Psychopharmacology (1998) 140 : 123–126

RAPID COMMUNICATION

Andrew B. Scholey · Mark C. Moss · Keith Wesnes

Oxygen and cognitive performance: the temporal relationship between hyperoxia and enhanced memory

Received: 8 July 1998/Final version: 10 July 1998

Abstract Oxygen administration coinciding with word presentation enhances word recall in humans, suggesting that elevated levels of circulating blood oxygen may be available to neural memory consolidation processes. This double-blind experiment examined the relationship between blood oxygen levels and cognitive performance when oxygen was inspired for 2 min at different times relative to a simple word recall task, forward digit span and backward digit span. Transient hyperoxia, measured by haemoglobin-bound oxygen, was evident following oxygen inspiration. Neither forward nor backward digit span was affected by oxygen administration. Word recall (12 min following word presentation) was enhanced when oxygen was administered 5 min prior to, immediately before or immediately following word presentation; but not 10 min prior to, 5 min following nor 10 min following, word presentation. These data suggest that oxygen administration can selectively enhance aspects of cognitive performance and support a hypothesis whereby supplemental blood oxygen is sequestered by neural mechanisms involved in memory consolidation.

Key words Oxygen · Memory · Digit-span · Hyperoxia

Introduction

Previous work in our laboratory has demonstrated that transient oxygen inspiration can improve performance on tests of long-term memory and attention, but not of working memory, in healthy young adults (Moss and Scholey 1996; Moss et al. 1998; Scholey et al. 1997). More words were recalled when oxygen was administered immediately prior to presentation of a word list, but not immediately before recall 10 min later (Moss and Scholey 1996). Similarly, oxygen was administered immediately prior to encoding of material in a study where subjects performed better on tasks of everyday memory (a cued shopping list and name-to-face matching). This effect developed following repeated tests of recall and was not apparent at immediate recall, again suggesting that working memory may be unaffected by hyperoxia (Winder and Borrill 1998). However, it is possible that the tasks used to assess working memory were not sensitive enough to measure hyperoxia associated improvement (Moss et al. 1998).

When blood haemoglobin oxygen saturation was measured in subjects who demonstrated oxygen-induced enhancement of verbal memory and simple reaction time (SRT), significant hyperoxia coincided with word presentation and SRT (Scholey et al. 1997). This finding supports our hypothesis that oxygen is sequestered by task-sensitive neural substrates during congnitively demanding aspects of the task, for example memory encoding. However, to date, no study has examined the effects of oxygen administration on both cognitive performance and blood oxygen levels when the gas is inspired at different times relative to a cognitive task.

We postulated that significant cognitive enhancement should occur only when oxygen-induced hyperoxia occurred immediately before, during or immediately following presentation of target material. Additionally, we were interested in whether transient hyperoxia could improve performance on forward digit span and backward digit span, tests of working memory where ceiling effects are avoided through the progressive, within-session increase of task difficulty. To this end, blood oxygen saturation was monitored

A.B. Scholey (✉) · M.C. Moss
Human Cognitive Neuroscience Unit,
Division of Psychology, University of Northumbria,
Newcastle upon Tyne NE1 8ST, UK
e-mail: a.scholey@unn.ac.uk, Fax: +44-191-227-3471

K. Wesnes
Cognitive Drug Research Ltd, CDR House, Portman Road,
Reading RG30 1EA, UK

during transient oxygen administration to participants with various time intervals between gas inspiration and cognitive tasks.

Materials and methods

Participants

Fourteen males and six females (mean age 21 years) were each paid £20 for participating in the study. Before the onset of the experiment, each gave written consent as approved by the Ethics Committee of the Division of Psychology at the University of Northumbria.

Materials

Medical quality air (placebo control) and oxygen were provided by British Oxygen Company (Guildford, Surrey, UK). These were administrated via a face mask at 8 l/min using double-blind methodology according to previously published procedures (Moss et al. 1998; Scholey et al., unpublished data). Arterial haemoglobin oxygen saturation (%) was sampled automatically at 30 s intervals using a finger cuff attached to a N100-P hand held pulse oximeter (Nellcor Puritan Bennet, Coventry, UK) according to the manufacturer's instructions.

Cognitive measures

Word recall was measured as follows. Fifteen words, matched for concreteness and frequency (Paivio 1968), were recorded at a rate of one word every 2 s onto a tape recorder in seven different, randomised orders. A 15 s period was allowed at the beginning of the word presentation phase to introduce the participant to the task, after which one of the lists was presented. A further 15 s was allowed following word presentation to replace the mask. Thirteen minutes following the onset of the word presentation phase, participants were allowed 2 min to write down as many words as possible. Items were scored for number correct and number of intrusions.

