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Hyperbaric Oxygen Therapy

The **hyperbaric oxygen therapy** (HBOT) is one of the most frequently studied non-invasive procedures in modern medicine. The database shows a broad but unevenly distributed body of evidence: while some areas of application such as **safety** or **cognitive disorders** are well documented, the study situation for other areas remains patchy or contradictory.

1,091

STUDIES IN
TOTAL

822

IN HUMANS

276

OF WHICH
CONTROLLED

5

IN ANIMALS

8

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-12

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Hyperbaric Oxygen Therapy at a Glance

ORIGIN:

Hyperbaric oxygen therapy (HBOT) is a medical procedure in which patients inhale 100 % oxygen in a pressure chamber under increased ambient pressure (1.5–3 bar). Originally developed for the treatment of decompression sickness, HBOT is now used for wound healing, neurological rehabilitation and inflammation modulation. The mechanism of action is based on hyperoxygenation of the tissue, which can influence oxidative stress, inflammatory processes and microvascular dysfunction.

EVIDENCE BASE:

1.091 evaluated studies · 276 controlled human studies · 546 observational studies · 79 review articles · 5 animal studies · 7 cell culture studies

STRONGEST INDICATIONS:

- Tissue oxygenation and inflammatory processes HBOT showed a significant increase in brain tissue oxygen partial pressure (PO₂) in a controlled study in patients with traumatic brain injury. Preclinical data suggest short-term reduction of pro-inflammatory markers and increase of pro-angiogenic cytokines, although with unclear clinical relevance.
- Cognition and psyche Randomised controlled studies in patients with prolonged post-concussion syndrome (PCS) after traumatic brain injury showed significant improvements in global cognitive function, attention and executive functions after 40 HBOT sessions. In healthy older adults, controlled studies showed improvements in attention and information processing speed as well as increases in cerebral blood flow in prefrontal and parietal regions.
- Post-COVID-19 Sham-controlled studies in post-COVID-19 patients showed significant improvements in neurocognitive functions, energy levels and sleep quality after 40 HBOT sessions. MRI data indicated microstructural changes and improved brain connectivity, although without long-term follow-up.

LIMITATIONS:

- The evidence base for classic indications such as bone healing consists predominantly of small controlled studies with contradictory results. Antiviral effects have so far only been investigated in preclinical models.
- Methodological quality of the studies is heterogeneous: many studies are based on observational designs without causal conclusions, and pressure protocols as well as outcome parameters vary widely.
- Lack of standardisation of measurement methods and short observation periods complicate statements on the sustainability of the effects, particularly in inflammation modulation and cognitive rehabilitation.

CLASSIFICATION:

Hyperbaric oxygen therapy is a well-studied, non-invasive procedure with initial indications of effects in neurological rehabilitation and inflammation modulation. The heterogeneous evidence base and lack of long-term data currently limit the strength of the statements.

1. What Hyperbaric Oxygen Therapy Is

The **hyperbaric oxygen therapy** (HBOT) is a medical procedure in which patients inhale **100 % oxygen** in a pressure chamber under increased ambient pressure (usually 1.5–3 bar). The increased pressure enables a significantly increased **physical dissolution of oxygen in the blood plasma**, independent of the binding capacity of haemoglobin. The therapy is usually carried out in series of sessions, the duration and pressure levels of which vary according to the indication.

The **decisive mechanism of action** of HBOT lies in the **hyperoxygenation of the tissue**, which cannot be achieved under normal conditions. The increased oxygen partial pressure allows oxygen to diffuse deeper into poorly perfused or hypoxic tissues, which can influence **oxidative stress**, **inflammatory processes** and **microvascular dysfunction**. At the same time, **stem cell mobilisation**, **angiogenesis** and **neuroplasticity** are discussed as possible secondary effects. These effects are usually measured via **biochemical markers** (e.g. inflammatory mediators), **imaging procedures** (e.g. MRI) or **clinical scores**, although the transferability of laboratory findings to the human organism often remains unclear.

2. What the Studies Show in Detail

The key human studies and the most important reviews — by field of application, with population, duration, preparation, measured variable and result, as reported by the original studies. Numbers appear only where the study states them.

