indicated by the observation that the width at half-height of the radiochemical peak is more than twice that of the corresponding chemical peak (*7*).

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References and Notes

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Sensitivity of Hamster to Colchicine

In 1952, Orsini and Pansky (*1*) reported that hamsters seem to possess a natural resistance to colchicine. They found that the hamster would survive when it was injected with dosages ranging from 0.12 to 10 mg per 100 g of body weight. Upon noting this work, we undertook an investigation to discover the lethal dosage for the hamster and to note any gross effects that might occur (*2*).

Young mature males 10 to 12 weeks of age were used for the entire series. The animals were deprived of food for 24 hours before injection but were allowed water at liberty. The weights, dosage, and subsequent history of the animals were recorded, and all animals were injected intraperitoneally in the morning.

Several animals were injected with dosages up to 10 mg/100 g of body weight, and no outward effects of the drug were noted. At the 15-mg level, slight paralysis and loss of weight were observed. The dosage was increased to 30 mg and increased by 10-mg steps thereafter. With the 30- and 40-mg dosages, all animals displayed slight paralysis in the rear quarters, drowsiness, inability to maintain equilibrium, and a marked loss of weight. The severity of these symptoms increased with increased dosages. When given 50 to 70 mg/100 g of body weight, the majority of the animals went into a coma preceded by paralysis and surges of transient tetany, from which they did not recover. One of the animals that received 50 mg and two of those that received 60 mg displayed severe nasal hemorrhages before death. No diarrhea or bloody stools were present, as has been reported for the rat (*2*). The results are recorded in Table 1.

On autopsy, pinpoint hemorrhages were present on the small and large intestines. Histological sections were made of the small intestines to observe any mitotic variation. In all cases there was a marked increase in the number of metaphase figures and an absence of spindle fibers in many cells.

Eleven males which survived the previous treatment were kept to observe any latent effects that might develop. The animals were checked, weighed, and placed with females in heat many times during the following 6 months. The males that received the 50- and 60-mg dosages never regained the tremendous weight lost, and two of the animals that received 60-mg dosages died within 3 months. Animals of these groups were hypersensitive and unsure of balance, as if their nervous or muscular system, or both, had been affected. Animals of the groups that received 30- and 40-mg dosages appeared normal and regained most or all of the weight lost.

None of the 11 males which received from 30 to 60 mg/100 g of body weight mounted a female, but all would go through the preliminary actions of breeding. However, males that received a dosage of 15 mg/100 g of body weight were fertile. Six months after the beginning of the experiment, the animals were sacrificed. In the two that had received 60-mg dosages, the following conditions were noted: the liver adhered to the diaphragm, the intestines were adhered to themselves and to the body wall, and the testes were approximately one-half of normal size. In the other groups, adhesions were not as evident and occurred only among the intestinal loops.

Histologically, the testes of these animals showed a conspicuous absence of secondary spermatocytes, spermatids, and spermatozoa. In many instances all cell types were sloughed in clumps into the lumen of the tubules. The secondary spermatocytes, spermatids, and sperm were completely absent in about one-third of the tubules of the groups that received 60 mg dosages but ranged to near normal in the group that received 30 mg dosages.

From the data given it is evident that the lethal dosage of colchicine for the hamster is approximately 70 mg/100 g of body weight. The presence of paralysis and the loss of consciousness indicate that the effects of colchicine on the nervous system are the main factor causing death. Colchicine will cause an arrest of cell mitosis in the metaphase stage in the hamster. In other work (*3*) the following is shown: (i) the effect of colchicine on the mitotic index of the crypts of Liberkühn at the 1 mg/100 g dosage level; (ii) the optimal dosage for maximal arrested metaphases; (iii) dosages that inhibit reproduction in the female; (iv) dosages that cause resorption of the fetuses in late pregnancy (*4*).

Table 1. Survival of hamsters following administration of various dosages of colchicine.

Dosage (mg/100 g of body wt.)	No. in group	Deaths		Survivals (No.)
		No.	Time after injection (hr)	
30	4			4
40	4	1	27	3
50	5	1	30	3
		1	45	
60	8	1	2	5
		1	3	
		1	108	
70	8	3	0.5	0
		2	2	
		2	3	
		1	45	
75	5	2	0.5	0
		2	2	
		1	3	

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References and Notes

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2. Colchicine was obtained from the Nutritional Biochemicals Corp., Cleveland, Ohio.
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4. This investigation was supported in part by research grant RG4473 from the National Institutes of Health, U.S. Public Health Service.

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Alpha-Rhythm Responsiveness in Normal, Schizophrenic, and Brain-Damaged Persons

Routine examination of electroencephalographic records does not show that the electroencephalograms of schizophrenics differ in any consistent manner from those of normal patients (*1*). However, more active electroencephalographic techniques which introduce experimental variables in order to test for electroencephalographic changes hold more promise. Berger (*2*) long ago noted that sensory stimulation produced alpha blocking among normal persons. Later, Liberson (3) reported less reduction in alpha activity in response to light (a flash every 2 seconds) among catatonics than among psychoneurotics. Mundy-Castle (*4*) has emphasized the usefulness of more rapid photic stimulation, capable of producing alpha driving (increased amplitude or change in frequency) for

Table 1. Alpha responsiveness to stimulation.

