Hyperbaric Oxygen Therapy DRIVES Functional Recovery & Neuroplasticity

60-daily sessions of Hyperbaric Oxygenation (1.5 ATA 100% O2 for 60-minutes) Induces Neuroplasticity and Improves Cognition Years After Anoxic Brain Injury Due To Cardiac Arrest

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Abstract
Cognitive impairment may occur in 42-50% of cardiac arrest survivors. Hyperbaric oxygen therapy (HBO2) has recently been shown to have neurotherapeutic effects in patients suffering from chronic cognitive impairments (CCI) consequent to stroke and mild traumatic brain injury. The objective of this study was to assess the neurotherapeutic effect of HBO2 in patients suffering from CCI due to cardiac arrest.

Methods
Retrospective analysis of patients with CCI caused by cardiac arrest, treated with 60 daily sessions of HBO2. Evaluation included objective computerized cognitive tests (NeuroTrax), Activity of Daily Living (ADL) and Quality of life questionnaires. The results of these tests were compared with changes in brain activity as assessed by single photon emission computed tomography (SPECT) brain imaging.

Results
The study included 11 cases of CCI patients. Patients were treated with HBO2, 0.5-7.5 years (mean 2.6 ± 0.6 years) after the cardiac arrest. The treatment was well tolerated and all patients completed the treatment protocol. No significant adverse reactions were recorded in any of the patients.
'Hyperbaric Oxygenation is a potent mean of delivering sufficient Oxygen to the brain for repair processes and induction of neuroplasticity'. HBO2 was found to induce modest, but statistically significant improvement in memory, attention and executive function (mean scores) of 12% , 20% and 24% respectively. The clinical improvements were found to be well correlated with increased brain activity in relevant brain areas as assessed by computerized analysis of the SPECT imaging.
Case 1: 52-year-old male, one year post ventricular fibrillation, suffering from ataxia and significant cognitive decline.
Baseline cognitive evaluation showed a very low memory index score and low executive function, verbal function, information processing speed, attention, and motor skills index scores.

After 60 HBO2 sessions, the patient had improvements in verbal function, executive function and attention from scores of 71, 73 and 68 to 106, 90 and 81, respectively. Improvement was also seen in memory from 25 to 43, yet the score was still low. Clinically, with regards to his ADL after HBO2, the patient was able to participate in housework, managing finances and shopping.

Brain SPECT evaluation showed the that the largest post HBO2 increase in brain activity was in the perirhinal cortex (BA 36) with over 50% increase, in the primary visual cortex (BA 17,18) with over 30% increase and in the cingulate gyrus (BA 23, 31) with over 20% increase (Fig. 4).

Case 2: 48-year-old male, 2 years post resuscitation, suffering from motordysphasia, left-right disorientation and significant cognitive dysfunction.

Cognitive evaluation at baseline showed low memory, visual spatial and executive function scores in addition to low attention and motor scores.

After 60 HBO2 sessions, the patient had improvement in memory, visual spatial and executive function from scores of 58, 70 and 74 to 68, 76 and 79, respectively. Clinically, he had complete resolution of dysphasia. Improvements were also noticed in ADL abilities such as ability to do laundry and manage finances. Additionally, he was able to return to his previous work.

Brain SPECT evaluation showed the largest post HBO2 increase in the parietal lobes (BA 5,7), temporal lobe with over 25% increase, in the inferior orbital gyrus (BA 45,47), cingulate gyrus (BA 23,24), in Wernike's area (BA 39) and in the primary visual cortex (BA 17,18) with over 15% increase (Fig. 5).

Discussion

'The most significant measurable improvements were in executive function, attention and memory'

The neurotherapeutic effects of HBO2 in patients suffering from CCI caused by cardiac arrest mediated anoxic brain injury, were evaluated by both clinical and brain imaging measures. Even though the acute injury was 5 months to 7.5 years (mean 31.3±7.7 months) prior to treatment, HBO2 was associated with significant cognitive improvement in all patients. The clinical improvements were well documented by neurocognitive tests and correlated with improved ability to perform the activities of daily living and quality of life. The most significant measurable improvements were in executive function, attention and memory.

Important validation and clues for future, larger scale studies were provided by the SPECT brain imaging. We found the clinical improvement to be well correlated with increased activity in the relevant brain area. More specifically, the brain areas that had the most significant increase in metabolic activation were in the perirhinal cortex (BA36), the pre-frontal cortex (BA 8,9,10,11), inferior frontal gyrus (BA 45,47), the anterior cingulate gyrus (BA 23,24) and the parietal lobes (BA 5,7).

A good correlation was found between the improved neurocognitive functions and the brain areas corresponding to these functions:

The perirhinal cortex activation after HBO2 was most prominent in patients that had significant memory improvement. The perirhinal cortex has a critical role in object recognition memory while interacting with the hippocampus (Brown & Aggleton, 2001).

Because the memory assessments in the cognitive tests were indeed recognition tasks, this area might be expected to be involved.

