

of dissociation can be clearly recognized; in such instances the entry includes two (or more) rows specifying the relations between the different aggregates.

In some instances an arbitrary decision has been made regarding the "natural" molecular weight, since some proteins form aggregating as well as disaggregating systems. Some such systems, such as the seed proteins, have been omitted entirely from Table 1 because it is still difficult to decide what is their "natural" state.

The most accessible references are given for each entry; they do not necessarily include the source most deserving of credit for establishing the subunit interrelations; such sources are mentioned in the cited works. Certain reviews (1) give less-complete compilations with more details for individual proteins.

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#### References

1. F. J. Reithel, *Advan. Protein Chem.* **18**, 123 (1963); H. Sund and K. Weber, *Angew. Chem. Intern. Ed. Engl.* **5**, 231 (1966).
2. D. Crowfoot, *Proc. Roy. Soc. London A* **164**, 580 (1938); L. S. Moody, dissertation, Univ. of Wisconsin, 1944; D. Waugh, *Advan. Protein Chem.* **9**, 359 (1954).
3. J. A. Gladner, K. Laki, F. Stohlmann, *Biochim. Biophys. Acta* **27**, 218 (1958); C. R. Harmison, R. H. Landaburu, W. H. Seegers, *J. Biol. Chem.* **236**, 1693 (1961); E. E. Schrier, C. A. Broomfield, H. A. Scheraga, *Arch. Biochem. Biophys. Suppl.* **1**, p. 309 (1962); L. Lorand, W. T. Brannen, Jr., N. G. Rule, *ibid.* **96**, 147 (1962); D. J. Winzor and H. A. Scheraga, *ibid.* **104**, 202 (1964).
4. H. B. Bull, *J. Amer. Chem. Soc.* **68**, 745 (1946); R. Townsend and S. N. Timasheff, *ibid.* **79**, 3613 (1957).
5. N. M. Green, *Biochem. J.* **89**, 609 (1963).
6. G. Braunitzer, K. Hilde, V. Rudloff, N. Hilschmann, *Advan. Protein Chem.* **19**, 1 (1964).
7. G. Pfeleiderer and F. Auricchio, *Biochem. Biophys. Res. Commun.* **16**, 53 (1964).
8. W. C. Deal and W. H. Holleman, *Federation Proc.* **23**, 264 (1964).
9. A. Garen and C. Levinthal, *Biochem. Biophys. Acta* **38**, 470 (1960); M. J. Schlesinger, *Brookhaven Symp. Biol.* **17**, 66 (1964).
10. J. A. Winstead and F. Wold, *Biochemistry* **3**, 791 (1964); **4**, 2145 (1965).
11. H. Theorell and A. D. Winer, *Arch. Biochem. Biophys.* **83**, 291 (1959); T. K. Li and B. L. Vallee, *Biochemistry* **3**, 869 (1964).
12. J. R. Brown, R. N. Greenshields, M. Yamasaki, H. Neurath, *Biochemistry* **2**, 867 (1963).
13. J. Travis and W. D. McElroy, *ibid.* **5**, 2170 (1966).
14. A. Ramel, E. A. Barnard, H. K. Schachman, *Angew. Chem.* **76**, 55 (1964).
15. I. M. Klotz and S. Keresztes-Nagy, *Biochemistry* **2**, 445, 923 (1963).
16. V. Henning, D. R. Helinski, F. C. Chao, C. Yanofsky, *J. Biol. Chem.* **237**, 1523 (1962); B. C. Carlton and C. Yanofsky, *ibid.* p. 1531; D. A. Wilson and I. P. Crawford, *Bacteriol. Proc.* **1964**, 92 (1964).
17. H. R. Levy, R. R. Raineri, B. H. Nevaldine, *J. Biol. Chem.* **241**, 2181 (1966).
18. J. I. Harris and R. N. Perham, *J. Mol. Biol.* **13**, 876 (1965).
19. E. Stellwagen and H. K. Schachman, *Biochemistry* **1**, 1056 (1962); W. C. Deal, W. J. Rutter, K. E. van Holde, *ibid.* **2**, 246 (1963); H. K. Schachman and S. J. Edelstein, *ibid.* **5**, 2681 (1966).
20. E. Appella and C. L. Markert, *Biochem. Biophys. Res. Commun.* **6**, 171 (1961); T. P. Fondy, A. Pesce, I. Freedberg, F. Stolzenbach, N. O. Kaplan, *Biochemistry* **3**, 522 (1964).
21. I. Harris, *Nature* **203**, 30 (1964).
22. C. B. Kasper and H. F. Deutsch, *J. Biol. Chem.* **238**, 2325 (1963); M. D. Poulik, *Nature* **194**, 842 (1962); W. N. Poillon and A. G. Bearn, in *The Biochemistry of Copper*, J. Peisach, P. Aisen, W. E. Blumberg, Eds. (Academic Press, New York, 1966), p. 525.
23. H. R. Whiteley, *J. Biol. Chem.* **241**, 4890 (1966).
24. J. Durell and G. L. Cantoni, *Biochim. Biophys. Acta* **35**, 515 (1959); W. Klee, *ibid.* **59**, 562 (1962).
