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Informativeness of neurophysiological diagnostic methods in the differentiation of motor neurons of spinal cord motor neuron disease

Objectives: Defining the principles and tactics of differential use of Neurophysiological (NPh) methods in cervical spondilotic myelopathy (CSM) diagnosis.

Materials and methods. Analysis of the clinical and NPh examination data of 160 patients (from 31 to 76 years of age) suffering from CSM. The examination techniques used: clinical and neurological; neurovisualizing (MRI, CT, functional spondylography); a set of NPh methods, namely: stimulation electromyography (ENMG) with F-wave recording (188 examinations); needle EMG (105); motor evoked potentials (MEP) (188); somatosensory evoked potentials (SSEP) (50); single fiber EMG with determination of average density of muscle fibers in motor units and reliability of neuromuscular transmission (32).

Results. An optimal scheme of the use of NPh diagnostic methods in patients with SCM was worked out and applied. Out of the total of 160 patients examined, 19 (11.9%) had motoneuron involved; 32 (20%) had ALS syndrome at the background of cervical spondylosis; 59 (36.9%) patients had concomitant radiculopathy, etc. The sensitivity of MEP technique in the identification of partial spinal cord compression in cervical spondylosis was confirmed – 134 (83.8%) cases; SSEP – 29 (58%). The clinical example illustrates the role of jitter-analysis in the cases when a subtle differentiation between the motoneuronal disease, ischemic and compression injury of the spinal cord motoneurons is necessary.

Conclusions. An optimal scheme of the use of NPh diagnostic methods in patients with CSM was suggested. Due to the use of motor and somatosensory evoked potential techniques, the diagnosis of the spinal cord conduction structures compression and evaluation of the degree of their functional disorders were improved. The use of jitter-analysis allows to increase the information value of NPh diagnosis of the spinal motoneuron involvment, especially at the early stages of the pathological process.

Key words: *cervical spondylotic myelopathy, diagnosis, jitter.*

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Introduction. In our previous studies [1,2] we analyzed the principles and tactics of the use of neurophysiological (NPh) diagnostic methods on the basis of the NPh examination of 160 patients with cervical spondylotic myelopathy (CSM) in the course of their surgical and non-surgical treatment. In spite of significant achievements of neurovisualizing technologies in the objective assessment of the functional condition of segmental and conduction structures of the spinal cord, there still remain unclarified questions, including the theoretical and purely methodological ones. The number of published works dedicated to NPh monitoring of the spinal function in patients with compression myelopathy has been steadily increasing lately, which reflects the importance of the problem of diagnosis and treatment of the pathology.

The spinal function disorders, especially that classified as myelopathy, occur in the neurologists' and neurosurgeons' clinical practice almost on the daily basis. It is due to high incidence of vertebral column pathology and the patients' delay in seeking medical advice on the one hand, and imperfection of the pathology diagnosis, insufficient effectiveness of treatment measures, as well as rather high degree of incapacitation of the patients, on the other hand. The cause of spinal cord compression is usually the median protrusion of the intervertebral disc at C_V-C_{VI}, C_{VI}-C_{VII} level.

The spinal cord dysfunction can occur both due to its direct mechanical compression, static or dynamic, at the moment of movement, and to the compression of the vessels supplying the spinal cord (myeloischemia). The factor contributing to the spinal compression at the cervical level of the vertebral column is a congenital or acquired vertebral canal stenosis (i.e.its diameter is less than 11 mm, and the correlation between the anteroposterior diameter of the vertebral canal and the vertebral body is less than 0.8 mm).

In certain cases the changes in the vertebral column revealed with the help of radiography, CT scan or MRI may be clinically asymptomatic. On the other hand, the finding of an intervertebral disc herniation, spondylosis or stenosis of the vertebral canal, does not necessarily mean that only they can cause the patient's neurological disorders.

According to etiology, the most frequent cause of the cervical myelopathy syndrome is the spondylogenic spinal cord compression as a result of: spondylosis, intervertebral disc hernia, acquired stenosis of the vertebral canal, compression by posterior osteophytes, hypertrophied ligament, etc. (according to ICD-10: codes

M50+, M47.1 (G99.2*); a likely spondylogenic vascular compression of the anterior spinal or vertebral artery with ischemic myelopathy (code M47.0+ (G99.2*). The range of diseases which require differential diagnosis is as follows: consequences of vertebrospinal trauma, tumours of this level (extra- and intramedullar), amyotrophic lateral sclerosis (ALS), syringomyelia, transverse myelitis, hereditary spastic paraplegia, disseminated (multiple) sclerosis, etc [3]. The etiological factor of the compression injury of the spinal cord may be a craniovertebral anomaly, in particular, Chiari 1 malformation (code Q07.0).