The pre-frontal cortex (BA10,11) and, more specifically, the inferior frontal gyrus (BA 45, 47) activation after HBO2 were prominent in all patients with significant executive function improvements. The right frontal gyrus is known to mediate a go/no go task (Aron, Robbins, & Poldrack, 2004), which was among the executive function tests used in the present study. The prefrontal gyrus is presumed to act as a filtering system that enhances goal directed

activities and inhibits irrelevant activations. This filtering mechanism enables executive control (Miller&Cohen, 2001).

The anterior cingulate gyrus (BA23, 24) activation after HBO2 was seen in the subjects with attention improvement. The anterior cingulate gyrus is presumed to be involved in error detection, especially in a Stroop task (Bush, Luu, & Posner, 2000), which was used in the attention tests. Lesions in this area can cause inattention to akinetic mutism (Bush et al., 2000).

The posterior parietal lobes are involved in visual spatial processing. Lesions in the right parietal lobe are known to cause visual spatial construction deficits (Mishkin & Ungerleider, 1982). Activations of these areas were seen in the patients with visual-spatial index improvement.

The changes revealed by inspection of the pre and post SPECT images indicate that HBO2 can induce reactivation of neuronal activity in stunned areas in agreement with earlier studies (Barrett, 1998; Churchill et al., 2013; Jacobs et al., 1969).

This implies that increasing the plasma dissolved oxygen with hyperbaric oxygenation is a potent mean of delivering sufficient oxygen to the brain for repair processes and induction of neuroplasticity.
'Any significant improvement after 5 months may be attributed to the intervention used'
This study has several limitations. The major one relates to the retrospective methodology and the relatively small number of patients. Still, the findings presented here are in agreement with and reinforce similar findings from previous prospective controlled trials in which the neuroplasticity effects of HBO2 ere demonstrated in chronic stages of other brain related injuries (Boussi-Gross et al., 2013). 'Hyperbaric Oxygenation can induce neuroplasticity at chronic stages in areas with metabolic dysfunction'.

Moreover, the natural history of anoxic brain injury implies that maximal recovery is expected during the first 3 months, and no further significant improvement is expected after 3 months (Lim et al., 2014). Accordingly, any significant improvement after 5 months may be attributed to the intervention used.

Although significant clinical improvement at a relatively late chronic stage and high correlation with the improved metabolic activity support the validity of the findings, larger randomized prospective controlled trials are needed.

Another important limitation relates to the HBO2 protocol. Although significant neurotherapeutic effects were achieved with 60 sessions of 1.5 ATA for 60 minutes, the exact protocol needed to induce maximal neuroplasticity with minimal side effects remains unknown. There is cumulative data that even smaller increase in pressure might be as effective (Efrati & Ben-Jacob, 2014).
As stated above, further randomized controlled trials with large patient cohorts are needed to better understand who the best candidates are and what the optimal HBO2 protocol is for patients suffering from ABI.
Conclusions
'Due to the growing numbers of cardiac arrest survivors, the application of HBO2 in this population should be considered'
Hyperbaric oxygen therapy may improve cognitive functions even during the late chronic phase after ABI resulting from cardiac arrest. Due to the growing numbers of cardiac arrest survivors, the application of HBO2 in this population should be considered. Further prospective randomized clinical studies should be carried out in order to evaluate the

patients who can benefit the most from the treatment and the optimal HBO2 protocol (dose and duration) for this population.

Hyperbaric Oxygen Improves Post Concussion Syndrome Years After Traumatic Brain Injury (TBI)

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Traumatic brain injury (TBI) is the leading cause of death and disability in the US. Approximately 70-90% of the TBI cases are classified as mild, and up to 25% of them will not recover and suffer chronic neurocognitive impairments. The main pathology in these cases involves diffuse brain injuries, which are hard to detect by anatomical imaging yet noticeable in metabolic imaging.

The current study tested the effectiveness of Hyperbaric Oxygen Therapy (HBOT) in improving brain function and quality of life in mTBI patients suffering chronic neurocognitive impairments.

Methods and Findings: The trial population included 56 mTBI patients 1–5 years after injury with prolonged postconcussion syndrome (PCS). The HBOT effect was evaluated by means of prospective, randomized, crossover controlled trial: the patients were randomly assigned to treated or crossover groups. Patients in the treated group were evaluated at baseline and following 40 HBOT (60-minute) sessions; patients in the crossover group were evaluated three times: at baseline, following a 2-month control period of no treatment, and following subsequent 2-months of 40 HBOT sessions.

The HBOT protocol included 40 treatment sessions (5 days/week), 60 minutes each, with 100% oxygen at 1.5 ATA. ‘‘Mindstreams’’ was used for cognitive evaluations, quality of life (QOL) was evaluated by the EQ-5D, and changes in brain activity were assessed by SPECT imaging.

Significant improvements were demonstrated in cognitive function and QOL in both groups following HBOT but no significant improvement was observed following the control period. SPECT imaging revealed elevated brain activity in good agreement with the cognitive improvements.

Conclusions: HBOT can induce neuroplasticity leading to repair of chronically impaired brain functions and improved quality of life in mTBI patients with prolonged PCS at late chronic stage.