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International Clinical Protocol on Vestibular Disorders (Dizziness)

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Abstract

26-28 May at 43 Congress of Neurootological and Equilibriometric Society (Budapest, Hungary) International Clinical Protocol on Vestibular Disorders (Dizziness) being discussed and accepted as Consensus Document. Cochrane reports estimates that dizziness has prevalence of 22.9% in the last 12 months and an incidence of 3.1%. Only 1.8% of adults consulted a physician in the last 12 months. Cochrane reviews suggest that the evidence base for dizziness evaluation is weak, thus necessitates the creation of evidence-based document. Protocol is based at the new concept of vestibular system, which involves the vestibular peripheral sensors, space orientation tetrad, vestibular presentations in the brain cortex and vestibular effectory projections in the brain. Labyrinth consists of sensors, for which six modalities are adequate: 1. acceleration, 2. gravitation, 3. low frequency whole-body vibration, 4. Infrasound, 5. magnetic impulse, 6. metabolic changes. Vestibular system from rhomboid fosse gets the inputs from visual, acoustic, somatosensory organs, integrating them and forming space perception and orientation. Interaction with space is realized through sensory, motor, vegetative and limbic projections. So, vestibular disturbances may manifest as paropsia, tinnitus, numbness. Vestibular evoked potentials (not VEMP) and craniocorpography have highest sensitivity (90% and more). As vestibular dysfunction has recurrent character patients need monitoring.

Keywords: vestibular disorder, hair cell, meniere's disease.

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SCOPE OF PROBLEM

Dizziness is the third reason of patient admittance to the doctor in USA[1]. According to Cochran reports a representative sample of 4869 adults in Germany being screened for dizziness, and 1003 individuals with dizziness underwent validated neurootologic interviews to differentiate vertigo from dizziness. Dizziness/vertigo has a prevalence of 22.9% in the last 12 months and an incidence of 3.1%. For vertigo, the prevalence is 4.9% and the incidence is 1.4%. 1.8% of unselected adults consulted a physician in the last 12 months (0.9% for vertigo). After 88-90 y.o. the figures increase to 51-45%, respectively[2]. Compared with dizziness, vertigo is more frequently followed by medical consultation (70% *vs.* 54%; $P < 0.001$), sick leave (41% *vs.* 15%; $P < 0.001$), interruption of daily activities (40% *vs.* 12%; $P < 0.001$), and avoidance of leaving the house (19% *vs.* 10%; $P = 0.001$). More than half of the participants with "vestibular vertigo" reported "nonvestibular diagnoses". Age and sex-adjusted health related quality of life was lower in individuals with dizziness compared with dizziness-free control subjects[3].

Objectives

Cochran reviews suggest that the evidence base for dizziness evaluation is weak. Meta-analyses and systematic reviews are particularly important for clinicians because these studies design minimize bias and summarize evidence in a manner useful to clinicians. Unique guidelines summarize important measures of diagnostic accuracy (e.g., sensitivity, specificity, and coherence) – the information which is the most useful when making medical decisions. When the sensitivity and specificity of posturography was assessed by a meta-analysis design, both of these operating characteristics were only about 50% for identifying vestibular disorders – indicating that the test results do not influence the probability of the outcome[4]. In fact, none of the guidelines were even intended to be a clinical practice guideline for dizziness. Other than BPPV and Ménière's disease, meta-analyses and systematic reviews were only found on alternative interventions[5]. The statement on acoustic neuroma stems from a National Institutes of Health Consensus Development Conference – which aim to present useful consensus information to health professionals, but is not intended to be clinical practice guidelines[4]. The guideline on ischemic stroke only briefly addresses dizziness[6]. All this has leaded to that unprofessional management is much worth, than no treatment.

Evidence for interventions – including re-positioning for BPPV – is insufficient and for medication therapy is absent entirely[5]. Thus, more empirical studies, systematic reviews and meta-analyses on relevant dizziness topics are needed so that evidence is established in a way that will inform clinicians and also research agendas. Guideline statements can then be developed to transform evidence into actual recommendations for clinical care. With these priorities, future work could make an important contribution to the efforts in optimization of healthcare utilization for one of the most common symptom presentations in the entire medicine[4]. Proposed in 2012 by Neurootological and Equilibriometric Society Consensus Expert Document "Guidelines on dizziness and space orientation disorders"[7] is decided to become the theoretical basis for creation of International Clinical Protocol on Vestibular Disorders (Dizziness). This Protocol has been voted by the 43 Congress of the Society to be Consensus Document 26-28 May in Budapest, Hungary and is proposed for development of the National and local protocols.