25. L. Kanarek, E. Marler, R. A. Bradshaw, R. E. Fellows, R. L. Hill, *J. Biol. Chem.* **239**, 4207 (1964).
26. V. Shore and B. Shore, *Biochem. Biophys. Res. Commun.* **9**, 455 (1962).
27. J. A. Hoch and B. D. De Moss, *Biochemistry* **5**, 3137 (1966).
28. A. Morawiecki, *Biochim. Biophys. Acta* **44**, 604 (1960); M. A. Steinmetz and W. C. Deal, Jr., *Biochemistry* **5**, 1399 (1966).
29. W. A. Schroeder, J. R. Shelton, J. B. Shelton, B. M. Olson, *Biochim. Biophys. Acta* **89**, 47 (1964); K. Weber and H. Sund, *Angew. Chem.* **77**, 621 (1965).
30. A. Hattori, H. L. Crespi, J. J. Katz, *Biochemistry* **4**, 1225 (1965); E. Scott and D. S. Berns, *ibid.*, p. 2597; D. S. Berns and A. Morgenstern, *ibid.* **5**, 2985 (1966).
31. H. S. Penefsky and R. C. Warner, *J. Biol. Chem.* **240**, 4694 (1965).
32. J. C. Gerhart and H. K. Schachman, *Biochemistry* **4**, 1054 (1965); H. K. Schachman and S. J. Edelstein, *ibid.* **5**, 2681 (1966).
33. G. Bernardi and W. H. Cook, *Biochim. Biophys. Acta* **44**, 96, 105 (1960); R. W. Burley and W. H. Cook, *Can. J. Biochem. Physiol.* **40**, 363 (1962).
34. T. Hofmann and P. M. Harrison, *J. Mol. Biol.* **6**, 256 (1963).
35. J. M. Creeth and L. W. Nichol, *Biochem. J.* **77**, 230 (1960); F. J. Reithel, J. E. Robbins, G. Gorin, *Arch. Biochem. Biophys.* **108**, 409 (1964).
36. N. B. Madsen and C. F. Cori, *J. Biol. Chem.* **223**, 1055 (1956).
37. P. W. Trown, *Biochemistry* **4**, 908 (1965); R. Haselkorn, H. Fernandez-Moran, F. J. Kieras, E. J. van Bruggen, *Science* **150**, 1598 (1965).
38. D. Zipser, *J. Mol. Biol.* **7**, 113 (1963); U. Karlsson, S. Koorajian, I. Zabin, F. S. Sjostrand, A. Miller, *J. Ultrastruct. Res.* **10**, 457 (1964); K. Weber, H. Sund, K. Wallenfels, *Biochem. Z.* **339**, 498 (1964).
39. W. W. Kielley and W. F. Harrington, *Biochim. Biophys. Acta* **41**, 401 (1960).
40. R. C. Valentine, N. G. Wrigley, M. C. Scrutton, J. J. Irias, M. F. Utter, *Biochemistry* **5**, 3111 (1966).
41. R. F. Steiner and H. Edelhoch, *J. Amer. Chem. Soc.* **83**, 1435 (1961); H. Edelhoch and B. de Crombrughe, *J. Biol. Chem.* **241**, 4357 (1966).
42. Y. Kaziro, S. Ochoa, R. C. Warner, J. Chen, *J. Biol. Chem.* **236**, 1917 (1961).
43. M. Koike, L. J. Reed, W. R. Carroll, *J. Biol. Chem.* **238**, 30 (1963); C. R. Williams and L. J. Reed, *Federation Proc.* **23**, 264 (1964).
44. C. Frieden, *J. Biol. Chem.* **237**, 2396 (1962); J. E. Churchich and F. Wold, *Biochemistry* **2**, 781 (1963); H. Sund, *Angew. Chem.* **76**, 954 (1964); E. Appella and G. M. Tomkins, *J. Mol. Biol.* **18**, 77 (1966).
45. S. M. Pickett, A. F. Riggs, J. L. Larimer, *Science* **151**, 1005 (1966); K. E. van Holde and L. B. Cohen, *Biochemistry* **3**, 1803 (1965); H. Fernandez-Moran, E. F. J. van Bruggen, M. Ohtsuki, *J. Mol. Biol.* **16**, 191 (1966); R. Lontie and R. Witters, in *The Biochemistry of Copper*, J. Peisach, P. Aisen, W. E. Blumberg, Eds. (Academic Press, New York, 1966), p. 455.
46. D. Guerritore, M. L. Bonacci, M. Brunori, E. Antononi, J. Wyman, A. Rossi-Fanelli, *J. Mol. Biol.* **13**, 234 (1965).
47. L. E. Bockstahler and P. Kaesberg, *Biophys. J.* **2**, 1 (1962).
48. R. Markham, *Discussions Faraday Soc.* **11**, 221 (1951); J. I. Harris and J. Hindley, *J. Mol. Biol.* **3**, 117 (1961).
49. F. A. Anderer and H. Restle, *Z. Naturforsch.* **19b**, 1026 (1964).
50. H. Yamazaki and P. Kaesberg, *Biochim. Biophys. Acta* **53**, 173 (1961).
51. J. J. Kellery and P. Kaesberg, *ibid.* **55**, 236 (1962); **61**, 865 (1962).
52. R. T. Hersh and H. K. Schachman, *Virology* **6**, 234 (1958).
53. M. E. Reichmann, *J. Biol. Chem.* **235**, 2959 (1960); ——— and D. L. Hatt, *Biochim. Biophys. Acta* **49**, 153 (1961).
54. F. A. Anderer, *Advan. Protein Chem.* **18**, 1 (1963); D. L. D. Caspar, *ibid.*, p. 37.
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## Activity and Responsivity in Rats after Magnesium Pemoline Injections