In agreement with modern concepts ideas of pathophysiological mechanisms of CSM develpoment, we analyzed a number of typical electrophysiological phenomena which are supposed to accompany the spinal cord compression at the cervical level, including the involvement of the anterior horn motoneurons in the pathologic process.

The objective of the study: to determine the principles and tactics of differentiated application of NPh methods in CSM diagnosis.

Materials and methods. We have been observing 160 patients with CSM since 2007. 96 (60%) out of them were male and 64 (40%) - female. The age range of the patients was from 31 to 76 (52.28±11.83 on the average). We used the following methods of examination: clinico-neurological, neurovisualizing (MRI, CT, functional spondylography). The set of NPh methods included: 1) standard stimulating ENMG with F-wave recording (188 tests); 2) needle electromyography (EMG) (105 tests); 3) motor evoked potentials (MEP) to transcranial magnetic stimulation (TMS) and spinal magnetic stimulation (MS) (188); 4) recording of somatosensory evoked potentials to median nerve stimulation (SSEP) (50).

EMG examination of a single fiber is very important for differentiation of incipient signs of the spinal motoneuron involvement and assessment of denervation-reinnervation changes [4]. It was necessary to use these more subtle (sensitive) methods of examination in 32 (20%) cases to confirm or disprove the involvement of spinal motoneurons in the pathologic process. The needle EMG allows to evaluate the morpho-functional organization of motor units, preservation of innervation, the extent of reinnervation (reorganization), i.e., characterize the condition of peripheral neuromotor system. The single fiber EMG enables us to study the electrical activity of separate muscle fibers, and also determine their density in motor units (MU) and reliability of neuromuscular transmission with the help of jitter-method [4]. Jitter is a deviation of the off period interval of the action potential of two muscle fibers which belong to one MU. The density of muscle fibers reflects the average number of muscle fibers belonging to one MU within a radius of 300 μm.

To measure the jitter, we placed the electrode for single fiber recording in the muscle so that it could be possible to record the potentials of two adjacent muscle fibers belonging to one MU. The value of jitter is normally 5 -50 μs. In case of a disorder caused by any pathology, the jitter value increases. We also determined the muscle fiber density in a MU. The average fiber density was measured in conventional units by means of calculating the average number of single muscle fiber potentials belonging to different MU. This value in healthy patients varies from 1.2 to 1.8, depending on the muscle and on the age. The increase of muscle fiber density in an MU reflects the change of MU structure.

NPh diagnosis was made on the «Neuro-MEP-4» («Neurosoft», RF) equipment with the use of «Neuro-MS» magnetic stimulator («Neurosoft», RF).

All the patients gave their informed consent to our conducting NPh examination.

The statistical data processing was carried out with the help of «Statistica 6» application package, the sampling method: sample mean value, mean error; for the definition of the likelihood of the difference between the groups – a nonparametric technique: for binary features - Pearson's chi-squared test; for two independent groups comparison – Mann-Whitney U-test. The difference was considered feasible when $p<0.05$. The correlation between the indices was estimated with the help of the Spearman correlation coefficient.

Results and discussion. The main complaints of the patients were as follows: bilateral numbness of the extremities (in 58% of patients), discomfort in walking (56%), weakness in the extremities (68%). the patients usually noted certain clinical manifestations with periods of occasional worsening. Clinically, myelopathy manifested itself in combined or isolated signs of Brown-Sequard syndrome, central spinal syndrome, anterior spinal cord syndrome.

In fact, the necessity of evaluation of degenerative dystrophic changes in the vertebral column in relation to clinical manifestations of myelopathy arises in clinical practice on a daily basis. Such a task, as well as the problem of differential diagnosis, as a rule, dictate the need for use of NPh techniques to diagnose the condition of segmentary and conduction structures of the spinal cord. We have developed and tried out the following scheme of NPh examination of the patients with CSM in our clinical studies ***(Fig.1)***.

MU – motor unit; MUP – motor unit potential, SNAP– sensory nerve action potential; CMAP – compound mixed nerve action potential; DRP – denervation-reinnervation process, FP – fibrillation potential; PShW – positive sharp wave; FscP – fasciculation potential; SF EMG – single fiber EMG; NCV – nerve conduction velocity; M- and F- muscle potential under stimulation ENMG; MEP – motor evoked potential; CMCT –central motor conduction time; SSEP – somatosensory evoked potential.

