USAARL-TECH-FR--2020-029

Hyperoxia as a Cognitive Enhancement Tool: An Annotated Bibliography

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
25-06-2020	Final Technical Report	

4. TITLE AND SUBTITLE
Hyperoxia as a Cognitive Enhancement Tool: An Annotated Bibliography

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Hayes, Amanda; Temme, Leonard; St. Onge, Paul

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
U.S. Army Aeromedical Research Laboratory
P.O. Box 620577
Fort Rucker, AL 36362-0577

8. PERFORMING ORGANIZATION REPORT NUMBER
USAARL-TECH-FR--2020-029

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
DISTRIBUTION STATEMENT A. Approved for public release; distribution unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This paper is an annotated bibliography intended to examine the available research using oxygen supplementation at sea level as a cognitive performance enhancement technique.

15. SUBJECT TERMS
Annotated bibliography, Hyperoxia, Oxygen, Cognitive performance, Cognition, Cognitive enhancement

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Loraine St. Onge, PhD
UNCLAS	UNCLAS	UNCLAS	SAR	20	19b. TELEPHONE NUMBER *(Include area code)* 334-255-6906

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Introduction

Enhancing physical and cognitive performance with low cost, highly reliable, and widely available solutions remains essential to overmatching the evolving capabilities of our adversaries. This annotated bibliography demonstrates that hyperoxia, or the supplementation of oxygen above 21% at sea level, increases cognitive performance in healthy individuals. This intervention offers a cost-effective improvement strategy; however, any resultant side effects are not discussed here.

This report provides a brief summary of the research specific to hyperoxia use as a cognitive performance enhancement tool. The researchers conducted Google Scholar searches to identify candidate articles. After reviewing each article, the researchers checked the references sections to locate additional articles. Through this process, the authors identified 15 articles that reported the effects of oxygen supplementation on cognitive performance in humans and provided a direct comparison between ambient air (~20.95% oxygen at sea level) and levels of hyperoxia (oxygen supplementation). The articles described in this review included cognitive measures of attention, memory, perception, verbal cognition, visuospatial ability, visual acuity, and reaction time. Tables 1 and 2 provide descriptions of each study, and the references section provides an expanded narrative summary of each study based on the availability of information provided in each article.

Table 1. Details of each article that tested the effects of 100% oxygen

Reference	Concentration of Oxygen	# of Participants	Research Design	Aspect of Cognitive Performance Tested	Dependent Measures	Performance Enhancement?
Andersson, J., Berggren, P., Gronkvist, M., Magnusson, S., & Svensson, E. (2002).	100%	48 (26 male)	Within-subjects	Perception, attention, memory	Letter identification task, Stroop task, reading span task, word-free recall task, event-based recall task	No
Andersson, J., Berggren, P., Gronkvist, M., Magnusson, S., & Svensson, E. (2002).	100%	48 (30 male)	Between-subjects	Perception, attention, memory	Letter identification task, Stroop task, reading span task, word-free recall task, event-based recall task	No
Connolly, D.M., & Barbur, J.L. (2009).	100%	12 (6 male)	Within-subjects	Visual acuity	City University Contrast Acuity Assessment at photopic and mesopic lighting	Yes, higher visual acuity at low contrast

					levels	
Moss, M.C., Scholey, A.B. (1996).	100%	105 (not reported)	Between-subjects	Memory, mood	Verbal memory task, Profile of Mood States (POMS)	Yes, accuracy increased. No significant differences in mood

Table 2. Details of each article that tested the effects of other levels of oxygen

