steps of the corrective procedures. This is possible due to the simultaneous observation of MEPs recordings and the camera picture of the surgical field in the theatre.

Summarizing above, the neuromonitoring comprises motor evoked potentials and somatosensory evoked potentials recordings, which assure the integrity of both afferent
Spinal cord monitoring requires supervision by a neurophysiologist who is active and informative during surgery. Real-time monitoring allows for neurophysiologist to alert the surgeon about any change in parameters of impulses transmission which could signify spinal cord malfunction. Immediate analysis of possible causes of abnormal motor or sensory potentials can result in modification of scoliosis surgery including implant removal, reduction of curve correction or others. Safety of the patient remains the main principle of scoliosis surgery and relies in part on good collaboration between surgeon, neurophysiologist and anaesthetiologist.

Taking into account the issue of health care management, the above introduced methods, among others at the Wiktor Dega Orthopedic and Rehabilitation Clinical Hospital in Poznań, significantly affect the safety of the performed spondyloorthopaedic procedures. Since the use of neuromonitoring not only before and after the treatment, but, what is very importantly intraoperatively, it has been found that the safety of the pediatric patient has increased. From the point of view of the Hospital Management Board, the procedure clearly increases safety and the lack of financial claims resulting from possible complications.

Keywords: neurophysiological neuromonitoring, neurosurgery surgery, scoliosis, health care management

**DOES PRIMARY PROGRESSIVE MS HAVE THE SAME IMMUNOPATHOGENESIS AS RR/SP MS?**

Jacek Losy
Department of Neurology, Poznan University of Medical Sciences, Poland

Multiple sclerosis (MS) presents with different clinical manifestations: RRn (relapsing-remitting), SP (secondary progressive) and PP (primary progressive). Inflammation, demyelination, remyelination and axonal damage are characteristic and fundamental pathological findings in MS. Differences observed in immunopathology among different diseases courses (types) do exist, but are more of quantitative than qualitative nature. Different phenotypes are part of disease spectrum modulated by individual genetic predisposition and environmental influences.

Keywords: multiple sclerosis, clinical manifestations

**STUDENTS SESSION**

**Neurostimulation as a possible therapeutic method in patients with long-COVID neurocognitive problems**

1Bartłomiej J. Czyżniewski, 2Magdalena Gibas-Dorna
1 Students’ Scientific Society, Collegium Medicum, University of Zielona Góra, Poland
2 Department of Applied and Clinical Physiology, Collegium Medicum, University of Zielona Góra, Poland

Micropolarization of the brain has long been recognized as a therapeutic approach for the treatment of neurological disorders. Due to their practicality, noninvasive methods, such as Transcranial Magnetic Stimulation (TMS), transcranial Electrical Stimulation (tES), and transcutaneous Vagal Nerve Stimulation (tVNS), are preferred in
both neurological and psychiatric treatment. These non-invasive techniques are applied directly through the scalp using electrodes or magnetic fields to evoke an electrical current to change cortical excitability, stimulate neuronal connections, and file cerebral neurotransmission. These methods are registered for clinical use worldwide as adjuvant therapy for many neurological disorders such as Parkinson’s and Alzheimer’s disease, vascular dementia, and chronic pain. The outbreak of the COVID-19 pandemic made it necessary to implement new strategies for COVID-19 medication, and what’s more – therapy of its non-pulmonary complications.

Although SARS-CoV-2 is generally considered a respiratory pathogen, it also displays a potent neurotropism, thereby many of the neurological dysfunctions are manifested during the acute phase of infection, and distressingly even months after infection, which is now termed as “Long-COVID”. Long-COVID affects patients through cognitive deficits, concentration and memory disturbances, headaches, which is now commonly defined as 'brain fog'. It also causes neuropsychiatric disorders such as dyssomnia, dementia, depression and even psychosis. Both viral affinity for nerve cells and hypoxia induced by decreased blood saturation as a result of breathing difficulties lead to neuronal damage. According to available data, it affects one third of infected people.

