STUDIES ON THE EFFECTS OF ALCOHOL, NICOTINE AND CAFFEINE ON WHITE MICE

II. EFFECTS ON ACTIVITY

L. B. NICE

From the Laboratory of Physiology in the Harvard Medical School

THREE FIGURES

CONTENTS

Historical.....	123
Methods.....	125
The growth of the mice.....	127
Weekly activity of the mice.....	129
Total activity.....	139
Comparison of the total activity of all the mice.....	143
Discussion of the effects of alcohol, nicotine and caffeine on the activity of white mice.....	146
Summary.....	149
Bibliography.....	150

HISTORICAL

During the past twenty years the effects of drugs on the activity of men and animals have been studied by many investigators. With but few exceptions however, these studies have extended over short periods of time and the drugs have been given intermittently.

Alcohol

Hodge ('03) compared the spontaneous exercise of a pair of alcoholic and a pair of control dogs and found that the alcoholic female exercised 57 per cent as much as the control female and the alcoholic male 71 per cent as much as the control male. Their activity was measured by means of pedometers in their collars.

Stewart ('98) gave two grey rats 20 per cent alcohol to drink. The activity of the alcoholic rats, as measured by revolving cages, surpassed that of the controls. Thirty per cent alcohol decreased the activity of white rats.

In investigations on men Lombard ('92), Frey ('96), Kraepelin ('99), Rossi ('94) and Schumburg ('99) showed that small doses of alcohol increased the amount of work done with the ergograph. Schnyder ('03) observed that alcohol when taken in a fasting condition, increased the amount of work done with the ergograph but when taken after or during a meal decreased it. With Hellsten ('04) 80 grams of absolute alcohol diminished the amount of work he could perform. These doses were so large, however, that they produced disturbances of digestion. Aschaffenburg ('96) found that wine decreased the efficiency of typesetters. Rivers ('08) considers that the increase of work noted by the above investigators under the influence of alcohol was due to faulty methods. The interest of taking the alcohol stimulated the subjects to extra exertions. His own experiments were carried on with control mixtures so the subjects did not know when they were taking alcohol. He states that "small doses, varying from 5 to 20 cc. of absolute alcohol have no effect on the amount or nature of the work performed with the ergograph, either immediately or within several hours of their administration."

Nicotine

So far as I can find, no experiments have been made on testing the effects of nicotine on muscular activity. Tobacco was found by Lombard ('92), Harley ('94), Féré ('04) and Rivers ('08) to decrease the amount of muscular work as recorded by the ergograph, although the pleasurable sensations connected with smoking would be expected to stimulate the subject and thus increase the amount of work done.

The fact that tobacco is forbidden to athletes when in training for tests that require great muscular strength shows that it is generally considered to have a depressing effect on muscular activity.

Caffeine

Caffeine was shown by Mosso ('93), Koch ('94), Hoch and Kraepelin ('96), Schumburg ('99) and Rivers ('08) to increase the capacity for work with the ergograph. From the results of these experiments Rivers ('08) says:

This stimulating action persists for a considerable time after the substance has been taken without there being any evidence, with moderate doses, of reaction leading to a diminished capacity for work, the substance thus really diminishing and not merely obscuring the effects of fatigue. When taken in excess the stimulating action may be so transitory, and followed by so great a decrease that it may legitimately be spoken of as an accelerator of fatigue.

METHODS

This study was undertaken to find the effects of alcohol, nicotine and caffeine on the spontaneous activity of white mice when kept under the influence of these drugs in moderate quantities all the time.

Sixteen male mice eight weeks old were used in the experiment. They were all descendents of one pair of mice whose offspring had been inbred for four generations. These mice belonged to the fourth generation and came from four different lots, each lot being the young of one male and several females. One mouse from each lot was placed in each of the experimental lines. Thus mice of the same sex, the same age, and very closely related were the subjects of this investigation.

Four lines were carried: one was given alcohol, a second nicotine, a third caffeine and a fourth was carried for controls. The alcohol and nicotine were given in the same proportions as in preceding experiments, as on these strengths the mice seemed to keep in good health. The caffeine was given in a 1:300 solution.

Each mouse in the alcohol line was given 35 per cent alcohol to drink instead of water, and every other day, 3 cc. of 35 per cent alcohol was added to its crackers and milk.

Each mouse in the nicotine line received 1:1000 nicotine sulphate solution to drink instead of water, and had 3 cc. of 1:1000 nicotine sulphate added to its crackers and milk every other day.

In the caffeine line each mouse drank 1:300 caffeine citrate solution instead of water, and every other day 3 cc. of 1:300 caffeine solution was added to the crackers and milk.

All of the sixteen mice were given the same food which consisted of buckwheat and oats, every other day crackers and milk, and once or twice a week meat.

The experiment continued from November 18 to June 8. During the winter months the room was heated with hot water and remained at about 65° F.

To study the spontaneous activity of these mice revolving cages were devised. These cages are similar to those used by Stewart ('98) and later by Slonaker ('07, '12) in their studies on rats. The cages are 6 inches wide by 10 inches in diameter, and made of 8-mesh galvanized wire. Each cage is fastened to an axle which revolves with the cage. The axle is $\frac{1}{4}$ inch in diameter and 18 inches long. The ends of the axle are pointed and set into the end of a bored out set screw forming a pinion which by reducing friction permits the cages to revolve very easily. By means of turning the set screw the pinions can be adjusted in case of wear. The cages are mounted as shown in the accompanying photograph (fig. 1).

The revolutions of each cage are recorded by means of an alarm clock whose balance wheel had been removed. A wire about 6 inches long is attached to the escapement lever of the clock and to one end of a wooden lever which rests on the axle near one end of a cage. In one brass hub of each cage two pins are set on opposite sides of the axle, and $1\frac{1}{2}$ inches from it. These pins are parallel with the axle. As a cage revolves the end of the wooden lever is raised by each pin in turn causing the clock to register. Each revolution of a cage corresponds to one second on the clock.

Each cage is supplied with a nest box made of galvanized tin $2\frac{3}{4}$ inches wide, $2\frac{3}{4}$ inches long and 2 inches deep. These are swung to the axle by two wire hooks attached to the top of the nest box near its ends. A tunnel $1\frac{1}{8}$ inches square having a wire mesh floor leads to the opening in one end of the nest box where the mouse enters. The floor of the nest box is a hinged door.

