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Cognitive enhancement of healthy young adults with hyperbaric oxygen: A preliminary resting-state fMRI study

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HIGHLIGHTS

- Hyperbaric oxygen (HBO) caused increases in spatial working memory and memory quotient.
- The alternation of regional homogeneity (ReHo) induced by HBO is related to the cognitive performance.
- HBO administration affects the functional connectivity of several subcortical regions.

ABSTRACT

Objective: To date, no study has examined the effect of hyperbaric oxygen (HBO) on the cognitive performance and spontaneous brain activity in healthy adults using resting-state functional magnetic resonance imaging (rsfMRI). Our aim was to reveal the neural mechanism underlying the change in cognitive performance caused by increased oxygen.
Methods: In this study, we acquired fMRI data from 20 healthy young adults and used placebo-controlled (PBO) rsfMRI to identify the effect of HBO on the cognitive measures and the regional homogeneity (ReHo) in healthy adults.
Results: Compared to the PBO group, the HBO group showed the following: (1) the scores of the spatial working memory and memory quotient were significantly increased after HBO administration; (2) the ReHo value was significantly increased in three clusters, the left hippocampus, right inferior frontal, and lingual gyri, and for these three clusters, their functional connectivity with the subcortical brain system was significantly increased after HBO administration; and (3) the changes of ReHo values in these clusters generated by HBO administration were correlated with several aspects of cognitive performance, clarifying the cognitive locus of the effect.
Conclusion: Our results suggested that the increased availability of oxygen can, to some extent, improve memory performance.
Significant: Our findings may improve our understanding of the role of HBO in clinical and practical applications.

1. Introduction

Humans have long used cognitive enhancement methods to reduce suffering and improve the quality of life, which has attracted a surge of interest in their effects on cognitive functions in health and diseases in recent years (Kennedy, 2004; Anon, 2007; Normann and Berger, 2008; Husain and Mehta, 2011; Clark and Parasuraman, 2014; Graf et al., 2013; Lane, 2013). A growing body of evidence suggests that some kinds of cognitive-enhancing drugs

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could improve the proficiency and the range of various mental activities that they engage in, including working memory, attention, and emotion, to achieve better performance in many aspects of daily life (Mehta et al., 2000; Zaninotto et al., 2009; Eickenhorst et al., 2012; McKendrick et al., 2014). The potential opportunities, limitations, and ethical problems of neuroenhancement have also been widely discussed in society (Partridge et al., 2011; Graf et al., 2013; Heinz et al., 2014).

The human brain is the most metabolically active organ in the body. Oxygen supply is essential for mental activities in the brain. Although the adult brain does not grow, divide, or move, it consumes up to 25% of the blood oxygen supply (Roland, 1993; Raichle, 2010). During brain neural activity, the energy used for information processing and transiting originates from the breakdown of glucose, which ultimately depends on the abundant supply of oxygen. Therefore, oxygen supply is regarded as a neurocognitive enhancer, and it is widely used in various brain diseases and healthy subjects. Moss and Scholey (1996) demonstrated that increased availability of cerebral oxygen can improve performance on cognition measures, such as memory consolidation in healthy young adults, but the effect appeared to be specific to consolidation. Likewise, Scholey et al. (1998) showed a significant effect of oxygen administration on word recall, but not forward or backward digit span by a double-blind design, which suggested that oxygen administration could selectively enhance several aspects of cognitive performance. In addition, Moss et al. (1998) showed that oxygen administration can improve performance of attention and vigilance, and the oxygen-induced cognitive enhancement changes with the duration of the oxygen administration.

Recently, some functional magnetic resonance imaging (fMRI) studies have reported the neural mechanism of oxygen-induced cognitive enhancement. Several studies demonstrated that the improvement of visuospatial task performance in the condition of higher oxygen concentration was related to increased brain activation in several brain regions, such as the cingulate gyrus, thalamus, and superior parietal regions (Chung et al., 2004; Choi et al., 2010). In addition, Chung et al. (2006) also found increased activation in the right frontal gyrus, left temporal gyrus, and left fusiform gyrus when subjects were exposed to higher oxygen concentration compared to air administration during verbal tasks. These findings revealed the positive effects of highly concentrated oxygen on brain function and cognitive performance.

