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WEEKThe impact of hyperbaric therapy on cognitive functions in patients treated for idiopathic sudden hearing loss or hard-to-heal chronic wounds

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Abstract

Background: Hyperbaric Oxygen Therapy (HBOT) may improve brain metabolism, synaptic plasticity and neurogenesis and modulate inflammatory processes, resulting in improvement of cognitive function in various neurological disorders.

Methods: 53 individuals aged 26 to 83 years, 23 women and 30 men, 23 patients treated for idiopathic hearing loss (group I) and 30 patients treated for difficult-to-heal chronic wounds (group II) were included to the study. The Mini Mental State Examination (MMSE) Verbal Fluency Test (VF), Trail Making Test (TMT), Ray Auditory Verbal Learning Test (RAVLT) and Color Word Interference Stroop tests were applied for assessment of different cognitive domains. Cognitive assessment were performed before and after HBOT treatment. For statistical analysis non-parametric tests were applied. Significance of differences between groups were conducted using the U-Mann-Whitney test. The statistical significance of changes in neuropsychological test results before vs after hyperbaric oxygen therapy (HBOT) was assessed using the Wilcoxon signed-rank test for paired samples. For correlation analysis the R-Spearman test was used.

Results: Cognitive decline was found in both patients groups. Group II at baseline show worse performance on most cognitive tests compared to group I. After HBOT significant improvement was observed in most cognitive parameters in both groups. No significant difference between groups after HBOT were observed in seven parameters of verbal tests (VF and RAVLT). No significant changes were noted in the first learning trial and word recall after distraction in the RAVLT and VF (phonological) in patients from group I, and word recall after distraction in the RAVLT in the patients from group II. Before HBOT older age correlated with worse cognitive abilities in booth groups. After HBOT older age correlated with worse results of the TMT A and B in group II, no such correlations were found in the group I. In group I before and after HBOT worse performance on cognitive tests correlated with greater cognitive impairment measured by the MMSE. In group II before HBOT results of MMSE were associated with poorer results in the TMT A and TMT B and in the fifth trial of the RAVLT. After HBOT, worse MMSE results correlated with the worse performance on Stroop A and one parameter of the RAVLT.

Conclusions: HBOT therapy showed positive influence on most cognitive domain in patients treated for chronic hard-to-treat wound and idiopatic hearing loss. Older age and general severity of cognitive decline is connected with worse cognitive improvement after HBOT.

1. Introduction

Idiopathic sudden sensorineural hearing loss (ISSNHL) is defined as a rapid-onset hearing loss of ≥30 dB across three consecutive audiometric frequencies within three days, occurring without an identifiable cause. Its estimated incidence ranges from 5 to 30 per 100,000 individuals, although the true prevalence may be higher, as a proportion of cases resolve spontaneously within approximately 30 days. The etiology of ISSNHL is thought to involve vascular occlusion, viral infections, and other microcirculatory disturbances, while poorer prognosis has been associated with advanced age and the presence of vertigo. Standard therapeutic approaches include corticosteroid therapy and hyperbaric oxygen therapy (HBOT) (Murray et al., 2022; Choi et al., 2024).

Chronic non-healing wounds, particularly in diabetic patients, represent a significant public health concern, affecting approximately 1–1.5% of the population. The development of these wounds is multifactorial, with contributions from vascular abnormalities, inflammatory dysregulation, peripheral neuropathy, hyperglycemia, and impaired tissue perfusion (Calis et al., 2020). Effective wound healing requires complex interactions among cellular, biochemical, and vascular processes. HBOT has been employed as a therapeutic modality in this context, demonstrating the ability to reduce oxidative and pro-inflammatory mediators, promote angiogenesis, modulate vascular tone, and enhance the activity of growth factors involved in tissue repair (Rangwala et al., 2023; Capó et al., 2023).

Hyperbaric oxygen therapy involves the inhalation of 100% oxygen under elevated atmospheric pressure, leading to a marked increase in oxygen dissolved in plasma and improved tissue oxygenation. Initially developed in the 19th century for neurological and psychiatric disorders, HBOT has recently gained renewed attention for its restorative effects on the central nervous system (CNS) (Corning, 1861). Contemporary research has explored its applications in brain injuries, including traumatic brain injury (TBI), stroke, and early-stage dementias, highlighting potential neuroprotective and neuroregenerative mechanisms.