Danger of vestibular disorder

Dizziness is a predictor of severe diseases[7,8]. The course of sickness is the same in the cases of light head trauma[9], ionizing or electromagnetic radiation[10], vibration disease[11,12] or intoxication[13]. Cunning feature of disorder is that initial reaction transforms into imaginable wellbeing. Both patient and doctor are sure that the disease is over. But, during 25-years monitoring dizziness in Chornobyl clean-uppers, it has been shown that after the period of imaginable wellbeing primary peripheral distortion in two-three years starts to involve higher levels of brain[10], involving motor, vegetative and limbic systems, resulting in organic pathology: neurologic, cardiovascular, psychiatric[8]. When the process reaches brain cortex, the balance of cortical processes is disturbed, causing immune failure[11], which finishes with chronic, autoimmune and oncologic diseases[14]. In the cases of severe damage this process is running quickly, in moderate – it becomes chronic and long lasting, but its development is the same[15].

Concept of vestibular system

Dizziness in its wide meaning is met either alone or associated with certain disease. It accompanies seasickness, meteosensitivity, diabetes and other metabolic disorders, hepatic dysfunction, it is met in gynecology: 14-15 years old girls, first trimester of pregnancy, and during climax; in the cases of cardio-vascular diseases, in postoperative period, in oncology, especially during chemotherapy, and as a result of stress, head trauma, intoxication or infection[16]. It may be of occupational origin in the form of vibration or monitor disease, the result of ionizing or electromagnetic fields irradiation[8].

In many cases it has functional and not organic character, among patients with dizziness complaints only in 29% the CT scans and in 40% MRI have shown abnormalities: atrophies, infarctions, demyelization[17]. In general being widely spread dizziness is not enough studied, often resistant to therapy and results in invalidity of patient[18]. Wide scale studies of dizziness, being done from 1974 till today by Neurootological and Equilibriometric Society, as well as knowledge accumulated by Barany Society and Society for Neuroscience, have lead to the *concept of vestibular system,* which involves the

vestibular peripheral sensors, space orientation tetrad, vestibular presentations in the brain cortex and vestibular effectory projections in the brain.

Vestibular peripheral sensors

Each analyzer consists of peripheral sense organ and its pathways to specific cortical zone[19].

From this point of view vestibular organ is unique because of several reasons. Its peripheral end organ is a composition of series of closed spaces, in which receptor structures are placed. Maculae with otoliths are located in sacculus, utriculus, while in the ampoules of semicircular canals – cristae and cupulae. Macula consists of otolith and sensory epithelium. First is the mass of small crystals (otoconia), connected by otoconial membranes – thin protein ligatures. Cupula differs from macula by presence of only organic components; it resembles the sail, closing most part of canal ampoule. Principle of vestibular inertial function is that mass, fixed at vivid spring, deflects proportionally to the acceleration applied. Mutual position of maculas and cupulas is such that they cover all the possible movement directions, both angular and linear. Signal perceived is coded into pattern of spikes, which in its turn is send to CNS[19]. Besides this, the structures named, also evaluate the changes of gravitational field direction, hypo, hypergravitation and weightlessness[20]. Gravitation sensor responds not only to the head position against gravitation field of the Earth changes, but also to microgravitation changes, occurring because of celestial bodies dislocations. Many patients feel excitation, sleeplessness, headache spells, and anxiety during full moon days[21].

Microstructure of labyrinths has macular lacinias (macula neglecta)[22]. They appear to be small macules distributed in sacculus and lagena and differ from ordinary macules by absence of gelatinous substance and otoconia. Hair cell cilia in these structures are most variable in length. This feature gives the researchers possibility to estimate macula neglecta as being morphological structure for perception of low frequency whole body vibrations. In nature they are met during earthquake, storm, hurricane and have dangerous meaning. Today cities are full of technogenic vibrations from underground, lorries, ventilations, etc. It is also important to note, that the cilia movement frequency being estimated as 7-10 Hz[23], thus explaining this frequency range to be the most horrifiable. In the activity of cilia they have identified Math1 as an essential gene for cilia movement in the hair cells and prestin – essential motor protein. The latter are considered to be serious breakthrough in the approach to management of hearing and vestibular function loss[24,25].

