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Citation: Scholey, Andrew B., Benson, Sarah, Sela-Venter, Shirley, Mackus, Marlou and Moss, Mark (2020) Oxygen Administration and Acute Human Cognitive Enhancement: Higher Cognitive Demand Leads to a More Rapid Decay of Transient Hyperoxia. Journal of Cognitive Enhancement, 4 (4). pp. 94-99. ISSN 2509-3290

Published by: Springer

URL: https://doi.org/10.1007/s41465-019-00145-4 <https://doi.org/10.1007/s41465-019-00145-4>

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Journal of Cognitive Enhancement (2020) 4:94–99
https://doi.org/10.1007/s41465-019-00145-4

BRIEF REPORT

Oxygen Administration and Acute Human Cognitive Enhancement: Higher Cognitive Demand Leads to a More Rapid Decay of Transient Hyperoxia

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Received: 14 February 2019 / Accepted: 15 July 2019 / Published online: 29 July 2019

Abstract
Both supplemental glucose and oxygen administration can improve aspects of cognitive performance. Previous research has established that more effortful cognitive processing results in reductions in peripheral blood glucose. We hypothesized that a similar phenomenon may be evident when measuring blood oxygen levels. This double-blind, placebo (air)-controlled, crossover study examined the effects of 100% oxygen administration and mental effort on heart rate and blood oxygen saturation. In counterbalanced order, twenty participants performed tasks where cognitive demand was relatively high (Serial Sevens) and relatively low (counting upwards) under conditions of normoxia and hyperoxia. Oxygen saturation and heart rates were co-monitored using a pulse oximeter. Oxygen administration was associated with significantly fewer errors during Serial Sevens and the generation of more responses during counting. Both hyperoxia and heart rate were differentially affected by gas and task. Following oxygen inspiration, transient hyperoxia decayed significantly more rapidly during Serial Sevens than during the counting task. In the air condition, blood oxygen levels were raised during Serial Sevens compared with counting. The opposite effects were observed for heart rate. These results suggest that, following oxygen inspiration, a high cognitive load results in measurable uptake of circulating oxygen. This is likely to involve somatic and central processes.

Keywords Oxygen · Cognitive demand · Hyperoxia · Heart rate

Introduction

Previous work has demonstrated that oxygen administration can improve performance on a number of cognitive measures in healthy adults (Choi et al. 2010; Chung et al. 2006, 2007, 2008a, b; Chung and Lim 2008; Chung et al. 2004a, b; Moss and Scholey 1996; Moss et al. 1998; Scholey et al. 1998, 1999; Sohn et al. 2005). Such improvement occurred only when concurrently measured hyperoxia coincided with encoding of target material in memory tasks, or with performance of a reaction time task (Scholey et al. 1998, 1999). These results support the idea that increased circulating oxygen is available to, and utilized by, metabolically active tissue including the neural substrates which underlie cognitive processing. This contention is supported by functional magnetic resonance (fMRI) studies showing cognitive enhancement and greater activation in brain loci associated with task performance under hyperoxic compared with normoxic conditions (Choi et al. 2010; Chung et al. 2004a, b, 2006; Yu et al. 2015; Kot et al. 2015).

Like oxygen, glucose administration is capable of enhancing cognitive performance (Smith et al. 2011). Of particular relevance to this study is the finding that, following ingestion of a glucose load and a subsequent peak in glucose levels, more rapidly falling blood glucose levels are associated with improved cognitive scores (Benton and Parker 1998; Parker and Benton 1995). Moreover, higher levels of cognitive demand have been shown to result in more rapid decay of blood glucose both during both hyperglycaemic (Scholey et al. 2001) and euglycemic (Fairclough and Houston 2004; Scholey et al. 2001; Scholey et al. 2006) conditions.

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If glucose and oxygen enhance cognitive performance via increasing the availability of metabolic substrates (Owen and Sunram-Lea 2011; Scholey 2001), one might predict that a similar relationship should exist between oxygen levels and task performance. Such a proposition is readily testable since brief inhalation of oxygen leads rapidly to measurable hyperoxia (as indexed by oxygenated haemoglobin using oximetry) which decays to baseline levels over the subsequent minutes.