On the top of the nest box is a feed box 3 inches long and 1 inch wide with two compartments, one for grain, the other for crackers and milk. The feed box is held in place by a spring clip. Another clip holds a small wide mouthed bottle which is inverted. This bottle contains the water or drug which the mouse drinks. In the mouth of this bottle is a rubber stopper with an opening through it $\frac{1}{2}$ inch in diameter. Through this opening a glass tube

Fig. 1 Revolving cages and recording clocks

$\frac{3}{8}$ inch in diameter inside is inserted. The lower end of the glass tube is drawn towards a point making an opening $\frac{1}{4}$ inch in diameter. This device compelled all the mice to drink directly from the bottles.

THE GROWTH OF THE MICE

The mice were weighed at the beginning of the experiment when they were eight weeks old. They were weighed once a week during the next two months and once each month the next five months.

TABLE 1
Weight of the mice in grams

LINE	EX- PERI- MENT	WEIGHT AT 8 WEEKS	WEIGHT AT 9 WEEKS	WEIGHT AT 10 WEEKS	WEIGHT AT 11 WEEKS	WEIGHT AT 12 WEEKS	WEIGHT AT 16 WEEKS	WEIGHT AT 20 WEEKS	WEIGHT AT 24 WEEKS	WEIGHT AT 28 WEEKS	WEIGHT AT 32 WEEKS	WEIGHT AT 36 WEEKS
		grams	grams	grams	grams	grams	grams	grams	grams	grams	grams	grams
Control...	1	19.0	20.0	19.0	20.0	20.0	21.5	24.0	22.5	24.5	25.0	25.0
	2	19.5	18.0	20.0	20.0	20.0	22.5	23.5	23.5	25.0	25.0	25.0
	3	20.0	19.0	22.0	22.0	22.0	25.0	25.0	28.0	32.0	33.0	35.0
	4	19.0	17.0	19.0	18.5	20.0	21.5	22.0	22.5	24.5	24.5	24.0
Alcohol...	5	16.5	20.0	19.0	19.0	19.0	20.5	21.5	21.0	19.0 ¹		
	6	18.5	18.0	20.0	18.0	19.0	21.5	23.5	25.0	25.5	25.0 ¹	
	7	18.0	19.0	19.5	19.0	20.5	22.0	23.5	24.5	27.0	26.5	19.0
	8	18.0	19.0	19.0	19.0	21.0	21.0	22.5	24.5	24.5	25.0	20.0
Nicotine...	9	16.5	20.0	19.5	21.0	21.5	22.0	21.5	22.5	24.5	24.0	23.0
	10	18.0	15.0	17.0	18.0	18.5	19.0	19.0	20.0	22.0	20.0	20.0
	11	19.0	17.0	17.0	17.5	20.0	21.0	22.0	24.5	25.5	26.0	23.0
	12	20.0	17.0	17.5	18.0	19.0	20.5	20.0	21.5	22.0	22.5	21.5
Caffeine...	13	16.5	17.0	20.0	20.0	19.0	22.5	24.0	25.0	26.5	26.5	27.0
	14	17.0	17.0	18.5	18.0	19.0	20.5	20.5	19.5	17.0 ¹		
	15	16.0	16.0	17.0	18.0	19.0	22.5	23.0	23.5	26.0	25.0	26.0
	16	15.5	15.0	19.0	19.5	20.0	21.5	21.0	23.5	26.0	27.5	30.0

¹ Mouse No. 5 died at the end of the twenty-seventh week, No. 6 at the end of the thirty-fourth week and No. 14 in the thirty-second week.

At eight weeks the control mice averaged 19.5 grams in weight, the alcohol mice 18 grams, the nicotine mice 18.5 grams and the caffeine mice 16 grams. At twenty-four weeks the control mice averaged 24 grams, the alcohol mice 24 grams, the nicotine mice 22 grams and the caffeine mice 23 grams. At thirty-six weeks the control mice averaged 27.3 grams, the alcohol mice 19.5 grams, the nicotine mice 22 grams and the caffeine mice 27.6 grams.

The control mice gained 4.5 grams each in the first sixteen weeks of the experiment and 3.3 grams in the last twelve weeks. The alcohol mice had gained 6 grams each when twenty-four weeks old, but had lost 4.5 grams on an average at the end of the experiment. The nicotine mice gained 3.5 grams each by the twenty-fourth week, and had gained no more at the end of the experiment. The caffeine mice gained the most of all, 7 grams in the first sixteen weeks and 4.6 grams in the last twelve weeks.

The average gain for the alcohol mice was 1.5 grams, for the nicotine mice 3.5 grams, for the control mice 7.8 grams and for the caffeine mice 11.6 grams.

WEEKLY ACTIVITY OF THE MICE

The number of revolutions registered by each clock was recorded at 12.30 P.M. every day. In the following tables the number of revolutions that each mouse ran are recorded by weeks.

Mouse No. 1 exhibited its greatest activity from the tenth to the eighteenth week, then became somewhat less active, increased again at the twenty-fifth week and then decreased rather gradually till the end of the experiment. Its maximum run was 139 078 revolutions at the thirteenth week and its minimum run was 48 380 revolutions at the thirty-fourth week. Its average run per week was 92 004 revolutions.

No. 2 exhibited its greatest activity from the eleventh to the seventeenth week and then had a second period of high activity from the twenty-fifth to the twenty-ninth week. Its maximum run was 147 576 revolutions at the fourteenth week and its minimum run was 59 320 revolutions at the thirty-fifth week. Its average run per week was 95 622 revolutions.

