Influence of comorbid diseases in the elderly on the efficiency complex conservative of pain in efficacy of treatment of back pain in the elderly with comorbidities

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Abstract: The aim of the study: to determine the structure of dorsalgia and comorbid diseases and the possibilities of rehabilitation in elderly patients with degenerative-dystrophic diseases of the spine (DDSD). The results of observation of 120 elderly patients who received sanatorium treatment in the Urgench sanatorium during 2020-21, aged 60-74 years, were analyzed, including 71 women, 49 men. All patients underwent a neurological examination, X-ray, CT or MRI of the spine, to identify comorbid diseases - ECG, ultrasound of internal organs, consultations with a general practitioner, urologist or gynecologist. According to the literature data and the results obtained, when selecting elderly patients with dorsalgia for treatment, it is necessary to take into account the "red flags" and refer such patients to specialized specialists. In addition, other comorbid diseases are identified in the elderly, which may limit the treatment of drug and physiotherapy (rehabilitation) therapy, which must be considered. Finally, in the elderly, it is necessary to take into account the so-called "yellow flags" - cognitive and depressive manifestations that affect the subjective sensation of pain.

1 Introduction

The growth of the economic development of countries, the improvement of the quality of life leads to a gradual increase in the life expectancy of the population, and, consequently, to its aging. If in 1950 worldwide, according to the Demographic Division of the UN Department of Economic and Social Affairs, there were 188 million people aged 60 and over, then by 2000 this figure had increased to 585 million. Approximately every tenth to twelfth inhabitant of the planet - These are people in the elderly (from 60 to 74 years) or senile (from 75 to 89 years) age. People who have reached the age of 90 years or more are considered centenarians [1].

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Elderly patients are characterized by high morbidity in general, among which cardiovascular, oncological diseases, as well as diseases of the musculoskeletal system are in the lead [2, 3].

Low back pain (LBP) is the most common problem in the elderly, leading to reduced quality of life and disability [4, 5, 6]. Worldwide, the prevalence of LBP in the elderly ranged from 13% to 50% [7, 8, 9]. A study conducted in Israel found that the prevalence of chronic LBP in the elderly aged 77 years and older was high at 58% [10]. Both the frequency and prevalence of chronic LBP have been found to increase with age. Thus, in the elderly aged 80 years and older, BNS is three times more likely to be observed than in people aged 50 to 59 years [11].

Since severe LBP is difficult to treat and leads to functional disability, timely treatment of LBP in the elderly is of great social importance [12].

Due to the high prevalence of cognitive impairment in the elderly, they cannot correctly assess their pain sensations. This leads doctors to underestimate the severity of BNS and inadequacy of treatment. This is supported by a study where 25% of older people in nursing homes with chronic pain did not receive analgesics, and only 50% of the elderly were prescribed analgesics as permanent prescriptions in suboptimal doses, which did not meet geriatric clinical guidelines [13].

Many studies have found that comorbidities are associated with chronic LBP in the elderly. One study found that in older women, hypertension, joint pain, and loneliness were factors in the development of chronic LBP [14]. Another study showed that the likelihood of LBP was 2.7 times higher among older people with one chronic comorbidity and 4.8 times higher for people with two or more comorbidities compared with older people without comorbidities [11].

The main types of potentially serious pathology of the spine and spinal cord that cause back pain:
1) traumatic fractures of the vertebrae;
2) compression fractures of the vertebrae against the background of osteoporosis;
3) tumors (including metastases) of the spine;
4) tumors of the spinal cord and spinal roots;
5) infections (osteomyelitis, epidural abscess, tuberculosis);
6) spondylarthritides (primarily ankylosing spondylitis);
7) secondary stenosis of the spinal canal with the "horse tail" syndrome;
8) diseases of internal organs (aortic aneurysm, gynecological pathology, kidney disease, etc.).

To identify a serious pathology, a system of "red flags" or "threat signs" is proposed, which are anamnestic and / or clinical signs that can be detected when questioning or examining a patient with LBP, indicating that he has an increased likelihood of developing a severe, possibly a life-threatening disease that causes LBP [15].