One, relatively straightforward, way of manipulating mental effort is to present mathematical tasks with varying difficulty. Serial Subtractions tasks (e.g. Serial Sevens) involve repeated subtraction of a given number from a starting number within a prescribed time period. Unsurprisingly, Serial Sevens was rated as significantly more subjectively demanding than simply counting upwards in ones (Kennedy and Scholey 2000). In that study, participants were constrained to match the number of counting responses to the number generated during preceding Serial Subtractions tasks (specifically they counted in time to a metronome which ensured the same number of responses). Without this constraint, participants inevitably generate more responses during counting than Serial Subtractions (itself an indication of the relative demands of the tasks). Thus, while counting upwards in ones is not particularly cognitively demanding, it involves a greater amount of articulation and so may have a greater somatic component than Serial Sevens.

It is also documented that cognitive processing is associated with an increase in autonomic activity, including raised heart rate—a response which may serve to increase the delivery of oxygen and glucose to the brain during periods of mental demand. For example, a mental arithmetic task raised heart rates above those predicted on the basis of oxygen consumption alone (Turner and Carroll 1985).

The aim of the present study was to compare the effects of oxygen inspiration on the profiles of hyperoxia and heart rate during a task with relatively high cognitive demands (Serial Sevens) compared with a task having relatively high somatic demands (counting upwards in ones). To this end, arterial haemoglobin oxygen saturation and heart rate were monitored during Serial Sevens (cognitively more demanding) and counting upwards (somatically more demanding) tasks, following inhalation of oxygen or air.

Based on the above, we hypothesized that oxygen administration would differentially improve Serial Sevens over counting and that Serial Sevens would be associated with a greater decrease in blood oxygen levels following hyperoxia. Based on previous research on supplemental glucose administration, we predicted that in the air administration condition compared with counting, Serial Sevens would be associated with a greater reduction in blood oxygen levels and an increase in heart rate.

Materials and Methods

Participants

Twenty undergraduates (13 males, 7 females; mean age 21.6 years, range 18–30) from the University of Northumbria volunteered to participate in this study.

Physiological Measures

Arterial haemoglobin oxygen saturation (%) and heart rate (beats per minute) data were sampled at 15-s intervals using a N100-P hand-held pulse oximeter (Nellcor Puritan Bennet, Coventry, UK) according to the manufacturer's instructions.

Gas Administration

Gas delivery was achieved using the assembly described in previous studies (Moss et al. 1998; Scholey et al. 1998), which was arranged so that neither experimenter nor subject were aware of whether oxygen or air was being administered. Cylinders containing medical quality compressed air and 100% oxygen respectively were purchased from British Oxygen Company, Guilford, UK. Attached to each cylinder was a bull nose regulator and an air flow metre which were set to deliver each gas at a rate of 8 l per min. Each subject self-administered one of the gases (depending on their experimental condition) for 30 s via a hand-held face mask.

Cognitive Tasks

One of the two tasks employed was Serial Sevens. Participants were instructed to count backwards out loud in sevens, as accurately and quickly as possible, from a randomly generated starting number between 900 and 1000. The other task comprised of counting upwards—participants were required to count upwards in ones from a randomly generated start number between 600 and 800. In the instance of an error in either task, subsequent responses were scored as positive if they were correct in relation to that new number. Performance on each task was recorded and scored later both for accuracy (number of errors) and speed (number of responses generated).

Procedure

A randomized, placebo-controlled, double-blind, cross-over design was employed. Participants were tested individually on two occasions at the same time of day within the same week. They were asked to refrain from smoking and drinking caffeinated drinks for 2 h prior to presenting themselves for testing. Upon entering the laboratory, participants were assigned to one of the two coded conditions corresponding to oxygen or air administration. They were then familiarized with the nature of the tasks, the gas delivery mask and the pulse oximeter. Data collection began with a 4-min baseline recording with the participant sitting quietly. This was followed by 30-s gas (oxygen or air) administration followed by either Serial Sevens or the counting task, lasting 4 min. Participants then rested for 1 min, inspired the other gas for 30 s and underwent the opposite (4 min) task. The order of both gas and task presentation was completely counterbalanced across participants.

Results

Cognitive and physiological results are presented in Fig. 1 and key findings are summarized below. Cohen's *d* effect sizes of 0.2, 0.5 and 0.8 are operationally defined as 'small', 'medium' and 'large', respectively (Cohen 1992).