Recently, as the COVID-19 pandemic continues, it has been suggested to implement brain neurostimulation for the treatment of neural complications resulting from Long-COVID. However, until now there are few studies, including clinical trials, confirming the effectiveness of this method. Since no authorized strategies and standards of Long-COVID therapy are formulated, neurostimulation may be considered as a potential therapeutic tool to alleviate neurological symptoms of Long-COVID.

70-year-old patient with hyponatremia mimicking ischemic stroke – a case report.
Maria Derkaczew, Victor Böhmeke Picallo
Collegium Medicum, Department of Neurology, University of Warmia and Mazury, Olsztyn

Introduction

Hyponatremia is a very common electrolyte disorder occurring in neurological patients. However hyponatremia mimicking ischemic stroke is not so widely seen in literature. Low level of sodium in blood serum can cause symptoms like headache, impaired concentration, confusion, imbalance and even symptoms characteristic for stroke like paresis, loss of sensation and one-sided facial drop [1].

Case report

We report a case of 70-year-old female patient admitted to the Stroke Unit of the Neurology Department with a suspicion of ischemic stroke. During examination patient was confused, she was not verbally responsive, she could not execute any of given commands, she presented with bilateral Babinski reflex and global aphasia, with an NIH stroke score of 15 and mRS 5. She vomited profusely before the admission to hospital. Apart from these symptoms no more abnormalities were found in the neurological examination. She was found unresponsive by her family and the day before patient was completely independent and living alone. Medical records revealed that patient was diagnosed with high blood pressure and had a history of depression. Patient’s family reported that she manifested with memory impairment for last couple of days. Computed Tomography (CT) showed no changes characteristic for stroke and the patient did not qualify for thrombolytic treatment or thrombectomy. Laboratory tests showed very low
level of sodium in blood serum (113 mmol/L) and CRP level and leukocytes were elevated. Intensive IV fluid therapy was applied to compensate electrolyte balance disorders. The patient received antiplatelet therapy, Low Molecular Weight Heparin (LMWH), statin and antihypertensive agents. Her Magnetic Resonance Imaging (MRI) showed no ischemic foci in the brain. During hospitalization, the patient’s condition gradually approved.

Conclusions
Many medical conditions such as brain tumors, psychiatric disorders, infections, metabolic disorders or even migraine - also called as Stroke Mimics (SM) in literature - can simulate acute ischemic stroke, therefore it is necessary to implement appropriate diagnostic methods including imaging such as CT or MRI and blood tests - especially glucose level and electrolyte panel [2]. Hyponatremia can cause appearance of many neurological symptoms and also the ones characteristic for ischemic stroke. When correcting the level of hyponatremia, it is important to gradually (less than 10 mmol/L per 24 hours) increase the level of sodium in blood serum to avoid serious complications, such as central pontine myelinolysis [3].

Keywords: ischemic stroke, hyponatremia, stroke mimics


Functional polymorphism of the μ opioid receptor
Magdalena Chrószcz, Jan Rodriguez Parkitna
Molecular Neuropharmacology Department, Maj Institute of Pharmacology Polish Academy of Sciences, Krakow, Poland

The μ opioid receptor is the primary target of opioid drugs. It is ubiquitously expressed in the central and peripheral nervous system where it is involved in the regulation of nociception, analgesia, motivation, reward and hedonic homeostasis. Prolonged or excessive activation of the receptor by drugs can lead to serious adverse effects like respiratory depression, tolerance to the analgesic effects and development of addiction. Despite years of extensive research, mechanisms behind the adverse effects remain poorly understood. One potential factor affecting various effects of activation of the receptor is its transcriptional polymorphism. M opioid receptor is a G-protein coupled receptor which is encoded by the murine Oprm1 gene. Multiple transcript variants of the gene were reported, products of alternative splicing, two possible transcription starts, and several termination signals. Altogether up to 30 distinct protein isoforms were reported as possible. The protein products may be divided into three sets, containing 7, 6, or one-transmembrane helices, that differ in length and also N- and C-termini. Diversity in protein sequence likely affects affinity for ligands and downstream signalling pathways. Importantly, the expression of the various isoforms was reported to be specific to discrete brain regions. Antisense mapping and studies on knock-out mice show that animals devoid of some of the isoforms express function changes like distinct response to morphine and other analgesic drugs. Here, I summarise the knowledge about various
isoforms of the μ opioid receptor, their functional significance and the potential of specific variants of the receptor to be a target for the new analgesic drugs.