"Red flags" for LBP:
1) age over 50–55 years or less than 18–20 years;
2) the pain is not associated with movement, is combined with pain of another localization and / or is widespread (more than one root is affected);
3) a serious spinal injury or a connection between the onset of the disease and a previous injury;
4) persistent fever;
5) the presence of an oncological disease in history;
6) unexplained weight loss;
7) unrelenting at night or constantly progressing back pain;
8) increasing neurological symptoms, including clinical signs of the "cauda equina" syndrome (urinary incontinence or difficulty urinating, "saddle" anesthesia with impaired
sensitivity in the anus and perineum, bilateral weakness and/or numbness of the lower extremities, impotence;
9) pulsating formation in the abdominal cavity;
10) back pain, aggravated at rest;
11) immunosuppression, HIV, drug addiction;
12) long-term use of glucocorticoids;
13) the presence of systemic diseases;
14) increase in pain syndrome over time;
15) lack of relief and reduction of back pain after lying down;
16) intense and daily pain mainly in the thoracic spine;
17) deformity of the spine, formed in a short time;
18) the general condition of the patient with prolonged malaise suffers.

Among the causes of LBP, less than 1% are associated with spinal tumors [16]. Incidence rates of all neoplasms increase with age [17]. Most tumors in the spine are associated with metastasis, and only a few of them are primary tumors [18-23]. Most often, breast cancer, prostate cancer, and lung cancer metastasize to the spine, and somewhat less frequently, melanoma, kidney cancer, and thyroid cancer [24]. Tumors of the spine may manifest as the only clinical symptom in the form of back pain. The pain does not go away at rest, worse at night and with percussion. Tumors of the spinal canal are characterized by acute pain of the radicular type [25].

Myeloma. Damage to the spine is also observed in multiple myeloma, in which flat bones (skull, pelvis, sternum, ribs) are also affected. It belongs to the group of paraproteinemic hemoblastoses, characterized by the proliferation of plasma cells with hyperproduction of monoclonal antibodies. With multiple myeloma, osteodestruction and osteoporosis of the spine are detected. The lumbosacral spine is more often affected; constant intense pain in the back and chest is characteristic, subsiding in the supine position (in contrast to pain in metastatic lesions). The presence of an M-gradient in the electrophoregram of blood serum proteins and/or the detection of Bence-Jones protein in the urine play a decisive role in making a diagnosis. The disease is characterized by a sharp increase in the level of total protein in the blood serum, persistent proteinuria, a persistent and prolonged increase in the erythrocyte sedimentation rate (ESR), hypercalcemia, hypogammaglobulinemia, plasma cell infiltration of the bone marrow (the number of plasma cells reaches > 15%) [26, 27].

Among infectious lesions of the spine in the elderly, osteomyelitis of the vertebrae, discitis and tuberculous spondylitis are distinguished. They can develop as a result of hematogenous spread of infection from skin lesions, genitourinary, gastrointestinal, respiratory tracts. Predisposing factors for the development of infectious lesions of the spine are long-term immunosuppressive therapy, alcoholism, diabetes mellitus and other comorbid conditions. In tuberculosis, the lumbar region is involved in 30% of cases. Destruction of 2 adjacent vertebrae (anterior wedge-shaped deformity) is characteristic. Back pain in osteomyelitis is intense, in 15% of cases it occurs with symptoms of radicular or spinal compression. Fever occurs in 50% of cases. X-ray, computed tomography (CT) and MRI combined are shown [28].

All elderly people to some extent have cerebrovascular disorders due to arterial hypertension, atherosclerosis, diabetes mellitus, heart disease, etc., leading to brain atrophy. Neuroimaging studies have shown that brain regions responsible for pain processing (e.g., cingulate gyrus, insula, striatum, hippocampus, cerebellum, and prefrontal cortex) decrease significantly with age [29, 30]. These brain changes in the elderly lead to changes in pain perception, central pain processing [31], and/or neuroplastic changes in pain responses [32]. It should be noted that central pain processing may be difficult in encephalopathies associated with dementia [33]. In general, age-related changes in the brain with distortion
of central pain processing may contribute to the development of severe or chronic LBP in the elderly, which may reduce the effectiveness of treatment in this category of patients [34].

There are a number of social and psychological factors that contribute to the transition of the pain syndrome into a chronic form. These factors are commonly referred to as the “yellow flags” of pain [35]. These include:

- comorbid anxiety, depressive, or mixed disorder in the patient
- catastrophizing pain
- restrictive, “painful” behavior
- hypochondriacal personality type
- job dissatisfaction or conflicts at work
- problems in family life
- initial decrease in physical, social, household activity
- rental installations
- low level of education
- background stress conditions
- insomnia.