TABLE 2

Number of revolutions per week of the mice in the control line

AGE OF MICE IN WEEKS	MOUSE NO. 1	MOUSE NO. 2	MOUSE NO. 3	MOUSE NO. 4
9	80 243	78 785	55 718	63 878
10	120 935	82 528	71 041	123 370
11	122 119	118 306	99 070	139 978
12	132 593	125 001	100 003	120 495
13	139 078	140 830	81 004	101 626
14	126 355	147 576	98 966	80 772
15	123 957	131 274	81 620	84 200
16	94 870	129 195	80 028	94 145
17	92 598	119 668	85 370	109 275
18	108 405	91 304	69 584	129 304
19	86 990	84 900	73 100	144 913
20	66 117	83 987	78 744	105 902
21	74 287	85 647	58 647	135,978
22	72 890	64 281	58 119	130 395
23	82 120	85 955	76 740	125 572
24	88 454	93 540	54 545	68 147
25	107 148	109 515	54 532	126 018
26	91 722	101 215	60 060	116 095
27	93 892	74 380	54 104	105 780
28	88 755	110 640	55 180	100 500
29	67 071	119 481	41 058	78 013
30	77 439	63 365	40 881	84 547
31	88 028	81 600	47 324	94 140
32	85 345	85 102	52 164	105 615
33	72 652	74 825	36 155	91 057
34	48 380	72 453	39 825	77 830
35	74 460	59 320	40 746	62 100
36	69 195	63 554	41 247	57 633
Average.....	92 004	95 622	63 770	102 045

No. 3 was the least active of all the controls. It reached its maximum of 100 003 at the twelfth week and decreased steadily to the end of the experiment. Its minimum run was 36 155 revolutions at the thirty-third week. Its average weekly run was 63 770 revolutions.

No. 4 was the most active of the control mice. It showed high activity from the tenth to the thirteenth week, from the seventeenth to the twenty-third week, from the twenty-fifth to the twenty-eighth week and finally at the thirty-second week. Its

maximum run was 144 913 revolutions at the nineteenth week and its minimum run was 57 633 revolutions at the thirty-sixth week. Its average run per week was 102 045 revolutions.

Mouse No. 5 ran its maximum amount of 125 301 revolutions during the eleventh week and decreased rather rapidly till the twenty-seventh week when it died. Its minimum run was 2464 revolutions the twenty-sixth week. Its average run per week was 57 615 revolutions.

TABLE 3
Number of revolutions per week of the mice in the alcohol line

AGE OF MICE IN WEEKS	MOUSE NO. 5	MOUSE NO. 6	MOUSE NO. 7	MOUSE NO. 8
9	57 634	41 370	28 430	45 395
10	74 915	81 694	76 230	122 193
11	125 301	58 444	132 113	131 473
12	56 542	15 404	96 680	93 965
13	104 745	31 693	142 762	61 901
14	34 380	32 522	128 495	83 629
15	80 092	63 128	129 393	86 196
16	69 722	79 258	113,560	83 327
17	74 074	86 895	117 005	83 658
18	56 969	69 616	99 138	72 748
19	52 830	71 204	96 925	68 684
20	57 087	57 318	112 247	81 660
21	51 785	54 427	97 093	61 738
22	47 297	63 423	89 195	69 655
23	45 628	66 502	96 835	77 245
24	43 680	71 510	76 733	67 364
25	56 831	75 558	97 210	67 607
26	2 464	54 630	85 420	66 063
27	2 700 ¹	63 116	67 990	29 535
28		69 428	67 600	27 432
29		54 997	51 083	12 728
30		46 795	49 736	177
31		70 095	71 074	25 638
32		69 675	74 660	50 189
33		33 820	54 982	29 610
34		21 315 ¹	60 107	3 610
35			58 600	5 012
36			62 650	13 001
Average.....	57 615	62 435	86 934	57 908

¹ Nos. 5 and 6 died at the end of the twenty-seventh and thirty-fourth week, respectively.

No. 6 ran uniformly low; its maximum run was 86 895 revolutions at the seventeenth week and its minimum run for an entire week was 15 404 revolutions the twelfth week. It died the thirty-fourth week. Its average weekly run was 62 435 revolutions.

No. 7 was the most active of the alcohol line. It showed great activity from the eleventh to the twentieth week. Its maximum was 142 762 revolutions at the thirteenth week and its minimum, not counting the first week, was 51 083 revolutions during the twenty-ninth week. Its average run per week was 86 934 revolutions.

No. 8 ran its maximum of 131 473 revolutions at the eleventh week. It decreased steadily and near the end of the experiment made some very small runs, of which 177 revolutions at the thirtieth week was the least. Its average weekly run was 57 908 revolutions.

No. 9 showed great activity from the tenth to the twentieth week, from the twenty-fourth to the twenty-seventh week and again the thirty-second week. Its maximum run was 134 027 revolutions at the eleventh week and its minimum run, not counting the first week was 67 089 revolutions at the thirty-fifth week. Its average weekly run was 99 693 revolutions.

No. 10 was the least active of this line; it rose gradually to its maximum run of 106 697 revolutions at the fourteenth week and then decreased to its minimum run of 10 253 revolutions at the twenty-ninth week, but increased somewhat later. Its average run per week was 58 843 revolutions.

No. 11 shows a reversed record, for it ran low until its twenty-seventh week. Its maximum run was 111 132 revolutions at the thirty-fifth week and its minimum run 14 947 at the thirteenth week when many of the mice were running their highest. Its average weekly run was 65 006 revolutions.

No. 12 exercised the most of all the sixteen mice. It reached its maximum of 192 395 revolutions at the thirteenth week and kept up its great activity throughout the experiment, not going below 100 000 revolutions until the thirty-fourth week. Its minimum run was 54 392 revolutions at the twelfth week. Its average run per week was 124 886 revolutions.

TABLE 4
Number of revolutions per week of the mice in the nicotine line

AGE OF MICE IN WEEKS	MOUSE NO. 9	MOUSE NO. 10	MOUSE NO. 11	MOUSE NO. 12
9	25 227	36 370	44 240	75 805
10	112 286	68 748	31 218	69 467
11	134 027	53 430	37 226	122 325
12	127 474	75 451	19 167	154 392
13	107 162	98 414	14 947	192 395
14	119 168	106 697	40 222	175 052
15	122 093	94 483	33 564	145 488
16	133 615	93 275	29 488	160 474
17	122 570	80 278	61 232	135 952
18	123 667	77 205	69 841	150 792
19	110 990	82 355	72 800	169 845
20	110 770	68 310	64 275	134 322
21	94 691	74 252	51 091	163 060
22	91 428	19 104	71 540	157 709
23	92 467	46 020	49 708	152 201
24	102 065	41 973	62 118	139 931
25	108 910	66 335	80 280	148 290
26	106 312	55 715	66 680	109 654
27	104 340	30 960	99 900	134 390
28	80 052	54 510	100 124	125 528
29	79 221	10 253	72 718	100 308
30	83 505	22 382	68 433	103 102
31	85 974	50 024	53 315	100 280
32	102 207	58 168	110 585	112 674
33	81 638	51 922	108 188	101 015
34	78 748	34 335	95 980	97 185
35	67 089	38 428	111 132	90 943
36	83 434	58 214	100 286	74 228
Average.....	99 693	58 843	65 006	124 886

No. 13 ran low during the entire experiment. Its maximum run was 79 613 revolutions at the sixteenth week. Its minimum run was 14 704 at the thirty-second week. Its average weekly run was 40 052 revolutions.