It is shown that labyrinth also percept sounds[26]. In patients with destroyed cochlear it is possible to record flat audiogram proceeding from infrasound to 16 kHz and sensitivity threshold of 30-40 dBA[27]. Saccular hearing is also used now for, "vestibular evoked myogenic potentials". Fine parameters of sound: frequency composition, direction, melody are percept by hearing organ, and dangerous meaning of abrupt sounds-labyrinth.

In the living organisms there are magnetic sensors; magnetic impulse perception system is related to macula as it is dynamic system. Magnetic particles in ethmoid bones have the function of magnetic compass indicating the direction of the magnetic field of the Earth, this system is rigid[28,29]. It is possible to make up conditioned reflexes to magnetic stimuli and memorize them[30,31]. Evoked potential in response to electromagnetic field (EMF) stimulus have been recorded, proving the presence of pathway from periphery to cortex in the human brain[32]. It appears that moderate magnetic loading impairs coordination in magnetic sensitive patients[33]. Magnetic impulses appear when negatively charged clouds are moving or thunderstorm discharges. In nature the clouds appear before rain, which is resulting in being wet and energy loss. Therefore the biological sense of EMF impulse specific sensor is not to provide spectral-phase or amplitude parameters, but storm prediction. This provides explanation of weather change reactions-somnability, fatigue. Tight connection of magnetic and vestibular sensors might also cause dizziness; disturbances in motor, vegetative, limbic vestibular projections. In this case becomes understandable the number of accidents in the days of solar storms or in geopathogenic zones. Modern people have changed the Earth, we live today in the condition of "magnetic smog", which is covering the entire Globe and acting constantly at all the living beings.

Important finding is that animals with enucleated labyrinths stop reacting to emetics[34]. Analysis of literary data has shown that just vestibular system is mostly sensitive to both inorganic[13], and organic toxins[35]. Many industrial poisons result in vestibular dysfunction in concentrations, which do not influence any other organism function. Chemical reductive agents are increasing the sensitivity, oxidative – reduce it[36]. Mechanism of this phenomenon is disclosed in the studies of vestibular organ of snails. Perfusion of its hair cell cilia with reductive agents increases the cilia rigidity, oxidants – decrease. In both cases the mode of mechano-electric transduction changes[23]. Hair cell sensitivity to reductive oxidizing potential changes is 2-5 orders higher than that of all the other organism tissues[37,38]. Data presented indicate that vestibular analyzer additionally plays the role of metabolism (condition of oxidative-reductive processes) sensor in the organism. In this context the correlation between vestibular sensitivity and radiation tolerance becomes understandable[39]. From the other side it explains the identity of symptoms of kinetosis and intoxication. Penetration of the toxin into the organism excites the sensor in the labyrinth, which initiates the evacuation of toxin from the organism. Kinetosis or motion sickness is also over scale vestibular irritation[35,40]. It also explains the dizziness, appearing in patients with diabetes, kidney disease, chemotherapy etc.

Resuming the data presented it is possible to

estimate that labyrinth consists of set of sensors, for which six modalities of stimuli are adequate[8]: 1. Acceleration, 2. Gravitation, 3. Low frequency whole-body vibration, 4. Sound, including infrasound, 5. Magnetic impulse, 6. Metabolic changes.