Keywords: μ opioid receptor, alternative splicing, isoforms, analgesia, opioid drugs

**BDNF, acute ischemic stroke and poststroke depression**
Eryk Wacka¹, Agnieszka Zembron-Lacny²
¹Collegium Medicum University of Zielona Gora
²Department of Applied and Clinical Physiology, Collegium Medicum University of Zielona

Acute ischemic stroke is a sudden neurologic dysfunction caused by focal brain ischemia. Also it is the most common serious manifestation of cerebrovascular disease, the dominant cause of death in the European Union (approx. 1.2 million incidents of strokes per year) and a major cause of severe disability including poststroke depression (PSD). It is very significant to identify potential markers that can help to detect patients with stroke at high risk of PSD development.

Brain-derived neutrophic factor (BDNF) is a growth factor of nervous system serving many critical functions. It has been demonstrated that BDNF has a role in processes such as neuronal maturation, synapse formation and synaptic plasticity among others in the brain. BDNF level is lower in acute ischemic-stroke patients compared to healthy population. There is a potential association between circulating BDNF concentrations at admission and subsequent PSD development, and it provides additional support for the involvement of BDNF in the PSD development.

Based on literature review the results demonstrated that serum levels of BDNF were significantly lower in patients with PSD compared with patients without depression at the acute stage of stroke. However, the exact mechanism of BDNF involvement in the development of PSD remains unclear at present. More epidemiological and laboratory research are needed in this area to draw more definite conclusions. Therefore, we present the current data on the role of BDNF in stroke patients, concentrating on lifestyle factors such as diet and daily physical exercise.

**Chemotherapy-induced neuropathy (CIPN)**
Brandon Bujak
Faculty of Biology, Jagiellonian University, Cracov, Poland

Chemotherapy induced peripheral neuropathy (CIPN) is one of the most common side effect of cancer drug related treatment that shows neurotoxicity effect on human body with the risk of getting it can get up to a level of 85% among cancer patients. The overall cause of its appearance lays in the damaged by chemotherapy peripheral nerves. On going CIPN is described as pathological sensory state that can spread to motor and autonomic nerves pathologies as well if left untreated. Clinical picture of this disease depends on many conditions, but it is mostly described as pain in various forms including tingling, burning, cramps and different degrees of its intensity, which depends on selected way of treating patient. Most popular anti-cancer drugs like platinum-based drugs, taxanes, Vinca alcaoids have a high risk of causing a CIPN. The neurotoxicity of the drugs depends on many conditions (e.g. age, intensity of treatment, drug dosage). Chemotherapy induced peripheral neuropathy can affect ability with daily activities like walking, writing, exercising, but not limited to changes in blood pressure, paralysis and
organ failure. Challenge has been thrown down not only on patients that suffers from constant felling of severe, chronic pain, but also on doctor prescribing therapies due to mentioned before conditions of treated patients, can lead to reduction or even complete cessation of the treatment. Accurate evaluation is crucial to enhance information round incidence and occurrence of CIPN. Consensus is needed to standardize evaluation and diagnosis, with use of proven tools. Detailed phenotyping of the clinical syndrome movements toward a precise medical approach, to individualize remedy. Understanding substantial threat elements and pre-current vulnerability can be used to enhance techniques for CIPN prevention, or to apply focused treatment for established CIPN.