Reference	**Concentration of Oxygen**	**# of Participants**	**Research Design**	**Aspect of Cognitive Performance Tested**	**Tests Used**	**Performance Enhancement?**
Choi, M., Lee, S., Yang, J., Choi, J., Kim, H., Kim, H., … & Chung, S. (2010).	30%	8 (8 male)	Within-subjects	Visuospatial cognition	Visuospatial task, fMRI	Yes; 23% increased average accuracy and fMRI activation in cingulate gyrus and thalamus
Chung, S., Lee, B., Tack, G., Yi, J., Lee, H., Kwon, J., …, & Sohn, J. (2008).	30%	12 (6 male)	Within-subjects	Visuospatial cognition	Visuospatial task, peripheral capillary oxygen saturation (SpO2)	Yes; 18% increased average accuracy and increased SpO2
Chung, S., Iwaki, S., Tack, G., Yi, J., You, J., & Kwon, J. (2006).	30%	10 (5 male)	Within-subjects	Verbal cognition	Verbal task, SpO2, heart rate	Yes, 34% average accuracy increase and increase in SpO2
Chung, S., Kwon, J., Lee, H., Tack, G., Lee, B., Yi, J., & Lee, S. (2007).	40%	10 (5 male)	Within-subjects	Working memory	N-back test, heart rate, SpO2	Yes, decreased reaction time, increased accuracy, but not statistically significant
Chung, S., Lee, B., Tack, G., Yi, J., You, J., & Son, S. (2006).	30%	8 (8 male)	Within-subjects	Visuospatial cognition	Visuospatial task, MRI images	Yes, approximately 23% accuracy increase, fMRI activation in the cerebellum, occipital lobe, parietal lobe, and frontal lobe
Chung, S., Lee, H., Choi, M., Tack, G., Lee, B., Yi, J., …, & Lee, B. (2008).	40%	20 (10 male)	Within-subjects		Addition task, SpO2, heart rate	Yes, increased accuracy, increased SpO2, decreased heart rate
Chung, S. & Lim, D. (2008).	30%	20 (10 male)	Within-subjects	memory	Memory task, SpO2, heart rate	Yes, increased accuracy of approximately

						26%, no significant change in reaction time
Chung, S., Sohn, J., Lee, B., Tack, G., Yi, J., You, J., … & Sparacio, R. (2006).	30%	9 (9 male)	Within-subjects	Verbal cognition	Verbal cognitive task, fMRI	Yes, mean accuracy increase of 19%
Chung, S., Tack, G., Choi, M., Lee, M., Lee, S., Choi, J., …, & Park, S. (2009).	43.2%	9 (9 male)	Within-subjects	Visuospatial cognition	Visual matching task	Yes, 15% decreased reaction time, no significant change in accuracy
Chung, S., Tack, G., Kim, I., Lee, S., & Sohn, J. (2004).	30%	8 (8 male)	Within-subjects	Visuospatial cognition	Visuospatial task, fMRI	Yes, increased accuracy, fMRI activation in bilateral occipital, parietal and frontal lobes
Connolly, D.M., & Barbur, J.L. (2009).	14.1%	12 (6 male)	Within-subjects	Visual acuity	City University Contrast Acuity Assessment at photopic and mesopic lighting levels	No, lower visual acuity in 14.1% condition
Moss, M.C., Scholey, A.B., Wesnes, K. (1998).	Not reported. Compared 4 durations of oxygen supplementation to ambient air	20 (14 male)	Within-subjects	Attention, delayed word recall, picture recall, reaction time, number vigilance, long term memory, memory scanning, spatial memory, alertness, calmness, contentedness	Cognitive Drug Research (CDR) computerized assessment system	Yes, attention, vigilance, and some memory functions were positively affected by oxygen administration
Scholey, A., Moss, M., Neave, N., & Wesnes, K. (1999).	Not reported	31 (11 male)	Between-subjects	Memory and attention	Word recall, reaction time task	Yes, increased word recall and improved reaction time
Scholey, A.B., Moss, M.C., Wesnes, K. (1998).	Not reported	20 (14 male)	Between-subjects	memory	Word recall, forward and backward digit span task	Yes, decreased reaction time and increased accuracy on word recall task

Conclusion

1. One hundred percent oxygen supplementation renders varying effects on measures of cognition.

2. In the range of 30-45%, supplemental oxygen significantly increases multiple aspects of cognition and information processing.

References

Andersson, J., Berggren, P., Gronkvist, M., Magnusson, S., & Svensson, E. (2002). Oxygen saturation and cognitive performance. *Psychopharmacology, 162*, 119-128.

This study compared the effects of inhaling 100% versus 21% oxygen on cognitive performance in a sample of 48 participants (26 male). The study used a within-subjects design. Oxygen was delivered to the participants through a mask while they completed five cognitive tasks. The tasks included a letter identification task that assessed perception, the Stroop task that assessed attention, a reading span task that assessed working memory, a word-free recall and an event-based recall task that assessed long-term memory. Prior to and following oxygen administration, participants completed the Mood States Questionnaire. Participants were unaware of which concentration of oxygen they received during each condition. Results showed no statistical differences among cognitive and mood measures. Due to the lack of a significant increase in performance in first experiment, the researchers repeated the study using a between-subjects design. All other variables in this experiment were identical to the first. Forty-eight participants took part in this study (30 male). The results of this second study replicated those of the first experiment; no significant findings emerged.