Space orientation sensory tetrad

Dizziness relates to space orientation disorders; so it is important to highlight the mechanisms of brain space perception. Even at the level of rhomboid fosse the information inputs have been shown from the other sensory organs. 28% of vestibular neurons, responding to horizontal canal excitation, also react to hearing and somatosensory stimuli. Reaction is always the increase of impulsation frequency. For somatosensory information its increase appeared to be greater, than for hearing (62-145% and 20% correspondingly). Latencies of these responses being in the time frame of from 5 to 40 ms, indicating both oligosynaptic and polysynaptic pathways[41]. Vestibular nuclei neurons respond also to visual stimuli (65% of cells, responding to linear accelerations). Cooperative action of visual stimuli and linear accelerations results in phase shift in the direction of maximal accelerations[42]. Moreover, in this zone there are neurons (about 24%), responding to passive eye movements, i.e. from proprioceptors of oculomotor muscles. Latencies for these responses are from 6 to 30 ms, thus indicating several pathways with different amount of synaptic transmissions[43]. 14% of Deiters nucleus neurons react to cornea stimulation with enough short latency (6-16 ms). It provides the reason to speak about special corneal connections with spinal motor system in the tight contact with vestibular. Such complex is the basis of nociceptive reflex, protecting face and eyes[44]. Studies of many other reflexes show their formation at the structures of rhomboid fosse[45]. The data presented bring evidence that vestibular nuclei are forming the most ancient primary associative area of the brain in the meaning of space perception, orientation and movement coordination. Primary coordinating vestibular associative center of rhomboid fosse is localized at the connection of lateral portion of medial vestibular nucleus, medial portion of lateral vestibular nucleus and descending vestibular nucleus. Physiological data reveal among other pathways intimate connections of this area with closely located vegetative centers, controlling blood redistribution, heart and breathing rate, during bending, standing up, locomotion and especially moving head up and down[46]. That is why big portion of orthostatic problems are related to the dysfunction of just this brain zone. In the space perception major role is played by upper brain structures: medial longitudinal fasciculus and lamina quadrigemina, where the direction estimation occurs[47]. Next is caudate nucleus and hippocampus, vestibular dysfunction results in their degeneration, which is manifested with spatial memory impairment and cognitive deficit[48,49]. Subjects recognition, praxis, gnosis, cognition belong to cortical functions[50]. Total spatial disorientation is described, if cortex is the subject of lesion.

Analysis of the influence of different sensory inputs on the rhomboid fosse neuronal function has shown the major input of somatosensory and visual systems and less of hearing. This is depicted in the idea that space perception is formed by three sensory systems (triad): visual, somatosensory and vestibular[51]. The other proposal is to regard hearing as important part of space orientation[52]. Phonation of patients during dynamic posturography allows revealing the acoustic dysfunction input into topography of dizziness and imbalance. Usually it appears at the level of rhomboid fosse and medial longitudinal fasciculus (MLF). At both locations acoustic and vestibular nuclei are tightly close. Moreover, lateral longitudinal fasciculus (LLF) is considered to be the very place, where the direction of sound origin is determined. Destruction of either MLF, LLF or lamina quadrigemina results in the fail to determine sound direction. Thus, intersensory interaction idea might be useful for understanding of dizziness origin, hearing function providing information about sound, vestibular – integrating sound information into space orientation[8]. Psychophysical studies of healthy volunteers have revealed significant deficit of visual cortical activity during caloric test[53]. In PET studies optokinetic stimulation in patients with vestibular lesion causes much more active visual cortex response, than in healthy persons[54]. The authors have interpreted the data as competitive interaction between vestibular and visual stimuli, though it might be also regarded from the space orientation process point of view, which is not only competitive[8,47]. Next problem is “nonvestibular dizziness”[55], “appearing somewhere in the eyes”[56]. Investigation of dizziness, appearing in the first hour of wearing of ‘improper’ glasses, have shown the excitation of the vestibular nuclei at the level of MLF or lamina quadrigemina, no visual nuclei function impairment is found[8]. These data provide evidence that space orientation is formed at the vestibular nuclei as a result of integrative processing, first of all of the information from tetrad – four principal inputs: vestibular, visual, somatosensory and hearing[47].

There is a big bulk of literature proving that dizziness is related to vestibular dysfunction. Vestibular dysfunction is present in dizzy patients with neurosis, encephalitis and epilepsy[57], it can cause arrhythmia[58]. Minor head trauma starts as a vestibular dysfunction[59]. Tinnitus is related to vestibular disturbances[52]. Low-frequency whole-body vibration cause vestibular damage[11]. In the patients with diabetes polymodal EP reveal peripheral nerves dysfunction, especially pronounced in vestibular peripheral organ[60]. Low doses of radiation cause primary vestibular damage and needs vestibular function correction[61], which crucially improves the patient condition[10]. Early vestibular damage in Chornobyl clean-uppers later leads to immune deficiency[8]. Monitoring of long-lasting consequences in patients with vestibular lesion has shown that primary peripheral distortion in two-three years spreads to higher levels of brain step-by-step involving motor, vegetative and limbic systems, resulting in organic

pathology: neurological, cardiovascular, internal organs damage, including glands of inner secretion, psychiatric disturbances[62]. When the process reach brain cortex, the balance of cortical processes is disturbed, causing immune failure, this is finished with chronic autoimmune and oncologic diseases[8].

Vestibular brain projections

Labyrinth pathways within CNS structures are multiple and rather complicated. They differentiate several groups of them united into projections[63]: 1. cortical (sensory), 2. motor, 3. vegetative, 4. limbic[64].