Based on the positive effect of higher oxygen concentration on brain cognitive performance, an increasing number of people, especially some students under the stress of examination in China, have been exposed to HBO administration for improving cognitive performance. Previous studies have revealed that HBO, 100% oxygen at two to three times the standard atmospheric pressure, can result in arterial oxygen tension in tissues and have a number of beneficial biochemical, cellular, and physiologic effects (Tibbles and Edelsberg, 1996). In clinics, hyperbaric oxygen therapy (HBOT) is widely used to treat the long-term sequelae of a variety of neurological diseases, for example, chemic stroke (Efrati et al., 2013), subarachnoid hemorrhage (Griessenauer et al., 2012), and traumatic brain injury (TBI) (Wolf et al., 2012; Boussi-Gross et al., 2013). Most importantly, these studies demonstrated that HBOT can improve the memory quotient (MQ) and intelligence of patients and can help recover brain function by promoting the reanimation of brain cells (Veltkamp et al., 2005). In an animal experiment, Harch et al. (2007) demonstrated that HBO therapy can improve spatial learning and memory in a rat model of TBI using the Morris water navigation task, and they observed the improvement in spatial learning to be strongly associated with the increased vascular density. However, to the best of our knowledge, no study to date has examined the neurocognitive enhancement of HBO administration in healthy adults.

Resting-state fMRI (rsfMRI) has been used to measure low-frequency spontaneous neural activity of human brain in vivo, and it is a crucial technique for uncovering the intrinsic brain functional architecture under both normal and pathological conditions (Fox and Raichle, 2007; Fox and Greicius, 2010; Zhang and Raichle, 2010). Regional homogeneity (ReHo), which measures the similarity of fMRI time courses of a given voxel with its nearest voxels, provides useful information about the degree of signal coherence (Zang et al., 2004). ReHo is a voxel-wise data-driven approach that takes into account the spontaneous neural activity across the entire brain in the resting state. Compared to model-driven methods, ReHo appears more sensitive in the detection of unpredictable hemodynamic responses that model-driven methods fail to identify (Zhang et al., 2014). Because ReHo measures the similarity of neural activity for a specific voxel with its nearest neighboring voxels, it can be widely used as a complementary tool to describe local brain spontaneous activity and regional stability. Previous studies have shown that ReHo is a valuable index to reflect the abnormality involved in cognitive function impairments, including depression (Yao et al., 2009), Parkinson's disease (Wu et al., 2009), Alzheimer's dementia (He et al., 2007), and schizophrenia (Liu et al., 2006). Several recent studies also used ReHo to estimate the effect of cognitive task training on the modulation of local spontaneous neural activity in healthy subjects (Zang et al., 2004; Lv et al., 2013). They demonstrated that the higher ReHo of BOLD signal may indicate higher synchronization of local neuronal activity in the human brain, and an evoked activity by the task may be associated with increased ReHo (Zang et al., 2004; Lv et al., 2013).

In this study, we used a placebo (PBO)-controlled parallel group design. The aim was to explore the effect of HBO administration on cognitive measures and ReHo values of the human brain in the resting state, and to reveal their relationship. We hypothesized that HBO administration could enhance the cognitive performance, such as memory and attention in healthy adults; correspondingly, the values of ReHo in the regions associated with memory and attention may be changed.

2. Materials and methods

2.1. Subjects

We recruited 20 healthy undergraduates/postgraduates (nine males and 11 females, aged 18–20 years) from the campus of the South China Normal University. All subjects were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). Each subject was randomly assigned to receive either hyperbaric oxygen (HBO) or hyperbaric-air administration. No one had a history of neurological or psychiatric disease or head injury. The protocols were approved by the Research Ethics Committee of the Guangzhou Liuhuaqiao Hospital. Written consent was obtained from each subject prior to the experiment.

2.2. Experimental procedure

According to the subject receiving either the HBO or hyperbaric-air administration during the experiment, 20 subjects were divided into two groups, with 10 subjects in the HBO group and the other 10 subjects in the placebo (PBO)-controlled group. Each subject of the HBO group inhaled 100% oxygen in a chamber under 2.0 absolute atmospheric pressure (ATA) for 80 min every day (excluding the time for the subject to adapt to the HBO administration and the resting time). Conversely, each subject in the PBO group received 2.0 ATA air in the same chamber for 80 min every day. The HBO and PBO groups were given the same instruction before