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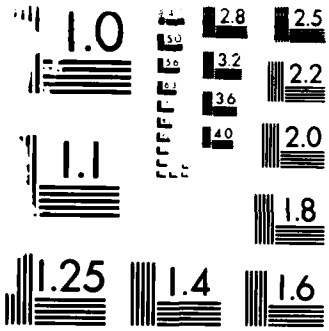

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Human Cerebral Function at High Altitude

Annual Report

Brenda D. Townes, Ph.D.
Thomas F. Hornbein, M.D.
Robert B. Schoene, M.D.

August 1983

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U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
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Subjects were the 21 members of the 1981 expedition. All were males between 25 and 52 years; fifteen subjects had M.D.'s or Ph.D's. Neuropsychological tests were administered to subjects prior to the expedition, during the ascent, upon descent to Kathmandu, and again one year after completion of the climb.

In this young and highly educated group of subjects using supplemental oxygen to climb Mount Everest, transient and long-lasting neurobehavioral effects were found after exposure to the extreme hypoxemia of high altitude. Transient effects included a mild deterioration in learning, memory, and expression of verbal material. These impairments were present within three days of descent into Kathmandu but not one year later. A bilateral reduction in motor speed characterized by rapid muscle fatigue persisted on year after completion of the study. One hypothesis is that cerebellar functions are negatively affected by prolonged exposure to hypoxia at altitude. Alternately, motor cortex functions may be impaired.

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SUMMARY

In the fall of 1981, the American Medical Research Expedition to Everest completed a series of physiologic and psychological studies on mountaineers ascending to the summit of Mount Everest. This expedition afforded the unique opportunity to observe the consequences of extreme, sustained hypoxia on human cerebral function. The goal was to ascertain whether exposure of healthy acclimatized individuals to extreme high altitude results in subsequent long term alterations in cognition or behavior indicative of hypoxic brain dysfunction.

Subjects were the 21 members of the 1981 expedition. All were males between 25 and 52 years; fifteen subjects had M.D.'s or Ph.D.'s. Neuropsychological tests were administered to subjects prior to the expedition, during the ascent, upon descent to Kathmandu, and again one year after completion of the climb.

In this young and highly educated group of subjects using supplemental oxygen to climb Mount Everest, transient and long-lasting neurobehavioral effects were found after exposure to the extreme hypoxemia of high altitude. Transient effects included a mild deterioration in learning, memory, and days of descent into Kathmandu but not one year later. A bilateral reduction in motor speed characterized by rapid muscle fatigue persisted one year after completion of the study. One hypothesis is that cerebellar functions are negatively affected by prolonged exposure to hypoxia at altitude. Alternately, motor cortex functions may be impaired.

FOREWORD

For the protection of human subjects, the investigator(s) have adhered to policies of applicable Federal Law 45CFR46.

HUMAN CEREBRAL FUNCTION AT HIGH ALTITUDE

In the fall of 1981 the American Medical Research Expedition to Everest completed a series of physiologic and psychological studies on mountaineers ascending to the summit of Mount Everest. This expedition afforded the unique opportunity to observe the consequences of extreme sustained hypoxia on human cerebral function. The goal of this study was to ascertain whether exposure of healthy acclimatized individuals to extreme high altitude results in subsequent long term alterations in cognition or behavior indicative of hypoxic brain dysfunction.

Laboratory studies of the effect of acute hypoxia upon cognition have been carried under simulated conditions. These investigations suggest impaired sensory perceptual and motor performance at altitudes to 6100m (3,7,9). While mild hypoxia (to 2,314m) may improve performance on simple motor tasks, more time is required to learn a new task at 3,048m. The mountaineer, therefore, might perform routine, well-practiced tasks adequately but be impaired in performing under unpracticed emergency conditions (5).

Naturalistic observations of alpine mountaineers suggest an increasing impairment in sensory, motor, and complex cognitive abilities as a function of severity of hypoxia with increasing altitude. At the highest altitudes the mountaineers' behavior may be similar to an individual with a known acute organic brain syndrome (10).

