Original Article

Hyperoxygenation Effect on Cognitive Functioning in the Aged

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Abstract

Article

References

Citing Articles (2)

Of the many changes known to accompany aging, those that involve cognitive functioning have provided a continuing challenge to behavioral scientists for many years. The processes involved in information storage (retention via memory traces), retrieval, recall. recognition, reproduction and conceptual efficiency (abstraction and generalization) are among the functions that are affected by aging.

Psychological studies have repeatedly demonstrated a high correlation between age and deficit in short-term memory. Other research indicates that subjects with known memory disorders do less well than others of their age on measures of intelligence, concept formation and retention, and new associations consistently give more difficulty than associations already firmly established from everyday life.

Most studies relating oxygen supply to cognitive functioning have involved the effects of acutely induced hypoxia on the learned behaviour of trained laboratory animals. e 1IiResults of such studies indicate that recent memory and learning are particularly sensitive to oxygen deprivation.

We know of no studies concerned with the effect of increased arterial oxygen tension on cognitive function in senescent man. In this study marked elevation of alveolar oxygen tension (Pa02) has been accomplished by intermittent increase of inspired oxygen tension by' administration of 100 per cent oxygen in a hyperbaric chamber."

Methods

Thirteen elderly male patients having a mean age of 68 years. and all exhibiting clinical manifestations of intellectual deterioration, were studied .:j· They were inpatients, having been continuously hospitalized for many months, and in some cases for several years because of the symptoms of senility. Medical records were throughly reviewed, and a physical examination was carefully carried out in an attempt to eliminate any subject whose cardiac, metabolic or respiratory status would present a calculated health risk on exposure to hyperbaric oxygenation procedures.

After clearance on the basis of physical criteria, each subject was individually given a battery of psychological tests geared to measure deficit in recent memory and conceptual efficiency. The Wechsler Memory Scale,2 consisting of seven subscales (Personal and Current Information, Orientation, Mental Control. Verbal Memories. Digit Span. Visual Reproduction and Associate Learning) was routinely given as the initial test in the battery. This test has two equivalent forms and either Form T or Form IT was given in the pre-experimental test battery. For each patient, the other form was given as part of the post-experimental battery, thereby minimizing any possible increase i.nscores attributable to "practice effects." The Bender-Gestalt test,l!l which involves the reproduction of nine geometric designs, followed by a recall phase. was given routinely as the second test in the battery. Since the Bender-Gestalt test is designed to detect organic deficit. most scoring systems currently used emphasize degrees of existing abnormality. A weighted scoring system designed to measure memory residuals on the recall phase of this test was used. Maxij Approval for the use of human subjects in this experiment was granted by the Sub-Committee on the Use of Human Subjects in Clinical Research, Research and Education Committee, Veterans Administration Hospital, Buffalo, New York, and tbe School of Medicine, State University of New York at Buffalo. Informed consent was obtained from each patient or his legal guardian.

mal weighted score attainable was 100 points. Subjects were given a stipulated number of points if each well known indicator of organic deficit was absent in the memory phase reproductions. Tien's Organic Integrity test. j] an abstract concept-perceptual test sensitive to organic brain damage, was used. It is standardized for repeated administrations and was routinely given as the final test.

Post-treatment psychological testing, consisting of a rc administration of the described battery above, was accomplished with each patient at a mean time of 12 hours after the last exposure in the hyperbaric chamber.

Each experimental subject was treated for 90 minutes, twice a day for J 5 days at 2.5 atmospheres absolute (aim abs) or 1900 mrn of mercury pressure. While at increased pressure, each of these men breathed 99 to 100 per cent oxygen from a cryogenic source. Each patient served as his own control in that pre-exposure test scores were compared to post-exposure scores at the completion of the treatment regimen.