Keywords: Chemotherapy-induced neuropathy (CIPN), cancer, peripheral neuropathy, neuropathic pain, chemotherapy

**Severe Raynaud's phenomenon in the course of systemic sclerosis – vascular and neurologic background**

Chanika Assavarittirong, Bogna Grygiel-Górniak
Department of Rheumatology, Rehabilitation and Internal Diseases, Poznan University of Medical Sciences, Poland

Introduction

Raynaud's phenomenon (RP) is a disorder characterized by vasoconstriction of the digital arterioles upon cold exposure or emotional stress. RP could be primary (idiopathic) or secondary to connective tissue disorders. Studies found that the pathogenesis of RP may involve genetic, vascular, and neurological factors. The autonomic nervous system may play an essential role in pathogenesis in secondary RP. The alpha 2c-adrenergic receptor relocates from the Golgi apparatus to the plasma membrane in the cold. Consequently, increased expression of alpha 2c-adrenergic receptors is observed and its activation through the rho kinase signaling pathway mediates cold-induced vasoconstriction. Increased expression of alpha 2c-adrenergic receptors has been reported in RP. The overproduction of vasoconstrictors such as endothelin-1 and angiotensin II plays a crucial role in RP pathogenesis. Moreover, it worsens vascular damage, mainly if RP is secondary to systemic sclerosis (SSc).

This case report presents a severe case of RP secondary to SSc, which resulted in feet necrosis and amputation of the hand and feet digits.

Case report

We present a case of a 57-year-old female patient diagnosed with SSc. Her initial symptoms appeared at the age of 15 in the form of RP, followed by wrinkles around the mouth and diffuse hardening of the skin, dysphagia, and telangiectasia. The patient presented severe RP, which evolved to the necrosis of the phalanges. There was an increase in the skin hardening and tension of the face and hands. During the hospitalization, the patient was administered intravenous immunoglobulin. A severe course of necrosis led to her hand and toes amputation. Upon admission, numerous foot ulcers were found on both sides. The medical history includes aortic stenosis, secondary Sjögren's syndrome, osteoporosis, right eye cataract, gastroesophageal reflux disease, a penicillin allergy.

Conclusion

RP is one of the most common initial symptoms of systemic sclerosis. Patients with SSc and RP are more prone to develop ulceration and necrosis of the digits. This case presented the complication of RP, which its neurological and vascular pathogenesis could
potentially explain the severe complications. Early intervention and patient education of SSc can reduce the risk of complication and maintain the patient's quality of life.

**A clinical application for Hindenberg's blimp; hydrogen in the treatment of brain injury**

Benjamin Shamiram Samantha, Au Tsz Yuen
Poznan University of Medical Sciences, Center for Medical Education in English, Poland

**Background**

Brain injury (BI) is well-known as a potential cause of irreversible brain damage in humans, often leading to impairment of bodily functions, paralysis, or even death. The etiology of BI may be linked to many factors including trauma, ischemic and hemorrhagic stroke, or ischemia-reperfusion injury, even intentional deep hypothermic circulatory arrest (DHCA) as part of surgical preparation. Currently, there exists no effective treatment in the reversal of BI in patients. However, experimental studies on using hydrogen-rich saline or gas inhalation in animal models has revealed neuroprotective effects; in the setting of BI, hydrogen serves as an antioxidant, anti-inflammatory, and a cytoprotective agent, ultimately aiding in the reversal of cellular damage.

**Methods**

A literature review of current studies was performed in 2022, utilizing the Pubmed database. Any studies which focused on the treatment of BI using hydrogen-rich saline were included; relevant keywords searched were: hydrogen-rich saline; brain injury; molecular hydrogen; hydrogen therapy; animal study. After compiling all applicable studies, a total of 16 studies were included in this review.