No. 14 showed its greatest activity from the eleventh to the seventeenth week, its maximum run being 135 316 revolutions at the fifteenth week. After that it decreased rapidly till its death in the thirty-second week. Its minimum run for an entire

TABLE 5

Number of revolutions per week of the mice in the caffeine line

AGE OF MICE IN WEEKS	MOUSE NO. 13	MOUSE NO. 14	MOUSE NO. 15	MOUSE NO. 16
9	27 395	25 160	51 796	51 991
10	43 205	79 935	22 685	79 617
11	41 960	102 615	33 712	143 242
12	55 474	121 164	44 478	83 853
13	34 623	87 722	44 476	141 494
14	53 403	97 081	66 508	149 307
15	47 585	135 316	64 128	128 433
16	79 613	110 157	79 980	105 980
17	48 182	104 390	46 347	112 592
18	56 228	55 084	60 028	88 598
19	51 672	82 158	58 585	103 555
20	66 583	65 340	72 885	123 895
21	53 286	66 561	58 847	87 510
22	49 292	83 704	45 256	92 468
23	58 332	61 774	48 048	72 504
24	45 728	61 374	38 114	90 872
25	35 560	26 366	47 217	111 157
26	33 015	12 512	40 410	74 635
27	33 246	4 230	43 822	70 652
28	23 602	12 657	38 868	77 981
29	24 812	451	36 690	66 117
30	18 800	1 182	29 057	44 623
31	21 940	1 007	44 248	54 748
32	14 704	72 ¹	51 550	72 710
33	22 393		59 412	66 271
34	26 256		42 240	71 520
35	26 797		41 616	77 685
36	27 790		45 855	54 098
Average.....	40 052	47 036	48 815	89 218

¹ No. 14 died in the thirty-second week of the experiment.

week was 451 revolutions at the twenty-ninth week. Its average run each week was 47 036 revolutions.

No. 15 ran much the same as No. 13, reaching a maximum of 79 980 revolutions at the sixteenth week. Its minimum run was 22 685 at the tenth week. Its average weekly run was 48 815 revolutions.

No. 16 was the most active of the caffeine line. It showed great activity from the eleventh to the twentieth week and rose

again at the twenty-fifth week. Its maximum run was 149 307 revolutions at the fourteenth week, and its minimum run, 44 623 revolutions at the thirtieth week. Its average weekly run was 89 218 revolutions.

Comparison of the weekly activity of all the mice

Although all these mice were of the same sex, the same age and closely related, yet even in the same lines they showed great individual variations in their activity.

Some time was necessary for the mice to get accustomed to the cages. The first week's runs are low, although the animals had been in the cages almost a week before the experiment was begun. All but one of the mice showed their greatest activity in the early part of the experiment. The decline in the latter part was probably due to increase in age. Slonaker ('07, '12) found that white rats are most active in early life.

The mice may be divided into two types, with one exception. Type 1 had a period of high activity falling within the tenth to the twenty-third week, and a second period of great activity occurring between the twenty-fourth and the thirty-second week. This would seem to be normal. This group includes six mice, controls Nos. 1, 2 and 4, nicotine Nos. 9 and 12 and caffeine No. 16. These six mice were more active than any of the others. None of them died.

Type 2 exhibited only one period of high activity which fell within the tenth to the twentieth week; the runs then decreased steadily to the end of the experiment. This includes nine mice, control No. 3, all of the alcohol mice, nicotine No. 10 and caffeine Nos. 13, 14 and 15. Only one of these, alcohol No. 7, is above the average in activity; all the others fall below the average. Three of these mice died. It is evident that these mice had less vitality than those of the first type.

No. 11 of the nicotine line is an exception to these two types. Its period of high activity did not begin until the twenty-eighth week, and its maximum run came at the thirty-fifth week.

Weekly activity of the average of each line

In order to compare the activity of the different lines the average of each line is recorded in table 6 and figure 2. Some of the mice in the alcohol and caffeine lines died during the course of the experiment. In such cases the last entire week of activity was counted in making the averages.

From table 6 and figure 2 it will be seen that the controls reached their maximum run of 119 523 revolutions at the twelfth

TABLE 6
Number of revolutions per week of the average of each line

AGE OF MICE IN WEEKS	CONTROL MICE	ALCOHOL MICE	NICOTINE MICE	CAFFEINE MICE
9	69 656	43 195	45 410	39 063
10	99 468	88 758	45 429	56 110
11	118 618	111 833	86 752	80 382
12	119 523	65 648	69 121	76 242
13	115 634	85 325	103 254	79 579
14	113 417	69 756	110 289	91 575
15	105 263	89 702	98 907	93 865
16	99 559	86 467	108 213	93 932
17	101 728	90 408	100 008	77 878
18	99 649	74 630	105 376	64 984
19	97 276	72 411	108 997	73 992
20	83 687	77 078	94 419	82 176
21	88 639	66 261	95 773	66 551
22	81 421	67 392	84 945	67 680
23	92 592	71 552	85 099	60 164
24	90 639	64 822	86 522	59 022
25	99 303	74 301	100 954	55 075
26	67 273	52 144	84 590	40 143
27	82 039	53 547	92 397	37 987
28	88 769	54 820	90 055	38 277
29	76 405	39 603	65 625	32 017
30	66 558	32 236	69 355	23 415
31	77 773	55 602	72 398	30 485
32	79 556	64 841	95 908	46 321
33	68 672	39 471	85 691	49 359
34	59 622	25 011	76 562	46 672
35	59 156	31 806	76 898	48 699
36	57 907	37 825	79 040	42 581
Average.....	87 493	63 767	86 321	59 079

Fig. 2 Curve showing the weekly activity of the average of each line. The abscissas represent the age of the mice in weeks, the ordinates the number of revolutions.

week and then showed a rather gradual decline in running to the end of the experiment. Their last run, 57 907 revolutions, was their least. Their average weekly run was 87 493 revolutions.