Distribution of **controlled human studies** by field of application — the numbers are not additive, as one study may be assigned to several fields:

FIELD OF APPLICATION	CONTROLLED STUDIES
Safety and tolerability	111
Cognition and psyche	65
Fatigue and stress	63
Inflammatory processes	58
Immune system	50
Skin	49

FIELD OF APPLICATION	CONTROLLED STUDIES
Metabolism	40
Musculoskeletal system	21

Inflammatory Processes

Participants received either 60 minutes of HBOT at 1.5 ATA, 3 hours of normobaric hyperoxia (NBH) with 100 % oxygen at 1 ATA or standard therapy within 24 hours of injury. Treatment was administered once daily for three consecutive days. Parameters measured included brain tissue oxygen partial pressure (PO₂), microdialysis, intracranial pressure, cerebral blood flow (CBF), cerebral oxygen metabolism rate (CMRO₂), liquor lactate and F₂-isoprostane concentrations as well as interleukin-6 and -8 in bronchoalveolar lavage. Compared with the control group, a significant increase in brain tissue PO₂ was observed during HBOT, but no significant differences in the other measured parameters. The study provides an indication of a short-term improvement in tissue oxygen supply, without however being able to demonstrate clinical effects in humans. A limiting factor is the short observation period of only three days, which does not permit statements on long-term effects ¹.

A systematic review from 2021 examined the effect of HBOT on markers of oxidative stress, inflammation and angiogenesis. The analysis included studies that measured these laboratory parameters in humans. The results suggest that HBOT-induced oxidative stress reduces the concentrations of pro-inflammatory acute-phase proteins, interleukins and cytokines while simultaneously increasing growth factors and pro-angiogenic cytokines. However, these effects often occurred only after the first HBOT session or for a short time after each session. The authors suspect that the observed changes could be mediated by the interference of hyperoxia with the NF-κB and IκBα signalling pathways. The clinical relevance of these laboratory findings has not been investigated and remains to be clarified, particularly with regard to the duration and sustainability of the effects. The included studies varied considerably in design, population and measurement methods, which limits comparability.

An observational study of 15 patients with prolonged post-concussion syndrome (PPCS) after traumatic brain injury examined the neurotherapeutic effect of HBOT using microstructural imaging. The participants received 60 daily HBOT sessions at 1.5 ATA for 60 minutes. Before and after treatment, dynamic susceptibility contrast-enhanced (DSC) and diffusion tensor imaging (DTI) were performed. The results showed significant increases in fractional anisotropy and significant decreases in mean diffusivity in white and grey matter. In addition, cerebral blood flow and volume increased significantly. Clinically, these findings correlated with improvements in memory, executive functions, information processing speed and global cognitive scores. The study suggests that HBOT could induce neuroplastic effects through angiogenesis and improvement of microstructure in both white and grey matter. A limitation is the lack of a control group, which makes causal conclusions difficult.

HYPOTHESIS Some of the controlled studies available suggest that HBOT can improve cerebral oxygen supply and modulate inflammatory processes in the short term. The observed effects on angiogenesis and neuroplasticity could be particularly relevant in chronic courses. However, long-term data are still outstanding that would demonstrate a sustained effect on inflammatory parameters or clinical outcomes. What is lacking are large-scale randomised controlled trials with longer follow-up periods and standardised measurement methods to validly assess the anti-inflammatory effect of HBOT – at present, controlled studies represent approximately one quarter of the evaluated works.

Cognition and Psyche

A randomised prospective study with 56 patients who suffered from prolonged post-concussion syndrome (PCS) 1–5 years after mild traumatic brain injury (mTBI) examined the effect of HBOT on cognitive functions and quality of life. The participants received either 40 HBOT sessions (100 % oxygen at 1.5 ATA for 60 minutes, 5 days/week over 8 weeks) or first underwent a two-month control phase without treatment before crossing over into the HBOT group. Cognitive functions were evaluated with "Mindstreams", quality of life with the EQ-5D. After HBOT, significant improvements were observed in global cognitive function, attention and executive functions. The study provides an indication of possible effects, but has limitations, including the absence of a placebo control group in the initial treatment phase and the possible expectation bias of the participants that could have influenced the results ².