How do increasing degrees of oxygen deprivation, together with extreme climatic conditions, produce the observed cognitive and behavioral changes? Selvamurthy, Saxena, Krishnamurthy, Suri, and Malhotra (14) made electroencephalographic recordings of 10 high altitude native and 10 lowlander soldiers at sea level and at 3,500m. Compared to native highlanders, lowlanders showed an increase in alpha activity during acclimatization suggestive of cortical depression. This change was associated with lethargic behavior attributed to cerebral hypoxia. Forster, Soto, Dempsey, and Hosko (6) recorded the electroencephalographic and visual evoked responses of seven healthy male subjects at sea level and for 12 successive days at altitude 4,300m. No changes in cerebral electrical activity were noted in the first two to three hours of hypoxia. Two subjects showed electrical changes during the first four days suggesting cortical depression. All remaining subjects showed electrical changes after the fifth day indicative of cortical excitation. Simultaneous changes in behavior were noted including anorexia, insomnia, irritability, increased ventilation, and depression. These data suggest that cognitive and behavioral changes observed during hypoxia at high altitudes were associated with measurable alterations in central nervous system function. In addition, individual differences during the initial stages of acclimatization occur in both the type and rate of change in cerebral electrical activity.

The physiological, cognitive and behavioral changes occurring at high altitudes are presumed to be caused by alteration in oxygenation of the tissues, either secondary to reduced supply and/or slower utilization (1). In acute hypoxia a reduction of arterial blood saturation to 85% leads to a decreased capacity for mental concentration and abolishes fine muscular coordination. A reduction to 75% leads to faulty judgment, emotional lability and impairment of muscular function (17).

The permanence of cognitive and behavioral changes observed at high altitudes once the hypoxic episode is resolved was investigated by Clark, Heaton and Wiens (4). They tested 22 mountaineers prior to and 16 to 221 days following Himalayan climbs above 5,100m on an extensive battery of psychological and neuropsychological measures (Wechsler Adult Intelligence Scale, Halstead Reitan Neuropsychological Test Battery, etc.). They found no evidence of permanent cerebral dysfunction due to altitude exposure. Sharma, Malhotra, and Baskaran (15,16), by contrast, found that lowlanders required to live for 10 months at high altitudes initially experience impairment of both motor coordination and speed; while the former resolved within a year, the latter persisted over a two year period. Ryn (13) followed a group of 20 male and 10 female Polish alpinists during and "for several weeks" after a Himalayan expedition. Only the male climbers ascended over 5,500m. Of these, half experienced symptoms similar to an acute organic brain syndrome; "for several weeks after the expedition they continued to feel poorly, showing signs of apathy and abulia, and impaired memory" (p. 461). In addition, 11 out of the 30 climbers (6 men and 5 women) had an abnormal EEG during the immediate period following the climb. On psychological testing (Bender and Graham Kendall) visual motor performance was normal in only 13, borderline in 12, and suggestive of organic pathology in 5 climbers. Although no pre-ascent measures were reported, these data tentatively suggest individual differences in the degree to which cognitive, behavioral, and central nervous system disturbances persist following a prolonged hypoxic episode. Whether or not such changes are permanent was a central question of the present study.

METHODS

Subjects:

Subjects were the 21 members of the 1981 American Medical Research Expedition to Mount Everest. All were males between 25 and 52 years with a mean age of 36.4. Fifteen had M.D.'s or Ph.D.'s.

Procedures:

Prior to the expedition the following psychological tests were administered to subjects at the Neuropsychology Laboratory, San Diego Veterans' Administration Hospital: Halstead Reitan Neuropsychological Test Battery (11), Repeatable Cognitive-Perceptual-Motor Battery (8), Selective Reminding Test (2), and the Wechsler Memory Scale (12).

