valine (12). These studies add to the accumulating evidence that the genetic code is, at least in its general features, the same in widely divergent species (13).

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References and Notes

1. The abbreviations are polyU, polyuridylic acid; PEP, phosphoenolpyruvate; ATP, GTP, CTP, UTP, adenosine, guanosine, cytidine, and uridine triphosphates; DOC, deoxycholate; sRNA, soluble RNA; TCA, trichloroacetic acid; polyUC, polyuridylic-cytidylic acid; polyUA, polyuridylic-adenylic acid; polyUG, polyuridylic-guanylic acid.
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Prolonged Immobilization of the Body: Changes in Performance and in the Electroencephalogram

Abstract. *Subjects who were immobilized for a week but otherwise were exposed to a normal and varied sensory environment showed intellectual and perceptual deficits similar in many respects to those occurring after prolonged visual and auditory deprivation. A significant change in the electroencephalogram was also observed.*

Severe deprivation of vision and hearing, in an isolation chamber, for periods up to a week can produce widespread impairments of intellectual and perceptual processes. Hallucinatory phenomena, to a limited degree, may also be present (1–3). Furthermore, these behavioral deficits are accompanied by significant changes in the electrical activity of the brain (4–6). The purpose of this experiment was to determine whether similar effects can be produced in subjects whose tactile-kinesthetic activity is reduced via immobilization but who otherwise are exposed to a normal and varied sensory environment. Fiske, in a recent review of the literature on perceptual deprivation, suggested that such results may be possible (1). Unfortunately, behavioral experiments specifically designed to appraise the role of kinesthesis are rare. Most of the research in this area has usually employed various degrees of immobility of the body concurrent with restriction of visual and auditory stimulation (1, 7). The results, therefore, are inconclusive. In the present study, tactile-kinesthetic stimulation alone was reduced.

The subjects were 22 male university students who were placed in a "coffin-like" box for 1 week—a period similar to the one we used in earlier experiments on visual and auditory deprivation (2, 3). This box was 7 feet long, 28 inches wide and 18 inches high. It was lined with a thick layer of foam rubber cut out in the shape of a human figure. At one end of the box was located an adjustable, padded head-holding device which fitted snugly against the forehead and side of the head. No padding was placed over the ear section. A plastic frame, to which pictures could be attached, was placed some distance above the head-holder. At the other end of the box, two V-shaped restraining devices immobilized the feet.

The subject was told to lie on the foam rubber with his head in the padded holder and his feet in the restraining holders. His legs and trunk were immobilized by means of belts fastened to the base of the box. The belts did not interfere with circulation. The arms were placed in comfortable but rigid cylinders which were fastened down but which permitted some degree of flexion of the elbow. To minimize such factors as pain and cramps the subjects were unstrapped periodically—for example, for 15 minutes at mealtimes and for 1 hour in the afternoon. During this hour they went to the washroom and also took a battery of intellectual tests. They were also unstrapped for 9 hours during the night but were not allowed to sit up or stand up. Apart from these restrictions on motor activity, they were exposed to as normal an environment as possible. They could hear people moving about and talking. They could listen to a radio whenever they wished. Various pictures were placed above them and changed from time to time, and the lights were put out at night. An experimenter was on duty at all times.

The subjects were given two batteries of tests, intellectual and perceptual-motor. These were identical with those used in our earlier experiments (2, 3). The intellectual tests, measuring 12 different abilities, were administered before the experiment and at daily intervals during the week. Eight equivalent forms of each test were used. Some of the tests measured fairly simple abilities involving overlearned material, while others appraised more complex abilities requiring deliberation and manipulation of ideas. The tests were all short, of several minutes' duration each, and consisted of the following: simple arithmetic problems, mathematical reasoning (solving numerical sequences), abstract reasoning (solving sequences of patterns), verbal fluency (writing words beginning with a certain letter), verbal reasoning (for example, *lend* is to *borrow* as *rich* is to ——), space visualization (selecting the exact parts which will form a certain design), digit span (forward and backward), rote learning of a list of nine three-letter words, recall of words presented a few minutes earlier, recognition of words presented earlier, cancellation test (picking out a particular number from pages of randomized numbers), and dexterity (placing a dot in a small triangle, making two check marks in a square, and tracing a line through a maze without touching the sides).