The chronicity of back pain in the elderly largely depends on the mental state of the person. Fear of pain increases depression and markedly reduces physical activity. A number of authors come to the conclusion that in elderly and old patients with prolonged pain syndrome, the plasticity of the CNS is noticeably reduced, which is clinically manifested by increased pain sensitivity and its slower recovery [36, 37, 38]. Anxiety, depression, kinesiophobia, and pain catastrophization are risk factors for persistent or debilitating LBP in the elderly [39]. A prospective study showed that older people with a high degree of depression were twice as likely to have LBP after 4 years of follow-up [40]. It is important to note that chronic LBP itself can be a factor in the development of depression and anxiety, so the study of anxiety and depression should be included in the examination of elderly patients with chronic LBP [36, 41]. The data obtained may help develop optimal multimodal approaches to the treatment of elderly people with LBP [36, 37, 42].

Patients with Parkinson's disease may experience increased sensitivity to pain due to decreased dopaminergic function of the striatum [43]. However, such pain can be alleviated by the administration of levodopa [44].

Elderly people with chronic LBP are characterized by a regional decrease in striatal gray matter density, which leads to less dopamine release, which leads to increased sensitivity to pain, forming a vicious circle and leading to LBP chronicity [45].

Dystrophic changes in the musculoskeletal system in old age lead to osteosclerosis and osteoporosis, which significantly reduces the functionality of the spine. Loss of elasticity of the intervertebral discs, facet joints and tendon-muscular apparatus against the background of erasing the boundaries of physiological curves both in the area of cervical and lumbar lordosis and thoracic and sacral kyphosis leads to a redistribution of the load on the spine. These changes cause pathological muscle tension, limitation of spinal mobility and rapid back fatigue and are the main cause of pain in most elderly patients [46].

The algorithm for diagnosing dorsalgia in the elderly should take into account the peculiarities of the combined pathology inherent in this age. Equally important is the somatic examination of the patient to exclude the pathology of the internal organs, accompanied by pain in the corresponding dermatomes. The next step is to confirm the degenerative process in the vertebrae themselves, intervertebral discs, and, which is especially important in elderly patients, facet joints [46].

The treatment of back pain is based on the principles of evidence-based medicine. The effectiveness of non-steroidal anti-inflammatory drugs (NSAIDs) has a high degree of evidence. The doctor must always remember that the treatment of back pain in the elderly,
very often with comorbidities, should be especially differentiated and sparing, giving preference to cyclooxygenase-2 (COX-2) preparations. The duration of admission is usually on average from 7 to 14 days [47].

An important step in the relief of muscle spasm that accompanies pain is the appointment of muscle relaxants. They reduce pain, reduce reflex muscle tension, improve motor functions, which allows more active rehabilitation measures, including physiotherapy exercises. Therapy with muscle relaxants in elderly patients begins with the usual dose (in malnourished patients, the dose can be reduced by 1/2 or 1/3) and continue from several days to several weeks during the entire period of the pain syndrome [48].

Radicular pain syndrome is characterized by significant intensity, peripheral distribution, limitation by the limits of the root and the conditions that cause it. Almost always, the pain spreads from the central part of the back (from the spine) to any part of the limb. Coughing, sneezing, tension are characteristic factors that increase pain. Any movement has the same effect. The pain associated with damage to the spinal root is primarily characterized by special signs of pain syndrome (pain can be acute paroxysmal piercing in nature or persistent burning, itching, cooling, sometimes deep and aching, may be accompanied by a sensation of current passing and a feeling of "crawling"). In addition, it is localized in the corresponding skin area, accompanied by a change in sensitivity, the development of muscle weakness, a decrease (loss) of the corresponding reflexes in the area of the nerve root concerned. Examination reveals tension and soreness of the paravertebral muscles, as well as a significant conflict on magnetic resonance imaging, indicating irritation or compression of the nerve root [49].

The results of recent systematic reviews indicate that among the drugs used in the treatment of radicular pain, the drugs of the gabapentinoids group: pregabalin and gabapentin are the most effective from a clinical point of view and patient safety, which makes them currently the drugs of first choice for the treatment of pain with neuropathic pain component [50, 51].