In a randomised controlled study with 63 healthy older adults (>64 years), the effect of HBOT on cognitive functions was examined. The participants received either 40 HBOT sessions (100 % oxygen at 2 ATA for 90 minutes, 5 days/week over 3 months) or no treatment. The primary endpoint was global cognitive function measured after the intervention. The HBOT group showed significant improvements in attention (net effect size 0.745) and information processing speed (net effect size 0.788). In addition, significant increases in cerebral blood flow in prefrontal and parietal regions were demonstrated by perfusion MRI. The study suggests that HBOT can improve cognitive functions in healthy older adults, possibly through regional changes in cerebral perfusion. A limitation is the lack of an active control group that could have controlled for placebo effects.

A randomised double-blind sham-controlled study with 71 military personnel suffering from persistent post-concussion symptoms after mTBI compared the effect of 40 HBOT sessions (1.5 ATA, 100 % oxygen, 60 minutes) with a sham intervention (1.2 ATA, room air, 60 minutes). Primary endpoints included symptoms, quality of life, neuropsychological tests and neurophysiological measurements. After 13 weeks, the HBOT group showed a significant improvement in the Neurobehavioral Symptom Inventory (mean change: -3.6 points vs. +3.9 points in the sham group, p=0.03). However, 49 % of participants were affected by post-traumatic stress disorder (PTSD), which limits the specificity of the results for mTBI. In addition, the effects on other cognitive or neurophysiological parameters were not consistent ⁸.

A randomised controlled study with 63 civilians and military personnel with persistent post-concussion syndrome (PPCS) after mTBI compared 40 HBOT sessions (1.5 ATA, 100 % oxygen, 60 minutes, 5 days/week over 8 weeks) with an untreated control phase. After HBOT, significant improvements were observed in symptoms (Neurobehavioral Symptom Inventory), memory, executive functions, depression, anxiety, PTSD symptoms, sleep quality and quality of life. After crossover into the HBOT group, the initial control participants showed similar improvements. The effects remained stable two months after the end of treatment. The study provides an indication of possible effects, but has the limitation of lacking a sham control, which does not exclude placebo effects ⁶.

HYPOTHESIS Some controlled studies suggest that HBOT can lead to measurable improvements in patients with chronic cognitive and psychological sequelae after mTBI as well as in healthy older adults. The effects could be mediated by a combination of improved cerebral perfusion, neuroplasticity and modulation of inflammatory processes. However, the results are limited by the absence of active control groups in some studies and the high

comorbidity with PTSD in military populations. What is lacking are studies with larger sample sizes, longer follow-up periods and specific biomarkers to clarify the underlying mechanisms and the sustainability of the effects.

Heart and Circulation

Intracranial pressure, cerebral oxygen partial pressure (PO_2), cerebral blood flow (CBF) and cerebral oxygen metabolism rate ($CMRO_2$) were measured. Compared with the control group, a significant increase in brain tissue PO_2 was observed in the HBOT/NBH group, but no significant differences in CBF, $CMRO_2$ or intracranial pressure. The preclinical data (animal experiments and cell cultures) suggest that the combined therapy can improve cerebral oxygen supply in the short term, although an effect on cerebral metabolism or intracranial pressure in humans has not yet been investigated.

HYPOTHESIS The present study suggests that HBOT in combination with normobaric hyperoxia can improve cerebral oxygen supply in preclinical models (animal experiments and cell cultures). Indications of a sustained effect on cerebral metabolic processes or intracranial pressure in humans are still outstanding. What is lacking are studies with longer treatment and observation periods as well as specific endpoints that would validly assess the clinical relevance of these effects for cerebral metabolism.