Following the above scheme of diagnostic examination we managed to pick out of the total number of the examined patients the 19 who had motoneuronal injury; we identified ALS syndrome at the background of cervical myelopathy in 32 (20%) patients; root(s) involvement – in 59 (36.9%) patients, and diagnosed concomitant tunnel syndromes: in 14 (8.8%) patients with carpal tunnel syndrome and 5 (3.1%) - with cubital tunnel syndrome; polyneuropathy – in 18 (11.3%) patients.

MEP is a sensitive technique for detection of subtle (pre-clinical) changes as a result of partial spinal cord compression in cervical spondylosis – the deviation of MEP indices was recorded in 134 (83.8%) cases whereas median SSEP deviation was registered in 29 (58%) out of 50 patients examined.

As is well-known, it is rather difficult to diagnose ALS at the early stages of the disease, especially when

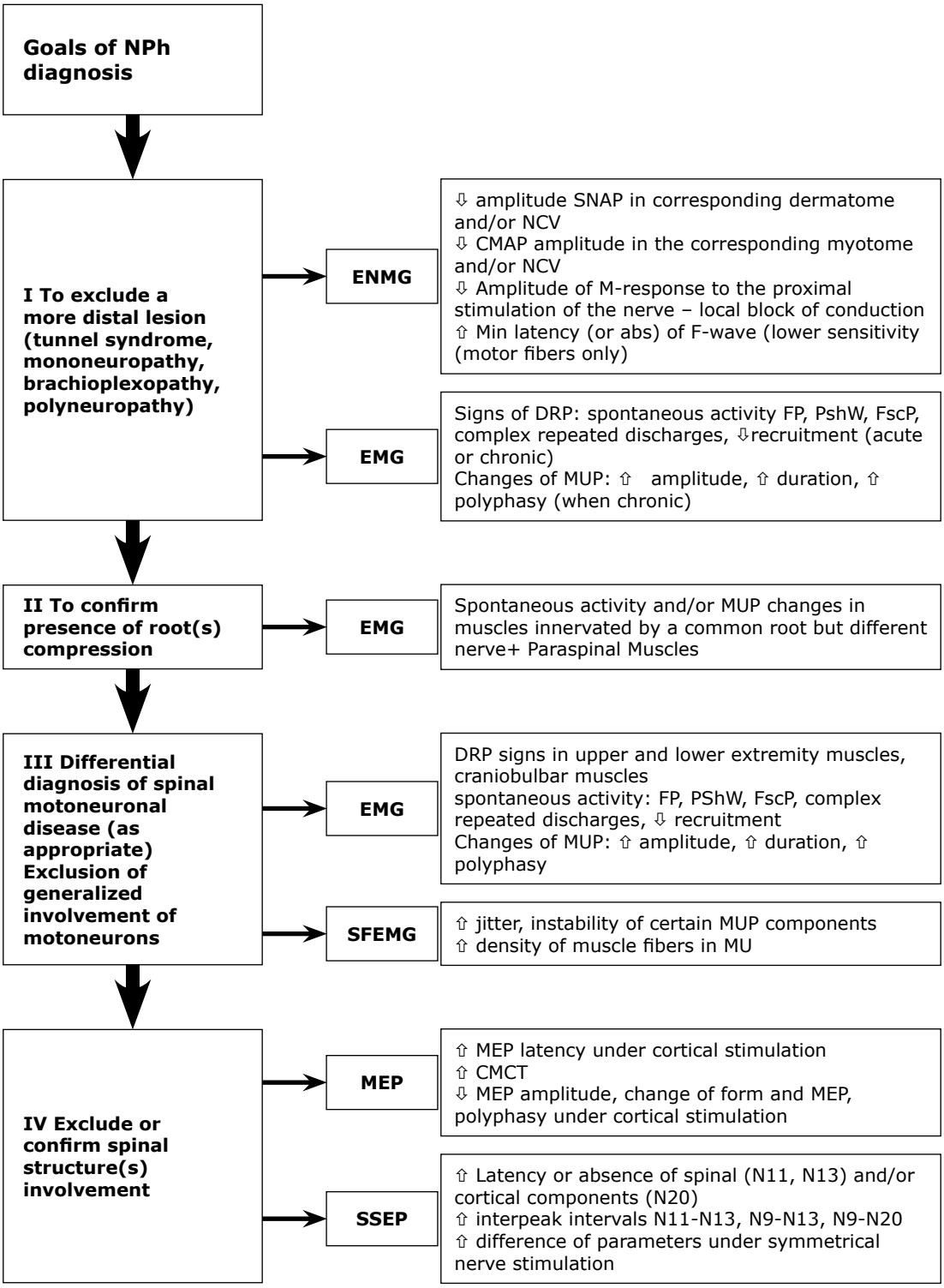

Fig.1. The scheme of complex NPh examination of a patient with CSM.

