Table 1. Disappearance duration, both/total ratio, and scale values for single forms and pairs. McG, McGill University; CU, Cornell University.

Form	Mean disappearance (sec)	Complexity	Similarity		Both/total (%)
			McG	CU	
A	83.3	14.7			
B	48.4	10.0			
C	31.8	13.9			
A	26.7				
B	28.2		14.4	2.7	9.2
Total (A or B)	46.7				
B	65.4				
C	49.4		10.0	1.7	15.0
Total (B or C)	92.4				
A	111.4				
C	96.8		4.9	0.6	24.8
Total (A or C)	144.6				

agreement between independent similarity estimates and the correlation between similarity and mean disappearance duration is obvious. The difference between McGill scaling estimates for pairs AB and AC was highly significant ($t = 15.9$, df 38, $P < .001$, t-test for correlated samples) and both estimates were significantly different from the standard of 10 ($t_{AB} = 9.2$, $t_{AC} = 11.4$, df 38, P's $< .001$). Coefficients of concordance (Kendall's W between observer's rankings) for the Cornell scaling ranged from .44 to .48 ($P < .01$).

There was no significant difference between mean disappearance duration for left and right fields, but the single forms showed a predominance of left-field disappearance (mean right-left duration difference, summed over both periods is −4.91 seconds), while the form pairs showed a predominance of right-field disappearance (mean right-left duration difference is 8.7 seconds). The mean (R − L) difference between single forms and pairs was almost significant ($t = 1.88$, df 62, $P < .1$).

Mean disappearance duration for form A alone (73.5 sec) was significantly greater than mean duration for C (31.7 sec, $t = 2.15$, df 20, $P < .05$), but the other differences between single forms were not significant. Neither were the differences between complexity estimates obtained for forms A (14.7) and C (13.9), although both were estimated as significantly more complex than the standard form B ($t_{A\text{-}B} = 6.7$, $t_{C\text{-}B} = 5.1$, df 38, P's $< .001$).

If disappearances under reduced stimulation are caused by cell fatigue (*1*), then the correlation between similarity and disappearances is understood by assuming that similar forms will excite in common a high proportion of cells, particularly at higher levels in the visual system hierarchy (*5*). High similarity means a smaller total population of cells stimulated and maximum input to those which are stimulated. This is the best opportunity for excited cells to become refractory, producing visual disappearances. High overlap should also mean high correlation between the disappearances of each stimulus; fatigue of cells for one stimulus will mean fatigue of cells for the other. The percentage of the time during which either form disappears that both forms disappear together, assuming that each form's disappearance is independent, equals $p_x p_y / (p_x + p_y - p_x p_y)$, where p_x and p_y are the percentages of disappearance for each form. This value was calculated for each subject and subtracted from the obtained percentage to give a corrected figure which is an index of the correlation between disappearances of the two forms. The mean corrected percentage (both/total) disappearances for the three form pairs is given in Table 1, and it increases with increasing similarity, although none of the differences are significant.

Linear extrapolation from Fig. 1 suggests a maximum disappearance duration of 190 sec for identical forms (distance = 0). There are in fact differences between disappearance duration for single forms, and identical pairs will probably be found to differ in mean disappearance duration as well. With similarity held constant, and with an adequate complexity scale, mean total disappearance should be an inverse function of form complexity—a scaled correlate of the width and breadth of the cell hierarchy stimulated by a form pair.

An alternative peripheral hypothesis suggests that dissimilar forms induce more gross eye movements than similar ones, and that these movements interrupt disappearances and shorten the mean duration for dissimilar pairs. Replication of these findings under optical stabilization, or with concomitant eye-movement recording, can resolve this uncertainty.

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Pentylenetetrazol Enhances Memory Function

Abstract. *Pentylenetetrazol, in oral doses of 1 to 30 milligrams per kilogram of body weight, significantly facilitated one-trial learning and memory retention in CF1 mice, whether administered before or immediately after the initial trial. The effects appeared significantly greater than those observed in earlier studies with oral administration of strychnine or picrotoxin at 0.2 to 0.8 and 2.4 milligrams per kilogram, respectively.*

There is great interest in finding drugs that can improve memory function, both as tools for research and for therapy. Lashley (*1*) was the first to report facilitation of maze learning by a drug—strychnine. This finding was confirmed for strychnine (*2*) and later

for picrotoxin (*3*). The dosage required for this effect, however, approached the toxic and was unacceptable for humans. Using a one-trial learning procedure, we have observed even greater effects on learning by pentylenetetrazol (Metrazol) at dosages commonly used to treat geriatric patients, whether oral administration preceded or immediately followed the initial experience. This report compares the effects of pentylenetetrazol with previously developed data for strychnine and picrotoxin (*4*).