Experimental and clinical studies indicate that HBOT positively influences multiple aspects of CNS structure and function. At the cerebral level, HBOT enhances cerebral blood flow and metabolism, stimulates angiogenesis, improves vascular function, promotes synaptic plasticity, supports axonal regeneration, and strengthens neuronal connectivity. It also mitigates brain edema and modulates inflammatory responses. At the cellular level, HBOT improves mitochondrial function, enhances neurotrophin expression (e.g., BDNF), inhibits apoptosis, and reduces oxidative stress, collectively contributing to the maintenance and restoration of neuronal integrity (Efrati et al., 2013; Tal et al., 2015; Gottfried et al., 2021). These neurobiological effects have been associated with measurable improvements in cognitive function in patients recovering from TBI and stroke (Hadany et al., 2020; Gottfried et al., 2021). Nevertheless, the elevation of tissue partial oxygen pressure (PO_2) inherent to HBOT can increase reactive oxygen species (ROS), potentially leading to peripheral and central oxygen toxicity if exposure is excessive (Groborz et al., 2025).

Given these mechanisms, HBOT represents a promising intervention not only for peripheral conditions such as ISSNHL and chronic wounds but also for cognitive rehabilitation. The present study aims to investigate changes in cognitive function in patients treated for idiopathic hearing loss or difficult-to-heal wounds under HBOT. All methods and procedures were performed in accordance with the relevant guidelines and regulations. The study was conducted in a hospital setting and received ethical approval from the Bioethics Committee (application number KB535/2022). In line with this approval, all patients provided informed consent prior to participation, including consent for the analysis of their results, which was deemed adequate and appropriate by the Bioethics Committee. The datasets generated or analyzed during this study are available from the corresponding author upon reasonable request.

2. Research Methods

2.1. Subjects

The study included 53 individuals aged 26 to 83 years (median age 55.0; interquartile range 39.0–67.0). The study group consisted of 23 women and 30 men. The participants were divided into two groups: Group I included 23 patients (13 women and 10 men) treated for idiopathic hearing loss. The median age of these patients was 39.0 years, with an interquartile range of 34.0–55.0. Three individuals (13% of the group) had well-controlled diabetes, and all participants had previously contracted COVID-19. The study was completed by 21 patients (12 women and 9 men). Group II comprised 30 patients (10 women and 20 men) treated for chronic, difficult-to-heal wounds. The median age in this group was 62.0 years, with an interquartile range of 53.0–70.0. The study was completed by 24 participants (8 women and 16 men). Nineteen individuals (63% of the group) had diabetes. Similar to Group I, all participants in Group II had a history of COVID-19 infection. Patients treated for chronic, difficult-to-heal wounds were significantly older compared to those treated for sudden hearing loss ($p<0.001$, U-Mann-Whitney test). During the Rey test, the participant underwent five learning trials. Delayed recall was subsequently assessed after a 20-minute interval. The testing environment was controlled, and no distractors or interruptions were observed. Attentional lapses were monitored throughout both the learning and recall phases, and none were detected. The interval between the two cognitive assessments were 10 weeks. Possible reasons for participant attrition in the study may include withdrawal due to time constraints, lack of continued interest, adverse effects or discomfort associated with the intervention, medical contraindications that emerged during the study, or logistical challenges such as transportation difficulties or scheduling conflicts. Additionally, some participants may have been lost to follow-up due to changes in health status or personal circumstances that prevented continued participation. Patients with depression, anxiety, fatigue, or those receiving psychotropic medication were also systematically excluded from the study.

Cognitive function assessments were conducted prior to the initiation of hyperbaric oxygen therapy and after its completion..

2.2. Neuropsychological Assessment

1. Structured Clinical Interview and Demographic Data Questionnaire
2. Minimental State Examination (MMSE) – a screening test for dementia-related changes, used to assess the global functioning of cognitive functions across various domains. Results: 30-27 points – no disorders; 26-24 points – mild cognitive impairment (MCI); 23-19 points – mild dementia; 18-11 points – moderate dementia; 10-0 points – severe dementia.
3. Verbal Fluency Test, letter and categorical versions. The task for the participant is to name as many words as possible starting with a given letter (K) or meeting a specified criterion (animals, sharp objects) within one minute. The result of the test is the number of words generated within three minutes.
4. The Trail Making Test A and B. This test is used to assess psychomotor speed and spatial function (Part A), as well as cognitive control, task-switching, attention, and executive functions (Part B). In Part A, the participant is asked to connect, as quickly as possible, circles numbered 1 to 12 in sequential order. In Part B, the participant is required to alternate between connecting circles numbered 1 to 12 and lettered A to L, maintaining both numerical and alphabetical order (1-A-2-B-3-C, etc.)
5. Rey Auditory Verbal Learning Test (RAVLT) – 15 words. The participant's task is to immediately recall a list of words (List A) read aloud in five trials, followed by recalling the words from List A after a distraction task using a different list of

words (List B). After a 20-minute delay, the participant is asked to recall the words learned from List A (delayed recall).