The alcohol line rose almost immediately to their maximum of 111 833 revolutions at the eleventh week, but after that declined rapidly and ran low throughout the experiment. Their last run was 37 825 revolutions and their minimum 25 011 revolutions at the thirty-fourth week. Their average weekly run was 63 767 revolutions.

The nicotine line reached their maximum of 110 289 revolutions at the fourteenth week. They retained a fairly constant level with a slight decline at the end of the experiment. Their last run was 79 040 revolutions and their least, if the first two weeks are left out of account, 65 625 revolutions at the twenty-ninth week. Their average weekly run was 86 321 revolutions.

The caffeine line rose slowly to their maximum of 93 932 at the end of the sixteenth week, and showed a rather steady decline to the end of the experiment. Their last run was 42 581 revolutions and their minimum run, 23 415 revolutions at the thirtieth week. Their average weekly run was 59 079 revolutions.

The control and nicotine lines ran close together for a large part of the experiment. The controls however reached a higher maximum and reached it sooner than the nicotine mice, but after the fifteenth week the nicotine line was generally slightly ahead of the controls. These two lines correspond to type 1.

The alcohol and caffeine lines ran close together, except at the maximum of the former. After the thirteenth week they ran entirely below the control and nicotine mice. Most of the time the alcohol mice ran somewhat higher than the caffeine mice. These two lines correspond to type 2.

The alcohol mice varied more than any of the other lines. The average weekly decrease from their maximum run to their final run was 3360 revolutions, that of the caffeine mice 2566 revolutions, the controls 2566 revolutions and the nicotine mice 1420. The nicotine line kept a more constant level than the others because both No. 11 and No. 12 were very active in the latter part of the experiment.

TOTAL ACTIVITY

The total activity of each mouse is shown in tables 7, 8, 9 and 10.

TABLE 7

Total work in revolutions done by the control mice

AGE OF MICE IN WEEKS	MOUSE NO. 1	MOUSE NO. 2	MOUSE NO. 3	MOUSE NO. 4
9	80 243	78 785	55 718	63 878
10	201 178	161 313	126 759	187 248
11	323 297	279 619	225 829	327 226
12	455 890	404 620	325 829	447 721
13	594 968	545 450	406 836	549 347
14	721 323	693 026	505 802	630 119
15	845 280	824 300	587 422	714 319
16	940 150	953 495	667 450	808 464
17	1 032 748	1 073 163	752 820	917 739
18	1 141 155	1 164 467	822 404	1 047 043
19	1 228 145	1 248 567	895 504	1 191 956
20	1 294 262	1 232 554	974 248	1 297 858
21	1 368 549	1 418 201	1 032 895	1 433 836
22	1 441 439	1 482 482	1 091 014	1 564 231
23	1 523 559	1 568 437	1 167 754	1 689 803
24	1 612 013	1 661 977	1 222 299	1 757 950
25	1 719 162	1 771 492	1 276 831	1 883 968
26	1 810 884	1 872 707	1 336 891	2 000 063
27	1 904 776	1 947 187	1 390 995	2 105 843
28	1 993 531	2 057 827	1 446 175	2 206 343
29	2 060 602	2 177 208	1 487 229	2 284 356
30	2 138 041	2 240 573	1 528 110	2 368 903
31	2 226 069	2 322 173	1 575 434	2 463 043
32	2 311 414	2 407 275	1 627 598	2 568 658
33	2 384 066	2 482 100	1 663 753	2 659 715
34	2 432 446	2 554 553	1 703 578	2 737 545
35	2 506 906	2 613 873	1 744 324	2 799 645
36	2 576 101	2 677 427	1 785 571	2 857 278

The total runs are 1 785 571, 2 576 101, 2 677 427 and 2 857 278 revolutions. Three mice in this line showed great activity while one was much less active. No. 3 ran 62 per cent as much as No. 4, No. 1 ran 90 per cent and No. 2 94 per cent as much as No. 4.

TABLE 8

Total work in revolutions done by the alcohol mice

AGE OF MICE IN WEEKS	MOUSE NO. 5	MOUSE NO. 6	MOUSE NO. 7	MOUSE NO. 8
9	57 634	41 370	28 430	25 345
10	132 549	123 064	104 660	167 538
11	257 850	181 508	226 773	299 011
12	314 392	196 912	333 453	392 976
13	419 137	228 605	476 415	454 877
14	453 517	261 127	604 910	538 506
15	533 609	324 255	734 303	624 702
16	603 331	403 513	847 863	708 029
17	677 405	490 308	964 868	791 687
18	734 374	559 924	1 064 006	864 485
19	787 204	631 128	1 160 931	933 169
20	844 291	688 446	1 273 178	1 014 831
21	896 076	742 873	1 370 271	1 076 569
22	943 373	806 296	1 459 466	1 146 224
23	989 001	872 798	1 556 301	1 223 469
24	1 032 681	944 308	1 633 034	1 290 833
25	1 089 512	1 019 876	1 730 244	1 358 438
26	1 091 976	1 073 906	1 815 664	1 424 501
27	1 094 676 ¹	1 137 022	1 883 654	1 454 036
28		1 206 520	1 951 254	1 481 468
29		1 261 517	2 002 337	1 494 196
30		1 308 312	2 052 073	1 494 373
31		1 378 407	2 123 147	1 520 011
32		1 448 082	2 197 807	1 570 200
33		1 481 902	2 252 789	1 599 810
34		1 503 217 ¹	2 312 896	1 603 420
35			2 371 496	1 608 432
36			2 434 146	1 621 433

¹ No. 5 and No. 6 died at the end of the twenty-seventh and thirty-fourth week respectively.

No. 5 had run 1 094 676 revolutions at its twenty-seventh week, No. 6 1 503 217 at its thirty-fourth week, and Nos. 8 and 7, 1 621 433 and 2 434 146 respectively at the end of the experiment. The record of No. 5 was 58 per cent of No. 7 at the twenty-seventh week, No. 6 65 per cent of No. 7 at the thirty-fourth week and No. 8 66 per cent at the end of the experiment. Three of this line showed little activity, while one was much more active.