A small number of tests were selected for administration during the ascent on the basis of requiring minimal equipment and ease of administration. These were the Selective Reminding Test, Finger Tapping Test from the Halstead Reitan Battery, and the Digit Symbol, Digit Vigilance, Trails B, Visual Search, and Peg Board tests from the Repeatable Battery. Pretest measures were re-administered in Kathmandu following descent from the mountain. At an expedition meeting held in Colorado a year later, the following tests were re-administered: Aphasia Screening, Trails B and Tapping tests from the Halstead Reitan Battery, the Digit Vigilance Task from the Repeatable Battery, and a verbal passage from the Wechsler Memory Scale.

Seventeen subjects participated in the pretest two months before the expedition and again at Base Camp (5,700m) within 3.3 days of arrival (range: 0 to 6 days). Of these, 16 subjects were tested at the Laboratory Camp (6,300m) within 6.4 days of arrival (range 1 to 18 days), and 9 subjects were tested at Laboratory Camp after returning from the South Col (8,050m) within 1.7 days of arrival (range 0-4 days). Post-testing occurred within three days of arrival in Kathmandu for 19 subjects; 2 subjects were tested in Seattle, Washington, within two months following the expedition. Fifteen subjects were tested at the 11-month follow-up examination. Data were analyzed by means of the Wilcoxon Signed Rank Test to compare differences in performance between the testing periods.

RESULTS

Table 1 summarizes the significant changes found between pre-expedition, post-expedition, and follow-up performance on the neuropsychological tests. Out of 21 comparisons made between performance prior to the expedition and in Kathmandu nine were statistically significant. This is greater than would be expected by chance alone. Performance improved between the pre- and post-expedition periods on tests of complex problem-solving including spatial problem-solving (Tactual Performance Test) and abstract reasoning (Category Test). This improvement was due to practice effects.

(see Table 1, page 7)

A significant decline was found in verbal learning and memory between pre-test and post-expedition testing in Kathmandu as measured by the Wechsler Memory Scale. Using Heaton's modification of this test, a verbal passage containing 24 items of information was read to the subject who then recalled as much information as possible. The passage was repeated until 14 items were recalled or 5 trials completed, whichever came first. Thirty minutes later subjects were asked to repeat as much of the paragraph as possible. Scores were the number of items recalled on the last trial (short-term verbal memory), number of trials to criterion, and the number of items recalled 30 minutes later (long-term verbal memory). As can be seen in Table 1, subjects in Kathmandu, compared to pre-expedition testing, took longer to learn the passage to criterion, recalled fewer items immediately, and showed decay in long-term verbal memory. As passages were not counterbalanced and different examiners were used at the two evaluation periods, these results are tentative and require replication. The observed decrements in verbal memory were transient as subjects had recovered to pre-expedition levels one year later.

On the Aphasia Screening Test there was a significant increase in the number of expressive language errors made between pre-test and post-test in Kathmandu. The types of errors made are shown in Table 2. With the exception of the error in multiplication, the reading, writing, spelling, etc. errors were not present prior to the ascent. Such errors, furthermore, are not expected among young, healthy and intelligent subjects. Pearson product moment correlations were computed between the highest altitude attained and change between pre- and post-expedition performance. Altitude attained was significantly related to an increase in the number of aphasic errors ($r = .55$, $p < .02$). These expressive language difficulties were transient as subjects were again functioning at pre-expedition levels one year later.

Table 1. Wilcoxon Signed Rank Tests Comparing Pre-, Post-(Kathmandu) and Followup-(One Year) - Expedition Performance