Choi, M., Lee, S., Yang, J., Choi, J., Kim, H., Kim, H., … & Chung, S. (2010). Activation of the limbic system under 30% oxygen during a visuospatial task: An fMRI study. *Neuroscience Letters, 471*, 70-73.

This study compared the effect of supplementing 30% and 21% oxygen concentrations on a visuospatial task. The study included eight male volunteers using a within-subjects design. The study conducted fMRI scans prior to and following oxygen supplementation. Participants completed the visuospatial task following oxygen supplementation with counterbalanced levels of oxygen concentration. Results showed a significant increase in accuracy from the 21% (M = 50.63, SD = 8.63) to 30% (M = 62.5, SD = 9.64) oxygen supplementation concentration, an approximate 23% performance increase. The fMRI results indicated increases in activations in the thalamus, cingulate gyrus, and cerebral cortex.

Chung, S., Lee, B., Tack, G., Yi, J., Lee, H., Kwon, J., …, & Sohn, J. (2008). Psysiological mechanism underlying the improvement in visuospatial performance due to 30% oxygen inhalation. *Applied Ergonomics, 39*, 166-170.

This study compared the effect of 30% oxygen supplementation to ambient air on a visuospatial task. Twelve volunteers (6 male) participated in this within-subjects study. Participants completed two versions of the visuospatial task, counterbalancing task order and oxygen concentration conditions. Results showed that percent accuracy on the visuospatial task increased significantly from the ambient air condition (M = 55.4) to the 30 % oxygen condition (M = 65.4), an 18% increase in accuracy. No significant differences emerged for response time between the two conditions. The results of this study indicated that 30% oxygen administration was effective in enhancing cognitive performance on this visuospatial task.

Chung, S., Iwaki, S., Tack, G., Yi, J., You, J., & Kwon, J. (2006). Effect of 30% oxygen administration on verbal cognitive performance, blood oxygen saturation and heart rate. *Applied Psychophysiology and Biofeedback, 31*(4), 281-293.

In this within-subjects study, cognitive performance was compared between 30% and 21% oxygen concentrations. Ten participants (5 male) completed both conditions in a counterbalanced order with an hour-long break between each condition. In the 30% oxygen condition, participants wore a mask that dispersed 21% oxygen for 6 minutes, 30% oxygen for 10 minutes, and then 21% oxygen for another 8 minutes. In the ambient air condition, participants were administered only 21% oxygen for the duration. The researchers monitored SpO2 and heart rate continuously and the participants completed a verbal cognition task. Accuracy results showed improved performance during the 30% oxygen condition. The mean accuracy on the task was 38.9 (*SD* = 5.3) for the 21% condition was 52.2 (*SD* = 6.4) for the hyperoxia condition. An improvement of 34%. The results also indicated that the SpO2 was significantly higher during the 30% oxygen condition, and SpO2 positively correlated with accuracy. No significant findings emerged for heart rate.

Chung, S., Kwon, J., Lee, H., Tack, G., Lee, B., Yi, J., & Lee, S. (2007). Effects of high concentration oxygen administration on n-back task performance and physiological signals. *Physiological Measurement, 28*, 389-396.

This study used a within-subjects design to compare performance differences between 40% supplemental oxygen to ambient air on cognitive performance by using an n-back task. Ten participants (5 male) completed all conditions with an hour-long break between conditions. Two levels of n-back task difficulty were included, an n-0 back task and a more difficult n-2 back task. Presentation order was counterbalanced across task difficulty and oxygen concentration. Dependent measures were reported as n-back accuracy and n-back reaction time. SpO2 and heart rate were also reported. The 40% oxygen-supplementation condition significantly enhanced cognitive performance by both increasing n-back accuracy and decreasing reaction time compared to the ambient air condition. Additionally, in the 40% condition the n-2 back had significantly higher SpO2 and heart rate than the n-0 back.

Chung, S., Lee, B., Tack, G., Yi, J., You, J., & Son, S. (2006). The effect of oxygen administration on visuospatial cognitive performance: Time course data analysis of fMRI. *International Journal of Neuroscience, 116*, 177-189.