A separate control procedure was designed to eliminate methodological bias in the results. Factors to be controlled by this manipulation were tester bias, [he effect of increased attention paid to the patient in the course of treatment, and effects possibly attributable to the environment or to high barometric pressure per se. Ten patients were exposed in pairs, one experimental subject, who breathed 99 to 100 per cent oxygen as described. and the other. designated as control. who was given 10 per cent oxygen in nitrogen. At 2.5 atmospheres absolute the control mixture provides an alveolar oxygen pressure only slightly higher than that associated with breathing air at normal ambient pressure. In all cases the chamber was pressurized with compressed air, and the patient's inspired gas "vas supplied by an oronasal mask with directly attached demand valve (Scott Aviation Company, Model BM19B-36). When this mask is properly sealed to the face, the demand valve makes a characteristic noise with inspiration. The trained attendant who accompanied patients during all treatments was alert to changes in the inspiratory sounds. Ile could thus detect and correct any gross loss of mask seal. and prevent inward leakage of chamber air. The pressure of oxygen in the inspired mixtures was confirmed by analysis with an Instrumentation Laboratories Model 113 gas analyzer, inside the chamber. The knowledge of which breathing medium was assigned to each paired patient was withheld from the investigator (E.AJ.) who scored the psychological tests. and was known only to the responsible physician (P.M.W.) and to the chamber operators.

Exposure to air at increased ambient pressure involves uptake of dissolved nitrogen and requires attention to decompression procedures. If a person breathes oxygen throughout exposure, he is protected from the possibility of decompression sickness. The increased nitrogen content of the 10 per cent oxygen mixture made it necessary to provide decompression based on the actual nitrogen pressure. the calculated "equivalent air depth," and the corresponding schedule from the United States Navy' standard air-decompression table. I: This was done and 150 control exposures were accompl ished with no incident of decompression sickness.

The experimental nature of the procedure as a whole was discussed freely with ward physicians. nurses and other interested hospital personnel. However, no mention was made of the control-paired procedure. and everyone was given the impression that each patient received 100 per cent ox) gen. In several cases questions arose because of obx ious failure of control patients to show the behavioral improvement obviously manifested by those who had been treated with 100 per cent oxygen. Such questions were handled by reference to "individual differences" rather than by any mention of the control procedure. Ward personnel were told that the patients who were given two series of 30 exposures (the first time on 10 per cent. and the second on 100 per cent oxygen) gave signs of potential further improvement as the result or the initial series and hence was selected as a candidate for further exposure.

Arterial-blood samples were obtained from each patient during an early exposure in his series.

A catheter was placed percutaneously in the radial artery. after it had been ascertained that there was adequate vascularization of the hand through collateral vessels. In all patients. samples were obtained during air breathing at normal pressure and at 20-rninute intervals when breathing the specified gas at 1.5 atm abs. Samples were also obtained during oxygen breathing at normal pressure in patients \\'110 were to breathe 100 per cern oxygen at pressure. Blood samples were collected in sealed. heparinized syringes and analyzed immediately at the same chamber pressure at which they were drawn. Readings of'Pao-, Pac02 and pH were obtained with an Instrumentation Laboratory Model 113 blood gas analyzer. These data were never revealed to the psychologist until post-exposure testing had been completed.

After the series of exposures to 10 per cent oxygen at 2.5 atm. and after post-exposure testing had been completed, control patients were given a series of 30 hyperbaric exposures breathing 100 per cent oxygen, as in the experimental group. The psychological-test battery was [ben repeated.

"This work was conducted at the Hyperbaric Medicine facility operated under the joint support of the State University of New York at Buffalo. the Veterans Administration and Union Carbide Corporation.

Results

Mean scores of psychological tests conducted before and after the series of ex experimental and control patients are presented in Figlll'e /Figure) Mean

Scores on the Wechsler },JeI11Oty Scale (WMS), Bender=Gestalt Memory Phase (B-G) and Tien's Organic integrity Tests (Tien's) before and after Hyperoxygenationfor Control and Experimental Subject Groups .. It is apparent from these data that the group breathing 100 per cent oxygen showed uniform and large increases in post-exposure test scores, whereas the subjects on low oxygen showed no significant improvement. A statistical analysis of these data is summarized in Table ITable 11 "~ J Comparison of Mean Pre-exposure and Po",

-exposure Psychological Test Scores/or Experimental and Control Subjects ..

When the control patients were given a second series of 30 hyperbaric exposures. this time with 100 per cent oxygen, their scores showed essentially the same degree or improvement that had been noted in the original experimental subjects (Table 2Table 2 Comparison

of Psychological Test Scores before and after Exposure TO J a pel' Cent Oxygen with Exposure Test Scores after 100 per Cent Oxygen in CO/lII'O/ Patients.).