**Results**

In reviewing the 16 studies found, 5 of them focused on subarachnoid hemorrhagic injury, 2 on traumatic injury, 1 on damage from cardiopulmonary bypass, 1 on a resuscitated cardiac arrest patient, 3 following ischemic-reperfusion, and 1 instance of DHCA (surgical procedure). One study observed the effect of hydrogen gas inhalation while the other 15 utilized hydrogen-rich saline infusion; each of the 16 studies illustrated that the therapeutic application of hydrogen alleviated BI.

**Conclusion**

In conclusion, though there have not yet been any clinical trials in human subjects, preliminary studies on animal models show promise in the treatment of various brain injury (BI) by means of therapeutic hydrogen in saline or gaseous forms.

**Can microbes save us from cognitive impairment in neuropsychiatric diseases, especially depression?**

Maria Dobieńska¹, Natalia Karina Bartosik¹, Michał Seweryn Karbownik²*

¹ Students' Research Club, Department of Pharmacology and Toxicology/Students’ Scientific Society of Pharmacology, Medical University of Lodz, Lodz, Poland
² Department of Pharmacology and Toxicology, Medical University of Lodz, Lodz, Poland

Cognitive impairment occurs in various neuropsychiatric diseases. Due to the gut's influence on the brain, a promising therapy might include microbiota-targeted interventions, which include probiotics, prebiotics and synbiotics.

One of the mechanisms of cognitive impairment among patients with depression or anxiety is excessive oxidative stress and inflammation. Possible utility of microbiota-targeted intervention derives from the fact that antioxidant properties of probiotics are
documented and multi-dimensional. For example, by reducing oxidative stress, probiotics increase the level of brain-derived neurotrophic factor, a protein contributing to neuroplasticity. Anti-inflammatory properties of probiotics have also been broadly discussed.

Cognitive impairment among these patients is also hypothesized to be caused by hypercortisolemia, triggered by disturbances in the hypothalamus–pituitary–adrenal axis. Research indicates that administration of probiotics could alleviate these abnormalities.

Synaptic plasticity might be also affected by reduced functionality of monoamines, typical in depressive patients. Probiotics have a broad impact on metabolism and functioning of monoamines.

Cognitive impairment in depression, especially late-onset depression, as well as in Alzheimer’s disease might be related to the presence of amyloid-beta in the brain. Preclinical studies revealed that probiotics administration decreased amyloid-beta aggregation in the brain and improved spatial memory.

Probiotics are also hypothesized to be an effective therapeutic option against arteriosclerosis, therefore they might as well prevent ischemic-related cognitive impairment.

Until now, the value of probiotics in the treatment of cognitive impairment in depression remains inconclusive. So far, only Rudzki et al. (2019) performed a clinical study in this field and the therapy using probiotics combined with SSRI was found successful. The potential that this treatment carries calls for more clinical studies.

Keywords: probiotics, depression, cognitive impairment, neuropsychiatric diseases

May addictive stimuli modulate adult neurogenesis in the nucleus accumbens?

Witkowska M.¹, Wiśniewska J.², Beroun A.²
¹Faculty of Medicine, Medical University of Warsaw, Poland
²Laboratory of Neuronal Plasticity, BRAINCITY, Nencki Institute of Experimental Biology PAS

Neurogenesis is the formation of new neuronal cells. Possibility of this process taking place in the adult mammalian brain has been hotly debated throughout decades. Nowadays, the presence of adult neurogenesis is widely accepted in the hippocampus in humans and additionally in the subventricular zone in rodents (Owji & Shoja, 2020). Moreover, two recently published articles have identified a subpopulation of neuroblasts in the nucleus accumbens (NAc) (Chen et al., 2021; García-González et al., 2020). It has been suggested that these neural progenitor cells originate during an adult neurogenesis, which was mediated by external stimuli - chronic pain (García-González et al., 2020). NAc is a structure crucial for addiction-related behaviours such as drug craving and drug seeking (Scofield et al., 2016). It has been shown before that administration of cocaine can affect adult neurogenesis in the hippocampus (Noonan et al., 2008). Therefore, it is reasonable to suspect that addictive stimuli would modulate adult neurogenesis in the NAc.