6. Stroop Test (Stroop Color-Word Interference Test) A and B. In Part A, the participant is asked to read aloud as quickly as possible 50 words, which are color names printed in black ink on a white sheet of paper. In Part B, the participant must name the ink color of each word, where the color of the ink differs from the color denoted by the word itself. The result is the time taken to complete the task, measured in seconds.

2.3. Procedure of the Study

Before inclusion in the study, a comprehensive assessment by a hyperbaric physician and a neuropsychological evaluation were performed. Clinical and psychometric assessments were conducted both before and after the completion of hyperbaric oxygen therapy (HBoT). Prior to inclusion in the study, a physical examination and a medical interview covering the patient's medical history and demographic data were conducted. Patients were required to provide complete medical documentation, including a description of their chest X-ray and an electrocardiogram (ECG) recording before therapy. Each patient had basic vital signs measured before the hyperbaric chamber session, including heart rate, blood pressure, body temperature, and blood glucose levels. In case of any reported discomfort, the patient was examined by the hyperbaric physician, who provided continuous medical supervision during the hyperbaric oxygen therapy.

One compression in a 12-person hyperbaric chamber, where patients breathe 100% oxygen at a pressure of 2.5 ATA, lasts approximately 90 minutes. 100% oxygen is administered for one hour in three 20-minute sessions. The oxygen is delivered through airtight face masks or hoods equipped with airtight rubber collars. In the chamber, alongside the patients, there is an attendant: a hyperbaric nurse or a paramedic. The compression process is supervised by a hyperbaric physician. The number of compressions is determined by the physician during qualification; for difficult-to-heal wounds, 30 compressions are prescribed, while for patients diagnosed with idiopathic sudden hearing loss, 15 compressions are administered.

Inclusion Criteria for the Study:

1. Diagnosis of a difficult-to-heal wound or sudden idiopathic hearing loss
2. Age 18 years or older
3. Ability to provide informed consent to participate in the study after being informed of its purpose and nature
4. No contraindications for hyperbaric oxygen therapy

Exclusion Criteria from the Study:

1. Severe comorbid somatic diseases (other than diabetes with controlled blood glucose), neurological and autoimmune diseases in an exacerbation stage, unstable coronary artery disease, NIHSS <3 points
2. Acute psychiatric disorders, alcohol or substance abuse
3. Pregnancy or planning pregnancy during the study
4. Failure to meet the positive qualification criteria for the study

End Point: Degree of change in the results of neuropsychological tests.

2.4. Statistical Analysis Methods

The distribution of variables was examined using the Shapiro-Wilk test. As the distribution of variables deviated from normality, non-parametric tests were applied in the analyses. In the first phase, internal consistency of the scales was assessed, and a principal component factor analysis was performed. Comparisons of statistical significance between the two groups were conducted using the U-Mann-Whitney test. The statistical significance of changes in neuropsychological test results after therapy versus before hyperbaric oxygen therapy (HBOT) was assessed using the Wilcoxon signed-rank test for paired samples.

2.5. Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

3. Results

It was found that participants in Group I (diagnosed with sudden idiopathic hearing loss) were significantly younger than those in Group II (diagnosed with difficult-to-heal wounds). In Group I, diabetes was diagnosed in 13% of participants, whereas in Group II, it was present in 63% of the participants. These factors should be considered when interpreting the results of the tests assessing cognitive functions.

Table 1 presents the results of the factor analysis based on the outcomes obtained in the administered neuropsychological tests.

test	The whole group N=53		Group I N=23		Group II N=30	
	Factor I	Factor II	Factor I	Factor II	Factor I	Factor II
MMSE	-0,80*	0,24	-0,86*	0,11	-0,65	0,01
VF „K”	-0,34	-0,66	-0,29	-0,84*	-0,49	0,36
VF animals	-0,62	-0,29	-0,73*	-0,29	-0,06	0,19
VF sharp objects	-0,40	-0,39	-0,44	-0,27	-0,55	0,14
VF whole	-0,67	-0,63	-0,70*	-0,62	-0,54	0,38

TMT A	0,77*	-0,42	0,83*	-0,39	0,60	-0,48
TMT B	0,76*	-0,32	0,85*	-0,31	0,75*	-0,28
Stroop A	0,66	-0,27	0,65	-0,33	0,73*	-0,37
Stroop B	0,79*	-0,23	0,90*	-0,22	0,54	-0,37
Rey 1	-0,69	0,31	-0,82*	0,31	-0,47	0,14
Rey 2	-0,79*	-0,21	-0,84*	-0,19	-0,54	-0,54
Rey 3	-0,80*	-0,00	-0,87*	0,05	-0,64	-0,56
Rey 4	-0,68	-0,32	-0,71*	-0,22	-0,58	-0,63
Rey 5	-0,90*	-0,01	-0,96*	0,03	-0,71*	-0,60
Rey after distr.	-0,66	0,14	-0,75*	0,08	-0,06	-0,55
Rey after 20 min	-0,72	-0,07	-0,74*	-0,23	-0,62	-0,07
Baseline variance	7,69	1,79	9,37	1,91	5,15	2,60
Participation==	0,50	0,11	0,59	0,12	0,32	0,16