So, with lumbosacral and cervical radiculopathy, the dose of pregabalin is 150-600 mg / day. As a rule, the starting daily dose is 150 mg (75 mg 2 times a day, morning and evening). After 3-7 days from the start, the transition to the optimal daily dose of 300 mg (150 mg 2 times a day) is carried out; if necessary, after 10-14 days, it is possible to increase the dose of pregabalin to a maximum of 600 mg/day (300 mg 2 times a day) [52].

In the complex therapy of radicular back pain, vitamins of group B are successfully used, according to indications - antidepressants and tranquilizers, with severe pain, paravertebral and sacral blockades with anesthetics and glucocorticosteroids are prescribed [53, 54].

In compression fractures and osteoporosis, along with effective pain relief, the appointment of anti-osteoporotic agents in combination with calcium and vitamin D3 preparations is indicated. Before starting the treatment of osteoporosis with pathogenic agents, it is necessary to study the levels of total calcium and phosphorus in the blood serum [55].

The elderly are often diagnosed with osteoarthritis and spondylarthrosis. Chondroprotectors are currently one of the principal prescriptions for patients with osteoarthritis. However, the effectiveness of only certain chondroprotectors (chondroitin sulfate and glucosamine) has been proven in multicenter randomized trials, and their use in osteoarthritis has a high (A1) degree of evidence [56, 57]. They are often referred to as symptomatic slow acting drugs for osteoarthritis (SYSADOA). There are combined preparations containing chondroitin sulfate and glucosamine sulfate). The duration of taking these chondroprotectors is usually up to 3-4 months; such courses are recommended 2 times a year. An important auxiliary component of the complex treatment of LBP is local
therapy. In order to reduce the intake of parenteral or oral drugs, it is advisable to use local anesthetic and/or chondroprotective creams or ointments [58].

Physiotherapy and rehabilitation of back pain in the elderly

To enhance the therapeutic effect, patients with dorsalgia add physiotherapy aimed at reducing reflex muscle spasm, reducing root compression, and improving microcirculation. However, for the treatment of back pain in the elderly with comorbid diseases, only gentle physiotherapy can be used, which include traction of the spine with light weight (in the absence of osteophytes), phonophoresis with papaya melon tree preparations, magnetotherapy (in the absence of a pacemaker), massage and exercise therapy [59, 60, 61].

Thus, back pain in the elderly has a diverse character, the diseases leading to them can be conditionally divided into three large groups: a) degenerative-dystrophic diseases of the spine, b) other diseases of the spine, c) diseases of the internal organs with reflected pain in the spine. Difficulties in the differential diagnosis between these nosologies are also associated with the fact that the elderly have symptoms blurring and chronic pain syndrome, layering of comorbid diseases, along with the increasing development of cognitive and dementia disorders in this age group of patients, complicating the subjectivization of pain syndrome assessment.

2 Results of own research

The aim of the study: to determine the structure of dorsalgia and comorbid diseases and the possibilities of rehabilitation in elderly patients with degenerative-dystrophic diseases of the spine (DDSD).

3 Materials and methods

The results of observation of 120 elderly patients who received sanatorium treatment in the Urgench sanatorium during 2020-21, aged 60-74 years, were analyzed, including 71 women, 49 men. All patients underwent a neurological examination, X-ray, CT or MRI of the spine, to identify comorbid diseases - ECG, ultrasound of internal organs, consultations with a general practitioner, urologist or gynecologist.

Depending on the presence of comorbid diseases, we divided our patients into 2 groups: the control group (CG) of 50 patients in whom comorbid diseases limited the receipt of full-fledged medical and physiotherapeutic treatment. In this group, patients received traditional treatment for DDSD: NSAIDs, muscle relaxants, chondroprotectors, vasodilator therapy, symptomatic therapy, lumbar massage and exercise therapy. The main group (MG) - 70 patients, patients in whom comorbid diseases did not limit the receipt of full-fledged medical and physiotherapeutic treatment. In this group, in addition to traditional therapy, patients received lumbar traction on a traction table with low weight, magnetotherapy and ultrasound therapy with hydrocortisone ointment.