Male CF1 mice aged 9 to 10 weeks were systematically randomized into treatment groups, housed in the experimental room for 16 hours before testing and throughout the study, and fasted for 3 to 4 hours before testing. For testing, the animals were placed in a narrow compartment (5 by 17.5 cm), with a grid floor, separated from a larger compartment (20 by 17.5 cm) by a hurdle 2.5 cm high. The animals normally crossed this hurdle with a mean of about 30 seconds on repeated trials; those failing to cross within 50 seconds on the first trial were eliminated from the study. If the mice received a foot shock (0.2 ma, 2 seconds) immediately after crossing the hurdle, they showed an increased latency for crossing during subsequent testing; the increase varied as a function of the time interval between tests (*5*). Except for special time-response studies, drug was orally administered immediately after the first trial, when the animals were returned to their home cages to be retested 27 hours later, with a 180-second cutoff time for response.

For the special studies with pentylenetetrazol and strychnine, different treatment groups of eight animals each received drug 30 minutes before or immediately after the first trial; their second trial came at various times after the first trial: 0, 5, 15, 30, or 90 minutes or 24 hours later. A control group received drug but no foot shock, to determine the effect of drug alone. Dosage was calculated as the free base, and the data were analyzed by the Wilcoxon rank-sum test (*6*).

Table 1 summarizes the results of several studies with strychnine and picrotoxin; Table 2, our results with pentylenetetrazol. The data show that memory retention was significantly improved by pentylenetetrazol at 1 to 30 mg/kg; effect was maximum at about 3 mg/kg. Memory was improved significantly by strychnine (0.2 to 0.8 mg/kg) or picrotoxin (2.4 mg/kg), but less markedly than by pentylenetetrazol—and less consistently reliable. In separate studies, convulsions, with or without death, required about 2 mg of strychnine, 12 mg of picrotoxin, or 200 mg of pentylenetetrazol (all per kilogram).

Previous studies (*5*) have shown a biphasic time-response curve for one-trial learning, evident in the saline data of Fig. 1. It was considered that the first response curve might reflect short-term memory retention, with rapid de-

Table 1. Strychnine and picrotoxin: mean latencies for hurdle-crossing.

Mice (No.)		Mean latency (sec)								
Exp.	Control (saline)	Strychnine (mg/kg)						Picrotoxin (mg/kg)		
		0.025	.05	.1	.2	.4	.8	0.6	1.2	2.4
40	46	48	60	76*	78*					
40	43		57	45	54	63				
40	59		51	58	52	80				
40	39				71*		89*	40	41	
40	43				76		57		41	73*

* $p < .05$.

Table 2. Pentylenetetrazol: mean latency for hurdle-crossing.

Mice (No.)		Mean latency (sec)						
Exp.	Control (saline)	Pentylenetetrazol (mg/kg)						
		1	3	7.5	10	15	30	60
40	47	76*	92*		46		54	
40	44	94†	111†		74*		85†	
16	36		64*					
16	56		116*					
16	81		108					
16	36				92*			
40	51			78*		81*	68†	56

* $p < .05$. † $p < .01$.

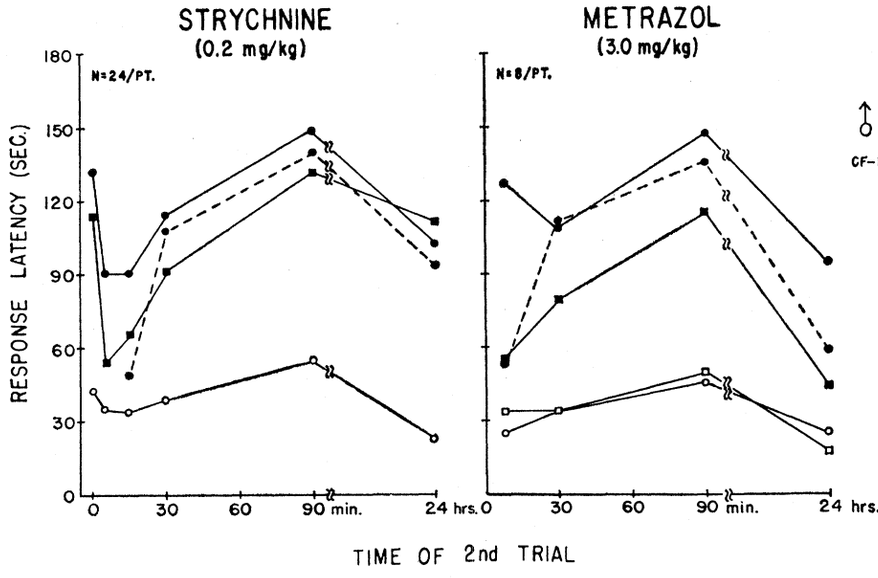

Fig. 1. Time-response curves for memory retention after treatment with strychnine or pentylenetetrazol (Metrazol). Each point represents a group of animals treated 30 minutes before (solid line) or immediately after (broken line) the first trial; a second trial followed at the intervals shown. Circles, drug-treated groups; squares, saline controls; open symbols, no foot shock; solid symbols, received foot shock during the first trial. Statistically significant in second-trial facilitation at the $p < .05$ level were: the 8-minute pretrial and 24-hour pretrial and post-trial pentylenetetrazol responses, and the 5-minute pretrial strychnine response.

cay (as in remembering a sequence of numbers), the second curve reflecting perhaps the actual process of "consolidation" of the memory trace for longer-term storage and retrieval. Parenthetically, we have also found the apprehension levels of the animals (subjectively rated on a blind basis during the first 15 seconds before crossing the hurdle) to directly correlate with latencies for hurdle-crossing—for example, to be lowest approximately 5 minutes after the foot-shock stimulus.