Cognitive Measures

During the Serial Sevens task, participants produced significantly fewer errors following oxygen breathing oxygen compared with air inspiration, $t(19) = 2.272$; $p < 0.05$, $d = 0.58$ (see Fig. 1a). Numerically, more Serial Sevens responses were generated in the oxygen condition than in the air condition

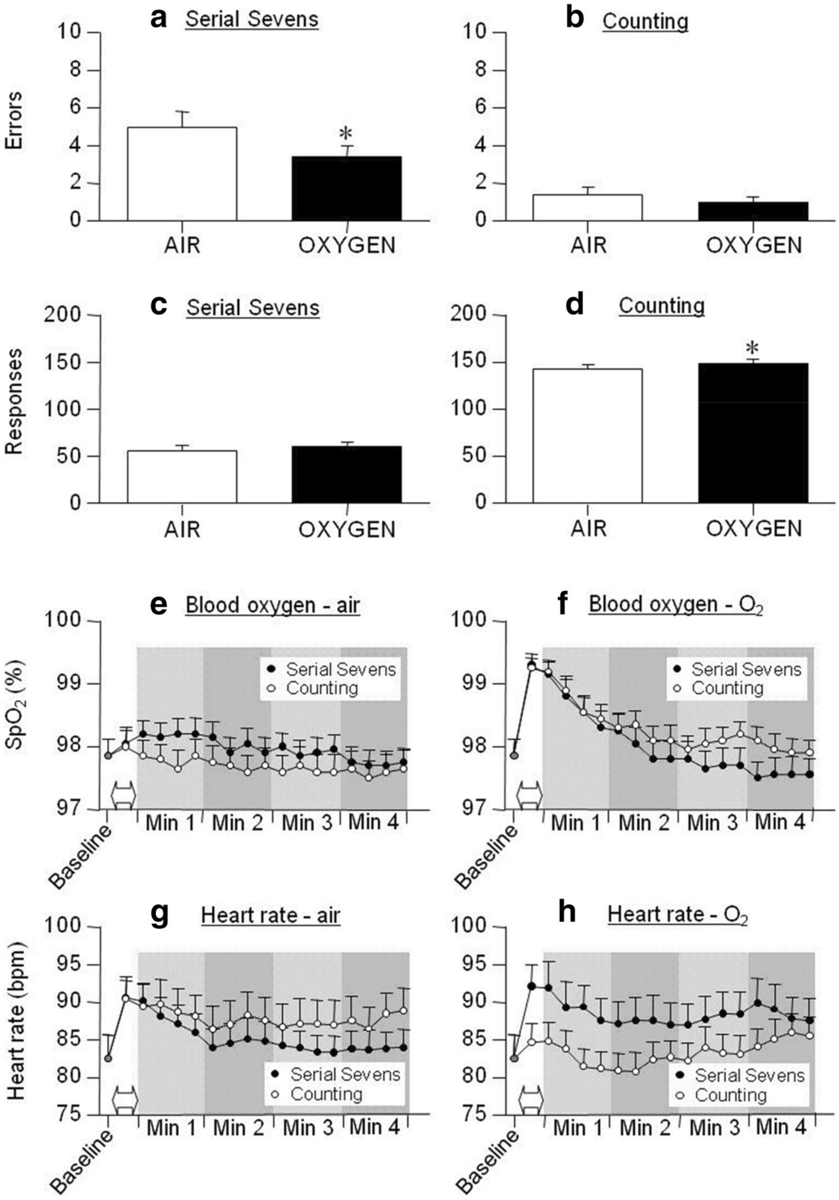

Fig. 1 **a**, **b**, **c**, **d** Effect of oxygen administration on task performance. **e**, **f**, **g**, **h** Physiological measures during the 4-min baseline, 30-s gas administration (⇔) and 4 min of the task (indicated by panels) in the air and oxygen (O_2) conditions. All figures present means; error bars depict standard errors. During Serial Sevens, participants made significantly (**a**) and numerically (**b**) fewer errors while in the oxygen condition; whereas during the counting task, numerically (**c**) and significantly (**d**), more responses were generated following oxygen inspiration ($*p < 0.05$ compared with air condition). Following air inspiration, blood oxygen saturation levels (SpO_2) were higher during Serial Sevens than counting (**e**), whereas heart rate (bpm) was increased more by counting than Serial Sevens (**g**). Conversely, following oxygen inspiration, blood oxygen decayed more rapidly (**f**) and heart rate increased more during Serial Sevens than counting (**h**)

(see Fig. 1c) although this was not statistically significant, $t(19) = 1.512$; $p = 0.146$, $d = 0.24$.