The battery of five perceptual-motor tests was only given before and after the week of immobilization. It consisted of the following: (i) Depth perception, measured by the Howard-Dohlman apparatus. The subject moved a vertical rod until it appeared to be at the same distance as a fixed rod. (ii) Size constancy. A black equilateral triangle, of variable height, was presented at a distance of 15 feet. The subject had to adjust the height of this triangle until it looked the same in size as the near one, the standard triangle, placed 4 feet away. (iii) Reversible figures. The subject fixated a point at the center of an ambiguous figure (reversible blocks) for 60 seconds, pressing a counter each time the figure changed. (iv) Color discrimination, measured by the Farnesworth-Munsell 100-hue test in which the subject is required to arrange caps in order so that they form a regular series between two fixed colored caps. (v) Pain sensitivity. Pain thresholds of the volar surface of the forearm were measured by the Hardy, Wolff, and Goodell dolorimeter using a radiant heat level of 150 m cal/cm^2 sec for a skin temperature of 34°C. A correction was made for skin temperature if it differed from 34°C by more than ±0.50°C. The threshold was determined by the time method—that is, in terms of the minimum duration in seconds of heat required to elicit the first trace of pricking pain.

In addition to these behavioral measures, electroencephalograms were taken from ten subjects before and after the week of immobilization. Records were also taken from ten controls, a week apart. These subjects were placed on a fixed feeding schedule, and records were taken in the morning, after breakfast. Precautions were taken to eliminate any drowsiness. The mean occipital lobe frequency was then determined by the method of Engel *et al.* (*8*). This involved counting the number of waves occurring in each of 200, 1-second samples of artifact-free occipital lobe tracings. In order to control for possible bias, a technician who was not associated with the project scored the tracings "blindly"—that is, he was not told whether the tracings came from the experimental or control group or whether they were taken before or after the period of immobilization. Each of the experimental subjects was paid $125. There were no failures. The first 22 subjects successfully endured the week of immobilization. The preimmobilization scores of these 22 subjects, on the 17 behavioral tests, were matched with the initial scores of 22 out of 40 control subjects. From this larger sample of controls it was possible to select 22 subjects whose "pre-" scores were almost identical with those of the experimentals. These control subjects received the same battery of tests and at the same time intervals as the experimentals. However, they were never immobilized. They merely came to the laboratory for the tests at the specified times. Two-tailed *t*-tests for correlated measures were used for statistical analysis.

An analysis of the data revealed that the mean performance of the experimental subjects during immobilization was worse than that of the matched controls on all 12 intellectual tests. Of these tests, cancellation ($p<.001$), recall ($p = .01$), and verbal fluency ($p>.02$) were impaired significantly, while the decreased scores on dexterity, space visualization, and numerical reasoning bordered on statistical significance ($.05<p\text{'s}<.10$). No reliable differences existed for verbal and abstract reasoning, digit span, arithmetic problems, rote learning, and recognition ($p\text{'s}>.20$). Of the five perceptual-motor tests, color discrimination ($p<.05$) and reversible figures ($p<.01$) were impaired significantly. On the latter test, several subjects complained that the ambiguous figures just would not reverse for them—a problem which they did not experience prior to immobilization. Depth perception, pain sensitivity, and size constancy were not affected ($p\text{'s}>.20$). An analysis of the electroencephalograms revealed a mean decrease in occipital lobe frequencies of 0.56 cycle per second after the week of immobilization. On the other hand, the sample of ten control subjects showed a mean difference of only +0.01 cycle per second over the same time interval. This difference between the two groups was significant at below the .001 level of confidence. Hallucinatory-like phenomena were quite rare. Only 3 of the 22 subjects reported their presence. One subject reported "flashes of light," another "cloudlike formations and circles contracting to nothing," and the third subject reported hearing music at a time when the radio was not in use. These phenomena appeared on only one occasion and in all cases occurred toward the end of the experimental period.

This study has demonstrated that reducing the level and variability of tactile-kinesthetic stimulation via immobilization can produce a disturbance of both performance and the electrical activity of the brain. These effects cannot be attributed to visual and auditory restrictions since none were imposed. They also cannot be due to the prone position which the subjects assumed. It has already been demonstrated that the recumbent position, maintained for a week, exerts no significant effect on our behavioral measures (*3*) or on the electrical activity of the brain (*5*). The results, therefore, appear to be related to the restrictions imposed on body movements. What little relevant literature there is seems to support these findings. For example, Goldman (*9*) has demonstrated that subjects who were strapped in a special chair which prevented movements of the limbs, trunk, and head showed a significant increase in the duration of the autokinetic effect in relation to a control condition. Unfortunately, no other perceptual processes were measured. More recently, Riesen (*10*) has shown that deficits of visual-spatial performance can occur in kittens and primates restrained in holders. Although reared in a normal visual environment they were deprived of the opportunity to move about freely. Finally, bodily movements are essential for readaptation after optically produced disarrangements of the visual field (*11*).

