from the same immunoglobulin preparation, the Red-II had to be used at seven times the concentration of the Green-II for satisfactory staining. Reagents used in combination (such as Red-I and Green-II) were mixed prior to application to the tissue.

Lymphoid tissue prints were obtained by touching microscope slides to the freshly cut surface of lymph node or splenic tissue obtained at surgery or autopsy. None of the specimens used came from patients with myeloma or macroglobulinemia. Stained specimens were examined under a Leitz ultraviolet microscope with a Corning #5840 exciting filter and K2, 23A, and 57A eyepiece filters.

Cells showing red, green, or mixed fluorescence under the K2 filter were differentiated according to the method of Cebra and Goldstein (*10*) in which Kodak gelatin barrier filters allow passage of only green light (57A) or red light (23A). From 100 to 300 cells were counted for each preparation and the relative percentages of each kind of staining were calculated.

The results of the experiments are summarized in Table 1. Fluorescent cells of preparations stained with both Red-I and Green-II (experiment 1) were either red or green but were rarely doubly stained. This clear and striking distinction of cells appears to indicate that, at a given time, a cell does not produce both kinds of L-chains. In all the experiments, the type I cells were more numerous, appearing approximately twice as frequently as those synthesizing type II chains. This is in accord with the relative concentrations of 7*S* γ-globulin molecules of types I and II found in normal serum.

Preparations stained with Green-Cr and either Red-I or Red-II (experiments 2 and 3) showed a significant percentage of doubly stained cells. This is interpreted to mean that single cells may produce at the same time both H-chains and L-chains of the type revealed by the appropriate stain. The green-staining cells in these experiments apparently contain 7*S* γ-globulin H-chains, either alone or together with L-chains of the other antigenic type. That the cells stain red in these experiments can indicate production of L-chains either alone or with H-chains of β_{2A}- or β_{2M}-globulins. The ratio of blended cells to green cells was generally in accord with the previously noted 2:1 predominance of type I cells.

The results of experiment 4 (Red-I, Red-II, Green-Cr) indicate the frequency of those cells staining for L-chain but not for H-chain of 7*S* γ-globulin (red-staining cells) and of those cells staining for H-chains but not L-chains of type I or type II (green-staining cells). Only a small percentage of cells stained green. Possibly the red-staining cells are producing β_{2A}- or β_{2M}-globulin. If so, such synthesis of these other immunoglobulins separate from 7*S* γ-globulin would be consistent with data of Mellors and Korngold (*11*), Burtin and Buffe (*12*), and the observations of Chiappino and Pernis on splenic cells (*13*). However, in this last investigation, some cells of the lymph node germinal center were found to contain both β_{2M}- and 7*S* γ-globulins.

Experiment 5 was performed as an internal control of the method. Preparations stained with Red-II and Green-II contained almost exclusively blended cells.

The results appear to indicate that spleen and lymph node cells may produce both L- and H-chains of 7*S* γ-globulin simultaneously but that they rarely, if at all, produce both kinds of L-chains. The ratio of type I to type II cells (2:1) is in accord with the relative amounts of these types of immunoglobulins in normal serum and also with the relative incidence of these antigenic types of myeloma globulins appearing in patients with multiple myeloma (*14*).

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Cutaneous Sensitivity after Prolonged Visual Deprivation

Abstract. *Subjects who were placed in darkness for a week but who were otherwise exposed to a normal and varied sensory environment showed an increase in tactual acuity and in sensitivity to heat and pain. This cutaneous supersensitivity was still present several days after the termination of visual deprivation.*

Exposure of human subjects to prolonged periods of sensory and perceptual deprivation can result in a variety of behavorial and physiological changes (*1*). One of the most perplexing of these is an increase in pain sensitivity (*2*) and in tactual acuity as measured by both a two-point (smallest distance separating two points of sensitivity) threshold (*3*) and a tactual fusion method (*4*). This increase in cutaneous sensitivity, which represents the only clear instance of supersensitivity following sensory isolation, is quite pronounced. Furthermore, it seems to occur in all, or almost all, experimental subjects. The purpose of this study was to demonstrate that an overall reduction in the level of visual, auditory, tactual-proprioceptive, and social stimulation is not essential for the appearance of this phenomenon. It can occur after visual deprivation alone.