**Abstract.** Rats injected intraperitoneally with magnesium pemoline avoided a buzzing sound (conditioned stimulus) associated with an electric shock to the feet (unconditioned stimulus) more frequently than controls. Drug-injected rats did not avoid the foot shock more frequently than controls, although the experimental rats did have shorter response latencies in the active avoidance task. In subsequent experiments which measured activity changes and response to the buzzing sound alone, it was found that magnesium pemoline caused a lesser decrease in activity level and a more sustained responsivity to the buzzer's sound than did control injections of tragacanth. This may account for the latency differences observed in the avoidance task.

Recently, Glasky and Simon (1) reported that magnesium pemoline, a mild stimulant of the central nervous system, also stimulates the synthesis of brain RNA polymerases in the rat (2). Plotnikoff (3, 4) investigated the effects of oral administration of magnesium pemoline on the subsequent active

avoidance behavior of rats. In the first of these behavioral studies (3), it was reported that rats receiving this drug had shorter response latencies after the first trial in an active avoidance task, and that this difference was still present 24 hours later during a retention test. Plotnikoff concluded, on the basis of

Table 1. Mean ( $\pm$  S.D.) "jump-out" time (in seconds) and percent avoiding shock on day 1, slow and fast learners.  $N = 24$  in each group. No drug administered.

Slow learners		Fast learners	
Mean $\pm$ S.D.	Percent avoiding	Mean $\pm$ S.D.	Percent avoiding
<i>Trial 1</i>			
27.8 $\pm$ 1.8	0	27.8 $\pm$ 1.5	0
<i>Trial 2</i>			
27.1 $\pm$ 2.6	4.2	24.6 $\pm$ 5.2	21
<i>Trial 3</i>			
26.4 $\pm$ 2.4	12.7	11.5 $\pm$ 5.0	100

these and other data (4), that such behavioral differences were due to an enhancement of learning and memory in the drugged rats, presumably due to the RNA synthesis-stimulating effects of magnesium pemoline. The present report concerns an attempt to replicate Plotnikoff's findings (3) and to explore alternative explanations for the behavioral changes observed following administration of magnesium pemoline.

Our first experiment followed the procedure of Plotnikoff (3). Our apparatus consisted of a 30.5- by 30.5-cm wooden box. Wire screening, attached to one wall, provided the means of escape for the rats, allowing them to reach a 30.5- by 30.5-cm escape platform 30 cm above the grid floor of the box. A 1.5-ma electric current, delivered equally to all parts of the grid floor, served as the unconditioned stimulus. A buzzing sound, approximately 75 db, served as the conditioned stimulus.