This study examined the effects of 30% oxygen versus ambient air on visuospatial tasks and blood oxygen level dependent (BOLD) responses using fMRI. The study used eight male participants and a within-subjects design, counterbalanced for the two oxygen levels. Participants were administered oxygen for five minutes prior to the visuospatial task. Following the task the participant took a 30-minute break and during that time the fMRI was conducted. Accuracy significantly increased in the 30% oxygen condition (t = 3.252). Scores increased from a mean of 50.6 (*SD* = 8.6) to 62.5 (*SD* = 9.6), an improvement of 23%. fMRI images revealed significant BOLD responses in the "…cerebellum, occipital lobe, parietal lobe, and frontal lobe" (p. 182). The results of this study indicated that oxygen administration enhanced performance on a visuospatial

cognitive performance task and that supplemental oxygen had an observable impact in the brain.

Chung, S., Lee, H., Choi, M., Tack, G., Lee, B., Yi, J., …, & Lee, B. (2008). A study on the effects of 40% oxygen on addition task performance in three levels of difficulty and physiological signals. *International Journal of Neuroscience, 118*, 905-906.

This study compared the effects of 40% oxygen supplementation to ambient air on an addition task using three difficulty levels. The three levels of difficulty on the addition task consisted of the following: low difficulty using single-digit addition, medium difficulty using double-digit addition, and high difficulty using triple-digit addition. Participants completed addition problems from the order of lowest to highest difficulty. This between-subjects study used 20 volunteers (10 male). SpO2 and heart rate were continuously recorded. Ambient air and 40% oxygen conditions were counterbalanced across subjects and an hour rest period occurred between conditions. For the 40% condition, oxygen was administered for the three minutes prior the start of the task and throughout the time necessary to finish the arithmetic task. Results showed that performance on all task difficulty levels improved in the 40% oxygen condition compared to the ambient air condition. The results also indicated that during the 40% oxygen condition, participants had a higher SpO2 and lower heart rate than in the ambient air condition.

Chung, S. & Lim, D. (2008). Changes in memory performance, heart rate, and blood oxygen saturation due to 30% oxygen administration. *International Journal of Neuroscience, 114*, 593-606.

These authors compared performance on a memory task resulting from 30% oxygen supplementation and ambient air. This study employed a within-subjects design, with 20 participants (10 male), and counterbalanced oxygen conditions and memory task difficulty levels. Each participant completed two sets of a memory tasks five minutes after receiving either 30% oxygen supplementation or ambient air. SpO2 and heart rate were collected continuously throughout the study. Participants took an hour break between oxygen conditions. Results indicated that accuracy and response time improved for all participants in the 30% oxygen condition as compared to ambient air. Although both were in the expected direction, only the measure of accuracy emerged significant ($t = 3.748$), with the 30% condition ($M = 38.5$, $SD = 9.4$) resulting in a 26% improvement in accuracy compared to the ambient air condition ($M = 30.5$, $SD = 6.4$). Also the 30% oxygen condition had higher SpO2 and lower heart rate than did the ambient air condition. Lastly, a correlation between memory task accuracy and the physiological changes were reported, indicating that the administration of 30% oxygen improved cognitive performance in this study.

Chung, S., Sohn, J., Lee, B., Tack, G., Yi, J., You, J., … & Sparacio, R. (2006). The effect of transient increase in oxygen level on brain activation and verbal performance. *Journal of Psychophysiology, 62*, 103-108.

This study compared the effects of 30% oxygen supplementation versus ambient air on a verbal cognitive task. This single-blinded, within-subjects study design included nine

male participants and assessed brain activity using fMRI. Oxygenation conditions were counterbalanced among subjects. The verbal cognitive task used in this study was developed by the research team. For both oxygen conditions, oxygen administration began five minutes prior to the start of the task and continued through task completion. Oxygen administration was discontinued for a 30-minute break between the two conditions during which time the fMRI scans were conducted.

A paired *t*-test showed significantly greater accuracy for the 30% oxygen condition (M = 52.75, SD = 5.55) compared to the ambient air condition (M = 63.07, SD = 12.53), an increase of approximately 19%. The results of this study indicated that the oxygen supplementation was effective in enhancing cognitive performance. The fMRI scans revealed significant activations in the occipital, temporal lobe and frontal lobes, with greater activations occurring during the 30% condition.

Chung, S., Tack, G., Choi, M., Lee, M., Lee, S., Choi, J., …, & Park, S. (2009). Changes in reaction time when using oxygen inhalation during simple visual matching tasks. *Neuroscience Letters, 453*, 175-177.