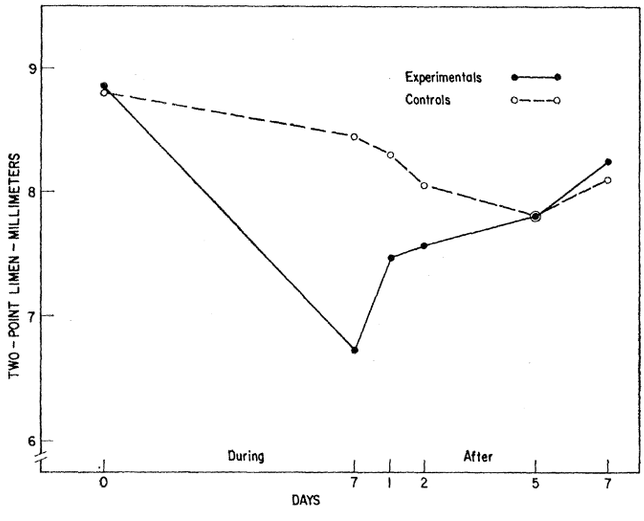
Sixteen male university students, each wearing a black mask, were placed in groups of two in an ordinary room for a period of 1 week. Apart from the exposure to constant darkness, their environment was quite normal. No gloves were worn and no restrictions were placed on their motor activity or on conversation with one another or with the experimenters. Furthermore, a radio was available in the room at all times. It was frequently in use. There were no failures; all 16 subjects successfully endured the week of darkness.

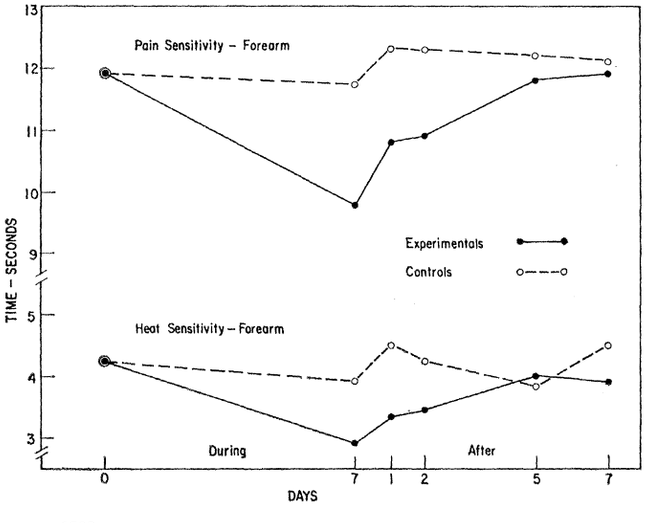
Measures of tactual acuity were taken from the palm, index finger, and forearm before and immediately after

the week of darkness as well as at intervals of 1, 2, 5, and 7 days after the termination of visual deprivation. The sensitivity of the palm was determined by the two-point threshold technique. The method of limits was used with two ascending and two descending series on each palm. One stimulation in every five was a "check test" in which only one point of the esthesiometer was used. The sensitivity of the index finger and forearm was measured by a fusion or "flicker" technique, described in an earlier publication (*5*). In this method an interrupted jet of air, at a specified pressure, is directed at the skin; the frequency of the air jet can be systematically increased until the subject reports a constant sensation of pressure. This threshold value is referred to as the critical frequency of percussion (CFP). Four experimental trials were given on each index finger and on the volar surface of each forearm, 8 cm below the elbow. All stimuli were presented in an ascending order and at a tank pressure of 1.4 kg.