Viral Infections

A randomised sham-controlled double-blind study with 73 patients suffering from post-COVID-19 symptoms examined the effect of HBOT on neurocognitive functions and symptoms. After treatment, the HBOT group showed significant improvements in global cognitive function (effect size $d=0.495$, $p=0.038$), attention ($d=0.477$, $p=0.04$) and executive functions ($d=0.463$, $p=0.05$). In addition, energy levels, sleep quality, psychiatric symptoms and pain perception improved. MRI demonstrated significant improvements in cerebral perfusion and microstructural changes in several brain regions. The study provides an indication that HBOT can alleviate neurocognitive deficits and symptoms in post-COVID-19 patients, possibly through improvement of cerebral perfusion and neuroplasticity. A limitation is the lack of long-term follow-up, which does not permit statements on the sustainability of the effects.

A further randomised sham-controlled double-blind study with 73 post-COVID-19 patients examined the effect of HBOT on functional and structural brain connectivity. The participants received 40 HBOT sessions (2 ATA, 100 % oxygen, 90 minutes) or a sham intervention. Before and after treatment, resting-state fMRI and diffusion tensor imaging (DTI) were performed. The HBOT group showed a significant decrease in internetwork connectivity that correlated negatively with improvements in attention and executive functions. In addition, significant changes in functional connectivity of the right hippocampus with the medial prefrontal cortex were demonstrated. The study suggests that HBOT can modulate brain connectivity in post-COVID-19 patients, which is accompanied by clinical improvements.

HYPOTHESIS Some controlled studies provide indications that HBOT could improve neurocognitive functions and symptoms in post-COVID-19 patients, possibly through modulation of cerebral perfusion and connectivity. However, long-term data on the sustainability of these effects are still outstanding. What is lacking are larger studies with longer follow-up periods and specific biomarkers to validly assess the underlying mechanisms and the clinical relevance of HBOT in post-viral syndromes.

Safety and Tolerability

A systematic review and meta-analysis from 2023 examined the adverse effects of HBOT. The analysis showed that the HBOT group had significantly more adverse effects than the control group (30.11 % vs. 10.43 %, $p < 0.05$). The most common side effect was ear pressure (113 cases). With more than 10 HBOT sessions or a chamber pressure above 2.0 ATA, the incidence of adverse effects was higher than in the control group. The study suggests that HBOT is relatively safe when used appropriately, but is associated with an increased risk of ear pressure and other mild side effects. A limitation is the heterogeneity of the included studies with regard to indication, treatment protocol and population.

A systematic review from 2018 summarised 40 years of clinical and preclinical research on the use of HBOT in acute severe traumatic brain injury (TBI). The analysis included eight clinical and 22 preclinical studies. The preclinical studies consistently showed positive treatment effects on various outcome parameters without notable safety concerns; these findings come from animal experiments, and transferability to humans has not been investigated. The clinical studies indicated that HBOT at 1.5 ATA for 60 minutes does not cause oxygen toxicity or cerebral/pulmonary damage. However, the clinical studies were often small and methodologically heterogeneous, which limits comparability. The authors emphasise the need for a multicentre randomised clinical trial to definitively clarify the safety and efficacy of HBOT in severe TBI ⁴.

A systematic review from 2004 examined the evidence on the efficacy and safety of HBOT in TBI. Randomised controlled trials and observational studies were included. Two randomised studies of fair quality reported conflicting results: one study found no differences in mortality or morbidity after one year, while the other showed a significant reduction in mortality in the HBOT group. However, the reduced mortality was accompanied by an increase in severe disabilities. The authors conclude that the evidence on the safety and efficacy of HBOT in TBI is limited and contradictory and requires further studies. What is lacking are large-scale methodologically robust studies with standardised treatment protocols and clearly defined safety endpoints ⁷.

HYPOTHESIS The available data suggest that HBOT is a relatively safe procedure when used appropriately, but is associated with an increased risk of mild side effects such as ear pressure. At higher pressures or longer treatment cycles, the risk of adverse effects increases. However, the evidence on the safety of HBOT in severe neurological diseases such as TBI shows limitations and contradictions. What is lacking are systematic safety studies with clearly defined protocols and long-term follow-up to validly assess the risk-benefit ratio.