Group	Number responding to stimulus						
	Visual	Auditory	Photic			Synchrony	Rest
			10-sec	20-sec	40-sec		
Normals	22	6	22	19	18	18	10
Schizophrenics	28	3	26	28	20	22	13
Brain-damaged	11	1	7	9	6	8	3

relating abnormal electroencephaiograms to deviation in behavior. Consistent with Liberson's observation of reduced response in psychotics, Rubin (*5*) has found fewer slow-wave responses to hyperventilation among psychotics than among normals.

In a preliminary paper (*6*), I have described observations of consistent imagery and electroencephalographic differences in response to photic stimulation among schizophrenic, normal, and brain-damaged persons. Schizophrenics resembled organics and differed from normal subjects in their reduced responsiveness in the production of patterns, colors, and depth movement aspects of visual images. Both patient groups reported fewer felt emotions accompanying stimulation and imagery than did normals. In addition, schizophrenic and brain-damaged patients failed to show as much change in alpha rhythm, either blocking or drive, in response to photic stimulation as did the normal subjects.

The present research (*7*) has concentrated on repeating—with more adequate instruments and samples—the observations on electroencephalographic response to stimulation. The problem was to test the hypothesis that schizophrenics will resemble brain-damaged patients in their failure to show normal responsiveness of the alpha rhythm to visual, auditory, and photic stimulation.

The sample consisted of 24 normal subjects (mean age, 38), 20 schizophrenics on tranquilizing drugs (mean age, 39), 20 schizophrenics not on tranquilizers (mean age, 40), and 20 brain-damaged patients (chronic brain syndrome, mean age, 66). The two schizophrenic groups were roughly matched for severity of illness. Age matching, which would have been desirable (*8*) was not feasible for the organic group.

Table 2. Chi-square categories.

Group	No.	No. responding to 6 or more stimulus conditions	No. responding to 5 or less stimulus conditions
Normals	24	11	13
Schizophrenics on tranquilizers	20	3	17
Schizophrenics not on tranquilizers	20	4	16
Brain-damaged	21	1	20

A Grass model III electroencephalograph machine and a Grass photic stimulator were employed. Two occipital electrodes with a lead to the right ear allowed bipolar and monopolar recording. Normal resting rhythms were established for each subject. Each period of stimulation was followed by a period of rest. The stimulation methods and the duration were as follows: 1-minute of eyes-open visual stimulation (looking at pictures); 1-minute of auditory stimulation (eyes closed listening to word association list); 30-seconds of photic stimulation at 10 flashes per second; 30-seconds of 20 flashes per second photic stimulation; 30-seconds of 40 flashes per second photic stimulation; and 1-minute of synchronized photic stimulation in which the subject's own alpha rhythm peaks served to trigger the flash.

Records were inspected to establish the responsiveness of the brain waves to each of the six stimulating conditions. In addition, responsiveness (suppression) of alpha rhythm at the onset of each rest was analyzed.

Since it has been shown (*9*) that the low reliability of judgments of electroencephalograms is a major problem, a second judge made independent ratings of the records on a random sample of 12 subjects (84 separate judgments). There was agreement between the two judges on 85 percent of the ratings. This is deemed satisfactory reliability.

Table 1 presents the results. Patients were categorized into those showing alpha change (drive, blocking) in response to six stimulating conditions (out of seven possible ones, including rest) and those showing responsiveness to less than six stimulating conditions. There were no significant differences between the groups with regard to the presence of normal resting alpha rhythm. The differences between schizophrenics on tranquilizing drugs and those not on tranquilizers were not significant, so the results obtained from these two groups have been combined. The Chi-square test was applied (see Table 2). The normals showed significantly greater alpha responsiveness to stimulation than did schizophrenics ($P = 0.05$). Normals showed significantly more alpha responsiveness than did organics ($P = 0.02$). Differences between schizophrenics and brain-damaged patients were not significant.

Schizophrenics resemble brain-damaged patients in their lack of brain-wave responsiveness to stimulation. Tranquilizing drugs appear to have no effect on responsiveness. That psychotics are often behaviorally unresponsive to stimulation has long been clinically observed. That their brain rhythms are now found also to be unresponsive is consistent with Pavlov's claim that schizophrenia was a protective inhibition of the cerebral cortex in the face of excessive traumatizing bombardment with stimuli. It is also consistent with more recent findings (*10*) which demonstrate the existence of a reticular excitatory center important for arousal and behavioral response to sensory stimuli. It has been shown (*11*) that this reticular region is subject, to some extent, to influence from the cortex.

One can surmise that in schizophrenia there are actual changes in brain function which closely resemble the states produced by demonstrable pathology in organic patients. The changes in schizophrenics appear to consist of a reduction in cortical responsiveness to external stimulation, possibly owing to the inhibition of afferent input in the reticular arousal centers. Whether or not the apparent inhibition of input in schizophrenics represents metabolic or tissue pathology in the excitatory center, or whether it represents learned inhibition through cortical influence, remains unknown (*11*).

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