In order to test that hypothesis a pilot study was conducted. The aim of the study was (1) to reproduce the identification of neuroblasts in the NAc and (2) to compare their quantity in mice that underwent addictive training with the mice from the control group. Herein, mice were exposed to either 7 days of cocaine or saline intraperitoneal injections. 2h after the last injection brains were extracted, fixed with paraformaldehyde and sliced on the vibratome. Finally, the protocol from the paper of Diego García-González et al. (2018) was
adopted in order to confirm that neuroblasts or glia-like fibers may be present in the area of NAc. Immunohistochemistry staining was performed on the mice brain tissues. Slices with immunolabeled markers of neuroblasts (DCX) and radial glia-like fibers (GFAP) were imaged with a fluorescent microscope. The results confirmed the presence of neuroblasts in NAc. Moreover, an increased number of neuroblasts was found in cocaine-treated animals. The results of this experiment are a message to continue further study to broaden knowledge about the origins of neuroblasts in the area of NAc.


Monoclonal antibodies blocking CGRP for prevention of migraine

Alicja Maziarczyk, Dominika Miazga
Students’ Neurology Society, Medical University of Lublin, Poland

Monoclonal antibodies blocking calcitonin gene-related peptide (CGRP) are a novel treatment strategy developed specifically for prevention of migraine. Four drugs belong to this group: eptinezumab, fremanezumab and galcanezumab, which bind to the peptide; and erenumab, which blocks the CGRP receptor. CGRP is involved in nociception and plays a crucial role in the pathophysiology of migraine, as it is released in the trigeminal ganglion as a response to local cerebral vasoconstriction in order to cause dilation of the vessels and maintain cerebral blood flow. Moreover, administration of CGRP, especially among migraineurs, induces a migraine-type headache.

The aim of the paper is to discuss the potential of monoclonal antibodies blocking calcitonin gene-related peptide for the prevention of migraine and to outline their safety and efficacy profile. Several randomised clinical trials have shown a significant efficacy of these drugs compared to placebo in reducing monthly migraine affected days, among patients suffering from both episodic and chronic migraine. Anti-CGRP monoclonal antibodies exhibit a superior benefit-to-risk ratio than established preventive treatments (topiramate, propranolol, onabotulinumtoxinA). Incidence rate of side effects is low; the most common were mild to moderate (e.g. pain at the injection site, upper respiratory tract infections, nasopharyngitis, back pain and urinary tract infection). Randomized controlled trials are still needed in order to compare different anti-CGRP monoclonal antibodies and assess their long-term safety profile. In addition, high costs of treatment
using monoclonal antibodies make this therapy available only for a limited number of patients. In conclusion, these drugs seem to provide promising prospects of improving the lives of migraineurs. As based on current knowledge, the benefits are superior to the likelihood of harm.

Keywords: CGRP monoclonal antibodies; Migraine prevention; Calcitonin gene-related peptide

**Issac syndrome-case report**

Dorota Bejga, Julia Kwaśniak, Jadwiga Wolińska, Beata Łabuz-Roszak

Students Neurological Association, Department of Neurology, Medical Sciences Institute, Opole University, Poland

Chanellopathies are described as congenital, autoimmune or transcriptional disorders of ion channels. Isaacs syndrome is an example of a rare genetically conditioned chanellopathy and it is a myotonia associated with potassium channels disfunction. The mutation determines a disorder of a resting potential as well as generation and propagation of an action potential. This results in dilution of a threshold level of a peripheral nerve excitability which is followed by the peripheral nerve hyperexcitability (PNH). Clinical signs of neuromyotonia are characterised by constant activity of muscle fibres resulting in twitches, stiffness at rest and delayed muscle relaxation after voluntary contraction. A diagnostic path of a 49-year-old patient, diagnosed towards Isaacs syndrome was described in a case report. All the knowledge on this disease as well as the diagnostic tests and available treatment has been gathered based on this example.