Tab. 1. The results of the factor analysis of the administered neuropsychological tests are presented. Cronbach's alpha values are provided, with significant loadings indicated by values > 0,70

As shown in the table 1 above, in the entire study group, poorer performance on most neuropsychological tests was most strongly associated with the first factor, particularly MMSE, TMT A and B, Stroop Test B, as well as trials 1, 2, and 5 of the Rey Verbal Learning Test. In Group I, consisting of individuals with idiopathic hearing loss, this relationship was observed for most tests, including MMSE, the Animal Category Fluency Test, the overall score of this test, TMT A and B, Stroop Test B, and all parameters of the Rey Verbal Learning Test. Poorer performance on the Phonemic Fluency Test for words beginning with the letter "K" was associated with Factor II. In Group II, composed of individuals undergoing treatment for chronic wounds, these associations were less pronounced. Factor I explained poorer performance in TMT B, Stroop Test A, and the fifth trial of the Rey Verbal Learning Test. In these categories, the Cronbach's Alpha coefficient exceeded 0.70.

Table 2 presents the results of neuropsychological tests conducted on patients qualified for HBOT therapy. The results of individuals treated for non-healing wounds were significantly worse compared to those treated for hearing loss in most parameters, except for five: the Phonemic Verbal Fluency Test (words beginning with the letter "K"), the Category Fluency Test (sharp objects), Stroop Test A assessing reading speed, and the first two trials of the Rey Verbal Learning Test. This suggests that fundamental language abilities related to word generation based on formal and categorical criteria, as well as the initial stage of auditory learning, were similar in both groups.

before HBOT				
	The whole group N=53	Group I 15 compressions N=23	Group II 30 compressions N=30	Comparison of Group I vs. Group II
Parameter	Median; 25-75%	Median; 25-75%	Median; 25-75%	

				U Mann Whitney Test
MMSE	28,00; 27,0 - 30,0	29,0; 27,0 – 30,0	28,0; 26,0 – 29,0	0,038
Fluency K	8,0; 5,0 – 12,0	9,0; 7,0 – 12,0	6,5; 5,0 – 11,0	0,250
Animals	12,0; 8,0 – 14,0	14,0; 12,0 – 16,0	9,5; 7,0 – 12,5	0,000
Sharp objects	7,0; 6,0 – 8,0	7,0; 6,0 – 8,0	7,5; 5,5 – 9,0	0,882
TMT A	31,0; 22,0 – 38,0	23,0; 20,0 – 38,0	33,0; 27,0 – 40,0	0,021
TMT B	64,0; 48,0 – 102,0	54,0; 42,0 – 72,0	72,0; 58,0 – 110,0	0,008
Stroop A	29,0; 24,0 – 38,0	26,0; 22,0 – 35,0	31,5; 26,0 – 41,0	0,088
Stroop B	61,0; 51,0 – 75,0	52,0; 48,0 – 70,0	71,5; 57,0 – 80,0	0,011
Rey 1	4,0; 4,0 – 6,0	5,0; 3,0 – 6,0	4,0; 5,0 – 6,0	0,184
Rey 2	6,0; 5,0 – 7,0	6,0; 5,0 – 8,0	6,0; 5,0 – 6,0	0,181
Rey 3	7,0; 5,0 – 8,0	7,0; 6,0 – 9,0	7,0; 5,0 – 7,0	0,041
Rey 4	8,0; 7,0 – 9,0	9,0; 7,0 – 10,0	8,0; 6,0 – 9,0	0,015
Rey 5	9,0; 7,0 – 10,0	10,0; 9,0 – 11,0	8,5; 7,0 – 9,0	0,009
After distraction	4,0; 3,0 – 5,0	5,0; 3,0 – 6,0	4,0; 3,0 – 4,0	0,039
After 20 min	7,0; 6,0 – 8,0	8,0; 7,0 – 9,0	6,0; 5,0 – 7,0	0,003

Tab. 2. Results of the participants before the start of HBOT therapy

Table 3 presents the results obtained by the participants after completing HBOT therapy, as well as the significance of changes in test scores post-therapy compared to baseline results in both clinical groups. After HBOT therapy, patients with non-healing wounds achieved similar results to those with hearing loss in seven assessed parameters: phonemic fluency (letter K) and categorical fluency (sharp objects), the first, third, and fifth learning trials in the Rey Verbal Learning Test, as well as word recall after distraction and delayed recall in the same test.