The subjects were 48 experimentally naive male Sprague-Dawley rats, 70 to 75 days old, weighing 230 to 250 g. On day 1, following Plotnikoff's procedure (3), three test trials were given to select the slow learners, defined as subjects showing at most one avoidance during the three trials, jumping onto the escape platform only after the grid floor was electrified. Each trial was as follows: The rat was placed on the grid floor and 15 seconds later the conditioned stimulus was presented. The duration of the stimulus was 15 seconds, and during the last 5 seconds of the stimulus the grid floor was electrified (unconditioned stimulus) (see Table 1). On day 2, 24 hours later, the experimental subjects were injected intraperitoneally with magnesium pemoline (either 5, 10, or 20 mg/kg) suspended in 0.3 percent tragacanth (10 mg/ml). Control rats received equivalent volumes of the 0.3 percent tragacanth vehicle. Training trials began 30 minutes later and ten trials, 10 minutes apart,

were given. On day 3 a series of extinction trials (5) was given in which neither the unconditioned nor the conditioned stimulus was administered. Our procedure differed from that of Plotnikoff only in that: (i) tragacanth, rather than saline, was given to the control rats; (ii) the drug (magnesium pemoline) was administered intraperitoneally rather than orally [Plotnikoff had indicated, however, that the apparent enhancement of the acquisition effect can be obtained with intraperitoneal as well as oral administration (6)]; (iii) although the groups were analyzed separately, fast as well as slow learners were tested.

The results represent a partial replication of earlier reports. The rats treated with magnesium pemoline did have shorter average response latencies for the ten acquisition trials ( $p < .02$  for the slow learners and  $p = .05$  for the fast learners, Mann-Whitney U-test, two-tailed). These latency differences were not present on each trial, and were more noticeable on later trials (see Table 2).

The extinction results on day 3 differed from those of Plotnikoff (3). The groups given 5 or 10 mg of the drug per kilogram of body weight did typi-

cally have shorter response latencies, but these differences were not statistically significant, with the exception of the difference between the 10 mg/kg group and the tragacanth controls on trial 5 ( $p < .01$ , two-tailed). In general, however, no significantly improved "retention" was observed, and the 20 mg/kg group had in general longer response latencies than did the tragacanth controls (see Table 3).

Further analysis of the acquisition data in Table 2 revealed that while the rats injected with magnesium pemoline had shorter response latencies, a somewhat more meaningful measure of learning did not reveal any differences whatsoever. The drugged rats did not avoid the foot shock more often than the control rats, all groups displaying a high percentage avoidance. Typically however, the drugged rats jumped out of the box before the conditioned stimulus sounded, thus avoiding this stimulus (the buzzer) more often than control rats. Also, on the first acquisition trial, before any drug-enhanced learning could have occurred, the median response latency for the drug-injected rats was 10 seconds, as compared with 18 seconds for the tragacanth-injected controls. Thus 70 percent (25/36) of the

Table 2. The effect of magnesium pemoline (MgPe) on acquisition phase, in slow and fast learners. Results are mean times ( $\pm$  S.D.) in seconds for "jump-out" responses, and percent avoiding shock. The means of the ten trials given the groups of slow learners and the means of the nine trials given the groups of fast learners are shown in italic type. Abbreviation: n.s., not significant.