The severity of the pain syndrome was assessed using the Visual Analogue Scale (VAS). ENMG and the study of somatosensory evoked potentials (SSEPs) were performed according to the standard technique by stimulating the tibial nerve from both sides using the MVP-4 apparatus of the Neurosoft Company, Russia. When studying the functional state of the peripheral nerves performed by the stimulation ENMG method, we paid attention to the study of the F-wave, and more precisely, to its loss (blocks). By its physiological nature, the F-wave is a muscle response to a return discharge resulting from antidromic stimulation of a motor neuron. Dropout or block of the F-wave is its absence on the registration line.
The cause of the loss or block of the F-wave can be a lesion of both the nerve and the motor neuron [62].

In the study of SSEP, the latency and amplitude of the N22 peak (sensory response measured from the tibial nerve at the level of the caudaequina and conus of the spinal cord) and the N22-P38 interval (the interval from the lumbar level to the cortical centers) were measured [63].

Cognitive changes were determined by studying cognitive evoked potentials (CEP) using the Neuronspectr-5 device (Neurosoft, Russia). CEP was studied by isolating P300 complexes at the expense of significant sound stimuli using 12 channels. To assess the motor component, the P300 method was carried out by pressing a key when recognizing significant auditory stimuli. For further analysis, the averaged values of the latency and amplitude of the P300 potential were taken [63].

4 Results and discussion

All patients, upon admission to the sanatorium, complained of back pain of various localizations. 35 (29.2%) subjects (including 18 (15%) people with lumbar ischialgia) complained of pain, mainly in the lumbar spine, 4 (3.3%) predominantly in the cervical spine, mainly in the thoracic region. - 10 (8.3%), 36 (30%) patients complained of cervicalgia in combination with lumbodynia, 35 (29.2%) complained of widespread pain throughout the spine.

According to CT or MRI data, 31 (25.8%) patients were found to have herniated intervertebral discs in the lumbar spine, no larger than 7 mm in size, 10 (8.3%) patients had hernias of the cervical spine, 48 (40%) patients protrusions of the intervertebral discs were found (mainly of the lumbar spine), in 45 (37.5%) cases spondyloarthrosis was detected, in 38 (31.7%) cases - spondylosis, in 8 (6.7%) cases an X-ray picture of relative vertebral stenosis was observed channel. Thus, our patients had confirmed signs of degenerative-dystrophic changes in the spine with greater localization in the lumbar region, then in the cervical region and, to a lesser extent, in the thoracic region.

All patients had certain comorbid chronic diseases of the internal organs, as well as the musculoskeletal system. On the part of the musculoskeletal system, patients were observed established (according to the clinical picture, x-ray studies) arthrosis of various localization: gonarthrosis - in 33 (27.5%) patients, coxarthrosis - 18 (15%), humeroscapularperiarthritis - 45 (37.5%). Of the comorbidities in patients, there were: hypertension and arterial hypertension of 1-2 degrees - 59 (49.2%) patients, coronary heart disease - 11 (9.2%), diabetes mellitus - 4 (3.3%), chronic obstructive bronchitis - 9 (7.5%), overweight (> 25) - 37 (30.8%) patients, obesity 1-2 tbsp. (> 30) - 18 (15%), 3 tbsp. (>40) - 1 (0.8%), nodular goiter - 20 (16.7%), benign prostatic hyperplasia in 15 (30.6%) men.

Before treatment, the intensity of dorsalgia according to VAS in both groups was comparable: 5.3±0.3 points in the control group and 5.2±0.2 in the main group. After the treatment, the intensity of dorsalgia in both groups decreased. In patients of the main group, the severity of dorsalgia according to VAS was 2.0±0.1 points, which was significantly lower than in the control group (2.6±0.4 points; p<0.05) (Table 1).

As a result of the study of the functional state of the peripheral nerves performed by the method of stimulation ENMG, F-wave blocks of various severity were detected in all patients. However, before treatment, F-wave block rates were comparable (Table 1). After treatment, in patients of the main group, F-wave blocks were 16.1±0.3%, which was significantly lower than in the control group (19.3±1.6%; p<0.05) (Table 1).