Three minutes was allowed for forward digit span, which was assessed as follows. Participants immediately repeated strings of randomly generated digits presented orally ar a rate of one item per second. Starting from single digits, the string length increased by one digit at each presentation. Digit span was taken to be the length of the string prior to the one in which a participant made their first error (transposition, omission or incorrect reporting of digits). Backward digit span was measured using a similar procedure except that participants were required to repeat the strings in reverse order to presentation.

Design

The study followed a pseudo-random, double-blind crossover procedure where every participant underwent a different one of seven inspiration regimes, and was presented with a different-order word list at each visit. The experimental conditions were as follows: air throughout the experiment (control); oxygen inspiration between 0 min and +2 min (starting 10 min prior to word presentation); oxygen between +5 min and +7 min (5 min prior to word presentation); oxygen between +10 min and +12 min (immediately prior to word presentation); oxygen between +12 min and +13 min (immediately following the end of word presentation and immediately prior to forward digit span); oxygen between +18 min and +20 min (immediately after forward digit span and immediately preceding backward digit span); oxygen between +23 min and +25 min (immediately following backward digit span and immediately prior to word recall). Air was delivered at all other times except during the periods allowed for cognitive tasks, when no gas was delivered in any condition.

Procedure

The order in which the participants underwent each gas inspiration condition was determined pseudo-randomly using a Latin Squares design. Each participant visited the laboratory on seven different occasions. On arrival the participant was allocated to the appropriate gas inspiration regime and randomly assigned to one of the word list conditions. Word presentation occurred between 12 and 13 min following the start of the experimental visit, forward digit span took place between 15 and 18 min, backward digit span between 20 and 23 min and word recall between 25 and 27 min. At the end of the seventh visit, the participant was thanked and debriefed.

Results

Cognitive measures were analysed by one-way analyses of variance. There was no effect of oxygen administration on forward digit span ($F6,114 = 1.15$, $P = 0.335$) or backward digit span ($F6,114 = 0.91$, $P = 0.491$). The results of oxygen administration on blood oxygen levels and word recall are presented in Fig. 1. Compared to the air inspiration control condition, there was a significant effect of oxygen administration on word recall ($F6,114 = 9.93$, $P < 0.001$). Sheffe post-hoc analyses of means revealed that significantly more word were recalled when oxygen was inspired 5–3 min prior to word presentation, 2–0 min prior to word presentation, and 0–2 min following word presentation when compared to all other conditions ($P < 0.01$ in all cases). The profile of oxygen haemoglobin saturation clearly shows that hyperoxia is evident immediately prior to, during, or immediately following word presentation only in the conditions where word recall was enhanced.

Discussion

These results confirm that transient oxygen administration to healthy young adults significantly enhances memory formation (Moss and Scholey 1996; Moss et al. 1998; Scholey et al. 1997; Winder and Borrill 1998). We have further demonstrated that this effect occurs specifically when hyperoxia occurs immediately prior to, during, or immediately following word presentation.

It is clear that availability of increased circulating oxygen may be available to the brain when hyperoxia occurs during or in the immediate aftermath of word presentation (when administrated at −2 min and at

