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Activation of the limbic system under 30% oxygen during a visuospatial task: An fMRI study

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ABSTRACT

The purpose of this study was to observe activation of the limbic system during the performance of visuospatial tasks under 21% O_2 or 30% O_2. Eight right-handed male college students were selected as subjects for this study. A visuospatial task was presented while brain images were scanned by a 3 T fMRI system. The experiment consisted of the following two runs: a visuospatial task under normal air (21% O_2) and a visuospatial task under hyperoxia (30% O_2). The accuracy rate on the visuospatial task was enhanced during 30% O_2 compared to 21% O_2. The neural activation areas of the limbic system were similar in the cingulate gyrus, thalamus, limbic lobe and parahippocampal gyrus. Increased neural activation was observed in the cingulate gyrus and thalamus under 30% O_2 compared to 21% O_2. Under 30% O_2, the improvement in visuospatial task performance was related to an increase in neural activation of subcortical structures, such as the thalamus and cingulate gyrus, as well as the cerebral cortex.

There have been reports that hyperoxia has a positive influence on cognitive abilities, such as memory, visuospatial and verbal abilities, n-back tasks and addition tasks [4–11,21,25,30]. Previous studies have reported that the administration of highly concentrated O_2 increases blood O_2 saturation [4–8] and results in an improvement in performance, such as an increase in accuracy rate [4–11,21,25,30], as well as a decrease in reaction time [8,10,21,25,30] during cognitive performance. A positive correlation has been found between blood O_2 saturation and accuracy rate [4,7,8] and highly concentrated O_2 is used more efficiently as the level of the difficulty of task is increased [5,6].

Recently, the positive effects of highly concentrated O_2 on cognitive performance have been verified using functional magnetic resonance imaging (fMRI) [9,11]. Increased activation in the right middle frontal gyrus, right inferior frontal gyrus, right superior frontal gyrus, left middle temporal gyrus and left fusiform gyrus were observed with 30% O_2 administration compared to 21% O_2 administration during verbal tasks [9]. During visuospatial tasks, increased cerebral activation has been demonstrated in the right postcentral gyrus, bilateral middle frontal gyri, right inferior frontal gyrus and left superior frontal gyrus by administration of high concentrations of O_2 [11]. These areas have a close relationship to each cognitive task. These results suggest that hyperoxia induced by a transient supplemental O_2 supply increased the O_2 in the brain vasculature and this residual O_2 was used only in areas associated with cognitive processing [2,4–11,14,20,22,25].

However, previous studies which have observed changes in neural activation by high O_2 administration only focused on cerebral cortical areas [9,11]. The cortical and subcortical areas interact during cognitive performance [19]. The limbic system of the subcortical areas includes subcortical structures associated with the limbic lobe [1] and relates to emotions and cognitive functions, such as memory, learning and visuospatial tasks [3,29]. Therefore, this study identified the effect of highly concentrated O_2 on the activation of the limbic system, which is one of the subcortical areas using fMRI.

Eight healthy right-handed male college students (mean age, 23.5 ± 3.2 years) participated in the study. None of the participants reported a history of psychiatric or neurologic disorders. The overall procedure was explained to all subjects who released consent for the procedure. All examinations were performed under the regulations of our Institutional Review Committee.

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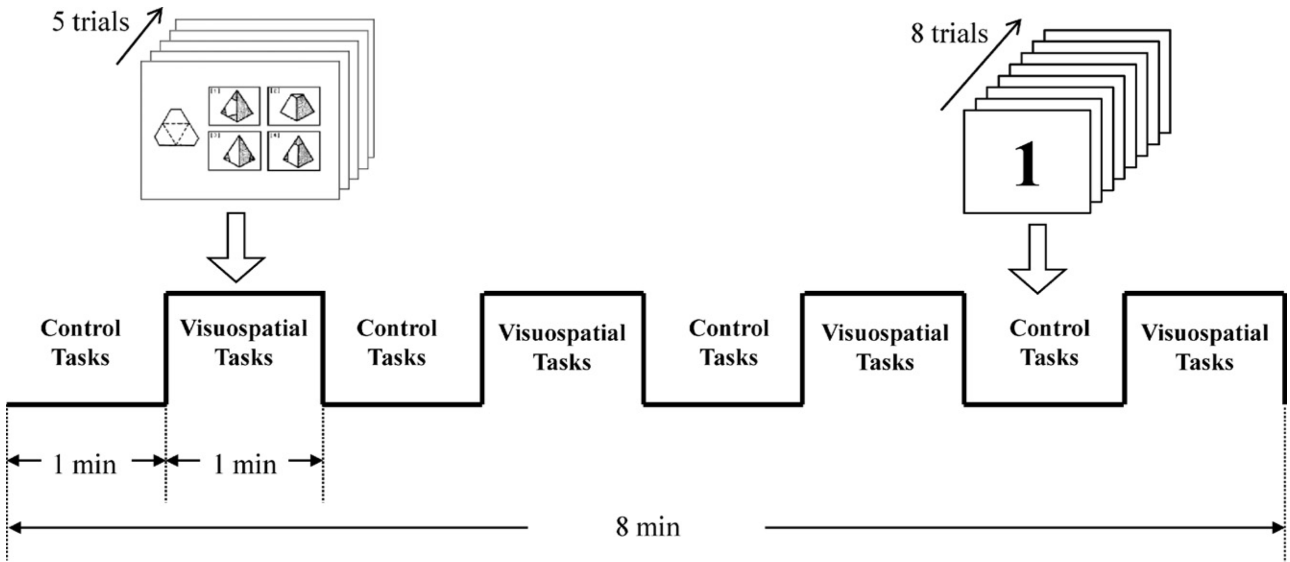

Fig. 1. The fMRI experimental procedure.