**The role of nerve growth factor in controlling anxiety-related and stress-related behaviors**

Hanna Nikanava

Institute of Zoology and Biomedical Research, Department of Neurophysiology and Chronobiology, Jagiellonian University in Kraków, Poland

Anxiety disorders are very common conditions in the human population. They affect both adults and children, and their consequences are associated with significant suffering. Anxiety plays an important adaptive role as one of the typical emotional symptoms of a stress response to threat. However, in anxiety and stress-related disorders such as generalized anxiety disorder (GAD), specific phobias, obsessive compulsive disorder (OCD), panic attacks, post-traumatic stress disorder (PTSD) and others, anxiety may appear in the form of persistent excessive worries occurring even in the absence of an appropriate stressor. The neural mechanisms underlying anxiety and stress-related behaviors are being intensively studied to develop more effective therapies for the above-mentioned disorders.

Nerve growth factor (NGF) is the first discovered and best described protein in the family of neurotrophins. It plays a key role in the differentiation and survival of sensory and sympathetic neurons, in the development of the nervous system, it participates in pain signaling and maintains the normal function of cholinergic neurons. Moreover, a growing body of research suggests that NGF is also implicated in the regulation of psychoneuroendocrine plasticity. The involvement of the nerve growth factor in the control of anxiety and stress-related behaviors has been demonstrated both in experiments on laboratory animals and in human studies. However, the exact mechanisms
by which NGF influences these behaviors are not fully understood and are still being investigated. The aim of my presentation is to show the current scientific knowledge on the participation of the nerve growth factor in the regulation of anxiety and stress-related behaviors and to describe the currently known mechanisms by which NGF influences them.

Keywords: nerve growth factor (NGF), hypothalamic-pituitary-adrenal (HPA) axis, stress, anxiety, mental disorders

A boy with newly described TUBB3 R262H syndrome.
Folga Barbara¹, Śmigiel Robert², Winczewska-Wiktor Anna³, Niedziela Marek⁴, Kolesińska Zofia⁴
¹Pediatric Endocrinology Research Group, Poznan University of Medical Sciences, Poland
²Department of Pediatrics, Division of Propaedeutic Pediatrics and Rare Disorders, Wroclaw Medical University, Poland
³Department of Developmental Neurology, Poznan University of Medical Sciences, Poland
⁴Department of Pediatric Endocrinology and Rheumatology, Poznan University of Medical Sciences, Poland

Introduction: The TUBB3 protein constitutes a beta-tubulin isoform in neurons, which serves as a component of microtubules, cytoskeletal structures implicated in neuronal migration and neurite growth. Missense mutations in the TUBB3 gene can lead to congenital fibrosis of the extraocular muscles type 3 (CFEOM3) with or without various neuropathies and endocrinopathies. Several distinct genotype-phenotype correlations have been described, including TUBB3 R262H syndrome in fourteen individuals.

Case report: A 20-month-old boy with bilateral congenital ptosis and facial weakness, left eye strabismus and nystagmus, poor right eye movements, psychomotor delay, sensorimotor polyneuropathy and hearing loss was referred to an endocrinologist because of suspected hypogonadism. On clinical examination, micropenis and bilateral cryptorchidism were observed. Low serum levels of inhibin B and anti-Müllerian hormone (AMH) with a normal gonadotropin rise following a gonadotropin releasing hormone (GnRH) stimulation test were indicative of hypogonadotropic hypogonadism (HH). MRI of the brain revealed hypoplasia of the corpus callosum with subsequent deformation of the ventricular system and hypoplasia of olfactory bulbs. Whole exome sequencing (WES) confirmed a heterozygous pathogenic variant R262H in the TUBB3 gene.

Conclusions: The newly described TUBB3 R262H syndrome constitutes the most severe form of syndromic CFEOM. With the help of enhanced genetic testing and established phenotype-genotype correlation, more tailored multidisciplinary medical care and genetic counseling can be assured.