TABLE 9

Total work in revolutions done by the nicotine mice

AGE OF MICE IN WEEKS	MOUSE NO. 9	MOUSE NO. 10	MOUSE NO. 11	MOUSE NO. 12
9	25 227	36 370	44 240	75 805
10	137 513	105 118	75 458	145 272
11	271 540	158 548	112 684	267 597
12	399 014	233 999	131 751	321 989
13	506 176	332 413	146 698	514 384
14	625 344	439 110	186 910	689 436
15	747 437	533 595	220 474	834 924
16	881 052	626 870	249 962	995 398
17	1 003 622	707 148	311 194	1 131 350
18	1 127 289	784 353	381 035	1 282 142
19	1 238 279	866 708	453 835	1 451 987
20	1 349 049	935 018	518 110	1 587 309
21	1 443 740	1 009 270	569 201	1 749 369
22	1 535 168	1 028 374	640 741	1 907 078
23	1 627 635	1 074 394	690 449	2 059 210
24	1 729 700	1 116 367	752 567	2 199 210
25	1 838 610	1 182 702	832 847	2 347 500
26	1 944 922	1 258 417	899 527	2 457 154
27	2 049 262	1 269 375	999 427	2 591 544
28	2 129 320	1 323 887	1 099 551	2 717 072
29	2 208 541	1 334 140	1 172 269	2 817 380
30	2 292 046	1 356 522	1 240 702	2 920 482
31	2 378 020	1 406 546	1 294 017	3 020 762
32	2 480 227	1 464 714	1 404 602	3 133 436
33	2 561 865	1 516 636	1 512 790	3 234 451
34	2 640 613	1 550 971	1 608 770	3 331 636
35	2 707 702	1 589 399	1 719 902	3 422 579
36	2 791 136	1 647 613	1 820 188	3 496 807

The mice in the nicotine line ran 1 647 613, 1 820 188, 2 791 136 and 3 496 807 revolutions during the experiment. One showed very great activity, another great activity while two were rather inactive. No. 10 ran 47 per cent as much as No. 12, No. 11 ran 52 per cent and No. 9 80 per cent as much as No. 12.

TABLE 10
Total work in revolutions done by the caffeine mice

AGE OF MICE IN WEEKS	MOUSE NO. 13	MOUSE NO. 14	MOUSE NO. 15	MOUSE NO. 16
9	27 395	25 160	51 796	51 991
10	70 600	104 095	74 481	131 608
11	112 560	206 710	108 193	274 850
12	168 034	327 874	152 671	358 703
13	202 657	415 596	207 147	500 197
14	256 060	512 677	273 655	649 504
15	303 645	547 993	337 783	771 937
16	383 258	658 150	417 763	883 917
17	431 440	762 540	464 110	996 509
18	487 668	837 624	524 138	1 085 107
19	539 340	919 782	582 722	1 188 662
20	605 923	985 122	655 608	1 312 557
21	659 209	1 051 683	714 455	1 400 067
22	708 501	1 135 387	759 711	1 492 535
23	766 833	1 197 161	807 759	1 565 039
24	812 561	1 258 535	845 873	1 655 911
25	848 121	1 284 901	893 080	1 766 068
26	881 936	1 297 413	933 490	1 841 703
27	914 382	1 301 643	977 312	1 912 355
28	937 984	1 314 300	1 016 170	1 990 336
29	962 796	1 314 751	1 052 860	2 056 453
30	981 596	1 315 933	1 081 917	2 101 076
31	1 003 536	1 316 940	1 126 165	2 155 824
32	1 018 240	1 317 012 ¹	1 177 715	2 228 534
33	1 040 633		1 237 125	2 294 805
34	1 066 889		1 279 367	2 366 325
35	1 093 686		1 320 983	2 444 010
36	1 121 476		1 366 838	2 498 108

¹ No. 14 died at the end of the thirty-second week.

One mouse in the caffeine line showed great activity and three were much less active. Nos. 13, 15 and 16 ran 1 121 476, 1 366 838 and 2 498 108 revolutions during the course of the experiment. No. 14 ran 1 317 612 revolutions to its thirty-second week when it died. No. 13's record was 49 per cent of No. 16. No. 15 was 55 per cent and No. 14 was 60 per cent of No. 16 at the thirty-second week.

COMPARISON OF THE TOTAL ACTIVITY OF ALL THE MICE

TABLE 11

*In the following table the mice are arranged in the order of their total activity.
Total activity of all the mice in revolutions and in miles*

	MOUSE NO.	NUMBER OF REVOLUTIONS	MILES RUN
Caffeine.....	13	1 121 476	556.06
Caffeine.....	15	1 366 838	677.72
Alcohol ¹	5	1 094 676 (at 27 weeks)	542.77 (at 27 weeks)
Caffeine ¹	14	1 317 012 (at 32 weeks)	653.01 (at 32 weeks)
Alcohol ¹	6	1 503 217 (at 34 weeks)	745.35 (at 34 weeks)
Alcohol.....	8	1 621 433	803.96
Nicotine.....	10	1 647 613	816.94
Control.....	3	1 785 571	885.34
Nicotine.....	11	1 820 188	898.72
Alcohol.....	7	2 434 146	1206.92
Caffeine.....	16	2 498 108	1238.65
Control.....	1	2 576 101	1277.31
Control.....	2	2 677 427	1327.56
Nicotine.....	9	2 791 136	1383.94
Control.....	4	2 857 278	1416.73
Nicotine.....	12	3 496 807	1733.83
Average.....		2 076 622	1010.30

¹ Nos. 5, 14 and 6 died at the twenty-seventh, thirty-second and thirty-fourth weeks respectively.

From table 11 it will be seen that below the average in activity are 3 caffeine mice, 3 alcohol mice, 2 nicotine mice and one control. Above the average are 1 caffeine mouse, 1 alcohol mouse, 2 nicotine mice and 3 controls. Caffeine No. 13 was the least active of all the mice. Nicotine No. 12 was the most active. No. 13 exercised only 32 per cent as much as No. 12. No. 13 is 54 per cent and No. 12 is 169 per cent of the average.

When the revolutions are reduced to miles the average daily run of all the mice is 4.93 miles. The average daily run of the mouse that ran the least is 2.84 miles, and of the mouse that ran the most 8.99 miles. The greatest run in one day of any mouse is 16.8 miles.