Vestibulo-cortical projection

According to the physiological findings it is composed of at least three pathways[65]: 1. Three neuron shortest pathway to the contralateral hemisphere; 2. Five neuron pathway to the ipsilateral hemisphere; 3. Multineuron pathway to the contralateral hemisphere.

The first of them is initiated by the thick fibers, innervating big type I hair cells localized in the central part of the peripheral receptor[66]. The first order neurons are presumably represent the crista-ampoular projections. The first transmission appears at the central part of the superior and partly in lateral vestibular nuclei[67]. Great neurons from this area are sending their axons to the ventral posterior area of thalamus, medial longitudinal fasciculus, Deiters nucleus and interstitial nucleus of Cajal. These second order neurons also send collaterals to the oculo-motor nuclei, being thus important nystagmus producer. Other electrophysiological data have revealed that vestibular responses might be found in the variety of somatic parietal areas (areas 2, 3a and 5). This input originates from great thalamic cells located in oral portion of ventro-postero-lateral nucleus and ventro-postero-inferior nucleus. These nuclei receive axon terminals from contralateral lateral and medial vestibular nuclei[68]. The latent time of this pathway is 3-5 ms if the vestibular nerve is stimulated directly in the electrophysiological experiment[65].

The second pathway is initiated by mostly thin fibers innervating the II type small hair cells, dispersed at the peripheral parts of all the receptor structures[68]. The first order neurons are dispersed in all the vestibular nuclei of the brainstem. The pathway seems to pass through medial longitudinal fasciculus, Deiters nucleus and interstitial nucleus of Cajal, archicerebellum and striopalidum subcortical system[68,69]. The latent time of this pathway is about 8 ms if the vestibular nerve is stimulated directly[65].

Multineuron pathway or pathways to the contralateral hemisphere has been revealed in the evoked potentials studies. Cortical peak P_2 has latency of 120-150 ms; the pathway passes through the reticular formation[70]. PET studies have confirmed localization of vestibular cortical representation in parieto-insular zone of primates[71]. Principal manifestation of its function is space perception, motion and time. Quantitative measure of its function is sensitivity threshold of the investigated subject[72]. Subjective sensation studies at the threshold level have revealed three types of sensations: undiscriminated, inverted and discriminated, which appear to be the fundamental feature of movement perception, no matter which is the direction of movement[73]. Quantitative measure of gravitation perception is considered to be vertical estimation, which is to be performed in total darkness[74]. Dizziness, vertigo, being in general space orientation disorders are manifestations of sensory vestibular disorders. Attention has been payed to the fact of dominance of vestibular cortical function in the non-dominant hemisphere (PET studies)[54]. Nystagmus studies in patients during caloric stimulation have shown that vertigo is presumably formed while left labyrinth stimulation (right hemisphere) and dizziness – right labyrinth (left hemisphere)[75]. As vertigo is more strong sensation, it might imitate the vestibular dominance in non-dominant hemisphere in PET studies, cited above. In reality a wide spectrum of symptoms are produced during vestibular stimulation or pathology[76].

Vestibulo-motor projection

It is characterized by vestibulo-spinal and vestibulo-ocular pathways[68]. In norm it provides wonderful coordination we see in sportsmen, dancers, and cascadeurs. In pathology it is manifested with coordination disturbances, distortions of balance, gait (static and dynamic ataxia), nystagmus and saccades[16].

Vestibulo-vegetative projection

This one influences cardio-vascular system and inner organs[46]. In normal conditions it provides vegetative reserve for normal function of the whole organism, in special conditions it enhances reconvalescence of postinfarctus patients[77], improve children physical development[78,79]. Overloading of it causes kinetosis[47]. Vestibulo-vegetative projection in some vital reflexes, i.e. standing up in bipedal living beings, appears to manifest rigid behavior[46]. Its dysfunction may initiate different vegetative disorders: cardiac arrhythmia[80] and even arterial hypertension[81].

Vestibulo-limbic projection

Physiological vestibular stimulation results in improvement of life quality, in pathology it results in limbic disorders[8].

Symptoms of vestibular dysfunction

Taking into consideration the presented material about the projections of the vestibular system, now it is possible to identify the symptoms, which manifest vestibular disorder.