there exist degenerative-dystrophic changes of the cervical spine and the combination of such changes in the lumbar spine. Controversial cases require NPh reevaluation and other retests. Needle EMG is considered the most important instrument of NPh detection of denervation changes in muscles. If there is a reason to suspect a motoneuron disease on the basis of NPh examination (Fig.1, block III), it is necessary 1) to confirm the peripheral motoneurons involvement in the most damaged muscles; 2) to detect the NPh signs of the peripheral motoneurons injury in the less clinically damaged muscles provided that the nerves are intact.

However, the results obtained are not specific for ALS, as they may be found in cases of spinal cord diseases (for instance, the spinal amyotrophy, poliomyelitis, syringomyelia), motor root diseases (e.g. polyradiculoneuropathy) and peripheral nerve diseases (axonal polyneuropathies) [5].

The absence of fasciculation potentials (FscP) causes doubts in the motoneuron disease diagnosis,

but does not exclude it. Jitter-analysis may be helpful for the unstable MUP detection in controversial cases. The considerable increase of jitter and the instability of certain MUP components is explained by the fact that the newly created (as a result of sprouting) terminals and immature synapses do not work with the sufficient degree of reliability. If this occurs, the patients with fast progression of the process demonstrate the most significant jitter and blocking of impulses. The stable form of MUP and the absence of impulse blocking in MUP recording will correspond to a relatively slow progression of the process and the effective reinnervation [6].

We believe the clinical case, which required the use of a number of diagnostic techniques and the consultations of various specialists, to be typical and at the same time totally individualized. The patient I., a 56- year-old female, was referred to the Institute of Neurosurgery with complaints of weakness in her lower and upper extremities, inability to walk unaided, pains in lumbar spine. The anamnesis: she was twice operated on for intervertebral disk herniation excision at L_V-S_I level, had adhesive epiduritis. The first complaints of weakness in her upper extremities appeared within a year after the last surgery. She arrived for the examination in a wheel-chair; lost 7 kg during the year. The meningeal and non-focal neurological symptoms absent; the cranial nerve function adequate; hypotrophy of upper extremity distal muscles; weakness in upper and lower extremities - tetraparesis in the form of upper spastico-atrophic paraparesis and lower spastic paraparesis; reduced sensitivity in the L_5-S_1 dermatomes; pelvic organ functions unimpaired.

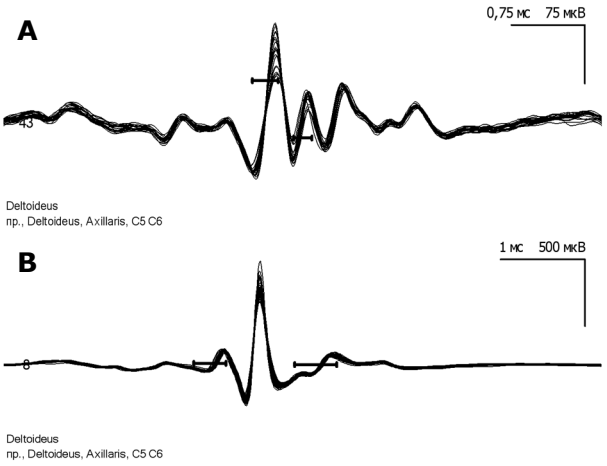

Fig.2. The single fiber EMG in the deltoid muscle (muscle strength 3 points). The jitter indices are within the normal range – 32.4 μs (normal up to 50 μs); impulse blocking was not observed. The muscle density in the given MU (the spike number) was increased in the 1st case (A) to 8 SI units, in the 2nd (B) – to 4 SI units.