MgPe (5 mg/kg)		MgPe (10 mg/kg)		MgPe (20 mg/kg)		Tragacanth controls		$p^*$
Mean time	Avoiding shock (%)	Mean time	Avoiding shock (%)	Mean time	Avoiding shock (%)	Mean time	Avoiding shock (%)	
<i>Slow learners (N = 6 in each dose group)</i>								
14.0 $\pm$ 9.9	67	15.1 $\pm$ 9.4	67	11.7 $\pm$ 9.0	83	17.8 $\pm$ 1.7	100	n.s.
8.9 $\pm$ 7.2	100	10.0 $\pm$ 5.2	100	6.9 $\pm$ 4.1	100	10.4 $\pm$ 5.3	100	n.s.
10.0 $\pm$ 4.9	100	14.1 $\pm$ 9.2	83	6.0 $\pm$ 2.3	100	13.9 $\pm$ 4.9	83	.05
8.5 $\pm$ 4.7	100	8.0 $\pm$ 6.2	100	14.3 $\pm$ 7.7	100	11.5 $\pm$ 5.5	100	n.s.
8.6 $\pm$ 9.9	100	9.3 $\pm$ 7.1	100	8.5 $\pm$ 4.8	100	14.6 $\pm$ 4.8	100	< .05
10.6 $\pm$ 9.4	83	9.1 $\pm$ 9.2	83	9.4 $\pm$ 6.1	100	13.4 $\pm$ 4.9	100	n.s.
6.0 $\pm$ 4.7	100	5.6 $\pm$ 2.3	100	12.4 $\pm$ 7.0	100	14.0 $\pm$ 6.9	100	< .05
8.0 $\pm$ 5.3	100	3.1 $\pm$ 1.9	100	9.2 $\pm$ 5.3	100	15.2 $\pm$ 7.8	83	.02
7.0 $\pm$ 5.0	100	10.1 $\pm$ 3.0	100	10.2 $\pm$ 1.7	100	12.9 $\pm$ 4.0	100	< .05
8.5 $\pm$ 7.6	100	3.2 $\pm$ 1.9	100	11.8 $\pm$ 6.4	100	13.6 $\pm$ 7.8	83	.10
9.0 $\pm$ 1.7	95	8.5 $\pm$ 2.8	93.3	9.8 $\pm$ 2.6	98.3	13.7 $\pm$ 2.8	94.9	< .02
<i>Fast learners (N = 6 in each dose group)</i>								
13.3 $\pm$ 4.8	100	10.7 $\pm$ 6.1	100	9.7 $\pm$ 5.4	100	15.5 $\pm$ 8.5	83	n.s.
13.7 $\pm$ 8.2	83	13.9 $\pm$ 11.6	67	10.5 $\pm$ 6.8	100	15.2 $\pm$ 5.7	100	n.s.
14.4 $\pm$ 7.2	83	9.0 $\pm$ 9.6	100	16.0 $\pm$ 9.4	83	17.0 $\pm$ 8.5	67	n.s.
10.6 $\pm$ 6.2	100	9.9 $\pm$ 6.1	100	7.6 $\pm$ 6.5	100	15.2 $\pm$ 7.9	83	n.s.
9.5 $\pm$ 4.8	100	9.8 $\pm$ 9.3	100	11.2 $\pm$ 8.9	100	16.4 $\pm$ 8.1	83	n.s.
7.4 $\pm$ 2.6	100	5.0 $\pm$ 2.7	100	11.2 $\pm$ 9.9	83	10.4 $\pm$ 4.9	100	n.s.
9.3 $\pm$ 8.6	100	9.3 $\pm$ 9.7	83	9.7 $\pm$ 2.4	100	8.4 $\pm$ 5.7	100	n.s.
6.3 $\pm$ 5.2	100	4.1 $\pm$ 1.9	100	8.5 $\pm$ 9.4	83	8.1 $\pm$ 6.6	100	n.s.
5.4 $\pm$ 3.1	100	3.7 $\pm$ 2.0	100	4.1 $\pm$ 2.4	100	12.1 $\pm$ 5.9	100	< .02
9.0 $\pm$ 1.9	96.2	7.7 $\pm$ 1.9	94.4	8.8 $\pm$ 3.0	94.3	11.5 $\pm$ 2.4	90.6	.05

\* Mann-Whitney U-test, two-tailed.

drugged subjects jumped out on trial 1 before the conditioned stimulus or the shock was activated, as compared with 42 percent (5/12) of the control rats. These facts of shorter response latencies with no differences in frequency of

shock avoidance for the rats treated with magnesium pemoline suggested to us that increased activity and/or increased responsivity to the buzzing sound used as the conditioned stimulus, rather than an enhancement of learn-

ing and memory, might serve as an alternative explanation for these results. A second experiment was designed to investigate this possibility.

In the second experiment, the apparatus used was capable of recording very small movements of rats. An accelerometer (modified RCA tube type 5734) was mounted at the top and center of the rear wall of a 27- by 20.5- by 20.5-cm wire home cage. A false bottom, 30 by 30 cm, containing a litter tray, was attached to the cage. Total weight of the apparatus was 3.4 kg. The apparatus rested on 2.5- by 9- by 4-cm foam rubber pads and was partially supported from above at each corner by taut elastic bands. The signals from the accelerometer were fed into a two-channel Offner-Beckman pen recorder, as were the signals from the buzzer used as the conditioned stimulus in the first experiment. A 4.5- by 0.2-cm glass rod, weighted with wax, was attached to the accelerometer in order to obtain sensitivity to movement in all three dimensions (7).