The O_2 supply equipment (OxyCure Co., Seoul, Korea), providing 21% and 30% O_2 in the air at a constant rate of 8 L/min was developed for this study. In order to maintain steady flow and a constant concentration level of O_2, the O_2 was administered to the subject through a mask without indicating the concentration.

Two versions of a visuospatial task with similar difficulty were developed from the Korean versions of an intelligence test, an aptitude test and a general aptitude battery (GATB) [17,18,23]. Two visuospatial tasks consisted of 20 items. Selected items consisted of choosing the same shape corresponding to the given figure from four given examples and choosing the development figure of the given diagram.

Fig. 1 shows the paradigm for the fMRI experiment. The experiment consisted of the following two runs of the visuospatial cognition testing: 21% level of O_2 and a 30% O_2 level. Every subject was to complete two runs and the order of 21% and 30% O_2 administration was counterbalanced. Each trial consisted of four blocks; each block had both control and visuospatial items (Fig. 1). Five minutes prior to the run, each subject was supplied with O_2 at either a concentration of 21% or 30%. Subjects were then given time to adapt to the O_2 administration. Oxygen supply was stopped after the first run. During a resting period of 30 min following the first run, anatomic images were scanned. The second run was carried out with the other concentration of O_2. The control and visuospatial tasks were presented using SuperLab 1.07 (Cedrus Co., San Pedro, CA, USA). Items were projected onto a screen and subjects were instructed to provide the correct answers. In response to control tasks, subjects were instructed to press the button corresponding to the number (1, 2, 3, or 4) projected on the screen (8 items per block). In the visuospatial task, subjects were asked to press the button as quickly as possible to indicate the item corresponding to the target figure (5 items per block). The two visuospatial tasks were counterbalanced across high and low oxygen levels. Prior to the experiment, each subject was asked to listen carefully to procedural instructions. Subjects were trained to do the task exactly in the same manner as would be expected in the scanner.

Imaging was conducted on a 3.0 T ISOL Technology FORTE (ISOL Technology, Seoul, Korea) equipped with whole-body gradients and a quadrature head coil. Single-shot echo planar fMRI scans were acquired in 35 continuous slices parallel to the anterior commissure-posterior commissure line. The parameters for fMRI include the following: repetition time/echo time [TR/TE], 3000/35 ms; flip angle, 60°; field of view (FOV), 240 mm; matrix, 64×64; slice thickness, 4 mm; and in-plane resolution, 3.75 mm. Five dummy scans from the beginning of each run were excluded to decrease the effect of non-steady-state longitudinal magnetization. T1-weighted anatomic images were obtained with a three-dimensional FLAIR sequence (TR/TE, 280/14 ms; flip angle, 60°; FOV, 240 mm; matrix, 256×256; slice thickness, 4 mm). These fMRI data were used to analyze the effects of 30% O_2 on visuospatial performance and cerebral cortical activation [11].

The fMRI data were analyzed with SPM99 (Wellcome Department of Cognitive Neurology, London, UK). All functional images were aligned with the anatomic images of the study by using affine transformation routines built into SPM99. The realigned scans were co-registered to the participant's anatomic images obtained within each session and normalized to the SPM99 template image that uses the space defined by the Montreal Neurologic Institute (MNI), which is very similar to the stereotaxic atlas Talairach and Tournoux [27]. Motion correction was done using Sinc interpolation. Time-series data were filtered with 240 s high-pass filter to remove artifacts due to cardiorespiratory and other cyclical influences. The functional map was smoothed with a 7 mm isotropic Gaussian kernel prior to statistical analysis. Statistical analysis was done both individually and as a group using the general linear model and the theory of Gaussian random fields implemented in SPM99. Using the subtraction procedure, activated areas in the brain during visuospatial tasks were color-coded by t-score. Finally, the double subtraction method was used to test the effect of the difference between the two oxygen level conditions (i.e., 21% of O_2 vs. 30% of O_2). To observe activation areas of the limbic system only, the WFU PickAtlas (Wake Forest University School of Medicine, Radiology Department, Winston-Salem, NC, USA), which is one of the toolboxes of SPM99, was used. Using the region of interest (ROI) analysis method, the number of activated voxels was calculated at the limbic system, which is separated into eight regions, such as cingulate gyrus, thalamus, limbic lobe, hypothalamus, hippocampus, parahippocampal gyrus, amygdala and the mammillary bodies.

The response accuracy rate of the task items was analyzed to identify the effect of O_2 on visuospatial performance. The mean accuracy rate was 50.63 ± 8.63 (mean ± SD) and 62.50 ± 9.64 for 21% O_2 and 30% O_2 administration, respectively, with a statistically significant difference between the two O_2 conditions ($t = 3.252$, df = 7, $p = 0.014$).