Vestibulo-cortical projection – vestibular analyzer – is the very brain structure, where the movement, space orientation and time perception is formed. In pathology we separate dizziness, vertigo[16], space[47] and time perception disorders[82]. Dizziness means the disturbance of the movement, space orientation and time perception. The subjects feel themselves unstable or moving, the

ground disappears, something is wrong in the head, sometimes it is heavy, sometimes it is somewhere in the glass sphere or it is impossible to explain what happens with this head[83]. Speaking about movement the patient, nevertheless, is unable to indicate the movement direction. This condition might be accompanied with general inhibition or irritation; excitation is rather rare, but also possible, like the feeling after big dose of coffee. The time might be either dragged out or running too fast[84]. The example of the physiological time perception changes might be in the situation, when the car after driving in the highway at the speed of 140 km/hour is entering the city and the speed is decreased to 30-40 km/hour. It seems to move so slowwwwly! Claustrophobia, agoraphobia, acrophobia, nyctophobia, orthostatics and optokinesis[85], discomfort while going up and down the staircase, ascendophobia and descendophobia, are also related to vestibular dysfunction, as spatial perception disorders[76].

Vertigo means the illusion of the non-existent movement[16]. In most cases the movement is rotatory like after carouser, less frequent is swinging or linear movement. It might be objective, subjective, giddiness[51] or kinetosis[86]. Usually, it accompanies acute cases of pathology and is combined with excitation or irritation and other additional symptoms: disequilibria, nausea, retching, up to consciousness loss[40].

Vestibular cortical representations

In the electrophysiological experiments the vestibular cortical area has been located in the anterior Sylvian sulcus posterior to the facial somatosensory zone and anterior to auditory cortex[87]. According to Brodmann's classification this is the area 2V. Neurons in the area 2V respond actively to caloric and electric direct stimulation of labyrinth. The pathway is bilateral, but contralateral features are strongly exaggerated. A second vestibular cortical projection area in humans is found in area 3 may represent the projection from the somatosensory arm field[88]. These data has been confirmed in 90th of 20 century with PET studies of primates[71] and humans[54]. Therefore, this part of the projection is supposed to represent the somatic afferents, involved into balance. Here, the integration of labyrinthine and somatic proprioceptive signals provides the subject of awareness of body orientation (horizontal). It is well known, however, that thalamic neurons transmitting vestibular information to parietal lobe also carry somatosensory signals, usually from proximal joints and muscles[22,89].

Because many secondary vestibular neurons with canal input also receive visual information from the optokinetic system, this signal is also evaluated in CNS. Thus, the vestibular system is unique among sensory systems, because of its integrative function. For example, head angular movements are based on information from a variety of sources including the labyrinth, the retina, the joint and the muscle receptors. Vestibular system, starting from rhomboid fosse level, is integrating sensory coordinator to produce effective movement of organism in space[47]. It has been shown that the orientation of visual cortical receptive fields might be changed by otolithic stimulation. In the other experiments the semicircular canals stimulation influences visual cortical background firing rates as well as the size of complex visual cortical receptive field. Vestibulo-cortical pathway is necessary for spatial orientation (depth) and vestibular memory[69]. Humans and animals without labyrinths cannot remember a path through which they have been transported. Such orientation ability seems to be mediated via a pathway through the vestibular nuclei, the magnocellular medial geniculate body and the caudal caudate nucleus[22,68].

Specifics of the vestibular analyzer means small cortical representation area and presence of the vestibular projections in somatosensory, visual and auditory cortical zones, besides vestibular cortical area itself. These projections seem to be based at the two parallel systems: type I hair cells-thick fibers-three synaptic pathways and type II hair cells-thin fibers-multisynaptic pathways[67]. They are the very substrate, where the sensations like numbness, black-outs, tinnitus of vestibular origin are formed[61,90].

Vestibulo-motor projection is responsible for the coordination function and locomotion. In the formation of this function several systems take part, including vestibular, vestibulo-motor pathways and motor effector system. The general coordination disorder terminology might be further detailed. In locomotion disorder swaying, staggering or stamped walk might dominate[47]. Static ataxia might be characterized by instability, swaying, and spastic disorder[51]. The patient might complain of momentary staggering, walking like drunkard, inability to fix the gaze, numbness, etc[16]. Pathologic eye movements, nystagmus and saccades, belong to the vestibulo-motor disturbances[91]. Patients complain of visual disturbances, inability to concentrate, while reading and writing, poor contrast of the subjects even in normal visual conditions[92].

