Neurological Findings After Prolonged Sleep Deprivation

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IN SPITE of the awareness that prolonged wakefulness has a detrimental effect on human beings, it was not until 1896 that Patrick and Gilbert [1] first studied three human beings for 90 hours of wakefulness and demonstrated decreases in sensory acuity, motor speed, ability to memorize, and the production of visual hallucinations. Since that time there has been a gradual increase in interest in sleep deprivation by psychologists, physiologists, and psychiatrists. Experiments have primarily taken the form of enforced abstention from sleep for varied lengths of time, with performance and learning tests being administered before, during, and after the prolonged vigil. Studies of the effect of prolonged sleep deprivation from a neurologic point of view, however, are relatively rare. Cooperman et al [2] demonstrated with von Frey hairs that pain occurred with a weaker stimulation after 60 hours of wakefulness; Freeman [3] described increased tone in the quadriceps muscle after sleep loss, and Furchtgott and Willingham [4] demonstrated an increased threshold to taste.

To date there has been no published study of serial neurological and electroencephalographic examinations on severely sleep-deprived individuals. West et al [16] observed a New York disc jockey for 201 hours, but their neurological findings have not been published.

The purpose of this report is to present the neurological findings on a high school senior who stayed awake for 264 hours without the aid of any kind of stimulants.

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Report of Case

A 17-year-old schoolboy came under the author's care at the Navy Medical Neuropsychiatric Research Unit, US Naval Hospital, San Diego, Calif, on Jan 7, 1964, with the history of going without sleep for 252 hours during which he had developed intermittent irritability, incoordination, slurred speech, partial nominal aphasia, difficulty focussing his eyes, slight astereognosis, and one brief visual illusion and one brief delusion. The initial aim for the excessive wakefulness was a planned project to evaluate the effects of sleep deprivation by the patient and two co-investigators for the San Diego Science Fair. A goal of 264 hours of deprived sleep was selected because the patient desired to establish a new record for staying awake (previous record was 260 hours).[5] In order to prevent the patient from falling asleep, he was constantly observed by one of his two co-investigators, and every six hours he was administered a series of tests to measure performance and ability to respond to stimuli. During the last three days of the vigil the patient was closely observed by Dr. William Dement.

During the second day of the vigil the patient noticed difficulty focusing his eyes. After the second day he stopped watching television for the rest of the experiment because his eyes were so extremely heavy and tired. At this time he also had mild astereognosis. By the third day he developed mood changes, ataxia, difficulty saying tongue twisters, and marked nausea. During the fourth day he became irritable and uncooperative; he developed memory lapses, difficulty concentrating, the feeling of a tight band around his head, and saw fog around the street lights. About 0300 that night he experienced the illusion that a street sign was a person. A short time later he imagined he was a great Negro football player and resented statements made about his ability and the Negro race. By the fifth day his equilibrium was normal, but he had intermittent hypnogogic reveries, such as seeing a path running through a quiet forest and plants in a garden. On the sixth day ataxia, mild astereognosis, and dysnomia were again present, and during the next three days slight irritability,

mild uncooperativeness, memory lapses, and inability to concentrate reappeared. Intermittent slurred speech was evident on the seventh day and it continued to deteriorate to a soft, slow, slurred, mushy quality by the end of the wakeful period. By the ninth day he occasionally thought in fragments and frequently did not finish sentences. Also, blurred vision became more of a problem. During the last two days of the vigil he felt a certain radio entertainer on whose show he later appeared was trying to make him appear foolish because he could not recall certain specific facts about the vigil. The patient finally went to sleep after 264 hours of wakefulness (Jan 8, 1964) and slept for 14¾ hours. The reason for terminating the vigil was simply that the patient had achieved his goal.

Examination.—Although the patient had been followed by a family doctor and a psychiatrist, he was not seen for neurological evaluation until late in the experiment. Three neurological examinations were performed during the period of sleep deprivation, and three post-vigil examinations were given ten days, six weeks, and seven months after the patient had resumed a normal sleep pattern.

Findings During Deprivation.—General physical examination revealed a well-developed, healthy high school boy who was ambulatory, oriented, and obviously weary. Blood pressure was 120/80 mm Hg. The pulse was 72, and the temperature (oral) was 97 F (36.1 C). Significant findings were: injected, dry sclerae and conjunctivae, congestion about Stenson's duct, moderate congestion of the soft palate and tonsillar pillars, severe pharyngeal lymphoid hyperplasia, and a grade 3 holosystolic murmur at the base of the heart with extension along the left sternal border which disappeared two days after the vigil ended.