The ENMG data of upper extremities: excitation conduction velocity indices along the motor and sensory nerve fibers in upper extremities within normal range; significant reduction of distal muscle M-response amplitude (up to 25-35% of the normal). According to needle EMG data in distal and proximal muscles of upper extremities, no signs of acute denervation process were detected. MUP had neuronal (type) changes. As the clinical data dictated the necessity of differentiation with ALS disease, we used the jitter method which is considered to be mainstream in the diagnosis of the fine mechanisms of denervation.

The jitter-analysis data in the deltoid muscle were within the normal range; an increased density of muscle fibers was noted which was the evidence of excessive complete reinnervation ***(Fig.2)***.

The needle EMG of the muscles innervated by L_4-S_1 roots (buttocks, lower legs, feet), rare cases of spontaneous activity in the form of PShW and FP in m.tibialis anterior dex were observed; the signs of moderate chronic denervation in the form of increased amplitude and MUP duration, significant polyphasy in mm.gluteus maximus, biceps femoris, tibialis anterior et extensor digitorum brevis were identified.

The ENMG examination allowed us to conclude that no signs of the spinal cord motoneurons generalized involvement were established. There was a maximum likelihood of cervical myelopathy with cervical intumescence motoneuron involvement. The changes in the needle EMG in the muscles of the lower extremities corresponded to the signs of root damage. The patient was recommended to do a cervical spine MRI ***(Fig.3)***.

The cervical spine MRI ***(Fig.3)*** showed: complicated osteochondrosis (antespondylolisthesis) of C_{IV} vertebra, uncovertebral spondylarthrosis deformans, spondylosis) of cervical spine, secondary myelopathy with myelomalacia or ischemic type spinal circulatory disturbance?

Thus, comparing the results of Nph and MRI tests, we received a confirmation of pathologic process with peripheral motoneuron degeneration at the cervical intumescence level (most likely, of ischemic origin). The absence of generalized motoneuron involvement according to needle EMG data and normal jitter indices, as well as the absence of impulse blocking, were indicative of neuromuscular contact stability, though the clinical presentations lasted for about 12 months. It conforms to the statements that in cases of neurogenic chronicity [5, 6], normal jitter indices and absence of impulse blocking is evidence of neuromuscular contact stability and completion of reinnervation processes in MU. According to the published research

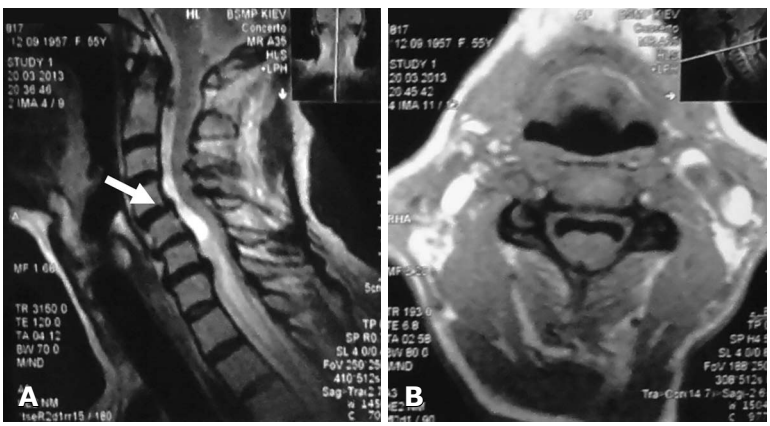

Fig. 3. The cervical spine MRI of the 56-year-old female patient. A - sagittal; B - axial section.

data, single fiber EMG may be very important for confirmation or exclusion of the deviations in mild manifestations of or doubts about neuronal diseases [7,8]. As a result of due to the verification of the sufficient number of muscles with the help of this technique, the presence of deviations may be established even in subclinical cases. A combination of jitter measurements and muscle fiber density allows us to identify the stage and completeness of reinnervation, as the increase of muscle fiber density and MU component stability reflect the reinnervation completeness.

Our research enabled us to systematize the approaches to clinical interpretation of NPh diagnosis results in patients with SCM. The use of a complex of modern NPh methods considerably improves the diagnostics of this pathology.

Conclusion

A scheme of the use of the optimal sequence of NPh methods for SCM diagnosis has been suggested.

The use of MEP and SSEP techniques makes it possible to improve the diagnosis of SCM, spinal cord conduction structures compression, and assess the degree of their function impairment.

The use of jitter-analysis is highly informative for the differential diagnosis of motoneuron disease, especially at the early stages of the pathologic process. In order to identify the involvement of the peripheral and central motoneurons in patients with SCM it is appropriate to use a complex of NPh techniques taking into account the predominant clinical presentations, the stage of the disease and its treatment, the dynamics of NPh sign changes.