This study compared the effect of 43.2% oxygen supplementation to ambient air on a visual matching task developed by the research team to assess reaction time and accuracy. Nine male participants completed the within-subjects study and conditions were counterbalanced. Oxygen administration commenced five minutes prior to the start of the task and continued for the duration of the visual matching task. Participants took a 30-minute break between conditions. A *t*-test compared reaction time and accuracy between conditions. Results showed no statistical differenced in accuracy between the two conditions. However, results showed a significant decrease in reaction time in the 43.2% condition (M = 1410.02 ms, SD = 266.16 ms) compared to the ambient air condition (M = 1626.6 ms, SD = 363.94 ms), a 15% decrease in reaction time. The authors of this study suggest that the administration of 43.2% oxygen increased cognition.

Chung, S., Tack, G., Kim, I., Lee, S., & Sohn, J. (2004). The effect of highly concentrated oxygen administration on cerebral activation levels and lateralization in visuospatial tasks. *Integrative Physiological & Behavioral Science, 39*(3), 153-165.

This study compared the effects of 30% oxygen and ambient air on visuospatial task performance. Eight male participants completed this within-subjects, single-blinded study. Conditions were counterbalanced between participants. The visuospatial task was developed by the research team. Subjects received supplemented oxygen five minutes prior to the start of the visuospatial task and continued through task completion. Task completion spanned approximately eight minutes, followed by completion of an fMRI . Paired *t*-tests and repeated measures ANOVAs were conducted. Results showed a significant improvement in accuracy in the 30% oxygen condition compared to ambient air (t = 3.252, df = 7). Further, fMRI results showed significantly greater activations in the "…bilateral occipital, parietal, and frontal lobes" areas (p. 153). The results of this study support that 30% oxygen supplementation significantly increased accuracy on a visuospatial task.

Connolly, D.M., & Barbur, J.L. (2009). Low contrast acuity at photopic and mesopic luminance under mild hypoxia, normoxia, and hypoxia. *Aviation, Space, and Environmental Medicine, 8*(11), 933-940.

Connolly and Barbur (2009) evaluated visual acuity at mesopic and photopic luminances while participants were mildly hypoxic, normoxic and hyperoxic. Unique to this body of literature, this study looked at visual contrast thresholds. The study used 12 healthy participants (6 male) who completed multiple inclusion screening tests including a physical exam, a urinalysis, and a detailed visual and eye health exam. Participants all had a Snellen acuity of 6/6. None of the participants reported using tobacco and refrained from caffeine and alcohol use prior to data collection. This study used a within-subjects design with three separate oxygen administration conditions: mild hypoxia (14.1% oxygen), normoxia (21% oxygen), and hyperoxia (100% oxygen). Oxygen administration was counterbalanced among subjects. Participants first completed the preliminary examinations ensuring they were fit to proceed with testing and then were administered oxygen for 15 minutes. During oxygen administration, participants sat with their eyes closed to adapt to the dark. Next, participants completed the City University Contrast Acuity Assessment (CAA) binocularly to measure contrast sensitivity thresholds using Landolt C's. Following this, the participants' pupil sizes were measured. Participants completed these tasks while undergoing the three differing levels of oxygen and in two separate lighting environments, photopic and mesopic.

Results indicated that when individuals were hypoxic (14.1% condition), they were less able to distinguish contrast in the mesopic condition. By contrast, when individuals were hyperoxic (100% oxygen condition) their threshold for identifying low contrast markers increased. Furthermore, the results of this study indicated that visual acuity was negatively impacted by hypoxia and the use of supplemental oxygen increased visual acuity by improving contrast acuity in mesopic lighting environments.

Moss, M.C., Scholey, A.B. (1996). Oxygen administration enhances memory formation in healthy young adults. *Psychopharmacology, 124*, 255-260.

This study encompassed a series of three experiments and evaluated the effect of administering 100% oxygen on measures of memory and mood. The overarching study used a between-subject design. In the first experiment, 45 participants were split into three groups, one group received oxygen before completing a memory test (while learning the material), one group received oxygen after learning and prior to completing a memory test, and one group served as a control and received no oxygen supplementation. Participants also completed the Profile of Mood States. The results of this study indicated that the group that received oxygen while learning the material and prior to taking the memory test had a significantly higher accuracy score than other two groups.

