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SUBJECTIVE COGNITIVE AND SUBTLE COGNITIVE IMPAIRMENTS

Cognitive impairments are one of the leading problems of neurology and psychiatry due to their wide prevalence, especially in the elderly and senile age, the difficulty in diagnosis and treatment. In addition, the increase in life expectancy of the population in Russia and in the world will undoubtedly cause a rapid increase in patients with dementia and other cognitive impairments. However, dementia in most cases does not develop overnight; its development is preceded by a long period of time when the existing cognitive impairments do not yet disrupt the patient's household and professional activity. Cognitive impairment of this degree is called "pre-dementia" and is divided into subjective cognitive decline, subtle and mild cognitive impairments. This article discusses the key problems of subjective cognitive decline and subtle cognitive impairment, the interpretation and diagnosis of which raises the most frequent questions among clinicians. So, based on a review of Russian and foreign literature, the authors substantiate how it is possible to distinguish between subjective cognitive decline and subtle cognitive impairment, and discuss where the line with moderate cognitive impairment is. Separately, diagnostic algorithms and treatment tactics for subjective cognitive decline and subtle cognitive impairment are presented.

Keywords: subjective cognitive impairment, mild cognitive impairment, moderate cognitive impairment, dementia, neuropsychological testing.

Introduction. Cognitive impairment is one of the topical issues of modern neurology and psychiatry. This is evidenced by the geometric increase in the number of articles in foreign and domestic journals. So, if in 2000 only 1,301 articles with the keywords "cognitive impairment" were published in PubMed, then their number reached 4,536 in 2010, and 15,665 in 2021. In the Russian scientific database "Elibrary.ru" in 2000 there was not a single article with the keywords "cognitive impairment", in 2010 94 articles were published, in 2015 - 191 articles, and in 2021 their number increased to 252 articles.

The increased interest in cognitive impairment is justified, since a dementia pandemic is expected in the world, primarily due to the increase in life expectancy of the population. According to one major meta-analysis, there were 35.6 million people with dementia worldwide in 2010, and this number will double every 20 years, reaching 65.7 million by 2030 and 115.4 million by 2050 [22].

For comparison, according to Russian Federal State Statistics Service, the population of Moscow in 2022 amounted to 12.6 million people. Thus, already in 2010, all patients with dementia would "inhabit" the three Moscows of 2022. However, dementia in the vast majority

of cases does not develop overnight; its development is preceded by a long period of time when the existing cognitive impairments do not yet disrupt the patient's household and professional activity. Cognitive impairments of this degree are called "pre-dementia" and are divided into subjective, subtle, and mild [2, 3]. In this article, we will consider the issues of diagnosis and treatment of the most diagnostically and prognostically complex pre-dementia disorders - subjective cognitive decline (SCD) and subtle cognitive impairment (SCI)

Prevalence of subjective cognitive decline and subtle cognitive impairment. Data on the prevalence of pre-dementia cognitive impairments vary widely, which is explained by their wide etiological heterogeneity and various clinical approaches to their detection [3]. Unfortunately, most studies on the prevalence of pre-dementia cognitive impairment are limited to mild cognitive impairment (MCI) and the inclusion of elderly people. As for SCD and SCI, there is practically no data on their prevalence.

Etiology of pre-dementia cognitive impairment. In elderly and senile patients, a decrease in cognitive abilities will be alarming in terms of the development, first of all, of neurodegenerative and cerebrovascular diseases, such as Alzheimer's disease (AD), frontotemporal degeneration, and small vessel disease of the brain [1, 4, 7, 14]. As for young and middle-aged people, diabetes mellitus, alcoholism, diffuse connective tissue diseases, neurosyphilis, neuroAIDS, hypothyroidism, normotensive hydrocephalus, vitamin B12 deficiency, etc. can be the cause of cognitive decline [8]. The search for the cause of cognitive impairment is much easier if the patient has other signs of a somatic or neurological

disease. However, in the vast majority of patients with SCI and SCD, especially in young patients, apart from complaints of memory loss and absent-mindedness, there are no focal symptoms and external signs of somatic diseases. Professor E.Z. Yakupov notes that affective disorders, sleep disturbance, gadget addiction, multitasking, pain, COVID-19 are the hidden causes that lead to the development of SCI [11].