Significant improvement was observed in most assessed parameters in both groups. However, after HBOT therapy, no significant changes were noted in the first learning trial and word recall after distraction in the Rey Verbal Learning Test in the hearing loss group, as well as in the phonemic fluency test (words beginning with the letter K), the first learning trial, and word recall after distraction in the Rey Verbal Learning Test in the chronic wound group.

These findings indicate a reduction in differences between the two clinical groups in neuropsychological tests assessing verbal abilities, including verbal learning strategies and efficiency. Additionally, they highlight a significant improvement in most cognitive test results in both groups following high-pressure oxygen therapy.

after HBOT					
	The whole group	Group I 15 compressions	Group I 30 compressions	Comparison of Group I vs. Group II	Significance of change after HBOT therapy vs. before

				U Mann Whitney Test	therapy – Wilcoxon Test	
Parameter	Mediana; 25-75%	Mediana; 25-75%	Mediana; 25-75%		Group I	Group II
MMSE	30,0; 29,0 – 30,0	30,0; 30,0 – 30,0	29,0; 29,0 – 30,0	0,020	0,002	0,001
Fluency K	9,0; 7,0 – 12,0	10,0; 9,0 – 11,0	7,5; 6,0 – 12,0	0,121	0,049	0,100
Animals	15,0; 12,0 – 19,0	18,0; 14,0 – 19,0	12,5; 11,0 – 17,0	0,047	0,007	0,000
Sharp objects	10,0; 8,0 – 11,0	10,0; 8,0 – 12,0	9,0; 8,0 – 10,5	0,657	0,000	0,001
TMT A	28,0; 21,0 – 34,0	22,0; 19,0 – 30,0	29,0; 25,0 – 35,0	0,030	0,001	0,000
TMT B	59,0; 49,0 – 92,0	49,0; 39,0 – 84,0	64,0; 53,5 – 93,0	0,025	0,001	0,000
Stroop A	25,0; 22,0 - 30	24,0; 21,0 – 25,0	29,0; 23,0 – 32,0	0,016	0,000	0,000
Stroop B	54,0; 46,0 – 68,0	49,0; 45,0 – 54,0	58,5; 53,0 – 69,0	0,010	0,000	0,000
Rey 1	5,0; 4,0 – 5,0	5,0; 4,0 – 5,0	4,0; 4,0 – 5,0	0,161	0,148	0,624
Rey 2	7,0; 6,0 – 7,0	7,0; 6,0 – 8,0	6,0; 5,5 – 7,0	0,020	0,001	0,003
Rey 3	8,0; 7,0 – 9,0	8,0; 7,0 – 9,0	8,0; 7,0 -9,0	0,316	0,006	0,000
Rey 4	9,0; 8,0 – 10,0	10,0; 9,0 – 10,0	8,0; 7,0 – 9,0	0,000	0,015	0,004
Rey 5	10,0; 9,0 – 11,0	10,0; 9,0 – 11,0	10,0; 9,0 – 10,5	0,516	0,010	0,000
After disctraction	4,0; 4,0 – 4,0	4,0; 4,0 – 5,0	4,0; 4,0 – 4,0	0,406	0,173	0,234
After 20 min	8,0; 7,0 – 9,0	8,0; 8,0 – 9,0	7,0; 7,0 – 8,5	0,094	0,019	0,001

Tab. 3. Results of the participants after completing HBOT therapy

Table 4 presents the results of the correlational analysis between the performance on neuropsychological tests and age in the subjects before and after the completion of HBOT therapy.

	Before HBOT			After HBOT		
	The whole group N=53	Group I N=23	Group II N=30	The whole group n=45	Group I N=21	Group II N=24
MMSE	-0,44*	-0,42*	-0,30	-0,44*	-0,28	-0,35
Fluency K	-0,25	-0,23	-0,13	-0,20	-0,20	0,04
Animals	-0,25	-0,18	0,12	-0,19	-0,27	0,20
Sharp objects	-0,19	-0,47*	-0,07	-0,15	-0,29	-0,03
TMT A	0,43*	0,27	0,42*	0,49*	0,27	0,44*
TMT B	0,40*	0,14	0,41*	0,52*	0,37	0,46*

Stroop A	0,18	-0,02	0,21	0,38*	0,19	0,29
Stroop B	0,31*	0,11	0,20	0,39*	0,21	0,26
Rey 1	-0,35*	-0,09	-0,36	-0,36*	-0,32	-0,16
Rey 2	-0,27*	-0,17	-0,25	-0,31*	-0,06	-0,25
Rey 3	-0,27*	-0,15	-0,43*	-0,33*	-0,28	-0,30
Rey 4	-0,13	0,27	-0,22	-0,42*	-0,34	-0,15
Rey 5	-0,37*	-0,24	-0,32	-0,20	-0,15	-0,24
After distraction	-0,35*	-0,19	-0,24	0,07	-0,05	0,39
After 20 min	-0,27	-0,11	-0,10	-0,34*	-0,29	-0,12