Total activity of the average of each line

TABLE 12

Total work in revolutions of the average of each line

AGE OF MICE IN WEEKS	CONTROL	ALCOHOL	NICOTINE	CAFFEINE
9	69 656	43 195	45 410	39 063
10	169 124	131 953	90 839	95 173
11	287 742	243 786	177 591	175 555
12	407 265	309 434	246 712	251 797
13	522 899	394 759	349 966	331 376
14	636 316	464 515	460 255	422 951
15	741 579	554 217	559 162	516 816
16	841 138	640 684	667 375	610 748
17	942 866	731 092	767 383	688 626
18	1 042 515	805 722	872 759	753 610
19	1 139 791	878 133	981 756	827 602
20	1 223 478	955 211	1 076 175	909 778
21	1 312 117	1 021 472	1 171 948	976 329
22	1 393 538	1 088 864	1 256 893	1 044 009
23	1 486 130	1 160 416	1 341 992	1 104 173
24	1 576 769	1 225 238	1 427 514	1 163 195
25	1 676 072	1 299 539	1 528 468	1 218 270
26	1 743 345	1 351 683	1 613 058	1 258 413
27	1 825 384	1 405 210	1 705 455	1 296 400
28	1 914 153	1 460 030	1 795 510	1 334 677
29	1 990 558	1 499 633	1 861 135	1 366 694
30	2 057 116	1 531 869	1 930 490	1 390 109
31	2 134 889	1 587 471	2 002 888	1 420 594
32	2 214 445	1 652 362	2 098 796	1 466 915
33	2 273 117	1 691 833	2 184 487	1 516 274
34	2 332 739	1 716 844	2 261 049	1 562 946
35	2 391 895	1 747 650	2 337 947	1 611 645
36	2 449 802	1 785 475	2 416 987	1 654 226

In table 12 and figure 3 the total activity of each line is averaged.

The average total activity of the caffeine line was 1 654 226 revolutions, of the alcohol line 1 785 475 revolutions, of the nicotine line 2 416 987 revolutions and of the control line 2 449 802 revolutions. The caffeine average is 68 per cent of the control average, the alcohol average is 73 per cent and the nicotine average is 99 per cent of the control average.

Fig. 3 Curve showing the total activity of the average of each line. The abscissas represent the age of the mice in weeks, the ordinates the total number of revolutions.

From figure 3 it will be seen that the control line leads throughout the entire time. The nicotine line excels the caffeine line at the sixth week and the alcohol line after the ninth week, and then gradually increases, keeping about an even distance from the control line, until the last two months when it more nearly approaches the control line. The alcohol average excels the nicotine line for eight weeks, but after that rises much more slowly. The caffeine average equals the nicotine average for five weeks, but after that is the lowest of all.

DISCUSSION OF THE EFFECTS OF ALCOHOL, NICOTINE AND CAFFEINE ON THE ACTIVITY OF WHITE MICE

Control line

The control mice have the highest total activity of all the lines. They also have the highest average maximum. Three of them, Nos. 1, 2 and 4, belong to type 1, having a second period of high activity. These three are well above the average in total activity. No. 3 is less active, coming below the average. It belongs to type 2. It weighed 35 grams while the other control mice weighed 24, 24 and 25 grams respectively. Only one other mouse, caffeine No. 16, weighed as much as 30 grams. There may be some correlation between the inactivity of control No. 3 and its weight. None of the controls died. They gained on an average 7.5 grams throughout the experiment.

Alcohol line

Of the mice subjected to alcohol three are decidedly below the average in total activity, while one is slightly above it. They all belong to type 2, none having a second period of high activity, as the six most vigorous mice did. Three of them, Nos. 5, 7 and 8, start out well, but all except No. 7 rapidly decrease in activity. No. 7 seems to be an average mouse of type 2; however it loses 20 per cent of its weight during the last month. No. 5 has a maximum of 125 301 revolutions but decreases very rapidly until its death when twenty-seven weeks old. No. 6 runs low all its life, its maximum being only 86 895 revolutions. It died

when thirty-four weeks old. No 8 drops from its maximum of 131 473 regularly until the twenty-seventh week; after that its runs are irregular and some are very small. At the same time, from the twenty-eighth week to the end of the experiment it loses 30 per cent in weight. This great loss of weight and its small irregular run indicate that it would have died soon.

This line of mice started out well. They reached a high average maximum of 111 833 revolutions during the eleventh week. This is much higher than the nicotine or caffeine line at the same time but a little lower than the maximum of the control line. In fact the nicotine line never reaches quite as high an average maximum, and the caffeine maximum is only 93 932 revolutions. But after that the alcohol line drops abruptly and only once exceeds 90 000 revolutions. Their total activity is 73 per cent of that of the controls.

The alcohol mice gained 6 grams each up to the twenty-fourth week, which is more than the control mice had gained during the same time. After this, however, they lost 4.5 grams on an average. None of the other lines lost any in weight except the nicotine mice.

The activity of all the mice in the alcohol line seems to have been checked and lessened. The viability of all the mice was weakened, for two died, one was evidently going to die soon and the fourth lost 20 per cent in weight. This loss in weight occurred during the last month of the experiment. The decreased activity began to show after the mice were twelve weeks old, but the loss of weight and lessened viability did not manifest themselves until after the mice were twenty-five weeks old. Thus it appears that alcohol had a markedly injurious effect on the viability an activity of these mice and that these effects were cumulative.

Nicotine line

The mice in the nicotine line show more variations than the mice in any of the other lines. No. 10 is the least active and belongs to type 2. No. 11 is below the average in total activity. It has a very unusual record, running its least at the twelfth week

when other mice are running their highest and reaching its maximum at the thirty-fifth week when the activity of all the other mice is decreasing. No. 9 and No. 12 belong to type 1 and both exhibit great activity. No. 12 has a remarkably high record, much higher than any of the other mice in the different lines of the experiment. It exercised 169 per cent as much as the average and 122 per cent as much as control No. 4, the second most active of all the mice.

The average total activity of these mice is almost equal to that of the controls.

None of these mice died. They gained 3.5 grams during the experiment, which was less than half what the control mice gained. The last month they showed an average loss of 1.5 grams.

Nicotine did not seem to affect the health of these mice but may have slightly checked their growth.

Whether the wide variations in the activity of these mice were caused by nicotine cannot be known without further experiments. Nicotine may have had a stimulating effect on activity, shown particularly in No. 12 with its remarkable record and in No. 9. No. 10 would be an exception to such a theory. No. 11 might be explained as being naturally a very inactive mouse but that the cumulative effects of nicotine stimulated him to activity. Or it is possible that all these variations were due to chance.