In addition to tactual acuity, sensitivity to heat and pain was measured on the forearm, before and after the week of darkness, by the Hardy, Wolff, and Goodell dolorimeter (*6*). The basal setting for the instrument was 100 mcal cm^{-2} sec^{-1} for a skin temperature of 34°C. A correction was made in the basal setting if the skin temperature differed from 34°C by more than ±0.50°C. The subjects were asked to indicate when they felt the first sensation of warmth and, subsequently, when they experienced the first sensation of pricking pain. The latency, in seconds, was measured by a Hunter Klockounter and a Standard high-speed timer. Both instruments were activated by the onset of the stimulus of radiant heat. Four heat and four pain trials were given on each forearm with the trials separated by a 1-minute interval. Practice trials on the various cutaneous measures were given a day before the experimental session. For purposes of statistical analysis, the predeprivation scores of the 16 experimental subjects, on the five cutaneous measures, were matched with the initial scores of 16 out of 30 control subjects. From this larger sample of controls it was possible to select a group of 16 subjects whose scores before deprivation were approximately the same as those of the experimental subjects. These control subjects received the same cutaneous tests and at the same time intervals as the experimental subject but they were never visually deprived. Two-tailed *t*-tests for correlated measures were used in the statistical analysis.

Figure 1 indicates that the experimental subjects, after a week of visual deprivation, showed a pronounced increase in tactual acuity of the palm in relation to that of the controls ($p < .001$). Furthermore, there are suggestions that this effect was still present 2 days after termination of visual deprivation. However, only the difference measured on the first day is significant ($p < .05$). Figure 2 indicates that the tactual acuity of the index finger





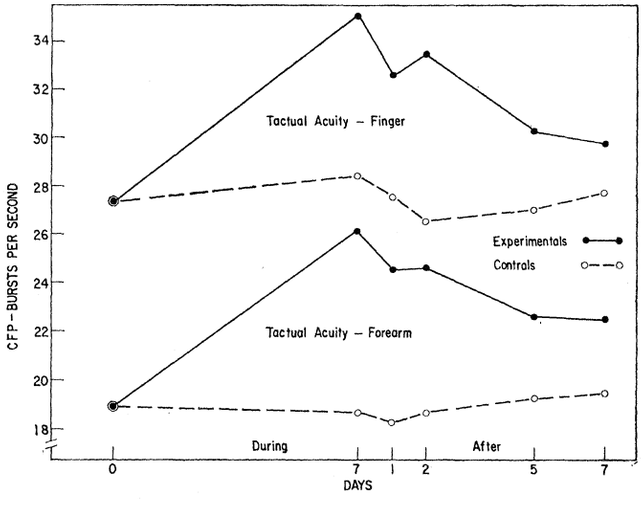


Fig. 1 (left above). Tactual acuity of the palm as measured by a two-point threshold method before and after a week of darkness, and 1, 2, 5, and 7 days later. Fig. 2 (right above). Tactual acuity of the index finger and forearm as measured by a fusion method before and after a week of darkness, and 1, 2, 5, and 7 days later. CFP, critical frequency of percussion. Fig. 3 (left). Heat and pain sensitivity of the forearm before and after a week of darkness, and 1, 2, 5, and 7 days later.

and forearm acuity of the index finger of darkness (in each test, $p < .001$). Again, the aftereffects seemed to persist for a number of days. However, for the finger, only the differences observed on days 1 and 2 are significant (in each test, $p < .01$); for the forearm, the day-7 difference is still significant ($p < .05$). In the case of the forearm, however, the unusually long aftereffect may partly be due to a change in standard of judgment. Finally, Fig. 3 shows that not only did tactual acuity increase but also sensitivity to heat and pain (in each test, $p < .01$). Furthermore, this supersensitivity still persisted on day 2 for pain ($p < .05$) and on day 1 for heat ($p < .05$).