For the counting task, an opposite pattern emerged. No significant differences were found for the number of errors made; although when in the oxygen condition, participants did produce numerically fewer errors than when in the air breathing condition, $t(19) = 1.483$; $p = 0.154$, $d = 0.28$ (see Fig. 1b), and participants generated significantly more responses in the oxygen breathing condition than in the air breathing condition, $t(19) = 2.252$; $p < 0.05$, $d = 0.43$ (see Fig. 1d).

Physiological Responses

The effects of both task and gas administered on blood oxygen saturation and heart rate are presented in Fig. 1e–h. Statistical comparisons were performed on the changes in both heart rate and blood oxygen saturation for each task in each gas condition. These were calculated by subtracting the mean value across 4 min of the baseline measurement from the mean value during 4 min of the task. The resulting measures were subjected to 2 (Gas; oxygen, air) × 2 (Task; Serial Sevens, counting) analyses of variance (ANOVA).

Blood oxygen saturation for both tasks, following air and oxygen inspiration respectively, are presented in Fig. 1e, f. With regard to blood oxygen levels, a significant Gas × Task interaction effect was evident, $F(1,15) = 42.85$; $p < 0.001$, demonstrating that the changes in oxygen saturation following inspiration of each gas were differentially affected by the tasks. Over 4 min of task performance following air inspiration, oxygen saturation levels increased during Serial Sevens and decreased during the counting task (mean changes in percent saturation = 0.07 ± SD 0.18 and − 0.22 ± 0.10, respectively; $d = 2.55$). Following oxygen administration, the change during Serial Sevens was less than during the counting task (mean changes = 0.09 ± 0.50 and 0.36 ± 0.37, respectively; $d = 2.19$). It is evident from Fig. 1f that this latter effect is due to a more rapid decay of hyperoxia during Serial Sevens. There were no main effects of Gas nor of Task on changes in blood oxygen saturation.

Heart rates for both tasks, following air and oxygen inspiration respectively, are presented in Fig. 1g, h. With respect to heart rate changes, there was a significant Gas × Task interaction $F(1,15) = 139.29$; $p < 0.0001$. Following air inspiration, the change in heart rate was higher during the counting task than during Serial Sevens (mean bpm changes = 5.32 ± 1.05 and 2.50 ± 1.94, respectively; $d = 2.72$). Conversely, in the oxygen condition, the change in heart rate during Serial Sevens was higher than during the counting task (mean changes = 5.86 ± 1.31 and 0.73 ± 1.67, respectively; $d = 3.09$). Additionally, there was a significant main effect of task, $F(1,15) = 17.3$, $p < 0.001$, with the Serial Sevens task eliciting higher heart rate changes than the counting task (mean changes = 4.17 ± 9.44 and 1.99 ± 7.60, respectively; $d = 0.18$).

Discussion

Our hypotheses were partially supported. These results confirm that oxygen inspiration enhances cognitive performance (Chung et al. 2007, 2008a; Chung and Lim 2008; Chung et al. 2004a; Moss and Scholey 1996; Moss et al. 1998; Scholey et al. 1998, 1999; Sohn et al. 2005; Choi et al. 2010; Chung et al. 2004b, 2006, 2008b). Participants made significantly fewer errors during Serial Sevens when in the oxygen condition than when in the air condition; the effect was relatively robust with a medium effect size. They also generated a (non-significantly) greater number responses during the task precluding the possibility that superior performance was the result of a ‘speed accuracy trade-off’.

Serial Sevens relies heavily on working memory and central executive function. In earlier studies, computerized tests of working memory, including both forward and backward digit span appeared to be selectively resistant to oxygen-induced cognitive enhancement, although methodological issues may account for these findings (see Moss et al. 1998; Scholey et al. 1998). We have previously speculated that tasks requiring a higher amount of ‘mental effort’ may be more amenable to the cognition-enhancing effects of oxygen administration. Serial Sevens may be associated with a higher cognitive load than the above measures of working memory and, as such, may be more susceptible to hyperoxic enhancement. Additionally, the task has a higher executive function load—requiring allocation of cognitive resources to ongoing demands. This itself may engender more cognitive resources and needs to be addressed in future studies.