Different disorders appear in *vestibulo-vegetative projection.* Most typical are the disorders related to kinetosis[40]. They are characterized by intensive nausea, retching and vomiting episodes[93]; usually they are accompanied by blood vessels spasms, palpitations, tachycardia, extrasystols[80,94], sweating, spasms of esophagus, laryngospasms. Persons are complaining of dyspnoe, pain in epigastrium and bronchi[95]. They depend on the exact vestibular pathway and level of the pathological process location[96]. It might involve this or that internal organ, forming sometimes exotic versions of disease structure. An extraordinary example: patient complains that after about quarter an hour in city traffic the uncontrolled urination happens. The treatment proposed – dimenhydrinate before trip appeared to be successful – thus being the support of vestibulo-vegetative projection existence[8].

Special attention has to be attracted to headache of vestibular origin, which is called *vestibular migraine*[97]. Sometimes it is considered as a substitute of vertigo,

sometimes as an additional symptom[98]. It might be complicated with other symptoms: nausea and vomiting, convulsions and even consciousness losses[95]. The criteria of the vestibular migraine diagnostics have to be based at objective instrumental methods. Vestibular origin of migraine is established with the help of Vestibular EP, ECG and pupillometry with vestibular loading tests. It demonstrates good regression during therapy with the medications, correcting vestibular function, especially histamine blockers[8].

Vestibulo-limbic connections are least studied and today the data about their disturbances looks like preliminary studies from the point of view of evidence-based medicine. Nevertheless, pioneering physiological studies have attracted the researchers' attention to this projection[64]. The clinical experience with Chornobyl clean-uppers has shown that up to 40% patients with dizziness are complaining of fears, nightmares and phobia[10]. This experience expands also to the patients with head trauma (including whiplash), poisoning and limbic disturbances triggered by kinetosis (sopit-syndrome). It is manifested with weakness, somnability, loss of initiative[99]. The correction of the vestibular function crucially influences the limbic symptoms, thus indicating its vestibular origin. Besides phobia and sopit-syndrome, limbic symptoms also include: disturbances of alimentary, drinking, sexual behavior, attacks of irritation, emotional lability, aggressiveness, etc[100]. In severe cases depression and anxious disorders might develop at the basis of vestibular dysfunction[101].

The experience of aviation and space medicine has shown that being closely related from one side, from the other side the vestibular projections might be enough autonomic. It means that clearly expressed disturbances in one projection, might not be necessarily accompanied by the same expression of the disturbances in the other projections[63]. In the cases of chronic pathology it means that the situations are possible, when we have enough expressed dysfunctions in vegetative or limbic systems, with minor vestibular symptoms. These patients spend years visiting hospitals and ambulances, diagnostic centers, circulating between the doctors – all in wane, they need only the vestibular investigation and correction of the leading trigger of the disease. The situation might be more pessimistic, because of patient might not relate poisoning, head trauma, visit of radar station several years ago with today palpitation episode or other dysfunctions[8].

Diagnostic methods evaluation criteria proposed: method tolerability, sensitivity, specificity, coherence[4], providing knowledge about the disease, influence on management strategy and cost.

For sensory projection condition documentation the most popular questionnaire is *NOASC*. Its use is mostly profitable in statistical studies of wide contingents. There are two different ways of result interpretation. First is the most simple, when they calculate the percentage of patients having this or that complaint[102]. Second is I_e, expression index, which characterize the number of signs from this group (for example, headache types or dizziness parameters) in one patient. Expression index is calculated as ratio of certain group symptoms sum to the number of patients examined[10].

Additionally to NOASC the differentiation of vestibulo-sensory complaints may be quantified with the help of *"Types of dizziness"* Questionnaire[76].

Vestibular evoked potentials (VestEP, not VEMP) method being independently initiated in at least three countries (Ukraine, USA, Germany)[70,103,104], passed verification procedure[8] and evaluated by independent NASA experts [NASA Contractor Report 3922, №№ 13 & 23. USSR Space Life Sciences Digest, 1987 & 1988]. The results of coherence ratio are in the frame of 95%, thus making these data highly important from the point of view of evidence-based medicine. Sensitivity of method has been evaluated in comparison to the amount of persons complaining of dizziness (n=912 examinations, 672 patients) – 90.57%, specificity – 98.57%[105].