The neurologic examinations showed the patient to be cooperative and oriented. He was somber in mood and had a short attention span. He repeated seven numbers forward and six numbers backwards; but he had considerable difficulty with serial sevens. The first time he attempted the test he stopped at number 65 and stated he could not remember what he was doing. Upon continuing with the test he made four mistakes. On the second try he made two mistakes. For a boy who made average to above average grades in high school, his fund of knowledge was below expectations. When asked to read a paragraph he was only vaguely able to recall what he had read and details were absent.

His pupils reacted normally, and extraocular movements were intact; however, conjugate lateral ocular deviation was reduced in the right eye on gaze to the right, and a right horizontal nystagmus was observed in the right eye on gaze to the right. Although convergence was present at 252 hours of sleep deprivation, at 264 hours of wakefulness this was impossible. In spite of the above observations, the patient always denied diplopia. Between 254 and 264 hours of sleeplessness the patient demonstrated a coarse clockwise rotatory nystagmus on gazing up and to the left and a coarse counterclockwise rotatory nystagmus on looking up and to the right. Ptosis of both upper eyelids was very marked, being more exaggerated on the right side than on the left (Fig 1). Repetitive elevation and depression of the eyelids did not accentuate the ptosis. Both corneal reflexes were very sluggish. The patient's general facial appearance was expressionless, although volitional and emotional movements were intact. Taste was intact, but a double test-dose of sugar was required to perceive sweetness on the left anterior aspect of the tongue. The voice was normal when he was encouraged to speak, but usually it was soft, slow, slurred, and listless, with no inflections. The gag reflex was hyperactive bilaterally.

The patient's posture and gait were normal, and there was no evidence of involuntary movements except for several examples of sudden clonic jerks of both upper extremities which were felt to represent nocturnal jerks or what de Lisi described as "physiological hypnic myoclonias." Upon extending his arms in front of his body, tremulous finger movements were observed. Coordination was normal as demonstrated by normal finger to nose, heel to shin, and Romberg tests. Such tests as rapid alternating hand movements, fine finger movements, tandem walking, and standing alone on each foot were also normal. All sensory modalities were present. On one occasion the patient confused right and left on double simultaneous stimulation when his attention began to wane. This was corrected when his attention was regained. The patient complained of very marked discomfort when his feet were stroked with a dull key. The deep tendon and superficial reflexes were markedly hyperactive on both sides of the body and the plantar reflexes were flexor.

Findings Post-Deprivation.—When the patient was examined ten days after he had resumed a normal sleep pattern, he was found to be almost normal. His mood had changed to a carefree, happy attitude, and his mental status was improved. Serial sevens were performed slowly, but correctly. He remembered only two out of three objects over a ten-minute period. The cranial nerve signs and the reflexes had also returned to normal. Neurological examination 38 days and seven months after the sleep-deprivation were completely normal.

Laboratory Findings.—Ancillary examinations at 264 hours of wakefulness disclosed a hemoglobin of 15.4 gm%; hematocrit of 44%; red blood cell count of 4.79 million; white blood cell count of 7,490; differential of 46% neutrophils; 45% lymphocytes; 8% eosinophils; and 1% basophils. The urine was amber and clear, had a pH of 5.0, had a specific gravity of 1.027, and had no albumin, sugar, acetone, bile, or occult blood. The spun sediment contained 1-2 white blood cells and a rare epithelial cell per high-power field. An aliquot of urine showed Na, 240.0 mEq/liter; K, 85 mEq/liter; Cl, 8.75 mEq/liter; and CO_2, 2.298 mEq/liter. Blood chemistry determinations showed BUN, 14 mg%; fasting glucose, 76 mg%; Na, 155 mEq/liter; K, 4.6 mEq/L; chloride 108.7 mEq/