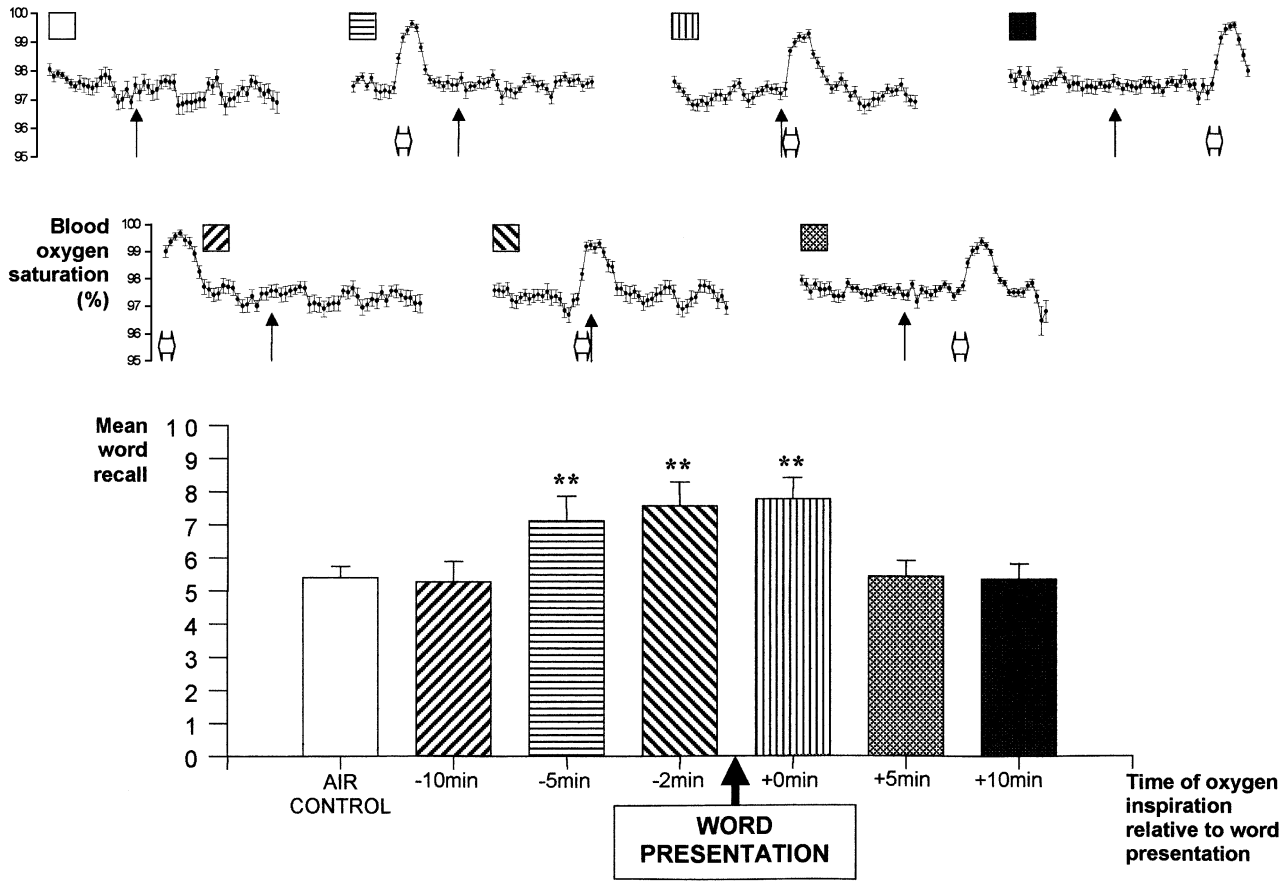

Fig. 1 Effects of different timings of transient oxygen inspiration on blood oxygen levels and word recall. *Top figures* show the effect of 2 min oxygen administration (⇔) on blood haemoglobin saturation (mean HbO_2 ± SE) at different times relative to the presentation of a word list (↑). The *bottom histogram* illustrates the effect on word recall (mean number of words ± SE) of each inspiration regime (**, $P < 0.01$ compared to air control, and oxygen delivered −10 min, +5 min or +10 min relative to word presentation). *Patterned panels* in the top figure refer to the corresponding bars in the bottom histograms

+10 min). However, it is interesting to note that the haemoglobin-bound oxygen has decayed to basal levels when oxygen is administrated between −5 and −3 min before word presentation (Fig. 1). These data do not conflict with previous behavioural findings (Moss et al. 1998), although the reasons remain unclear. It is possible that increased oxygen is still available to the brain, which accounts for some 30% of basal oxygen metabolism (Roland 1993), at levels beyond the sensitivity of the measures used here. Alternatively, the effect may be due to an increase in a dissolved oxygen fraction which would be available to the brain's perfusate but, again, would not be measurable using the methods employed here. Finally, it is possible that oxygen administration is involved in some kind of "priming" of neural substrates involved in the establishment of a memory trace, a phenomenon which would, presumably, have decayed in the condition where oxygen is presented 10 min prior to word presentation.

No effect was found on performance on forward or backward digit span. The reason for this is unclear although the neuropsychology and psychopharmacology of digit span performance is less than straightforward. Digit span has been shown to be selectively preserved following frontal and hippocampal lesions in humans (Cave and Squire 1992; Hermann et al. 1994; Petrides 1995; Richer et al. 1996), in elderly non-insulin-dependent diabetics (Aitiea et al. 1995; Helkana et al. 1995), and has shown no or marginal deterioration in Korsakoff's syndrome (Wiegersma et al. 1991; Cave and Squire 1992).

