Official title: The efficacy of normobaric oxygen on chronic cerebral ischemia

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Study protocol

Objective

The aim of this study was to investigate whether the normobaric oxygen (NBO) could correct the chronic cerebral ischemia (CCI) induced EEG anomalies.

Design and methods

This was a prospective randomized cohort study and had been approved by the Institutional Ethic Committee of Xuanwu Hospital, Capital Medical University (Beijing, China) in accordance with the guidelines of the 1964 Declaration of Helsinki. Informed consent was obtained from all individuals before collecting any data. From December 2018 through December 2019, the patients who diagnosed as intracranial arterial stenosis or internal carotid arterial stenosis in Xuanwu Hospital, Capital Medical University and Beijing Fengtai You'anmen Hospital were enrolled in this study with random number table. The diagnosis of intracranial arterial stenosis and internal carotid arterial stenosis was confirmed by magnetic resonance angiography (MRA) and/or computed tomographic angiography (CTA). All of the enrolled subjects should comply with the following inclusion and exclusion criteria.

Inclusion criteria: (1) age from 18 to 80 years; (2) diagnosis of ICAS and/or ECAS; (3) NIHSS≤4 and mRS≤2; (4) signed informed consent.

Exclusion criteria: (1) brain infarction occurring within recent two months; (2) intracranial arterial aneurysm, dissection or malformation; (3) history of cerebral hemorrhage or subarachnoid hemorrhage; (4) history of cerebral trauma; (5) history of other brain injury or disorders; (6) austere diseases such as cancer, heart failure, respiratory failures; (7) respiratory diseases; (8) poor compliance.

The participants underwent 30-minute EEG recording two times. Between the two time recordings, they were randomly performed with NBO (received oxygen supplement with 8L/min, via Venturi mask, maintaining 45min) and rest (had a rest like lying, sitting or walking for 45min), which were labeled NBO group and control group in this study.

The EEG recording was conducted with an EEG recording equipment (EEG YAL PN-NET, Beijing Yunshen Science and Technology Corporation). Ag/AgCl electrodes were positioned at Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, T3, T4, T5, T6, O1, O2, A1, A2 (21 channels) according to the international 10-20 system, with electrode impedances all less than 5kΩ. The sampling rate was 256 Hz for all channels using a 16 bit AD convertor. Channel A1 and A2 were as references. Five minutes of artefact-free data was selected from EEG recordings in each subjects at random, and these participants should maintain awake and lying quietly with eyes closed as much as possible. Data filtering (band pass, 1 to 30Hz) was performed in EEGLAB (version 2019.1) with supplementary scripts operating in the MATLAB

environment. The artefact removal (blink artefact and electromyogram artefact) was performed again automatically using BSS algorithm (sobi) that was implemented into EEGLAB software packages.

The absolute power (AP, with units uV^2) was computed using Fast Fourier Transform (FFT) for each electrode over the delta (1-4 Hz), theta (4-8 Hz), alpha (8-13 Hz) and beta (13-20 Hz) frequency bands, and the relative power (RP) was a ratio of the frequency band of interest power to the total power across the 1-20Hz range. The power spectral density (PSD) for each channels was estimated via Welch's procedure with a 2-s Hamming window length. Besides over all channels, fronto-central electrodes (F3, F4, Fz, C3, C4, Cz) which were with mild occipital alpha oscillation impact, were also used to reflect the actual frequency activities in the forehead. Proceeded by python software, the EEG wavelet entropy was calculated via nonlinear dynamics method in order to evaluate the complex of brain function.[34] Power ratio index (PRI) was defined as AP ratios of theta/alpha (TAR), delta/alpha (DAR), (delta+theta)/(alpha+beta) (DTABR), and fronto-central alpha/occipital alpha (FOAR) in this study. Each frequency band AP and RP reduction rate was calculated as a ratio of pre-intervention minus post-intervention bandpower to pre-intervention bandpower.

Statistical analysis

R software (http://www.r-project.org) was used for analysis in this study. The continuous data was expressed as mean±standard deviation (SD) or median

(interquartile range, IQR). Dataset following a Gaussian distribution was analyzed with Student's t test; otherwise analyzed with Mann-Whitney U test. As for multiple comparisons among groups, LSD method was used to remove the statistical bias from repeated measure. The comparison between the prior to and post-intervention was performed with paired samples t test and Wilcoxon test. Categorical data was presented as num. (percentage) and proceeded by chi-square test. Multiple analysis using linear regression model was to rule out the confounding effect of other covariates that may affect the EEG measures. p-value <0.05 was indicative of statistical significance.