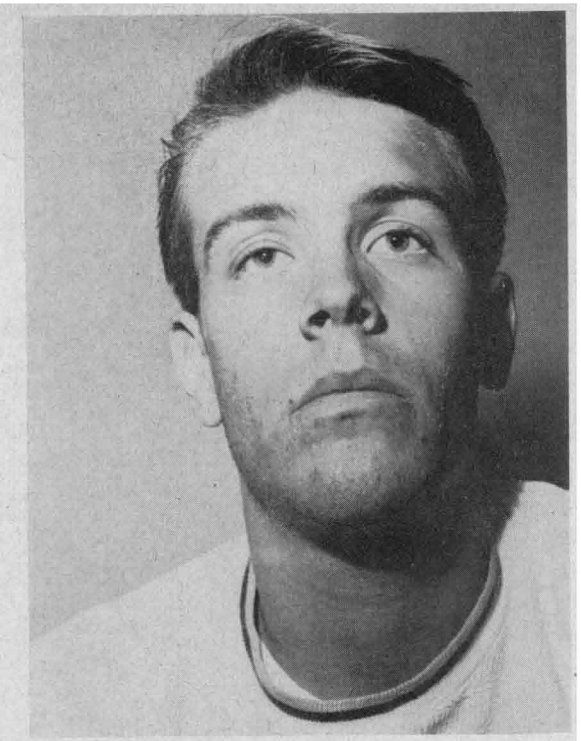

Fig 1.—The patient after ten days of wakefulness. (Photo courtesy of the *San Diego Evening Tribune.*)

liter; cholesterol, 142 mg%; total protein, 7.4 gm%; and albumin, 5.2 gm%. Chest x-rays and ECG's were normal.

The EEGs at 236 and 249 hours of wakefulness showed a marked reduction in α-activity and an increase in both low voltage δ- and θ-activity (Fig 2). The reduction in α-activity was evident when the patient's eyes were closed as well as when they were open. Sound stimuli did not produce α-enhancement. Ten days after the patient had resumed a normal sleep pattern the α-waves had returned to the tracing. An interesting finding was the presence of excessive θ-activity seven months after the vigil, but this may be the subject's normal EEG pattern. A more thorough analysis of the EEG and autonomic findings will be presented by Johnson et al [6] in a report to be published.

Comment

The behavior of this young man was similar to that described by other investigators of sleep deprivation. He first demonstrated signs of abnormal behavior during the third day of wakefulness, and subsequently he experienced sporadically the tactual misperception, temporal disorientation, cognitive disorganization, and visual misperception that others have experienced. Of particular interest in this case, however, was the fact that he did not show the characteristic progressive deterioration to the point that his contact with reality was grossly impaired. When the patient was examined the last two days of the vigil, he was alert and oriented, but tests requiring any concentration or increased length of time to do the tasks showed short lapses in his attention. These lapses in attention in sleep-deprived patients have been reported by Warren and Clark,[7] Bjerner,[8] Williams et al,[9] and Wilkinson.[10,11] Wilkinson [12] also described an irregularity in the rhythm of the responses of sleep-deprived persons that was also observed in this patient. These observations agree with the phenomenon which Bills [13] called "blocks."

Not observed previously, but seen in this patient, were nystagmus of the right eye on gaze to the right, defective conjugate lateral deviation of the right eye, complete loss of voluntary conjugate adduction of both eyes, bilateral rotatory nystagmus on lateral upward gaze to both sides, sluggish corneal reflexes, mild weakness of the orbicularis oculi muscles, and very hyperactive deep tendon reflexes. After 14¾ hours of sleep some of these signs persisted, but ten days later all signs had cleared except for a slight difficulty with memory. Six weeks and seven months after the sleep deprivation experiment, the patient was perfectly normal.

A review of previously published case reports pertaining to individuals sleep-deprived for 120 hours or longer was done. Of the five persons studied,[14-18] all were male. Their ages were 32, 24, 27, >21, and >29. A listing of their occupations showed two were disc jockeys, one a radio announcer, one a medical student, and one unknown. Their past histories showed one was eccentric and paranoid, another was unstable and had received a medical discharge from the Army, another was an adopted child who had been in a children's mental institution for arson and theft and who had held 20 different jobs in six years, and one was crippled as a child and had an abnormal electroencephalogram prior to the experimental insomnia. It was interesting to note that four of the five had abnormal psychiatric or neurological histories. The reasons for undertaking the vigils were: radio marathon, three; research, one; and to bolster one's ego, one.