The subjects for the second experiment were experimentally naive male Sprague-Dawley rats, weighing 300 to 375 g, approximately 90 days old. As in experiment 1, 30 minutes before testing, the experimental rats were injected intraperitoneally with magnesium pemoline (either 5, 10, or 20 mg/kg) in 0.3 percent tragacanth suspension (six rats per group). Ten control rats were injected with equivalent volumes of tragacanth. Subjects were given six trials 20 minutes apart. On each trial the rat was placed in the activity apparatus and 15 seconds later the conditioned stimulus used in experiment 1 was activated for 15 seconds. Subjects remained in the apparatus for an additional 15 seconds after termination of the buzzing sound, for a total of 45 seconds per trial. Response to the buzzing sound as well as pre- and postbuzzer activity was recorded as deflections on the pen recorder chart. As shown in Fig. 1, the entire 45-second period was divided into 15 3-second episodes for analysis. No significant differences in prestimulus spontaneous activity or buzzer responsivity occurred among subjects on trial 1. By trial 6, however (approximately 1 hour and 40 minutes after trial 1), large activity and responsivity differences between the experimental and control subjects were readily apparent ( $p < .001$ , for each of the three periods, prebuzzer, buzzer, and postbuzzer), the rats treated with magnesium pemoline being significantly more active. Essen-

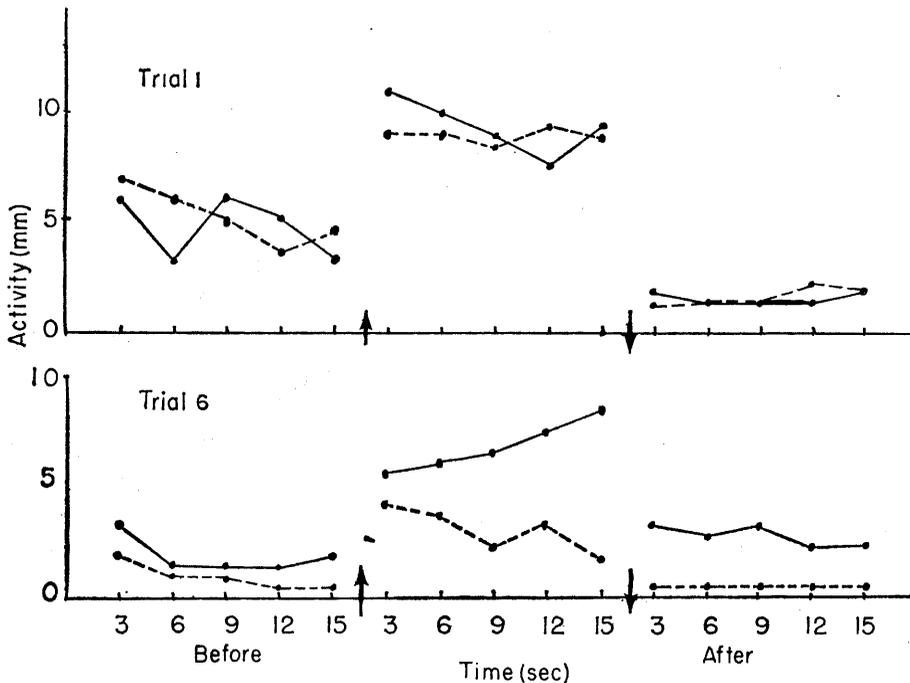


Fig. 1. Mean activity and buzzer responsivity of magnesium pemoline-injected (solid line) and control (dashed line) rats for each of three 15-second periods, before, during, and after presentation of the conditioned stimulus. Arrows indicate onset and offset of conditioned stimulus. On trial 6 (bottom) but not trial 1 (top) all differences between groups are statistically significant ( $p < .001$ ,  $t$ -test, two-tailed). A deflection of 1 on the ordinate would be equivalent to a turn of the head by subject.

Table 3. Effect of magnesium pemoline on the extinction phase, in slow and fast learners. Results are mean times ( $\pm$  S.D.)\* in seconds for "jump-out" response. The mean latencies for the ten trials, for slow learners and fast learners respectively, are shown in italic type.