Metabolism

A systematic review and meta-analysis from 2022 examined the efficacy of HBOT in diabetic foot ulcers (DFU). The analysis showed that HBOT significantly increased the healing rate of diabetic foot ulcers (relative risk 1.901; 95 % CI 1.484–2.435, $p < 0.0001$) and shortened healing time (mean difference -19.360 days; 95 % CI -28.753 to -9.966, $p < 0.001$). In addition, HBOT reduced the incidence of major amputations (relative risk 0.518; 95 % CI 0.323–0.830, $p < 0.01$). However, the studies varied greatly in design, treatment protocols and outcome definitions, which limits comparability. In addition, many studies lacked information on concomitant therapies such as wound debridement or antibiotic administration that could have influenced the results.

HYPOTHESIS The available data suggest that HBOT can accelerate the healing of diabetic foot ulcers and reduce the risk of amputation. The effects could be mediated by improved oxygen supply, angiogenesis and modulation of inflammatory processes. However, standardised protocols and long-term data are lacking to validly assess the clinical relevance of these effects for wound healing. What is lacking are larger methodologically robust studies with clearly defined endpoints and longer follow-up periods.

Fatigue and Stress

A randomised controlled study with 30 women suffering from fibromyalgia syndrome (FMS) with a history of childhood sexual abuse examined the effect of HBOT on clinical symptoms and neuroplastic changes. The participants received 60 HBOT sessions (100 % oxygen at 2 ATA for 90 minutes, 5 days/week over 12 weeks). After treatment, significant improvements were observed in all FMS questionnaires (Widespread Pain Index, Symptom Severity Scale, functional impairment), quality of life, PTSD symptoms and psychological distress. In addition, MRI demonstrated structural and functional changes in brain regions associated with pain processing and emotional regulation. The study suggests that HBOT can induce neuroplastic effects in FMS patients with a trauma background and alleviate the symptoms recorded in the questionnaires.

HYPOTHESIS The study suggests that HBOT can lead to measurable improvements in patients with fibromyalgia syndrome and a trauma background, possibly through modulation of neuroplastic processes and reduction of stress responses. However, long-term data and larger studies with active control groups are lacking to clarify the sustainability and specificity of these effects. What is missing are studies with longer follow-up times and specific biomarkers for stress and exhaustion.

Bones and Joints

A combined analysis of two randomised controlled multicentre studies examined the effect of HBOT on osteoradionecrosis (ORN) of the mandible. A total of 65 patients with ORN and indication for surgical treatment were randomised: Group 1 received surgical removal of the necrotic bone combined with 30 pre- and 10 postoperative HBOT sessions (243 kPa for 90 minutes), Group 2 received only the surgical treatment. The primary endpoint was healing of the ORN one year after the operation, evaluated using a clinically adapted version of the Common Toxicity Criteria of Adverse Events (CTCAE) v 3.0. In Group 1, 70 % of patients healed (21/30), in Group 2 51 % (18/35). HBOT was associated with an increased chance of healing, independent of baseline ORN grade or smoking status. In addition, xerostomia, unstimulated salivary flow and dysphagia improved in the HBOT group. A limitation is the high drop-out rate of 33 %, which limits the significance of the results.

HYPOTHESIS The study indicates that HBOT can positively influence functional parameters such as salivary flow and dysphagia. Whether these effects are clinically relevant for bone healing stands out. To be clarified are studies with longer follow-up times and standardised outcome parameters.

Skin

A review from 2021 summarised the therapeutic effects of various therapies and also discussed the underlying mechanisms of hyperbaric oxygen therapy (HBOT). Specifically for HBOT it is described that it is used for the treatment of wound-healing disorders because it improves tissue oxygen supply and modulates inflammatory processes. The work mentions that HBOT promotes angiogenesis, stimulates collagen synthesis and supports the proliferation of fibroblasts and keratinocytes. In addition, HBOT can enhance the effect of antibiotics and reduce the development of bacterial resistance. The authors emphasise, however, that the evidence for the efficacy of HBOT in chronic wounds is heterogeneous and depends on the aetiology of the wound. A limitation is the absence of specific clinical studies that systematically compare the effect of HBOT on different wound types ¹¹.

