

Review Article

Current Review: Hyperbaric Oxygen Analysis with Appropriate Cognitive Assessment

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Abstract

Hyperbaric Oxygen Therapy (HBOT) is a medical treatment that involves placing a patient in a pressurised chamber and administering 100% oxygen. Recently, there has been growing interest in the cognitive benefits of HBOT, with research showing improvements in cognitive functioning, especially in domains such as memory. HBOT has been proposed as an adjunctive therapy for Traumatic Brain Injury (TBI) since the 1960's and a growing body of work demonstrates consistent cognitive benefits for those suffering from TBI [1]. The use of HBOT in the treatment of TBI is based on the theory that injured neurons would benefit from increased oxygen delivery from HBOT, which may electrically or metabolically reactivate the cells. This may help to improve any cognitive impairments resulting from the TBI [2]. These benefits may be partially due to HBOT leading to an increased level of oxygen in the blood, which is believed to promote neurogenesis, neuronal integrity and synaptogenesis, factors that may influence cognitive functioning. This review examines research on the cognitive benefits of HBOT and provides an overview of the methods by which cognitive performance can be measured. While the optimal treatment protocol for HBOT needs further clarity, existing research highlights its potential for enhancing cognitive performance.

Keywords: Hyperbaric Oxygen Therapy; Oxygenation; Traumatic Brain Injury; Stroke; Cognition, Memory; High Metabolic Brain Regions; Cognitive Assessment; Mini Mental State Exam; NeuroTrax

Introduction

Originally developed for the treatment of decompression sickness in divers, HBOT is increasingly utilized for the treatment of a variety of medical conditions [3]. Currently the FDA has approved HBOT for 13 uses, including for the treatment of burns, severe anaemia and carbon monoxide poisoning [4]. Beyond these treatments, researchers have started to explore the impact of HBOT on cognitive functioning [5].

Based on a growing number of clinical trials, HBOT seems to enhance cognitive performance in individual's suffering from neurological conditions, particularly in cognitive domains such as memory [6]. A handful of recent studies provide evidence that HBOT may have cognitive benefits for healthy individual's as well, demonstrating its promising applications for general cognitive improvement.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore was exempt.

Cognitive Effects of HBOT in Neurocognitive Disorders

The potential for HBOT to improve memory has been documented in numerous studies investigating HBOT and TBI [7]. TBI refers to any injury to the brain caused by an outside force i.e. a forceful blow to the head. Symptoms range from mild to severe, depending on the trauma and can result in temporary or permanent cognitive impairment, such as memory loss [8]. An early study investigating this theory was conducted by Harch, et al., where military personnel with TBI underwent 40 HBOT sessions, 90 minutes long, at 100% oxygen at 1.5 Atmospheres Absolute (ATA). Results demonstrated an increase both in working memory and delayed memory, following HBOT, in addition to measures of general cognition. A later study by Tal, et al., confirmed these findings [9]. Patients with chronic neurocognitive impairment as a result of TBI were given 60 sessions of HBOT, 90 minutes long, at 100% oxygen at 2 ATA. Significant improvements were found in all cognitive domains, particularly in memory, information processing speed and global cognitive score. Additionally, results found that HBOT induced cerebral angiogenesis (the formation of new blood vessels) and recovery of brain microstructure in TBI patients. The authors concluded that HBOT may enhance integrity of brain fibres in TBI patients, providing a potential explanation for the cognitive benefits associated with it (Tal, et al., 2017). Similar findings were also reported in a later study by Hadanny, et al., who administered HBOT in TBI patients for 40/70 sessions for 60/90 minutes of 100% oxygen at 1.5/2 ATA [10]. Clinical improvements were observed in all cognitive domains, with the most prominent improvements being in memory. These findings were observed in parallel with increased activation in relevant brain areas.

Additionally, evidence for the effects of HBOT on memory can be found in research on the use of HBOT for patients suffering from a stroke [11]. A stroke is the result of a ruptured blood vessel or a blockage in an artery [12]. Cognitive deficits following a stroke are very common and can lead to a decline in the ability to function in everyday life [13]. Increased oxygenation has been suggested as a potential treatment for a stroke, as this may lead to tissue repair and the formation of new synaptic connections [13]. A study by Boussi-Gross, et al., explored the use of HBOT for addressing memory impairments in patients at chronic, late-stage recovery from stroke [14]. Patients received 40-60 HBOT sessions, 90 minutes long, at 100% oxygen at 2 ATA. Results revealed statistically significant improvements in all memory domains, which were associated with improvements in brain metabolism, predominantly in temporal regions. More recently, Rosario, et al., conducted a study examining HBOT and cognitive performance in patients who had suffered a stroke [15]. Significant improvements were observed in memory and general cognition, as well as in sleep and an increased quality of life [15]. Similar findings were reported in a later study by Hadanny, et al. [10]. Patients suffering from a stroke that occurred over 3 months prior to treatment were given 40-60 HBOT sessions, 90 minutes long, at 100% oxygen at 2 ATA. Significant improvements were observed in all cognitive domains, with memory demonstrating the highest mean absolute change. These studies provide further evidence that HBOT can improve memory in patients suffering from neurological damage.