Treated with magnesium pemoline			Tragacanth controls
5 mg/kg	10 mg/kg	20 mg/kg	
<i>Slow learners (N = 6 in each dose group)</i>			
14.8 $\pm$ 8.9	12.1 $\pm$ 12.0	16.8 $\pm$ 11.4	19.7 $\pm$ 11.0
14.5 $\pm$ 10.1	19.6 $\pm$ 12.9	17.4 $\pm$ 12.7	18.8 $\pm$ 12.9
10.9 $\pm$ 10.5	18.8 $\pm$ 11.4	21.5 $\pm$ 13.3	19.5 $\pm$ 11.6
11.9 $\pm$ 10.6	18.7 $\pm$ 12.5	22.4 $\pm$ 12.0	18.6 $\pm$ 12.6
13.5 $\pm$ 12.6	17.6 $\pm$ 13.6	23.4 $\pm$ 10.2	19.3 $\pm$ 11.8
14.0 $\pm$ 12.5	21.7 $\pm$ 11.8	21.5 $\pm$ 13.3	19.0 $\pm$ 12.1
14.4 $\pm$ 12.2	18.1 $\pm$ 13.2	20.9 $\pm$ 14.1	19.6 $\pm$ 11.7
15.8 $\pm$ 11.2	18.0 $\pm$ 13.6	24.8 $\pm$ 11.2	19.2 $\pm$ 11.7
15.6 $\pm$ 11.3	17.6 $\pm$ 13.5	22.6 $\pm$ 12.2	18.8 $\pm$ 11.3
14.2 $\pm$ 12.3	17.1 $\pm$ 14.0	25.3 $\pm$ 11.6	19.6 $\pm$ 11.4
<i>13.9 <math>\pm</math> 11.2</i>	<i>17.9 <math>\pm</math> 12.8</i>	<i>21.7 <math>\pm</math> 12.2</i>	<i>19.2 <math>\pm</math> 11.8</i>
<i>Fast learners (N = 6 in each dose group)</i>			
5.9 $\pm$ 2.5	10.5 $\pm$ 2.2	13.1 $\pm$ 10.9	11.9 $\pm$ 9.2
4.4 $\pm$ 1.4	6.8 $\pm$ 3.8	15.9 $\pm$ 12.3	10.1 $\pm$ 10.1
5.1 $\pm$ 1.9	3.8 $\pm$ 1.6	11.8 $\pm$ 11.3	10.8 $\pm$ 9.8
5.3 $\pm$ 3.8	5.9 $\pm$ 4.2	13.7 $\pm$ 12.7	13.5 $\pm$ 13.2
5.6 $\pm$ 4.0	3.2 $\pm$ 1.4	14.1 $\pm$ 10.7	14.5 $\pm$ 12.5
6.8 $\pm$ 2.8	5.2 $\pm$ 3.5	13.9 $\pm$ 10.3	11.0 $\pm$ 10.1
9.2 $\pm$ 10.4	5.4 $\pm$ 2.3	13.6 $\pm$ 10.4	13.3 $\pm$ 9.8
9.8 $\pm$ 10.4	6.7 $\pm$ 3.8	14.5 $\pm$ 12.5	14.6 $\pm$ 10.4
11.1 $\pm$ 11.7	6.6 $\pm$ 2.5	16.3 $\pm$ 11.0	15.8 $\pm$ 12.4
9.5 $\pm$ 10.2	9.4 $\pm$ 6.6	17.2 $\pm$ 10.6	18.3 $\pm$ 12.9
<i>7.3 <math>\pm</math> 5.9</i>	<i>6.8 <math>\pm</math> 3.2</i>	<i>14.4 <math>\pm</math> 11.3</i>	<i>13.4 <math>\pm</math> 11.0</i>

\* S.D. may not be an appropriate indication of variance, since the distribution typically was not normal.

tially identical results were obtained a week later with a group of 16 pigmented (Long-Evans) rats. In this latter experiment, subjects were male rats, 270 to 370 g, and about 90 days old. Eight tragacanth-injected controls were compared with eight rats injected with magnesium pemoline (10 mg/kg).

Thus, the major finding of our second experiment was that rats injected with magnesium pemoline (either 5, 10, or 20 mg/kg) maintained a higher level of spontaneous activity and responsiveness to the buzzing sound used as the conditioned stimulus in experiment 1. There appear to be two major interpretations that could account for the observed increased activity and sustained stimulus responsiveness in these drug-treated rats. Since no noticeable differences occurred on trial 1, the growing difference across trials between experimental and control subjects could be interpreted as a slower rate of habituation to the buzzing sound in the drug-treated rats, resulting in the significant differences seen in succeeding trials.

An alternative proposal is that the magnesium pemoline effects are time dependent and the full behavioral effects of the drug are seen only on trials 2 to 6 (50 to 130 minutes after injection). Our experimental design does not allow us to choose between these two alternatives. It is interesting to note, however, that brain RNA polymerase *in vivo* increases in a linear fashion up to at least 2 hours after intraperitoneal injection (20 mg/kg) in Sprague-Dawley rats, according to Glasky and Simon (1).