Our case report and those of others bring up the question of the seriousness of prolonged loss of sleep in patients; that is, what permanent changes might occur in the mental or neurological functions of these individuals? So far as we know, the medical literature does not contain any case reports of human beings who died as a direct result of sleeplessness, but this is not true of animals. We do not believe our patient suffered any permanent neuropathological damage from his ordeal, as two complete examinations six weeks and seven months post-deprivation showed no abnormalities. His waking electroencephalogram seven months later still showed some θ-activity, but this may be his normal pattern. The patients described by Katz and Landis [14] and Brauchi and West,[15] however, had psychiatric complaints six months and three months, respectively, after their ordeal, and it is interesting that both of these men had psychiatric histories some months and years before their vigils. The patient studied by West et al [16] was very anxious and denied all of his bizarre behavior for four days after resuming his normal sleep pattern. During the next six months he had many personal problems, became depressed, and finally developed paranoid behavior. These three patients seem to support the assertion by Bliss et al [19] that in susceptible persons the combination of psychological distress and prolonged sleeplessness may precipitate some schizophrenic illnesses. These same authors also demonstrated that the hallucinogenic properties of *N,N*-diethyl-D-lysergamide (LSD-25) were considerably enhanced by prolonged wakefulness.

In the brains of puppies who were sleep deprived and died, capillary hemorrhages in the cerebral gray matter were observed by Manacéine.[20] In a group of adult dogs who died at 9 to 17 days after constant wakefulness, Daddi [21] reported a diffuse chromatolysis and vacuolation of the cytoplasm in the cells of the cerebral cortex, especially the frontal lobe. Similar changes were seen by Agostini,[22] Okazaki,[23] and Jorda.[24] Legendre and Piéron,[25,26] who deprived dogs of sleep for 30 to 505 hours, reported shrinking of neurons, displacement of nuclei, vacuolization of cytoplasm, and disappearance of Nissl's bodies primarily in the fifth and sixth layers of the frontal cortex. These changes were reversible if the dogs were allowed to sleep.[27] Upon studying sleep-deprived rabbits, Bast et al found changes in the cells of the medulla [28] and spinal cord.[29] Thus it appears that sleep-deprived animals do develop neuropathological evidence of changes in the cortex of the frontal lobe and in the medulla and spinal cord, depending upon the species of animal that was studied. The fact that our patient had clinical signs that could be due to altered function in the cerebral cortex and brain stem is indeed intriguing.

Summary

A case of a 17-year-old male who was sleep-deprived for 264 hours is described, and the previously reported cases of prolonged wakefulness (greater than 120 hours) are briefly reviewed. Psychiatrically the patient experienced the visual misperceptions, temopral dis-

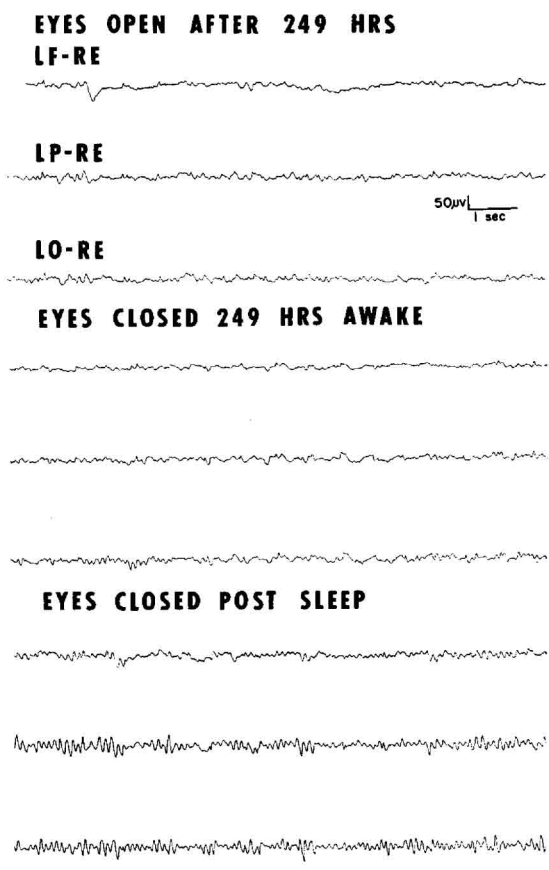

Fig 2.—EEG activity after 249 hours of sleep deprivation and ten days after the first recovery sleep. The lead placements were LF-RE, left frontal to right ear: LP-RE, left parietal to right ear; LO-RE, left occipital to right ear.

orientation, cognitive disorganization, and tactual misperceptions that others had experienced, but at the end of the vigil he was psychiatrically much healthier. During the vigil he showed difficulty with focusing his eyes, stereognosis, equilibrium, and speaking. Multiple neurological examinations demonstrated that aside from quite evident physical and mental fatigue, the patient showed no significant abnormalities.

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Randy Gardner was the subject and Joe Marciano, Jr., and Bruce McAllister were the student collaborators on the Science Fair project.

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