Somewhat contradicting this notion, and counter to our hypotheses, is the finding that the simple counting task was also enhanced in the oxygen condition, in this case reflected by a significantly greater number of responses (again with a medium effect size). Counting upwards in ones can hardly be described as a cognitively demanding task; it seems possible that, in the absence of a cognitive load, increased circulating oxygen may be available to the musculature serving articulation—thus facilitating simple response generation. Certainly, with respect to a physical exercise regime, induced hyperoxia has been shown to increase individuals’ time to exhaustion by some 40% (Plet et al. 1992). Clearly the counting task used here is not equivalent to exercise and the extent to which performance on such tasks are enhanced by supplemental oxygen requires further investigation.

Examination of the relationships between blood oxygen saturation, heart rate and task revealed some interesting interactions, albeit with small or small-to-medium effect sizes. Following oxygen inspiration, participants’ blood oxygen decayed more during Serial Sevens than the counting task (see Fig. 1f). It is possible that this is partly due to increased uptake of oxygen by the neural substrates underlying cognitive processing. This suggests that, during hyperoxia, such processing is associated with a greater amount of energy expenditure than the somatic demands of response generation in the counting task—a suggestion which is supported to some degree by the increased heart rate associated with Serial Sevens in relation to the counting task. Nevertheless, the fact that Serial Sevens was also associated with a relatively higher heart rate during hyperoxia—a finding which is consistent with those reported elsewhere for other cognitive tasks (Scholey et al. 1999)—begs the question as to the extent to which cardiac activity is responsible for the increased uptake of oxygen. Additionally, accelerated heart rate may itself contribute to cognitive enhancement (Nielson et al. 1996); it is clearly important to determine the extent to which such effects impinge on the results of studies such as this. It seems clear that such changes cannot account for the oxygen-related improvement in the counting task. During this task, heart rates were consistently higher following air inspiration than following oxygen (compare Fig. 1g and h); although under hyperoxia, participants generated significantly more responses.

The differential effect of tasks on heart rate and blood oxygen levels between the air-breathing and oxygen-breathing groups appears to reflect very different physiological responses during normoxia and hyperoxia. Specifically, in the air-breathing condition, heart rates rose more during the counting task than during Serial Sevens. Moreover, in both gas conditions, during the counting task, more responses were generated (compare Fig. 1c and d) and fewer errors were made (compare Fig. 1a and b) than during Serial Sevens, thus supporting our supposition that counting is associated with a relatively higher somatic demand. It seems reasonable to suppose that the increased heart rate and lower oxygen levels during the counting task under normoxic conditions reflect an uptake of oxygen by the somatic component of this task. Intriguingly, during hyperoxia, such responses appear to be differentially targeted at cognitive components (in this case, Serial Sevens). The mechanisms underlying such different responses remain unknown at present but may reflect a positive feedback mechanism whereby hyperoxia and increased heart rate exert a mutually agonistic influence during cognitive processing. In a somewhat related study, examining the interactions between glucose, heart rate and cognitive demand, it was found that when the somatic demands of a counting task are matched with those of serial subtraction tasks, heart rate changes in the former are minimal (Scholey et al. 2001). It would clearly be of interest to examine the effects of oxygen administration on hyperoxia and heart rate comparing a task such as Serial Sevens with somatically matched, non-demanding control tasks.

In this context, the magnitude of cognitive enhancement from oxygen ($d = 0.58$) is similar to that seen following glucose administration ($d = 0.56$, Riby 2004), with those effects being more evident during conditions of cognitive demand (Macpherson et al. 2015; Scholey et al. 2009).

Finally, it should be mentioned that the increased uptake of oxygen during cognitive demand is consistent with brain imaging studies of focal neural activity, which rely on differential utilization of labelled oxygen, and which suggest that there is a substantial increase in oxygen utilization by active neural tissue (e.g. Malonek and Grinvald 1996). It would be of great interest to apply more recently developed methodologies to this problem (Catchlove et al. 2018). In particular, the extent to which increased neural activity observed in such studies correlates with the decay in blood oxygen, measured using the techniques described here, requires further investigation.

Compliance with Ethical Standards

All participants signed informed consent forms as approved by the Northumbria University Psychology Divisional Ethics Board.

Conflict of Interest The authors declare that they have no conflict of interest.

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