When analyzing the obtained SSEP data, it was found that patients initially had an increase in N22 latency in both compared groups and were comparable. After treatment in patients of the main group, the latency of N22 decreased to 21.2±0.4 ms, while in the
control group it decreased to 22.8±0.4 ms (p<0.05) (Table 1). When analyzing the N22 amplitude, it was also revealed that patients initially had low N22 amplitude values, however, these indicators were comparable in the compared groups (Table 1). After treatment, the amplitude of N22 increased in patients of the main group, while in the control group it remained at the same values (Table 1).

In the study of CEP in patients, it was found that patients initially had an increase in P300 latency in both compared groups and were comparable. After treatment in patients of the main group, the latency of P300 decreased to 353.1±2.3 ms, while in the control group it decreased only to 363.8±3.2 ms (p<0.05) (Table 1). When analyzing the P300 amplitude, it was also revealed that the patients initially had low P300 amplitude values, however, these indicators were comparable in the compared groups (Table 1). After treatment in patients of the main group, the P300 amplitude increased to 8.9±0.1 mV, while in the control group it increased to 7.9±0.3 mV (p<0.05) (Table 1).

5 Conclusions of own researches

1. In the elderly, dorsalgia of the lumbar and cervical localization of the process predominates in the structure of degenerative-dystrophic diseases of the spine.

2. For the rehabilitation of this category of patients in sanatoriums, it is necessary to take into account comorbid chronic diseases, which sharply limit the possibility of rehabilitation measures and thereby reduce the effectiveness of treatment.

3. Identified changes in the study of the CEP; an increase in latency and a decrease in the amplitude of P300 can be considered as a psychogenic component of the pain syndrome in the elderly with degenerative-dystrophic diseases of the spine.

4. In the elderly with degenerative-dystrophic diseases of the spine with comorbid diseases in a sanatorium, a rehabilitation complex consisting of NSAIDs, myorelaxants, chondroprotectors, symptomatic prescriptions and physiotherapy: lumbar traction on a traction table, ultrasound therapy with hydrocortisone ointment, massage and therapeutic exercises, has recommended itself as an effective complex method of treatment in this category of patients, which does not cause an increase in the manifestations of concomitant pathology.

6 Conclusion

According to the literature data and the information we obtained as a result of the study, we can conclude that when selecting elderly patients with dorsalgia for treatment, it is necessary to take into account the "red flags" and refer such patients to specialized specialists. In addition, older people have other comorbid diseases that must be taken into account when prescribing drug and physiotherapy (rehabilitation) therapy. Because, with some comorbid diseases, there are restrictions on prescribing drugs and physiotherapy. Finally, in the elderly, it is necessary to take into account the so-called "yellow flags" - cognitive and depressive manifestations that affect the subjective sensation of pain.

Table 1. Dynamics of clinical and neurophysiological parameters during treatment in the compared groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Maingroup, n=70</th>
<th>Controlgroup, n=50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>Pain intensity according to VAS</td>
<td>5.2±0.2</td>
<td>2.0±0.1*</td>
</tr>
</tbody>
</table>
cognitive and depressive manifestations that affect the subjective sensation of pain. Some comorbid diseases, there are restrictions on prescribing drugs and physical therapy. Therefore, when prescribing drug and physiotherapy (rehabilitation) therapy, it is necessary to take into account the “red flags” and refer such patients to specialized medical institutions. We can conclude that when selecting elderly patients with dorsalgia for treatment, it is important to consider the category of patients, which does not cause an increase in the manifestations of concomitant dystrophic diseases of the spine.

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control Group</th>
<th>Main Group 1</th>
<th>Main Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENMG, % blocks Fwave</td>
<td>20.5±0.6</td>
<td>16.1±0.3*</td>
<td>21.6±0.6</td>
</tr>
<tr>
<td>SSEP Latency N22 (ms)</td>
<td>23.3±0.6</td>
<td>21.2±0.4*</td>
<td>23.2±0.3</td>
</tr>
<tr>
<td>SSEP Amplitude N22 (mV)</td>
<td>1.1±0.1</td>
<td>1.3±0.1*</td>
<td>1.1±0.1</td>
</tr>
<tr>
<td>CEP Latency P300 (ms)</td>
<td>366.2±2.2</td>
<td>353.1±2.3*</td>
<td>365.9±2.2</td>
</tr>
<tr>
<td>CEP Amplitude P300 (mV)</td>
<td>7.6±0.1</td>
<td>8.9±0.1*</td>
<td>7.7±0.1</td>
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