Tab. 4. The results of the correlation between the scores obtained in neuropsychological tests before and after HBOT therapy and age

Age correlated with most of the cognitive test results. Before and after the completion of HBOT therapy, older age correlated with worse MMSE scores, longer completion times for the TMT A and TMT B tests, longer completion times for the Stroop B test, and fewer words remembered in the Rey verbal learning test. However, after dividing into groups, in the group of patients with hearing loss before HBOT therapy, statistically significant correlations were observed in two parameters: MMSE and categorical fluency (sharp objects). After HBOT therapy, no such correlations were found. In the group of patients with chronic wounds before the initiation of HBOT therapy, the correlation with age was observed in the TMT A and TMT B tests (the older the age, the longer the task completion time) and with the number of words recalled in the third trial of the Rey test. After therapy, the correlation was only observed in the results of the TMT A and TMT B tests.

Table 5 presents the results of the correlational analysis between the performance on neuropsychological tests and overall cognitive functioning measured by the MMSE test in the studied patient groups before and after HBOT therapy. In Group I – patients treated for idiopathic hearing loss, before and after hyperbaric oxygen therapy, worse results in most neuropsychological tests significantly correlated with greater cognitive impairment measured by the MMSE. In Group II, patients treated for chronic wounds, such correlations were much fewer. Before therapy, a general decline in cognitive functioning measured by the MMSE was associated with poorer results in the TMT A and TMT B tests and in the fifth trial of the Rey Verbal Learning Test. After HBOT therapy, such a correlation was found only in the Stroop A test and in the fifth trial of the Rey Learning Test.

Correlations with MMSE	Group I		Group II	
	Before HBOT N=23	After HBOT N=21	Before HBOT N=30	After HBOT N=24
VF „K”	0,26	0,53*	-0,09	0,08

VF animals	0,53*	0,52*	0,30	0,15
VF sharp objects	0,40	0,40	0,08	0,00
VF general	0,53*	0,60*	0,07	0,26
TMT A	-0,66*	-0,59*	-0,40*	-0,23
TMT B	-0,60*	-0,57*	-0,43*	-0,29
Stroop A	-0,58*	-0,47*	-0,29	-0,46*
Stroop B	-0,60*	-0,51*	-0,28	-0,28
Rey 1	0,49*	0,65*	0,03	0,12
Rey 2	0,59*	0,52*	0,04	-0,13
Rey 3	0,62*	0,54*	0,26	0,01
Rey 4	0,24	0,61*	0,28	0,08
Rey 5	0,71*	0,54*	0,46*	0,47*
Rey after distraction	0,59*	0,48*	0,31	-0,06
Rey after 20 min	0,38	0,19	0,39*	0,33

Tab. 5. The correlations between the results obtained in neuropsychological tests and overall cognitive functioning measured by the MMSE before and after HBOT therapy in the studied patient groups

4. Discussion

This study included patients who underwent HBOT for the treatment of idiopathic hearing loss or chronic wounds that were difficult to heal, whereas cognitive function impairments were not the direct reason for initiating treatment. However, the neuropsychological assessment before starting HBOT therapy revealed that cognitive impairments were present in both groups, with the deficits being more pronounced in the group of patients treated for chronic wounds.

There is a lack of research on cognitive function in patients with chronic wounds that are difficult to heal. Cognitive decline may be associated with the age of patients suffering from this condition and with the presence of diabetes. A meta-analysis of studies on memory impairments in patients with type II diabetes indicated that in certain patient groups, there may be a weakening of memory functions, and this deterioration can progress in a more dynamic manner over time. Longitudinal studies, which controlled for other risk factors for cognitive impairment, such as insulin resistance, vascular diseases, hypertension, and previous strokes, showed that these factors can accelerate the deterioration of cognitive functions and even increase the risk of dementia (Arvanitakis et al., 2020). In the studied group of patients with chronic wounds, the prevalence of type II diabetes was significantly higher than in the group of patients with hearing loss, which could have been one of the reasons for their poorer results in neurocognitive tests.