HYPOTHESIS The available data suggest that HBOT can promote wound healing by improving oxygen supply and modulating inflammatory processes. Whether these effects are systematically demonstrable in different wound types and stages stands out. To be clarified are randomised controlled studies with clearly defined wound-healing parameters and longer follow-up times.

Overall Picture

Some controlled studies show that hyperbaric oxygen therapy (HBOT) can exhibit effects in clinical areas such as neurological, cognitive and inflammatory diseases. They report effects on attention, executive functions and quality of life after mild traumatic brain injury (mTBI) and post-COVID-19 syndrome. In addition, there are indications from controlled studies of a possible effect in diabetic foot ulcers, osteoradionecrosis and chronic wounds, whereby the effects could be mediated by improved oxygen supply, angiogenesis and modulation of inflammatory processes.

However, the evidence in many areas is limited or contradictory. Thus, many controlled studies lack active control groups that could control for placebo effects, and the follow-up times are often short. In addition, treatment protocols vary widely, which limits the comparability of the results. Particularly limited is the data on the long-term safety and efficacy of HBOT in severe neurological diseases such as severe traumatic brain injury or neurodegenerative diseases. Here, large-scale, methodologically robust studies with standardised protocols and clearly defined endpoints are urgently required.

Methodology of the Study Situation

The included studies cover a broad spectrum of designs, including randomised controlled trials (RCTs), observational studies, systematic reviews and meta-analyses. Most RCTs examined the effect of HBOT in specific indications such as traumatic brain injury, post-COVID-19 syndrome or diabetic foot ulcers. Primary endpoints were frequently cognitive functions, clinical symptoms, healing rates or cerebral perfusion parameters. Secondary endpoints included quality of life, neurophysiological measurements and structural imaging findings. Systematically lacking, however, are active control groups in many studies that could have controlled for placebo effects. In addition, follow-up times are often short (mostly <6 months), and there are hardly any long-term data on the sustainability of the effects. Another deficit is the heterogeneity of the treatment protocols, which makes meta-analysis and comparability of the results more difficult.

HBOT: A Procedure with Broad Application, but Limited Evidence for Many Indications

The
HIGH NUMBER OF STUDIES

on hyperbaric oxygen therapy belies the fact that the evidence for many areas of application is still under development or contradictory. While acute indications such as decompression sickness or carbon monoxide poisoning are well established, long-term, placebo-controlled studies are often lacking for chronic or neurodegenerative diseases. Even in frequently cited works (e.g. on fibromyalgia or diabetic foot ulcers) the effect sizes are small and the follow-up times short. In addition, the therapeutic relevance of laboratory findings (e.g. stem-cell activation or neuroplasticity) is rarely confirmed in clinical studies.

A
CENTRAL PROBLEM

is the lack of comparability of the study protocols. Pressure levels, session durations and concomitant therapies vary so widely that meta-analyses often cannot derive clear recommendations. For example, some works on traumatic brain injuries show positive effects, while others find no significant differences compared with the control group. In addition, the placebo effect is rarely controlled systematically in HBOT studies: the chamber environment and the intensive care can trigger subjective improvements independently of the oxygen effect. Reviews therefore call for standardised protocols and longer follow-up times to assess the actual efficacy of HBOT better.

3. How Robust the Research Is

The human studies are distributed across a broad spectrum of application areas, with safety studies and cognitive disorders accounting for the largest shares. Further focal points lie on fatigue syndromes, inflammatory processes, immunomodulation and skin diseases. Notable is the low number of controlled studies on classic indications such as bone healing or antiviral effects, although these are frequently mentioned in practice. The most frequently cited controlled studies focus on neurological sequelae of trauma (e.g. traumatic brain injuries, post-concussion syndrome) and post-viral syndromes (e.g. Long-COVID), while metabolic or dermatological applications are investigated less frequently.

The methodological quality of the studies is heterogeneous. While some randomised controlled trials (RCTs) have high citation counts (e.g. on post-concussion syndrome or Long-COVID), many works are based on observational designs that do not permit causal conclusions. In addition, pressure protocols, session durations and control conditions vary widely, which complicates comparisons between studies. Another problem is the lack of standardisation of outcome parameters: while some studies measure clinical improvements (e.g. cognitive tests), others focus on surrogate markers (e.g. inflammation values) whose relevance for the course of the disease is unclear. Reviews emphasise the therapeutic potential of HBOT but regularly point to methodological weaknesses and missing replication studies.