These effects of prolonged immobilization resemble in many ways those obtained in the prolonged visual and auditory deprivation experiments carried out in our laboratory (*2, 3*) and elsewhere (*6, 12, 13*). Some valid comparisons can be made, since identical tests and durations were used in most cases. The differences lie largely in the magnitude of the effects. First, a decrease in occipital lobe frequencies occurs in both types of experiments (*4–6*). The mean decrease, however, is less after immobilization—0.56 vs. 0.85 cycle per second after a week-long period of darkness and silence (*5*). Second, many of the same intellectual and perceptual abilities are impaired—for example verbal fluency (*3, 6*), recall (*2*), cancellation (*2, 3*), color perception (*2, 3, 12, 14*), and reversible figures (*3, 15*). However, immobilization does not affect as wide a range of performance tasks as does visual and auditory deprivation (*2, 3*). This seems to be in keeping with its less severe disturbances of brain wave activity. Third, certain behavioral measures appear to be immune to both immobilization and visual and auditory isolation —for example, rote learning (*2, 3, 6,* *16*), digit span (*2, 3, 6, 17*), verbal reasoning (*2, 3*), size constancy (*2, 3*), and depth perception (*2, 3, 12*). Finally, hallucinatory phenomena were rare. This is in agreement with the more recent deprivation experiments (*3, 13, 18, 19*) which indicate that these phenomena are not as common as was originally believed (*1, 6*).

It is possible that our effects and their resemblance to the "deprivation" phenomena would have been even greater if a more severe condition of immobilization had been employed. The fact that all of the volunteers endured the week quite easily and that there were no failures indicates that our procedure was not particularly stressful. Furthermore, it would appear to be less stressful than prolonged isolation where approximately a third of the volunteers fail to endure periods longer than 4 days (*13, 20*).

These behavioral and physiological changes are probably mediated by the same neural mechanisms that are believed to be involved in producing the classical perceptual deprivation phenomena—that is, a disturbance of the activity of the ascending reticular activating system as a result of a decrease in the level and variability of sensory input (*6, 21*). In the present experiment, however, the decreased variability of input is from the tactile-kinesthetic (and vestibular) rather than visual and auditory senses. Interference with these sense modalities alone may be sufficient to produce certain behavioral changes, especially in the light of several reports pointing to the "powerful excitatory influence of somatic sensory excitation" upon the reticular activating system (*22*). In addition to this nonspecific reticular system, it appears that the specific sensory systems may also be involved in these behavioral effects (*23*).

These results have important implications for the numerous sensory and perceptual deprivation experiments in which the subjects are instructed to lie quietly, often for long periods of time (*1*). They raise the possibility that the behavioral deficits reported in these studies may be as much a function of restricted motility as reduced visual and auditory input, if not more. Our findings are also relevant for the treatment of hospitalized patients, particularly those whose condition is such that it requires prolonged immobilization in a cast or in an iron lung. Adverse psychological effects may occur if appropriate measures to stimulate bodily activity are not taken. The findings, incidentally, are also applicable to the "man-in-space" program. Finally, the results have some relevance for the centuries old practices of swaddling and cradling of infants. Although these practices have now virtually dispeared, they still exist among some peasants of Central Europe and Italy, as well as in Lapland and in certain North American Indian tribes (*24*). In the light of our data it is possible that these practices may produce some degree of intellectual retardation. This view is supported by Hill and Robinson (*25*), who reported a case of retarded mental development which they believed was brought about "almost entirely by the drastic restrictions made to his movements." This was a 6-year-old boy who, because of a skin condition, had severe restrictions placed on arm and leg movements. Although this is a single case, the results, nevertheless, are suggestive. These swaddling and cradling practices may also retard perceptual development, particularly in view of Riesen's (*10*) demonstration of perceptual deficits in kittens and primates who were merely restrained in holders (*26*).

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Carbon Tetrachloride Poisoning in Rats: Alteration in Ribosomes of the Liver

Abstract. *Microsomes from livers of albino rats treated with carbon tetrachloride were compared with those from normal rats with respect to their ability to incorporate amino acid. Acute carbon tetrachloride poisoning results in depressed capacity of microsomes to incorporate amino acid. From ultracentrifugal data, there is an apparent dissociation of 79*S *ribosomes into 54*S *components.*

Carbon tetrachloride (CCl_4) causes hepatic necrosis, and a single sufficient exposure produces acute liver injury in many animal species (*1*). Injury occurs with such regularity and with such similarity of pattern that one can only conclude that some fundamental process is deranged by this toxic agent. How it acts has been the subject of considerable conjecture and experiment (*2–5*). The first subcellular elements suggested as the seat of the injury were the mitochondria (*2, 3*). Examination of the data revealed that the functional changes in the mitochondria occur at a time when the liver already shows significant damage when examined with the light microscope. With the electron microscope a much earlier and more subtle injury can be detected in the coarse endoplasmic reticulum (*3, 5, 6*). Coincident with this change there appears a depression in protein synthesis, the metabolic activity now known to be associated with the coarse endoplasmic reticulum (*5, 7, 8*). This report deals with experiments which extend the evidence for the site of action of CCl_4 in