Cognitive Effects of HBOT in Healthy Individuals

The above studies provide evidence suggesting that HBOT can have cognitive benefits for patients suffering from neurocognitive damage, particularly with regard to memory. Recently, a handful of studies have also demonstrated that HBOT may have the same cognitive benefits for healthy individuals. A pioneering study conducted by Hadanny, et al., examined the effects of HBOT on cognition for the first time in a group of healthy ageing adults [10]. Participants were administered 60 HBOT sessions, 90 minutes long at 100% oxygen at 2ATA. Results demonstrated improvements in all cognitive domains, post HBOT, including memory, attention and information processing speed. The effects of HBOT on cognition in healthy controls was also examined in a case report by Maroon [16]. The participant underwent 60 sessions for 100 minutes, at 2 ATA. A number of cognitive domains demonstrated improvement following HBOT, the most notable being in memory. Increased perfusion in temporal and medial regions of the brain were observed alongside this, which the author languages and high levels of acceptance among researchers and health professionals 8yas a valid measure of cognitive performance [17].

Effects of HBOT on the Brain

The brain regions implicated in memory include areas such as the hippocampus, the medial temporal lobe and the prefrontal cortex, regions that are high in metabolic activity [18]. Higher metabolic brain regions consume significantly more energy to function, typically in the form of oxygen or glucose and it may be the case that these regions benefit preferentially more from HBOT than areas of the brain lower in metabolic activity [15]. HBOT works by delivering oxygen at higher atmospheric pressures, leading to an increased amount of oxygen dissolved in the blood [19]. The result is enhanced oxygen delivery to tissues such as the brain. Brain regions higher in metabolic activity rely more heavily on oxygen to sustain their needs and thus may

benefit more from increased oxygenation [20]. Additionally, during injury to the brain, for example via stroke or TBI, high metabolic regions can become oxygen starved, leading to cellular dysfunction [21]. By increasing oxygen delivery, HBOT may help restore neuronal activity in damaged, higher metabolic brain regions. As such, the targeted improvement in memory observed from HBOT trials, may arise because memory-related brain areas, having high metabolic activity, stand to gain the most from enhanced oxygenation.

Diagnostic Tools for HBOT

Cognition is a complex process, encompassing many mental domains such as perception, attention and memory [22]. To effectively study this process, it is important to use cognitive tests that have the required scope to assess cognition across these domains [23]. Tests that assess single aspects of cognition such as memory or only provide an overall score, are limited in their use because they do not provide information about other domains such as attention and perception [24]. Therefore, to fully understand the effects of HBOT on cognition, it is important to identify suitable cognitive tests, that comprehensively represent multiple cognitive domains.

The Mini Mental State Exam (MMSE) has often been thought of as the gold standard for cognitive testing and has been used to assess cognitive improvement of HBOT in previous trials [23]. The MMSE, is a brief, 30-point cognitive test, designed to screen for cognitive impairment across multiple cognitive domains, including attention, visuo-spatial construction and memory. A score of 25 or above signifies healthy cognitive function, whereas any score below 24 indicates cognitive impairment [25]. Advantages of the MMSE include rapid administration, translation across multiple languages and high levels of acceptance among researchers and health professionals as a valid measure of cognitive performance [17]. Recently, computerised screening tools have been developed that assess cognition in greater detail over a variety of domains [26]. While these computerised cognitive batteries take longer to complete than shorter form assessments, such as the MMSE, they provide a more detailed representation of each cognitive domain. This allows researchers to examine which specific cognitive domains HBOT may affect compared to others [27]. Additionally, computerised screening tools hold advantages over written cognitive tests in that results are instantly normalised and testing supervision is not required, reducing manpower and potential human error [28].

One such computerised cognitive assessment that has been developed is NeuroTrax, a screening tool that combines a battery of cognitive tests to assess cognition over an array of domains [29]. NeuroTrax offers both a global cognitive score and seven individual domain scores [30]. NeuroTrax employs an adaptive approach to cognitive testing, whereby the difficulty of tasks is adjusted according to the users performance [31]. For example, if an individual is performing unusually well on the test, the difficulty of cognitive testing will increase. This reduces the likelihood of floor or ceiling affects, whereby an individual's true cognitive ability may be overestimated or underestimated due to the test being too difficult or too [32]. Neurotrax has been validated for the detection of mild cognitive impairment across the domains it assesses, showing good construct validity when compared to traditional neuropsychological tests [13]. This, in addition to its comprehensive approach to cognitive testing, makes NeuroTrax a sensitive measure of cognitive performance. Therefore, it is recommended that future research employs computerized cognitive assessments, such as NeuroTrax, to explore the effects of HBOT on cognition. This will allow researchers to identify specific cognitive domains impacted by HBOT, potentially leading to more targeted treatment options. This review details a number of trials showing the cognitive benefits of HBOT both for individuals with and without neurocognitive deficits, however it must be noted that the field remains controversial [33]. Much of the debate, however, relates not to the effectiveness of HBOT, but to a lack of clarity regarding optimal treatment protocol [34-38]. In the studies included in this review, duration of treatment time ranged from 60 - 100 minutes and atmospheric pressure ranged from 1.5 ATA to 2 ATA. The optimal HBOT protocol that would elicit maximal neuroplasticity, must be determined in future research.

Conclusion

Of the studies reviewed in this paper, HBOT shows promise as a method for enhancing cognitive functioning. Research has shown that HBOT can increase cognitive performance, specifically with regard to memory, both in individual's suffering with neurological conditions and those without. Future studies should continue to examine the effects of HBOT on cognitive performance using computerized assessments like NeuroTrax, which offer a thorough overview of how HBOT impacts different cognitive domains. Additionally, future research should aim to determine the minimum effective number of HBOT sessions needed to achieve improvement, reducing unnecessary use of time and resources.

Conflict of Interest

Dr. Gordon Slater has a pecuniary interest in Integrant a biotechnology company and Regen U clinics where he actively advises on treatment protocols and implant design.

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Consent to Participate

Informed consent was obtained from each participant prior to specimen collection.

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Data Availability

Data is available for the journal. Informed consents were not necessary for this paper.

Author's Contribution

The authors contributed equally.

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