From this framework it was of interest to determine the effects of strychnine and pentylenetetrazol on the biphasic response curve—that is, whether the agents accelerated the presumed "consolidation" process. Administration of strychnine (0.2 mg/kg) or pentylenetetrazol (3 mg/kg) 30 minutes before the first trial produced no change in the hurdle-crossing latency of animals not receiving a foot shock (Fig. 1). In animals receiving a foot shock, however, pretreatment with pentylenetetrazol completely prevented "memory" decay of the first phase and significantly increased the response latencies for all intervals of testing. Strychnine, in three separate studies with similar results (integrated in Fig. 1), produced comparable effects of lower magnitude. With both drugs, facilitation of one-trial learning appeared greater when administration preceded rather than followed the learning experience.

The dosage of pentylenetetrazol that facilitated one-trial learning in the mouse approximated 1/100th to 1/200th of the convulsant dose; thus facilitation cannot be readily ascribed to the mechanisms underlying its convulsant action. However, since other convulsants such as strychnine and picrotoxin also facilitate one-trial learning, such mechanisms cannot be ruled out entirely. Eccles *et al.* (*7*) have shown that the three agents differ significantly in their neurophysiologic modes of action: strychnine blocks postsynaptic inhibitory pathways, picrotoxin blocks presynaptic inhibition, and pentylenetetrazol blocks neither presynaptic nor postsynaptic inhibition. The excitatory effect of pentylenetetrazol on the nervous system seems rather to result from decrease in neuronal recovery time (*8*), without reference to inhibitory pathways; effects of small doses on behavior may derive from this acceleration of neuronal and synaptic transmission throughout the nervous system, as well as from possible specific regional effects on the brain that remain unknown.

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Organic Matter in Carbonaceous Chondrites

In a recent article, Studier, Hayatsu, and Anders (*1*) report mass spectrometric analyses of volatile compounds from the Orgueil meteorite and interpret the results as due to the establishment of chemical equilibrium in the solar nebula. In a subsequent review article, the impression was given that this was a very definitive piece of work (*2*). We should therefore like to express our criticisms.

1) The analytical data are very approximate and are compared to theoretical data which are based on an improbable postulate. Mass spectrometric data on a complex mixture of carbonaceous compounds lead to an exceedingly complex spectrum of molecular fragments, and it is very difficult to sort out the possible compounds present. This was true when Nagy *et al.* (*3*) previously reported similar mass spectrometric analyses, and, in fact, the analytical data were severely criticized on these grounds by Anders (*4*). Studier *et al.* attempted in no way to present the original data and gave only their final results, expressing them only in very qualitative terms. The data as presented could hardly be expected to establish a quantitative agreement with any theory for the formation of these compounds. No attempt has been made to justify even the qualitative character of these analyses. Some of the criticisms that Anders directed against the previous work must be applicable to the work of Studier *et al.*, as well as any other similar mass spectrometric work on this material.

The qualitative analyses for some 16 compounds consisting only of positive and negative signs are compared with the corresponding calculated concentrations of Dayhoff, Lippincott, and Eck (*5*), which vary by a factor of 10^6 for those reported as present in the meteorites. Moreover, their equilibrium calculations were made on the assumption that graphite did not appear. This is an *ad hoc* assumption which we regard as doubtful. It seems improbable that chemical reactions producing very complex molecules such as benzene, naphthalene, anthracene, xylene, and others, could take place in spite of the fact that, under the postulated conditions, graphite is exceedingly stable thermodynamically (see Table 1). It is true that carbonaceous compounds persist on the earth through long periods of time, and possibly at 500°K, without graphite having appeared, but these compounds were not made by equilibrium processes but by the very nonequilibrium processes of living organisms. We object to the hypothesis of an *equilibrium* origin of the compounds in the *absence* of graphite. It would appear that very qualitative analytical data have been compared to a theory in which an arbitrary assumption, that is, the absence of graphite, is made.

2) The physical conditions and the composition of materials assumed by Studier *et al.* are improbable and difficult or impossible to attain in the solar nebula. They assume that a condition existed in the nebula with a high total pressure and a temperature of about 500°K, the constituents of the atmosphere being principally hydrogen, carbonaceous compounds, oxygen compounds, and nitrogen compounds, making a total pressure of one atmosphere, with hydrogen depleted very markedly from all estimates of solar abundances.