4. What Is Frequently Claimed — and What the Data Support

STATEMENT	STUDY STATUS
HBOT has been investigated for accelerating the healing of chronic wounds (e.g. diabetic foot); the controlled results are inconsistent.	Controlled studies show mixed results: Some studies report improved wound healing, others find no significant differences compared with standard therapy.
HBOT has been investigated for improving cognitive functions in healthy older people; the results are preliminary.	A single controlled study shows slightly improved cognitive scores, but without long-term follow-up. The body of evidence is not yet sufficient to make general statements.

STATEMENT	STUDY STATUS
HBOT has been investigated for antiviral effects (e.g. in Long-COVID); the results are inconsistent.	One controlled study shows improvements in post-COVID symptoms , yet without a mechanistic explanation or replication . The evidence is preliminary and inconsistent .
HBOT has been investigated for promoting bone healing after fractures; the results are contradictory.	The majority of controlled studies examine this area, with inconsistent results . The data are too weak to derive clinical recommendations .

5. The Most Robust Studies

Ordered by strength of evidence, not by prominence. The complete evaluation includes significantly more studies; the most robust ones are listed here.

Controlled Studies in Humans

- ¹ A prospective, randomized clinical trial to compare the effect of hyperbaric to normobaric hyperoxia on cerebral metabolism, intracranial pressure, and (2010)
- ² Hyperbaric oxygen therapy can improve post concussion syndrome years after mild traumatic brain injury - randomized prospective trial (2013)
- A prospective, randomized Phase II clinical trial to evaluate the effect of combined hyperbaric and normobaric hyperoxia on cerebral metabolism, intra (2013)
- Hyperbaric oxygen therapy improves neurocognitive functions and symptoms of post-COVID condition: randomized controlled trial (2022)
- Hyperbaric Oxygen Therapy for Patients With Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-analysis (2022)
- Current controversies in the management of patients with severe traumatic brain injury (2006)
- ³ Hyperbaric oxygen in traumatic brain injury (2007)
- ⁴ Hyperbaric Oxygen Therapy in the Treatment of Acute Severe Traumatic Brain Injury: A Systematic Review (2018)
- ⁵ Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury (2012)
- Cognitive enhancement of healthy older adults using hyperbaric oxygen: a randomized controlled trial (2020)
- ⁶ Hyperbaric oxygen therapy for mild traumatic brain injury persistent postconcussion syndrome: a randomized controlled trial (2020)
- Efficacy of hyperbaric oxygen therapy for diabetic foot ulcers: An updated systematic review and meta-analysis (2022)
- ⁷ Hyperbaric oxygen therapy for traumatic brain injury: a systematic review of the evidence (2004)
- Hyperbaric Oxygen Therapy Can Induce Neuroplasticity and Significant Clinical Improvement in Patients Suffering From Fibromyalgia With a History of Ch (2018)
- Adverse effects of hyperbaric oxygen therapy: a systematic review and meta-analysis (2023)
- Hyperbaric oxygen treatment of mandibular osteoradionecrosis: Combined data from the two randomized clinical trials DAHANCA-21 and NWHHT2009-1 (2022)
- ⁸ Hyperbaric oxygen for post-concussive symptoms in United States military service members: a randomized clinical trial (2018)
- Effects of hyperbaric oxygen therapy on functional and structural connectivity in post-COVID-19 condition patients: A randomized, sham-controlled trial (2022)
- Long term outcomes of hyperbaric oxygen therapy in post covid condition: longitudinal follow-up of a randomized controlled trial (2024)
- A phase 2B randomised trial of hyperbaric oxygen therapy for ulcerative colitis patients hospitalised for moderate to severe flares (2020)
- ⁹ Systematic Review and Dosage Analysis: Hyperbaric Oxygen Therapy Efficacy in Mild Traumatic Brain Injury Persistent Postconcussion Syndrome (2022)
- Hyperbaric oxygen therapy for long COVID (HOT-LoCO), an interim safety report from a randomised controlled trial (2023)
- ¹⁰ Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury (2004)
- The effect of hyperbaric oxygen therapy on myocardial function in post-COVID-19 syndrome patients: a randomized controlled trial (2023)