The results obtained by patients with idiopathic hearing loss were diverse: some patients' results fell within age-appropriate norms, while others were significantly lower. There is a lack of studies on this topic in the scientific literature, perhaps because in most cases of this condition, there is spontaneous remission of symptoms without medical intervention (Pecorari et al., 2020). Additionally, spontaneous improvement or its absence depends on several factors, such as the degree of hearing loss, age, the presence of dizziness, and the audiogram profile. Age is recognized as a study limitation. However, upon stratifying the results by age group, older patients demonstrated greater severity of cognitive dysfunction, consistent with findings reported in the literature. This study included individuals with significant impairments that hindered normal functioning (Kuhn et al., 2011). In these cases, considering the neuronal nature of the condition, functional changes involving cognitive domains can be suspected. This hypothesis is supported by the results obtained in the MMSE screening scale, where in the group of patients with idiopathic hearing loss, 18 individuals (78.3% of the group) scored within the normal range (27–30 points), while the remaining patients showed a significant decrease in scores (at the level of MCI or mild dementia). In the group of patients with chronic wounds, 22 individuals (73% of the group) scored within the 27–30 points range (normal), while the others scored at the level of MCI or mild dementia. Based on the screening scale results, it can be concluded that both groups showed significant cognitive impairments with similar frequencies.

Eight out of 16 neuropsychological parameters were significantly worse in the group of patients with chronic wounds. They performed worse on the MMSE test, categorical fluency (animal category), TMT A, TMT B, Stroop A and Stroop B tests, as well as in the 2nd and 4th trials of word repetition in the Rey Verbal Learning Test, compared to the group of patients with idiopathic hearing loss. This indicates poorer overall cognitive functioning, weakened verbal functions (including fluency and immediate memory), more impaired working memory, and cognitive control processes, with a similar level of resistance to distractive stimuli and delayed memory.

Factor analysis, on the other hand, showed that in the group of patients with idiopathic hearing loss, poorer performance on neuropsychological tests was associated with the main factor I, while factor II was strongly associated with poorer performance on the phonological fluency test. In the group of patients with chronic wounds, the association with factor I was observed in only three out of the 16 tested parameters. This may suggest that the mechanism underlying cognitive impairments differs between the two patient groups.

The most important finding of the study was that after HBOT therapy, improvement in cognitive functions in most of the tested parameters was significant in both studied groups. This allows the conclusion that hyperbaric oxygen therapy has a beneficial effect on cognitive functions, both in the younger group of patients with idiopathic hearing loss and in the older patients with chronic wounds, according to the treatment regimens prescribed for each group. In the group of patients with idiopathic hearing loss, the treatment involved 15 sessions, while in the group of patients with chronic wounds, it involved 30 sessions. In both studied groups, compared to the baseline assessment before therapy, improvement was observed in most tests (except for the number of words recalled in the first trial of the Rey Auditory Verbal Learning Test and the number of words remembered in the trial after applying a distractor). In Group II (patients treated for chronic wounds), no changes were observed in the phonological fluency task. Unfortunately, the protocol of this study did not include an analysis of the mechanism of improvement (such as neuroimaging or biochemical studies), so the neurobiological mechanisms of this improvement cannot be described.

As mentioned earlier, HBOT is a recognized method for supporting the treatment of central nervous system (CNS) dysfunctions of various etiologies. Israeli researchers noted the beneficial effects of HBOT in patients 6-36 months after hemorrhagic or ischemic strokes, finding that HBOT induces neuroplasticity processes in the late post-stroke period, which translated into clinical improvement, cognitive functioning, and daily living abilities (Efrati et al., 2013). Similarly, Italian researchers demonstrated the benefits of HBOT in stroke patients (Catalogna et al., 2023). Rockswold et al. (2013) found improvements in various brain parameters related to brain recovery in patients with severe traumatic brain injury (Glasgow Coma Scale 5.5). The authors showed that HBOT significantly improved brain metabolism, reduced intracranial pressure and brain swelling, and was associated with a 26% reduction in mortality in this group. Tal et al. (2015) observed significant clinical improvement, overall improvement in cognitive functions, particularly in the areas of processing speed, visual-spatial orientation, and motor functions in patients many years after brain injury. This effect was mainly associated with the induction of angiogenesis, which improved perfusion in the damaged brain. It was noted that early use of HBOT with 1.4 ATM (one-hour daily session for 10 days) in adults with moderate TBI significantly improved Glasgow Coma Scale scores after 10 days. Early complementary HBOT treatment was also associated with significant improvement in outcomes 3 months after the injury compared to standard treatment (Chaturvedi et al., 2024). Notably, a study described significant improvement in cognitive functions in older individuals with type 2 diabetes. This was a randomized, double-blind study where neurobiological parameters (cerebral blood flow measurement and arterial spin labeling via MRI, glucose metabolism assessed by fluorodeoxyglucose positron emission tomography, and various cognitive areas and daily activity measurements) were examined. After HBOT therapy, significant improvements were observed in the studied parameters (BenAri et al., 2020).