Reports of the effects of acute pharmacological challenge on digit span are also unclear. Span was significantly reduced as part of a global cognitive impairment by 6.13 mg midazolam or 6.4 mg diazepam (Hennessey et al. 1991), but was selectively preserved following 2 mg lorazepam (Kirkby et al. 1995). Additionally, the sensitivity of digit span to alcohol has been questioned (Koelega 1995). Acute nicotine exposure improved other aspects of cognition, but not digit span, in Alzheimer's patients and young and elderly controls (Jones et al. 1992). Alzheimer's patients showed a selective resistance to digit span improvement

by L-deprenyl and physostigmine treatment (Sevush et al. 1991; Marin et al. 1995). Similarly, chronic estrogen treatment to menopausal women did not improve digit span although performance on other tasks was enhanced (Phillips and Sherwin 1992). On the other hand, it is relevant to the present study that chronic exposure to carbon monoxide impaired digit span exposure while increasing levels of carboxyhaemoglobin (Amitai et al. 1998), and an exercise regime improved span in older women (Hassmen et al. 1992). Such results suggest that digit span performance may be susceptible to change following chronic intervention or as part of a global cognitive change, but is relatively resistant to acute pharmacological manipulation where aspects of cognition are differentially affected. However, we cannot rule out the possibility that digit span (and indeed other aspects of working memory) may be sensitive to appropriate durations of oxygen not thus far examined (Moss et al. 1998).

Our laboratory is currently further investigating these issues and others relating to oxygen inspiration, oxygen utilisation and aspects of cognitive performance.

References

Aitiea JA, Moses JL, Sinclair AJ (1995) Neuropsychological function in older subjects with non-insulin-dependent diabetes-mellitius. Diabet Med 12:679–685

Amitai Y, Zlotogorski Z, Golankatzav V, Wexler A (1998) Neuropsychological impairment from acute low level exposure to carbon monoxide. Arch Neurol 55:845–848

Cave CB, Squire LR (1992) Intact verbal and nonverbal short-term memory following damage to the human hippocampus. Hippocampus 2:151–164

Hassmen P, Ceci R, Backman L (1992) Exercise for older women – a training method and its influences on physical and cognitive performance. Eur J Appl Physiol Occup Physiol 64:460–466

Helkala EL, Niskanen L, Viinamaki H, Partamen J, Uusitupa M (1995) Short-term and long-term memory in elderly patients with NIDDM. Diabetes Care 18:681–685

Hennessy MJ, Kirkby KC, Montgomery IM (1991) Comparison of the amnesic effects of midazolam and diazepam. Psychopharmacology 103:545–550

Hermann BP, Wyler AR, Somes G. Dohan FC, Berry AD, Clement L (1994) Declarative memory following anterior temporal lobectomy in humans. Behav Neurosci 108:3–10

Jones GMM, Sahakian BJ, Levy R, Warburton DM, Gray JA (1992) Effects of acute subcutaneous nicotine on attention, information-processing and short-term memory in Alzheimer's disease. Psychopharmacology 108:485–494

Kirkby KC, Montgomery IM, Badcock R, Daniels BA (1995) A comparison of age-related deficits in memory and frontal lobe function following oral lorazepam administration. J Psychopharmacol 9:319–325

Koelega HS (1995) Alcohol and vigilance performance – a review. Psychopharmacology 118:233–249

Marin DB, Bierer LM, Lawlor BA, Ryan TM, Jacobson R, Schmeidler J, Mohs RC, Davis KL (1995) L-Deprenyl and physostigmine for the treatment of Alzheimer's disease. Psychiatry Res 58:181–189

Moss MC, Scholey AB (1996) Oxygen administration enhances memory formation in healthy young adults. Psychopharmacology 124:255–260

Moss MC, Scholey AB, Wesnes K (1998) Oxygen administration selectively enhances cognitive performance in healthy young adults: a placebo-controlled crossover study. Psychopharmacology 138:27–33

Paivio A, Yuille JC, Madigan SA (1968) Concreteness, imagery, and meaningfulness values for 925 nouns. J Exp Psychol S76: 1–25

Petrides M (1995) Functional organization of the human frontal cortex for mnemonic processing – evidence from neuroimaging studies. Ann NY Acad Sci 769:85–96

Phillips SM, Sherwin BB (1992) Effects of estrogen on memory function in surgically menopausal women. Psychoneuroendocrinology 17:485–495

Richer F, Decary A, Chouinard MJ, Lepage M (1996) Working memory capacity is not preferentially affected by frontal excisions. Brain Cognit 30:422–425

Roland PE (1993) Brain activation. Wiley-Liss, Chichester

Scholey AB, Moss MC, Wesnes KA (1997) Is oxygen a smart drug? Proc Brit Psychol Soc 5:58

Sevush S, Guterman A, Villalon AV (1991) Improved verbal-learning after outpatient oral physostigmine therapy in patients with dementia of the Alzheimer type. J Clin Psychiatry 62:300–303

Wiegersma S, Dejong E, Vandieren M (1991) Subjective ordering and working memory in alcoholic Korsakoff patients. J Clin Exp Neuropsychol 13:847–853

Winder R, Borrill J (1998) Fuels for memory: the role of oxygen and glucose in memory enhancement. Psychopharmacology 136:349–356