To vestibule-motor projection study methods belong posturography and nystagmography__Posturography has sensitivity between 35 and 54% and specificity up to 90%[106]. Our preliminary data coincide with the opinion of the author: sensitivity related to the amount of patients complaining of dizziness is 37.04% (n = 54). The sensitivity of Uemura and Fukuda tests for the same patient group appeared to be 98.15%[105]. Unterberger stepping test means marching at a spot with eyes closed (100 steps or 1 min.)[107]. The interpretation is based at the measuring of amplitudes for head and shoulders sways (separately), linear and angular displacement and rotation[108]. Sensitivity of this test is 82.89%, and specificity – 99.78% (n = 912)[105]. Prof. Uemura has proposed the test of standing on one foot with eyes closed[109]. Its sensitivity appeared to be of 98.90% (n = 912)[105].

Caloric test sensitivity for acoustic neurinom below 15 mm is 70%[110]. Method low sensitivity is somehow compensated by its value in the establishment of hyper or hyporeactivity of the vestibular system, because the latter influences strongly the management of the disease.

Pendular test, if criterion of vestibular reactivity decrease (VRD) is accepted to be 25% method sensitivity is evaluated as 33.5%, and specificity – 92.5%, accepting VRD 20% authors have obtained sensitivity 41.2% and specificity – 85%[111].

Stages of management must be: continuous, progressive, upgrading. Each new step has to upgrade and not refuse previous management[112]. The process has to be organized according to severity degree of disease[113].

Outcome from vestibular lesion

According to the WHO requirements the Benefit is done in Perspective for patient, doctor, assurance, politics and society in whole. Also other parameters are to be included such as prevention, reconvalescence both full

and partial, improvement, compliance and life quality[114]. From the other side most clinical evidence-based trials does not provide the data about long-lasting monitoring of the patients. Therefore, we have studied 229 patients (37.16 y.o.) treated with combination of low doses of cinnarizine and dimenhydrinate (Arlevert®) in 367 examination sessions during the period from 3 months to 2 two years. Just after one month therapy 70 (30.57%) of them have attended the doctor for control. Most of them have reported partial improvement. The other patients have skipped the examination. Only 5 (2.18%) of them have reported no effect by phone. The motivation not to attend the doctor for the other ones has been the crucial improvement of their condition. Three and more examinations (up to five) have passed 41 (17.90%) patients. The detailed examinations of the results have provided the next picture. According to the 20-point battery we have significant decrease of symptoms which has been preserved longtime after one month therapy in the most patients. These data indicate satisfactory reconvalescence of the patients in the long-lasting period. Next in our study has been investigation of these same patients with the aid of VesEPs, which have revealed the statistically significant decrease of the pathology just after treatment with Arlevert and restoration of the pathology in the delayed monitoring time period. The data are significant according to T-test and not to F-test indicating only quantitative, but not qualitative changes in patients. The statistical significance is recorded between before treatment and after treatment, before treatment and just after the treatment databases according both to T-test and F-test. No difference has been revealed between before treatment and in longtime monitoring results, indicating absence of the long lasting treatment effect.

General conclusions from these data are: 1. Pathology has different development in different vestibular projections. 2. Pathology is first formed in the sensory projection. 3. Vestibular evoked potentials is the earliest method to detect the pathology (even earlier then the complaints). 4. Patients with vestibular disorders need monitoring.

Attachments are proposed to show how to use cloud technologies for protocol. Each doctor creates his own cloud, which is attached to the cloud of the hospital. Hospital clouds are united into one pool in the Dizziness Center Register. Use of the standard table Questionnaire “Types of Dizziness” allows monitoring local and general problems and tendencies related to vestibular pathology. It also makes transparent the activities of each doctor, makes possible to have evidence-basis for better therapeutic technologies. It gives the chance for family physician in the far away village to consult on-line the difficult patient at the specialized Center.

Questionnaire “Types of dizziness” is modification of two Questionnaires: Claussen’s NODEC[9] and Jacobson GP & Newman CW[115]. The Questionnaire “Types of dizziness” is used as the basis for standard databasis formation in the clouds of individual doctors, specializing at dizziness, as well as clinics and specialized Dizziness Centers. Besides standard Questionnaire, texts, pictures and video can be easy inserted into the cells of the table.

The Questionnaire “Types of dizziness” and the details for management and updates are presented in the full version of the Protocol at websites: http://sites.google.com/site/dizzylita http://happyvertigo.com

NB! Neurootological & Equilibriometric Society Reg. Headquarters is in Budapest, Hungary**.**

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