In this study, both patient groups shared one factor – having had a COVID-19 infection. Patients reported noticeable changes in attention and short-term memory after the infection, which persisted in some of them for several weeks, roughly until the symptoms of smell disturbance and fatigue subsided. However, this is merely a retrospective subjective assessment from the patients, not supported by medical or neuropsychological examination. It can, however, be suspected that this factor may have been significant in the worsening of cognitive functions in both studied groups. Therefore, it was decided to investigate whether there would be any change in the cognitive functioning of these patients after receiving hyperbaric oxygen therapy, especially since many previous studies have shown the effectiveness of HBOT in treating neuropsychiatric disorders, including cognitive dysfunctions of various etiologies.

Based on the analysis of 8 articles on the effectiveness of HBOT in the treatment of COVID-19, its beneficial effects during the acute infection phase in patients with respiratory failure were noted (Oliaei et al., 2021). Notably, a study by authors from the University of California and the University of Connecticut explains the potential neurobiological mechanism of cellular and tissue improvement in patients with severe respiratory failure during COVID-19. Currently, HBOT is recommended as an effective adjunctive therapy for the treatment of COVID-19 by the Oxygen-Ozone Therapy Scientific Society (SIOOT) in Italy (Valdenassi et al., 2020).

Recently, attention has been drawn to the effectiveness of HBOT in treating post-COVID symptoms. A randomized prospective study demonstrated that HBOT has a positive impact on memory functions, attention, executive functions, and neuropsychiatric symptoms in patients who have recovered from COVID-19. The study showed that this effectiveness is related to the regeneration of the brain's neuronal network and improvement in heart function (Pawlik et al., 2024). It was observed that patients with long COVID exhibit prolonged systemic inflammation, accompanied by various symptoms such as fatigue, deterioration of psychophysical condition, and cognitive disorders. HBOT may help reduce inflammation, and this mechanism can be linked to the symptomatic improvement observed in these patients, including in neurocognitive functions after HBOT therapy (Mrakic-Sposta et al., 2023).

However, it is worth mentioning that one of the latest systematic reviews, which included 42 studies on the impact of HBOT on cognitive functions in various neurological disorders, did not provide definitive information on this matter. The authors point out methodological issues, the lack of standard neuropsychological research protocols for specific diseases, the concentration of researchers on selected cognitive domains without considering others, and the lack of longitudinal studies (Marcinkowska et al., 2021). This raises the reflection that the methodology of neuropsychological research in different neurological disorders is not uniform, which complicates comparative studies. Furthermore, there is often a lack of a well-founded disease concept justifying the choice of the most appropriate measurement methods. In the case of this study, no relevant references were found in the literature in this regard for both patient groups.

In summary, this study showed that patients qualified for HBOT due to idiopathic hearing loss or chronic difficult-to-heal wounds present cognitive dysfunctions to a similar extent, with more pronounced changes in cognitive functioning observed in older patients treated for chronic wounds. The higher age of patients is a risk factor for more severe cognitive impairments. Treatment with hyperbaric oxygen significantly improves cognitive functioning in both groups, regardless of whether the patients are treated for idiopathic hearing loss or chronic wounds. The etiopathogenetic mechanisms behind cognitive dysfunctions may differ between the two patient groups. Additionally, the impact of a previous COVID-19 infection on the deterioration of cognitive functioning cannot be ruled out.

5. Conclusions:

HBOT therapy according to proper treatment protocol may positive influence on most cognitive domain in patients treated for chronic hard-to-treat wound and idiopatic hearing loss. Older age and general severity of cognitive decline is connected with worse cognitive improvement after HBOT. For future studies, it is recommended to incorporate a matched control group, implement an extended follow-up period—preferably exceeding two months—and include a functionality questionnaire to obtain more relevant and comprehensive outcomes, thereby strengthening the validity of the findings.

6. Limitations of the study

This study was not randomized or controlled and was observational in nature. Its aim was to observe potential changes in cognitive functioning in patients referred for HBOT for reasons other than cognitive dysfunction. Some information regarding the course of COVID-19 infection obtained from patients was retrospective and based on the subjective perception of the subjects. The sample size of the groups was relatively small. The study protocol did not include neuroimaging or biochemical studies that could have enabled the interpretation of the etiological mechanisms of cognitive dysfunction and the mechanisms of their improvement under the influence of HBOT. An additional limitation pertains to the potential for practice effects. Although the influence of repeated testing cannot be entirely excluded, the magnitude of the observed improvements surpassed the variation typically attributable to retesting. It is acknowledged that the cognitive assessments employed are primarily developed for dementia screening and may exhibit limited sensitivity to subtle cognitive deficits. However, within the clinical context of HBOT referral, these instruments were both feasible and validated for comprehensive cognitive evaluation. These limitations mean that the results of this study should be interpreted with caution, although it provides a basis for further planned randomized studies.

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7. References

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