Subjective evaluation by ward personnel confirmed measured improvement in the experimental group. Failure of response inthe patients on the 10 per cent oxygen mixture was also noted and commented upon, although ward personnel did not know of the existence of the control series. Such comments were frequent and unsolicited. Patients, too, noted subjective improvement in themselves and commented spontaneously that their memory seemed better.

A comparison of mean arterial oxygen tension levels obtained in experimental and control subjects is presented in Figure :2 Xlean Arterial Oxygen Tensions

(Pa02) in Experimental and Control Subjects ..

Values of Pacoj and pH obtained at 2.5 arm abs were not significantly different from those during air breathing at normal pressure. The experimental group showed large increases in arterial P02 under hyperoxygenation, whereas control patients on 10 per cent oxygen at the same pressure retained arterial Po:? near the normal range.

Discussion

Cortical oxygen deprivation can impair cognitive function in general and memory storage for recent events in particular. Such effects of hypoxia are firmly established, but there has been relatively little direct evidence for the assumption that the psychological symptoms of senescence arise from relative hypoxia of brain tissue. Oxygen delivery to any tissue depends upon arterial oxygen tension, hemoglobin level, blood flow, the state of the microcirculation and capillary-tissue diffusion of oxygen. All these factors may be impaired to some degree in the aged, but no direct correlation has been established between any such impairment and senility in man. To our knowledge the present study represents the first systematic attempt to determine whether symptoms of senility can be influenced by methods capable of producing marked improvement of cerebral oxygenation.

The data of this experiment indicate with a high degree of statistical significance that intermittent hyperoxygenation can materially improve psychological symptoms of senility for at least the period studied. It is suggested that high oxygen input affects the oxygen delivery system at some point and influences the function of tissue that is assumed to be marginally hypoxic. It is well known, however. that oxygen storage is minimal, and it bas been shown that tissue oxygen tension may be expected to return to pre-exposure levels within 30 minutes of cessation of high oxygen breathing at this level. The period is probably much shorter for tissue with a high rate of oxygen extraction, such as brain. Thus the measured effect on function is shown to outlast by far the increase in oxygen tension. Since consecutive retesting of patients is of questionable validity with available tools, data are not yet available on the total duration or presumable fall-off curve of this effect. That it does outlast the increase in oxygen tension by a factor of at least 24 raises questions about the role of oxygenation and energy storage in cerebral metabolism that should provide fruitful ground for further research.

Much remains to be learned about the practical value of hyper oxygenation in senility. It is not likely that the treatment modifies basic degenerative processes, but we know of no other form of therapy that offers statistically significant improvement of function. The value of such symptomatic benefit will depend largely on its duration and whether a retreatrnent schedule will maintain the effect. Both aspects remain to be investigated. The pattern of treatment also requires further study. There is no physiologic basis for thinking that 2.5 atm abs of oxygen, treatments twice a day for 90-minute exposures are in any way optimal. Higher tensions of oxygen probably cannot be safely used because of the risk of Central-nervous-system oxygen toxicity, but it is possible that lower tensions would have a similar effect. Indeed. it must be ascertained whether this improvement in function can be achieved by the use of 100 per cent oxygen at normal pressure.

The patients treated in this study were all suffering from severe deterioration of cognitive function, which was essentially incapacitating and prevented them from caring for themselves. It has been shown, however, that memory and learning curves peak at an early age: between 15 and 20 years .2 Thus, it is likely that many people in functional stages between those of peak learning and gross senility are undergoing slow, but progressive and measurable decreases in memory and learning function. It would be or importance to ascertain whether improvement Could be brought about in this segment of society by similar techniques.

Our work indicates only that the psychological symptoms of gross senility can be markedly and reliably alleviated by intermittent oxygenation and that the effects persist much longer than can be explained purely on the basis of elevated brain-tissue oxygen tension. The basic mechanisms of this demonstrated effect are as yet unknown, and the utility and optimal treatment method remains to be delineated. Further work in this area is potentially of great importance.

Source Information

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