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Інформативність нейрофізіологічних методів діагностики в диференціації ураження мотонейронів спинного мозку

Мета дослідження — визначити принципи і тактику диференційованого застосування комплексу нейрофізіологічних (НФ) методів в діагностиці спондилогенної шийної мієлопатії (СШМ).

Матеріали і методи дослідження. Проаналізовані результати клініко-нейрофізіологічного дослідження у 160 пацієнтів віком від 31 до 76 років з СШМ. Використані методи: клініко-неврологічний; нейровізуалізуючі (МРТ, КТ, функціональна спондилографія); комплекс НФ методів — стимуляційна електронейроміографія (ЕНМГ) з реєстрацією F-хвилі; голкова ЕМГ; моторні викликані потенціали (МВП); соматосенсорні викликані потенціали (ССВП); ЕМГ поодинокого м'язового волокна з визначенням середньої щільності м'язових волокон в рухових одиницях і надійності нервово-м'язової передачі.

Результати. Розроблена і застосована в дослідженні схема оптимальної послідовності використання методів НФ діагностики у пацієнтів з СШМ. У 19 (11,9%) пацієнтів виявлене ураженням мотонейронів, у 32 (20%) — синдром БАС на тлі СШМ; у 59 (36,9%) — супутня радикулопатія тощо. Доведено чутливість методу МВП щодо виявлення часткової компресії спинного мозку при шийному спондильозі — у 134 (83,8%) хворих, ССВП — у 29 (58%). На клінічному прикладі визначена роль джиттер-аналізу за необхідності тонкої диференціації хвороби мотонейронів, ішемічного та компресійного ураження мотонейронів спинного мозку.

Висновки. Запропоновано схему оптимальної послідовності використання методів НФ діагностики у пацієнтів з СШМ. Завдяки застосуванню методів МВП і ССВП удосконалено діагностику компресії провідних структур спинного мозку та тяжкості порушення їх функцій. Використання джиттер-аналізу дозволяє підвищити інформативність НФ діагностики ураження мотонейронів спинного мозку, особливо на ранніх стадіях патологічного процесу.

Ключові слова: *спондилогенна шийна мієлопатія, діагностика, ЕМГ, джиттер-аналіз.*

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Информативность нейрофизиологических методов диагностики в дифференциации поражения мотонейронов спинного мозга

Цель исследования — определить принципы и тактику дифференцированного применения комплекса нейрофизиологических (НФ) методов в диагностике спондилогенной шейной миелопатии (СШМ).

Материалы и методы исследования. Проанализированы результаты клинико-нейрофизиологического исследования у 160 пациентов в возрасте от 31 до 76 лет с СШМ. Использованы методы: клинико-неврологический; нейровизуализирующие (МРТ, КТ, функциональна спондилография); комплекс НФ методов — стимуляционная электронейромиография (ЭНМГ) с регистрацией F-волны, игольчатая ЭМГ, моторные вызванные потенциалы (МВП), соматосенсорные вызванные потенциалы (ССВП), ЭМГ единичного мышечного волокна с определением средней плотности мышечных волокон в двигательных единицах и надежности нервно-мышечной передачи.

Результаты. Разработана и применена в исследовании схема оптимальной последовательности использования методов НФ диагностики у пациентов с СШМ. У 19 (11,9%) пациентов выявлено поражение мотонейронов, у 32 (20%) — синдром БАС на фоне СШМ, у 59 (36,9%) — сопутствующая радикулопатия. Доказана чувствительность метода МВП для выявления частичной компрессии спинного мозга при шейном спондилезе — у 134 (83,8%) больных, ССВП — у 29 (58%). На клиническом примере определена роль джиттер-анализа при необходимости тонкой дифференциации болезни мотонейронов, ишемического и компрессионного поражения мотонейронов спинного мозга.

Выводы. Предложена схема оптимальной последовательности использования методов НФ диагностики у пациентов с СШМ. Благодаря применению методов МВП и ССВП усовершенствована диагностика компрессии проводящих структур спинного мозга и тяжести нарушения их функции. Использование джиттер-анализа позволяет повысить информативность НФ диагностики поражения мотонейронов спинного мозга, особенно на ранних стадиях патологического процесса.

Ключевые слова: *спондилогенная шейная миелопатия, диагностика, ЭМГ, джиттер-анализ.*

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