Caffeine line

Three of the mice in this line have low records of total activity. Nos. 13 and 15 run very low throughout the experiment. They have the lowest records of total activity of all the mice used in the experiment. No. 13 ran 54 per cent as much as the average and 39 per cent as much as No. 4, the most active mouse in the control line. No. 14 starts out well but soon decreases in activity and dies when thirty-two weeks old. These three mice belong to type 2. No. 16 belongs to type 1 and is above the average in total activity.

The average activity of these mice is the lowest of all the lines. Their average maximum weekly run is only 93 932 revolutions

and their minimum weekly run is 24 415. Their average total activity is 68 per cent of the controls.

The caffeine mice, with the exception of No. 14, gained 11.6 grams each, which was more than any other line gained. But as they started out the smallest of all the mice and at the end of the experiments equalled the controls in weight, they apparently grew normally. No. 14 gained 3.5 grams and lost it again before its death.

The growth of three of these mice does not seem to have been affected by caffeine. One, however, seems to have been injured, for it died when thirty-two weeks old.

Caffeine appears to have decidedly lessened the activity of the mice.

SUMMARY

1. The control mice gained 7 grams on an average during the experiment. None of them died. Three were above the average in activity. Their total activity was greater than any other line.

2. The alcohol mice gained 6 grams on an average up to the twenty-fourth week, but lost 4.5 grams later. Two died and one probably would have died soon. Three were below the average in activity. Their total activity was 73 per cent of that of the controls. Alcohol appears to have had a markedly injurious effect on the viability and activity of these mice.

3. The mice subjected to nicotine gained 2 grams each on an average. None died. Two were below the average in activity and two above, one being far more active than any other mouse in any of the lines. Their total activity was 99 per cent of the controls.

Nicotine apparently did not injure the health of the mice, but seems to have checked their growth.

Nicotine may have had a stimulating effect on the activity of three of the mice. Or it is possible that the variations shown in this line were due to chance.

4. Three of the mice subjected to caffeine gained 11.6 grams each on an average, but since they started out the smallest of all

the mice and at the end of the experiment equalled the controls in weight it appears that they grew normally. One mouse died.

These mice were the least active of all the lines, their total activity being 68 per cent of that of the controls. Three were below the average in activity and one was above.

Caffeine seems to have had no influence on the growth of three of the mice, but apparently had an injurious effect on one mouse, resulting in its death.

Caffeine seems to have greatly lessened the activity of these mice.

BIBLIOGRAPHY

- ASCHAFFENBERG, GUSTAV 1896 *Praktische Arbeit unter Alkoholwirkung*. Kraepelin's Psychologische Arbeiten, Bd. 1. S. 608-626. Leipzig.
- FÉRÉ, CH. 1904 *Travail et plaisir*. p. 316. Paris.
- FREY. 1896 *Ueber den Einfluss des Alkohols auf die Muskelermüdung*. Mitth. aus Klinken u. med. Instituten der Schweiz. Reihe 4, Heft 1. Basel u. Leipzig.
- HARLEY, V. 1894 The value of sugar and the effect of smoking on muscular work. *Journ. Physiol.*, vol. 16. pp. 97-122.
- HELLSTEN, A. F. 1904 *Ueber den Einfluss von Alkohol, Zucker und Thee auf die Leistungsfähigkeit des Muskels*. Skand. Arch. f. Physiol., Bd. 16., S. 139-221.
- HOCH, A., AND KRAEPELIN, E. 1896 *Ueber die Wirkung der Theebestandtheile auf körperliche und geistige Arbeit*. Kraepelin's Psychologische Arbeiten, Bd. 1, S. 378-488.
- HODGE, C. F. 1903 The influence of alcohol on growth and development. In *Physiological aspects of the liquor problem*. 1 Ed. by J. S. Billings. Houghton-Mifflin, New York, pp. 359-375. 396 pp.
- KRAEPELIN, E. 1899 *Neure Untersuchungen über die psychischen Wirkungen des Alkohols*. Münch., med. Wochenschrift. Jg. 46., S. 1365-1369.
- KOCH, W. 1894 *Inaug. Diss.* Marburg.
- LOMBARD, W. P. 1892 Some of the influences which affect the power of voluntary muscular contractions. *Journ. Physiol.*, vol. 13. pp. 1-58.
- MOSSE, U. 1893 *Action des principes actifs de la noix de kola sur la contraction musculaire*. Arch. ital. de Biol. t. 19., pp. 241-256.
- NICE, L. B. 1912 Comparative studies on the effects of alcohol, nicotine, tobacco smoke and caffeine on white mice. I. Effects on reproduction and growth. *Jour. Exp. Zool.*, vol. 12, no. 1, pp. 133-152.

- RIVERS, W. H. 1908 The influence of alcohol and other drugs on fatigue. Arnold, London, 136 pp.
- ROSSI, C. 1894 Ricerche sperimentale sulla fatica dei muscoli umani sotto l'azione dei veleni nervosi. *Rivista sper. di Freniatria*, vol. 20, pp. 442-480.
- SCHUMBURG. 1899 Ueber die Bedeutung von Kola, Kaffee, Thee, Maté und Alkohol für die Leistung der Muskeln. *Arch. f. Anat. u. Physiol. Abth., Suppl. Bd.* S. 289-313.
- STEWART, C. C. 1898 Variations in daily activity produced by alcohol and by changes in barometric pressure and diet, with a description of recording methods. *Am. Jour. Phys.*, vol. 1, pp. 40-56.
- SLONAKER, J. R. 1907 The normal activity of the white rat at different ages. *Jour. Comp. Neur.*, vol. 17, pp. 342-359.
- 1908 Description of an apparatus for recording the activity of small mammals. *Anat. Rec.*, vol. 2, no. 3, pp. 116-123.
- 1912a The normal activity of the white rat from birth to natural death its rate of growth and the duration of life. *Journ. Animal Behav.*, vol. 2, no. 1, pp. 20-42.
- 1912b The effect of a strictly vegetable diet on the spontaneous activity, the rate of growth, and the longevity of the albino rat. Leland Stanford Junior Univ. Pub., Stanford Univ., Cal., 36 p.
- SCHNYDER, L. 1903 Alkohol und Muskelkraft. *Arch. f. d. ges. Physiologie*, Bd. 93, S. 451-484.