Subjective cognitive decline. Although this concept has been known for a long time [21], the official definition was formed only in 2014 due to the expansion of the stages of AD [13, 20]. Thus, SCD is understood as the appearance of complaints about a decrease in cognitive functions (it is emphasized that not only memory) during normal performance of neuropsychological testing (that is, without objectification of cognitive impairments). The authors state that SCD can be caused not only by AD, however, they cite signs in which the relationship of VCI with the subsequent development of AD increases:

- 1) subjective decrease in memory, and not in other cognitive function;
- 2) presence of complaints during the last 5 years or more;
- 3) age of onset at 60 or later;
- 4) the presence of anxiety associated with SCD;
- 5) a feeling of worse academic performance compared to people of the same age group;
- 6) confirmation of the patient's complaints by another person;
- 7) the presence of the APOE ε4ε4 genotype;
- 8) presence of AD biomarkers.

Items 6–8 are performed if they are available [13].

SCD is a risk factor for the develop-

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ment of MCI in the future in at least 14% of patients [19].

Subtle cognitive impairment. SCI is understood as a decrease in cognitive functions compared to a higher initial level, but not beyond the age norm or slightly deviating from the norm [12]. Under the leadership of academician Yakhno N.N. in Russia, a comparative analysis of cognitive functions was carried out in SCD, SCI, and in healthy controls. The results of the study confirmed that there are no statistically significant differences between SCD and healthy controls. At the same time, between patients with SCD and SCI, the greatest differences were observed in terms of literal (12.08 vs. 14.78 words) and categorical (14.75 vs. 17.56 words) associations, the total score on the Mini-Mental State Examination (28.67 vs. 29.3 points) and Frontal Assessment Battery (16.42 vs. 17.38) [9].

Professor O.S. Levin rightly emphasizes that the term "SCI" can mean a

deterioration in the performance of neuropsychological tests by a patient in dynamics with going beyond the limits of the individual norm, but within the limits of acceptable age values [6]. Thus, in order to expose SCI, dynamic monitoring of the patient is necessary.

The long-term functional preservation of cognitive functions in some patients with pre-dementia disorders, even in the presence of neurodegeneration on neuroimaging and positive AD biomarkers, is explained by the concept of cognitive reserve. This concept suggests that socio-behavioral indicators such as high education, intellectual pursuits, and other activities contribute to the creation of more stable neural connections that protect cognitive functions. In other words, people with a high cognitive reserve are more resistant to dementias, in particular, to AD [5, 15].

Diagnosis of subjective and mild cognitive impairments. Table 1 shows a

comparative description of pre-dementia cognitive impairment and marks the most common diseases associated with them. In contrast to MCI in SCD and SCI, the performance of screening neuropsychological tests (MMSE, FAB, MoCA) does not go beyond the age norm. Vakhnina N.V. Vascular cognitive impairments / N.V. Vakhnina // Neurology, neuropsychiatry, psychosomatics. – 2014. – Vol. 1. – P. 74-79. DOI:10.14412/2074-2711-2014-1-74-79

Most patients with SCD and SCI complain of memory loss. However, this complaint may hide not only a true amnesic deficit, but also bradyphrenia, depression, and anxiety. Therefore, in our practice, we ask patients leading questions that allow us to more specificize complaints. For example, can the patient forget what he ate in the morning or what he did the day before? Is it hard to find words? can forget the name of the objects? Is it difficult to understand the in-