In experiment 2, spontaneous activity and stimulus-responsivity differences developed without training and within a time period comparable to that of ex-

periment 1 and Plotnikoff's report (3, 6). Thus we consider the important finding of this study to be that an alternative explanation, based on increased spontaneous activity and sustained stimulus-responsivity, can be offered to account for the shorter response latencies of the rats treated with magnesium pemoline in experiment 1. This alternative explanation, rather than "enhancement by magnesium pemoline of learning and memory," must also be entertained regarding Plotnikoff's findings (3). The fact that percent avoidances, a more meaningful measure of learning, was not increased in the drug-treated rats supports the supposition that when the effects of magnesium pemoline are evaluated on a short time scale, as in the present and previous (3, 4) experiments, the behavioral changes observed are primarily due to the effect of the drug on performance systems, not directly on "learning and memory."

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#### References and Notes

1. A. J. Glasky and L. N. Simon, *Science* **151**, 702 (1966).
2. Cylert; Abbott-30400; a combination of 2-imino-5-phenyl-4-oxazolidinone and magnesium hydroxide. We thank Abbott Laboratories, North Chicago, Illinois, for providing the magnesium pemoline.
3. N. Plotnikoff, *Science* **151**, 703 (1966).
4. ———, *Federation Proc.* **25**, 262 (1966).
5. Plotnikoff referred to day 3 as *retention*. However, since the test employed is a questionable measure of memory, and since the unconditioned stimulus is not presented, we prefer the term *extinction*. Also, slow extinction could be regarded as a failure of learning rather than an enhancement of memory.
6. N. Plotnikoff, personal communication.
7. A circuit diagram for this apparatus is available on request.
8. Supported by PHS grant MH-08545-03, D. P. Kimble, principal investigator. We thank Lee Vernon for technical assistance.

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rare-gas contents of another variety of primitive chondrites, the carbonaceous chondrites, we expected the UOC to be systematically richer than ordinary chondrites proper in these gases. Since little could be concluded from available data (7), we have determined by mass spectrometry the rare-gas contents (He, Ne, Ar, Kr, and Xe) of nine UOC; the experimental methods and results will be detailed elsewhere (8). We now report two salient results that seem to have interesting implications for further work on these chondrites.

First, the noble gases in all the UOC listed in Table 1 are strongly fractionated with respect to their "cosmic" proportions because the  $Xe^{132}$ ,  $Kr^{84}$ , and  $Ar^{36}$  abundances are about  $10^{-4}$  to  $10^{-5}$ ,  $10^{-6}$ , and  $10^{-8}$ , respectively, of their cosmic abundances (9). Only Khohar contains a significant amount of primordial  $Ne^{20}$ — $20 \times 10^{-8}$  cm<sup>3</sup>/g (standard temperature and pressure)—corresponding to about  $10^{-10}$  of the cosmic abundance of this isotope.

Second, the absolute amounts of primordial  $Ar^{36}$ ,  $Kr^{84}$ , and  $Xe^{132}$  are roughly proportional to the percentage mean deviation of the Fe contents of the olivine (5); this trend is seen in Fig. 1, and plots for  $Kr^{84}$  and  $Xe^{132}$  are similar. The quantity plotted along the abscissa (Fig. 1) is calculated from measurements of the Fe contents of many olivine grains (5). In UOC, the Fe contents usually differ substantially from the mean, or bulk, Fe content of the Fe-Mg orthosilicate. Thus, a high value for percentage mean deviation corresponds to a highly unequilibrium chondrite, and vice versa. Note that high primordial rare-gas contents occur in general among the most highly unequilibrium UOC, and vice versa.

It is generally accepted that the strongly fractionated noble gases were acquired by the meteorites, together with carbon and other volatiles, at an early stage in their history (for discussion of this point see 10). In this respect it is interesting that UOC generally have significant carbon contents and that several contain organic compounds, although not to the degree of carbonaceous chondrites of types I and II (4). The relatively high contents of fractionated noble gases are thus compatible with structural and compositional characteristics.

The trend of Fig. 1 suggests that the recrystallization of the UOC and the redistribution of Fe in the silicates

## Primordial Rare Gases in Unequilibrium Ordinary Chondrites

**Abstract.** *The primordial gases of eight unequilibrium ordinary chondrites are strongly fractionated with respect to "cosmic" proportions. The absolute amounts are roughly proportional to the degree of disequilibrium. Apparently, ordinary chondrites originally contained considerably larger amounts of primordial rare gases.*

A few ordinary chondrites (currently some 24 are known) have recently received considerable attention because they contain olivines and orthopyroxenes highly variable in content of Fe (1-5). This feature is remarkable because ordinary chondrites proper have silicates of virtually uniform composi-

tion (1). The unequilibrium ordinary chondrites (UOC) are obviously less recrystallized than the ordinary chondrites proper (3, 4); in fact, it has been argued that UOC are the "primitive" precursors of the ordinary chondrites (6).

Judging from the known primordial