In the second experiment, three groups of 12 were assigned to one of three groups: a group that received oxygen while learning the memory test material, a group that received oxygen after learning the material or a control group that received no oxygen supplementation. All groups returned to the laboratory 24 hours after the learning session to complete the memory test and mood questionnaire. Results showed that, similar to the

first experiment, the group that received oxygen while learning the material scored significantly higher than the other two groups.

The third experiment looked at whether subjects in the oxygen administration group performed better because they expected enhanced performance due to the oxygen received. In this experiment, 24 subjects were split into two groups learned material while in their respective oxygenation condition. One group received 100% oxygen and the other received compressed air. Following the learning session, participants returned 24 hours later to complete the test and the mood questionnaire. The results demonstrated that the individuals in the oxygen group performed significantly better than those in the compressed air group. Regarding the mood questionnaire, no significant differences existed among the groups in any of the three experiments. These results show that oxygen supplementation enhanced performance on a memory task, but this treatment had no effect on mood.

Moss, M.C., Scholey, A.B., Wesnes, K. (1998). Oxygen administration selectively enhances cognitive performance in healthy young adults: A placebo-controlled double blind crossover study. *Psychopharmacology, 138*, 27-33.

This study examined the use of oxygen supplementation compared to ambient air on a number of cognitive tasks. The study's authors did not specify the concentration of oxygen supplementation, but stated that the study used double blinding. The experiment used several methods of timing between oxygen inhalation and task performance as the study took place over a course of seven weeks. Twenty volunteers participated in the study (14 male, M_{age} = 24.5). The study used the Cognitive Drug Research task battery, which tests several functions of cognitive ability.

Results of this study indicated that the supplementation of oxygen significantly influenced attention, delayed word recall, and picture recognition reaction time. Variables that approached, but were not significant, included simple reaction time, choice reaction time, number vigilance and long-term memory. Measures that reflected no significant improvement from oxygen supplementation included word recognition, memory scanning, spatial memory, alertness, calmness, and contentedness. The authors concluded that oxygen administration is more effective in bursts rather than when administered continuously. Overall, oxygen supplementation benefitted attention, vigilance, and some memory functions.

Scholey, A., Moss, M., Neave, N., & Wesnes, K. (1999). Cognitive performance, hyperoxia, and heart rate following oxygen administration in healthy young adults. *Physiology & Behavior, 67*(5), 783-789.

This study examined the use of oxygen supplementation on cognitive tasks that examined memory and reaction time. Thirty-two participants (11 male) were split into either an oxygen supplementation condition or an ambient air condition in this between-subjects double-blind study. The authors of this study did not indicate the concentration of oxygen used. Participants received oxygen or ambient air through a facemask for approximately three minutes prior to completing a word recall and reaction time task. Tasks were administered through the Cognitive Drug Research Ltd. battery of cognitive assessments

program on a computer. SpO2 and heart rate were continuously collected throughout data collection. Participants were also asked to determine which condition they believed they were assigned to following data collection.

Compared to baseline performance, results indicated that those in the hyperoxia condition had faster reaction times and increased accuracy on the memory task than individuals in the ambient air condition. Individuals in the hyperoxia condition also exhibited significantly higher SpO2 than those in the ambient air condition. Further, in both conditions, a significant interaction existed between increased heart rate and improvement reaction time. The results of this study support the notion that hyperoxia enhances cognitive performance.

Scholey, A.B., Moss, M.C., Wesnes, K. (1998). Oxygen and cognitive performance: The temporal relationship between hyperoxia and enhanced memory. *Psychopharmacology, 140*, 123-126.

This study assessed cognitive and physiological effects of oxygen administration on healthy young adults. In the double-blinded experiment, 20 subjects (14 male) were assigned to either receive pure oxygen or ambient air. Six phases of the experiment included the following: baseline, gas inhalation, word presentation, reaction time, distractor task, and word recall accuracy. During these phases, SpO2 and heart rate were monitored. Results confirmed that oxygen supplementation significantly enhanced cognitive performance compared to the ambient air group. Participants who were received supplemental oxygen recalled more words, had faster reaction times, and exhibited significant hyperoxia during gas administration, word presentation, and the reaction-time task. Both groups showed increased heart rate during supplementation administration. In the oxygen group, the greatest improvements in performance were recorded in participants with higher SpO2. In the control group, greater cognitive improvement was associated with increased heart rate.

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