Direction of Change	Variable	Time	$\bar{x}$	SD	Pre-Post Z	Post-Follow Z	Pre-Follow Z
A. Improved Performance	Tactual Performance Test						
	Right Hand	Pre-	4.68	1.56	2.72**		
		Post-	3.86	1.46			
	Category Test	Pre-	24.29	15.46	3.48***		
		Post-	11.05	8.39			
B. Decline in Performance	Finger Tapping Test						
	Right Hand	Pre-	53.71	4.07	3.39***	1.32	2.20*
		Post-	45.40	6.18			
		Follow-	48.40	6.60			
	Left Hand	Pre-	47.65	4.60	2.30*	.66	2.93**
		Post-	42.25	5.96			
		Follow-	41.73	5.23			
	Criterion Right	Pre-	1.00	0	3.06**	.73	2.67**
		Post-	.14	.36			
		Follow-	.27	.46			
	Criterion Left	Pre-	1.00	0	2.93*	.54	2.93**
		Post-	.14	.36			
		Follow-	.13	.35			
	Wechsler Memory Scale						
	Short-Term Verbal Recall	Pre-	18.12	1.90	2.60**	2.12*	.98
		Post-	15.90	2.15			
		Follow-	17.13	2.20			
	Trials to Criterion	Pre-	1.24	.44	2.37*	0	2.67**
		Post-	2.40	1.54			
		Follow-	2.27	.70			
	Long-Term Verbal Recall	Pre-	16.35	2.91	2.32*	2.75	.94
		Post-	12.70	3.78			
		Follow-	14.50	2.85			

Table 1. (Cont'd.)

Direction of Change	Variable	Time	$\bar{x}$	SD	Pre-Post Z	Post-Follow Z	Pre-Follow Z
	Aphasia Screening Test	Pre-	.59	.79	2.22*	2.31*	.47
		Post-	1.25	1.25			
		Follow-	.47	.52			

*p < .05 **p < .01 ***p < .001

(see Table 2, page 10)

Finger Tapping speed decreased significantly over the course of the expedition (Table 1). Mean taps for the right hand were 53.7 (pre-test), 52.6 (Base Camp), 50.8 (Lab Camp), 48.1 (return from South Col), and 45.4 (Kathmandu); mean taps for the left hand were 47.6, 46.1, 47.4, 45.1, and 42.2, respectively. The standard method of administering the Finger Tapping Test is to obtain five trials of 10 seconds each on each hand with no greater difference than five taps between trials. Before the expedition all subjects reached criterion. At Kathmandu 15 out of 20 subjects could not sustain motor speed, and 13 out of 16 subjects could not do so one year later. Given a minute's rest, motor speed improved but would again decline. Immediately following the expedition and up to one year later rapid muscle fatigue was present bilaterally.

DISCUSSION

In this young and highly educated group of subjects using supplemental oxygen to climb Mount Everest, transient and long-lasting neurobehavioral effects were found after exposure to the extreme hypoxemia of high altitude. Transient effects included a mild deterioration in the learning, memory, and expression of verbal material. These impairments were present within three days of descent into Kathmandu but not one year later. A bilateral reduction in motor speed characterized by rapid muscle fatigue persisted one year after completion of the study. Clark, Heaton, and Wiens (4) tested subjects 16 or more days following descent to sea level with no observed impairment over pre-test performance. As in the present study Ryn (13) found signs of memory impairment "for several weeks after the expedition" (p. 461).

Our findings, together with those of Ryn, support at least transient decrements in verbal memory and expression. Possible involvement of the hippocampus and/or temporal areas of the brain in producing the observed decrements in verbal memory will be tested in the future by separating out learning from the retrieval of information across visual, auditory, and tactile modalities.

As prolonged motor impairments have been found by Sharma, Malhotra, and Baskaran (15,16) as well as in our studies, the finding appears to be reliable. One hypothesis is that cerebellar functions are negatively affected by prolonged exposure to hypoxia at altitude. Alternately, motor cortex functions may be impaired. We expect to test these hypotheses in the future using a more detailed examination of motor functions (8,9).

Table 2. Types of Aphasia Errors at Post-Test in Kathmandu

	Type of Error	Item	Response
1.	Reading	7 six 2	6 - 7 - 6 - 2
2.	Writing	warning	warninG
3.	Calculation	17 x 3	49, 52, 57
4.	Spelling	triangle	trangle
5.	Pronunciation	Massachusetts Episcopal	Massachusess, Massachutetts Ekpiscopal
6.	Confusion of Body Parts	Place left hand to right ear	Right hand placed to right ear

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