An examination of the individual performance of the 16 experimental subjects revealed that the effect of visual deprivation was uniform. The supersensitivity was shown by all subjects, on all skin areas, and on all cutaneous measures. On the other hand, the control subjects exhibited a chance distribution of increases and decreases in sensitivity. It is of interest that the subjects' spontaneous remarks seem to support some of the experimental results. Several individuals reported that during darkness the soles of their feet or their arms were very sensitive. One subject also stated that he was ticklish for the first time in his life. There were also indications of auditory hyperacuity. Several subjects reported, on their return home, that the radio was unusually loud. It is possible, therefore, that a general enhancement of sensory functioning may occur as a result of visual deprivation. This possibility is currently under investigation.

These results suggest that a severe reduction in sensory input from several modalities may not be essential for the appearance of cutaneous supersensitivity and of certain other deprivation phenomena. Some of these may be specific to a particular sense modality or, alternately, may be produced by interference with any one modality. In this regard, it is interesting to note that diminished proprioceptive stimulation alone can produce many of the classical deprivation effects (*7*). These results on cutaneous supersensitivity also suggest that one of the effects of the functional deafferentation produced by the visual deprivation technique may be to "sensitize" certain areas of the central nervous system. Some support for this hypothesis is offered by Grey Walter (*8*) who reported that in some congenitally blind children the nonspecific cortical responses evoked by tactile and auditory stimuli are unusually large in relation to those of sighted children of the same age. Krech *et al.* (*9*) have also demonstrated that rats, subjected to peripheral blinding at the time of weaning, subsequently show an increase in the weight and cholinesterase activity of the somesthetic cortex. Furthermore, Krech (*10*) recently observed similar somatosensory changes in sighted rats reared in darkness. Thus, it would appear that visual deprivation alone can produce cortical changes of a type which could result in cutaneous supersensitivity. Whether the cortical changes in man, however, are similar to those reported by Krech is open to speculation, particularly in the light of our short deprivation period.

Although some of the studies on blind organisms appear to support our findings, others do not. For example, if pronounced increases in cutaneous sensitivity can occur after only a week of darkness, similar or even greater increases might be expected in blind human subjects. This, however, does not appear to be the case. What literature is available is contradictory in nature, both increases and decreases in sensitivity being reported (*11*). Although the reasons for this discrepancy are not clear, our results, together with those of Krech, suggest that perhaps a "new look" at the centuries-old controversy over sensory compensation in the blind may be justified.

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Prevention of a Mental Defect of Phenylketonuria with Serotonin Congeners such as Melatonin or Hydroxytryptophan

Abstract. *Mice made phenylketonuric from birth until maturity by continuous administration of phenylalanine plus tyrosine had a subnormal maze-learning ability which was largely prevented when serotonin congeners such as melatonin or 5-hydroxytryptophan were administered continuously from birth to maturity. These results were interpreted to mean that the mental failure of experimental phenylketonuria is attributable to the serotonin deficiency imposed by it in infancy.*

In previous papers (*1–3*) we have presented evidence to suggest that the mental defect of the inherited idiocy of phenylketonuria is the result of a serotonin deficiency imposed in infancy. In this paper we want to offer direct proof of this idea by showing that the mental defect can be prevented (at least in part) through correction of the serotonin deficiency by means of continuous administration of those serotonin congeners which can penetrate into the brain and act there. All of these experiments have been done in laboratory animals (mice) because the nature of the disease in human beings is such that it is impossible to make the trials with them. Because an effective preventative treatment is available for human beings (the phenylalanine-low diet) it would be morally unjustifiable not to use it in preference to some other treatment.

Phenylketonuria was produced in newborn mice by the method previously described (*1*). It consisted of continuous oral administration of DL-phenylalanine and L-tyrosine from birth to maturity. Whenever a serotonin derivative was to be tested, it was also administered continuously from birth to maturity. Care was taken that all animals (controls as well as test) were handled to the same extent so as not