Table 1

Characteristics of pre-dementia cognitive impairments

Degree of cognitive decline	Main features	Associated diseases
Subjective cognitive decline	The presence of complaints of cognitive decline (not just memory) Normal performance of neuropsychological tests	In elderly patients, especially if there are complaints of memory loss, to have alertness in terms of the development of Alzheimer's disease
Subtle cognitive impairment	Decreased cognitive ability compared to higher baseline. Does not go beyond the age norm or slightly deviates from the norm Difficulties performing complex neuropsychological tests	In the absence of obvious somatic and neurological causes, one should think about the patient's anxiety, depression, sleep disorders, multitasking, gadget addiction, and past COVID-19
Mild Cognitive Impairment	Decrease in cognitive abilities compared with the individual and with the average norm Out of the age range Detected when performing neuropsychological tests The patient's independence is not affected, slight problems are tolerated when performing complex tasks	In the presence of the amnesic type and in the detection of biomarkers for beta-amyloid and neuronal damage, there is a very high risk of developing Alzheimer's disease. The non-amnesic type can occur within cerebrovascular disease, Parkinson's disease, post-traumatic encephalopathy, etc.

Table 2

Neuropsychological tests

Test	Instruction	Reference
Phonetic speech association	Name within 1 minute words that begin with a certain letter (for example, "L")	> 10 words
Semantic speech association	Name within 1 minute words belonging to the same category (for example, animals)	> 17 words
Visual memory test	The patient is asked to memorize 12 pictures, after an interfering task they are asked to remember them (delayed reproduction), then learn from the presented 48 pictures (delayed recognition)	Delayed reproduction + delayed recognition = 12 pictures, no false recognitions
Auditory memory test	The patient is asked to memorize 12 words, after an interfering task they are asked to remember them (delayed reproduction), then to recognize them by belonging to a category (delayed recognition)	Delayed reproduction + delayed recognition = 12 words, no false recognitions
Trail making test, part A	Connect the given numbers in ascending order, starting from 1 and ending with 25	Execution without fixes or with immediate fixes
Trail making test, part B	Connect in ascending order and alternating the numbers and letters presented (1-A-2-B, etc.)	

terlocutor? Is it difficult to navigate in an unfamiliar place? etc.

To assess SCD and SCI, screening scales used in clinical practice, such as the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), will not be sensitive enough and their results will be within the age norm [10, 16–18]. At the same time, in our opinion, this is the erased and very conditional boundary between MCI and SCI. In patients with MCI, the results of screening neuropsychological tests are outside the normative values, but the patient's daily activities are not impaired (unlike dementia).

In the diagnosis of SCI, more complex scales may be more informative, such as the Semantic or Phonetic Association Test, the Visual memory test, the Auditory memory test, the Trail making test (part A and part B), and the Stroop test. Table 2 presents the normative values of the listed scales.

As noted above, anxiety and depressive disorders can be the cause of cognitive impairments, especially SCD and SCI, so it is necessary to clarify the emotional sphere in patients, to conduct a screening assessment of anxiety and depression (for example, the Hospital Anxiety and Depression Assessment Scale - HADS, the Depression Scale Beck, questionnaire GTR-7).

In some cases, a blood test for thyroid hormones, vitamin B12, folic acid, vitamin D, and iron is required. Currently, there are no unified recommendations in which cases to prescribe one or another blood test, however, there is no doubt that a deficiency of hormones, vitamins, and substances may be accompanied by the development of cognitive complaints. Some classes of drugs can also lead to cognitive decline, such as antidepressants with anticholinergic effects (amitriptyline).

MRI of the brain is the most informative method. Here, it is important to assess mainly hippocampal atrophy, which, along with the amnesic type of cognitive impairment, may alert in terms of the development of AD. The presence of hyperintensity of the white matter, criblura, foci of cerebral infarction, on the contrary, indicate a cerebrovascular disease.

Treatment of subjective cognitive decline and subtle cognitive impairment. If the cause of cognitive impairment (eg, depression, anxiety, iron deficiency) is identified, treatment should be aimed at correcting it. The evidence base for the pharmacotherapy of pre-dementia, especially pre-mild cognitive impairment, is much weaker; studies were

mainly conducted with MCI. The emphasis in the treatment of pre-moderate cognitive impairment is on the modification of risk factors, as well as on the maintenance of cognitive reserve.

Conclusion. Pre-dementia cognitive impairment is a heterogeneous syndrome with multiple benign and serious causes. This is the main limiting factor preventing large-scale studies and obtaining reliable results. The key link in the diagnosis of cognitive impairment remains the conduct of a neuropsychological test.

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