6. Summary

Hyperbaric oxygen therapy (HBOT) is a well-documented procedure with proven safety and efficacy in specific areas of application. **It has been shown** that HBOT improves oxygen supply to hypoxic tissues in the short term, particularly in neurological trauma such as traumatic brain injury or post-concussion syndrome. Controlled studies demonstrated significant increases in brain tissue oxygen partial pressure (PO₂) as well as improvements in cognitive function; changes in cerebral perfusion and microstructural brain alterations, by contrast, are physiological and imaging findings. In post-COVID-19 patients, positive effects on neurocognitive deficits and quality of life were also observed. Evidence for inflammation modulation is promising, yet limited to short-term effects, such as the reduction of pro-inflammatory markers or the increase of pro-angiogenic cytokines.

HYPOTHESIS The observed effects of HBOT could be based on a combination of hyperoxygenation, modulation of oxidative stress, angiogenesis and neuroplasticity. Particularly in chronic courses of neurological diseases or post-viral syndromes, the therapeutic potential appears plausible, as the therapy can positively influence both cerebral blood flow and the microstructure of the brain. **It could follow from this** that HBOT might gain importance as a supportive measure in neurological rehabilitation or in inflammatory processes, provided the sustainability of the effects is confirmed in long-term studies. However, the underlying mechanisms are not yet fully understood, and the transferability of laboratory findings to clinical outcomes remains unclear. In addition, placebo effects or patient expectations could influence the results, especially in studies without active control groups.

To validly assess the efficacy and safety of HBOT, **studies would need** to clarify the following aspects: 1) **Long-term data** with standardised follow-up periods to examine the sustainability of effects on inflammatory parameters, cognitive functions and clinical outcomes. 2) **Large-scale randomised controlled trials (RCTs)** with active control groups to exclude placebo effects and increase the specificity of the results. 3) **Standardised measurement methods and outcome parameters** to improve comparability between studies and validate the clinical relevance of surrogate markers. 4) **Specific biomarkers** that map the underlying mechanisms such as angiogenesis, neuroplasticity or immunomodulation and enable a more precise evaluation of therapeutic effects. 5) **Investigations into classical indications** such as bone healing or antiviral effects, whose exploration is still pending despite frequent use in practice.

7. What Remains Open

- **Long-term effects:** Whether HBOT produces **permanent structural changes** (e.g. in the brain) is unclear. Most studies have **short follow-up periods**.
- **Optimal protocols:** Which **pressure levels, session durations and intervals** are most effective for which indication remains **insufficiently researched**.
- **Combination therapies:** Whether HBOT acts **synergistically with other procedures** (e.g. physiotherapy, stem-cell therapy) is **barely investigated**.

Frequently Asked Questions

Is HBOT suitable for the treatment of Long COVID?

One **controlled study** shows **improvements in cognitive symptoms and fatigue**, yet without **long-term follow-up**. The **study situation is still developing**, and **comparisons with other therapeutic approaches** are lacking. HBOT cannot be regarded as a **standard therapy** for Long COVID, but should be examined **individually within controlled studies**.

Can HBOT help with neurodegenerative diseases (e.g. Alzheimer's)?

Some **review articles** discuss **possible neuroprotective effects** through **reduction of oxidative stress** and **promotion of neuroplasticity**. **Clinical studies in humans** are, however, **rare and methodologically weak**. The **evidence is insufficient** to recommend HBOT as a **therapeutic option**. At present the application remains **experimental**.

How safe is HBOT? Are there risks?

Controlled studies examine the **safety** of HBOT, with **rare but serious complications** (e.g. **barotrauma, seizures**) documented. More common are **mild side effects** such as **ear pressure or fatigue**. The risks depend strongly on the **pressure protocol and patient selection**. An **individual benefit-risk assessment** is required.

Sources

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