

# Hyperbaric Oxygen Induces Late Neuroplasticity in Post Stroke Patients - Randomized, Prospective Trial

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## Abstract

**Background:** Recovery after stroke correlates with non-active (stunned) brain regions, which may persist for years. The current study aimed to evaluate whether increasing the level of dissolved oxygen by Hyperbaric Oxygen Therapy (HBOT) could activate neuroplasticity in patients with chronic neurologic deficiencies due to stroke.

**Methods and Findings:** A prospective, randomized, controlled trial including 74 patients (15 were excluded). All participants suffered a stroke 6–36 months prior to inclusion and had at least one motor dysfunction. After inclusion, patients were randomly assigned to "treated" or "cross" groups. Brain activity was assessed by SPECT imaging; neurologic functions were evaluated by NIHSS, ADL, and life quality. Patients in the treated group were evaluated twice: at baseline and after 40 HBOT sessions. Patients in the cross group were evaluated three times: at baseline, after a 2-month control period of no treatment, and after subsequent 2-months of 40 HBOT sessions. HBOT protocol: Two months of 40 sessions (5 days/week), 90 minutes each, 100% oxygen at 2 ATA. We found that the neurological functions and life quality of all patients in both groups were significantly improved following the HBOT sessions while no improvement was found during the control period of the patients in the cross group. Results of SPECT imaging were well correlated with clinical improvement. Elevated brain activity was detected mostly in regions of live cells (as confirmed by CT) with low activity (based on SPECT) – regions of noticeable discrepancy between anatomy and physiology.

**Conclusions:** The results indicate that HBOT can lead to significant neurological improvements in post stroke patients even at chronic late stages. The observed clinical improvements imply that neuroplasticity can still be activated long after damage onset in regions where there is a brain SPECT/CT (anatomy/physiology) mismatch.

**Trial Registration:** ClinicalTrials.gov NCT00715897

**Citation:** Efrati S, Fishlev G, Bechor Y, Volkov O, Bergan J, et al. (2013) Hyperbaric Oxygen Induces Late Neuroplasticity in Post Stroke Patients - Randomized, Prospective Trial. PLoS ONE 8(1): e53716. doi:10.1371/journal.pone.0053716

**Editor:** Jens Minnerup, University of Münster, Germany

**Received:** June 17, 2012; **Accepted:** December 5, 2012; **Published:** January 15, 2013

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**Funding:** The study was supported by the research fund of Assaf-Harofeh medical center, by the Tauber Family Foundation and the Maguy-Glass Chair in Physics of Complex Systems at Tel Aviv University and by Joseph Hackmey. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing Interests:** The authors hereby declare that, although Prof. Eshel Ben-Jacob is a PLOS ONE Editorial Board member, this does not alter the authors' adherence to all the PLOS ONE policies on sharing data and materials.

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## Introduction

Intensive functional therapy and rehabilitation programs for post stroke patients are considered essential for maximizing the patients' quality of life [1,2]. Unfortunately, these programs are often just partially successful, and additional therapeutic approaches towards metabolic recovery of affected cerebral tissues are called for. While a considerable amount of preclinical research supports the use of hyperbaric oxygen therapy (HBOT) for post-stroke damaged brain tissue, so far, only 5 articles reported controlled clinical trials of HBOT for stroke patients. These studies, in which the treatment started during the early-acute phase immediately after stroke, yielded non conclusive and somewhat contradicting results [3,4,5,6,7]. In contrast, a recent

phase-I study evaluating the effect of HBOT on chronic neurological deficiencies (due to traumatic brain injury) revealed promising results [8]. However, to date the effects of HBOT on neurological deficiencies due to stroke during the late-chronic phase (the focus of the current report) have not yet been investigated in a prospective randomized trial.

Years of clinical experience revealed that the dramatic spontaneous recovery from stroke occurs mainly within the first 30 days, though moderate and severe stroke survivors continue to improve for at least 90 days [9]. Most of the recovery involves brain regions rendered dysfunctional, but not dead [10]. Accumulated data from visualizations of these non-active (stunned) regions indicates that they may persist alive but dysfunctional for months, even years, after the acute injury [11,12,13]. It was