

The Age of Reproduction as a Factor of Transmissible Divergences in Learning Ability in the Mouse

A number of studies devoted to the establishment of divergences by systematically choosing young or old genitors have been made in asexual, as well as in sexual organisms (PARSONS¹). While some of them concern behavioural characteristics, such as sexual activity (WATTIAUX²), learning ability has not been, as yet, an object of these investigations.

In the present experiments two strains of a commercial stock of albino mice selected according to maternal age have been used. A so-called 'bradygenetic' strain was obtained by reproduction from old mothers (more than 12 months of age), and a 'tachygenetic' by reproduction through young females (less than 3 months). Within each line a close inbreeding was avoided by choosing each time an uncle as father of the following generation. These males were always middle aged (between 5 and 7 months) to avoid all interfering influence of paternal age.

Our experimental subjects were members of the third bradygenetic and of the twelfth to fourteenth tachygenetic generations. At 2, 5, and 12 months, their learning ability was tested in the double-T VICARI's maze³ to determine how efficiently bradygenetic and tachygenetic fasted subjects would learn to run through the maze directly to food. The same procedure was used throughout the whole experiment, according to VICARI: 'The animal of its own accord left the starting box and entered the maze through a small circular opening.... The problem consisted in finding the food by choosing the left-hand exit of the first compartment, and the right-hand exit of the second one, and avoiding the closed doors'. The latency reaction time, the running time, and the number of errors were recorded. The training lasted three weeks and a trial a day was given each week from Monday to Friday (five trials a week), the data for the same week being cumulated.

Table I gives the mean number of errors during learning for the tachygenetic and bradygenetic animals at 2, 5, and 12 months, with 95% confidence limits. Table II gives the mean running times. For the latency reaction time, the differences are never significant.

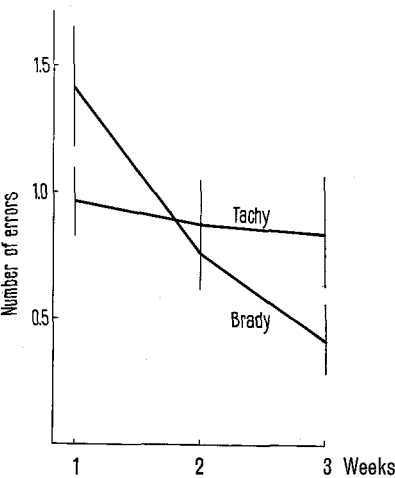
The major result of the study is summarized in the Figure which gives the decrease in the mean number of errors for the three weeks of the training period for

subjects 12 months of age. The superiority in learning ability of the bradygenetic individuals is obvious, although their mean number of errors was greater in the first week. The tachygenetic individuals do not learn at all. For 2 and 5 months of age, the differences between tachygenetics and bradygenetics are similar in orientation, but never significant. For the running time as for the latency reaction time, the two strains do not differ.

To evaluate the importance of our findings in natural populations, they may be compared with data describing natural conditions under which tachy- or bradygenesis is favoured (ODUM⁴) and especially the more recent study of CALHOUN⁵ which establishes that 50% of a rat population did not become pregnant before at least 165 days, although they were able to be so after 2 months. In this context it is interesting to notice that, according to

Table II. Mean running time (in sec)

Age in months	Strains	1st week	2nd week	3rd week
2 to 3	Tachy N = 39	18.746 ± 3.448	9.120 ± 3.464	6.671 ± 1.085
	Brady N = 43	16.088 ± 1.912	6.700 ± 0.520	5.879 ± 0.801
5 to 6	Tachy N = 17	12.882 ± 3.252	8.600 ± 1.851	8.541 ± 2.928
	Brady N = 20	9.870 ± 1.742	6.235 ± 1.296	5.895 ± 1.267
12	Tachy N = 23	14.456 ± 2.336	8.300 ± 1.303	8.465 ± 1.717
	Brady N = 42	18.076 ± 2.808	7.377 ± 0.786 (N = 40)	5.934 ± 0.786 (N = 38)



Mean number of errors for tachygenetic and bradygenetic mice of 12 months, with confidence limits for $t = 0.05$.

Table I. Mean number of errors

Age in months	Strains	1st week	2nd week	3rd week
2 to 3	Tachy N = 39	1.353 ± 0.221	0.887 ± 0.219	0.735 ± 0.196
	Brady N = 43	1.465 ± 0.186	0.804 ± 0.152	0.420 ± 0.137
5 to 6	Tachy N = 17	0.870 ± 0.290	0.823 ± 0.320	0.847 ± 0.303
	Brady N = 20	0.935 ± 0.248	0.565 ± 0.149	0.550 ± 0.227
12	Tachy N = 23	0.960 ± 0.143	0.869 ± 0.184	0.834 ± 0.224
	Brady N = 42	1.419 ± 0.245	0.747 ± 0.123 (N = 40)	0.415 ± 0.141 (N = 38)

¹ P. A. PARSONS, Quart. Rev. Biol. 39, 258 (1964).
² J. M. WATTIAUX, in press (1966).
³ E. M. VICARI, J. exp. Biol. 54, 31 (1929).
⁴ E. P. ODUM, Fundamentals of Ecology (Philadelphia 1959).
⁵ J. B. CALHOUN, Public Health Serv. Pub. (Washington D.C. 1962), p. 1008.

JOHNSON and STRONG⁶, after repeated early reproduction in mice a delay in sexual maturity is observed, while in bradygenetic individuals the opposite is true.

The purpose of this paper is not to contribute to the discussion of the mechanisms responsible for cumulative parental age effects in sexual organisms, which has been done at some length by WATTIAUX². It has been shown by HEUTS^{7,8} and AIZENSTAT⁹ that the segregation ratio of mendelian genes and presumably also of polygenes (WATTIAUX and HEUTS¹⁰) can vary with parental age. In the human species, the frequencies of many congenital defects are correlated with the age of the mother, and it is well known that for mongolian idiocy this correlation is the result of the increased frequency with which chromosomally abnormal eggs are produced in relatively older women¹¹. On the basis of a mechanism analogous to the latter, superior performances in bradygenetic mice, as described in the present report, can scarcely be expected.

Experiments are in progress to exclude possible effects of inbreeding itself on learning performance. Although similar effects of inbreeding have not come to our knowledge, their influence cannot a priori be rejected, while the breeding scheme adopted in our experiments has been applied for a different number of generations to our tachy- and bradygenetic mice.

Résumé. A partir d'un stock de souris albinos non inbred, deux lignées ont été formées, l'une par reproduction

à l'âge de deux à trois mois, l'autre par reproduction à plus d'un an. Les individus de 3^e génération de cette seconde lignée se montrent, à l'âge d'un an, supérieurs aux individus de même âge des générations 12 à 14 de la première lignée pour ce qui concerne l'apprentissage du parcours dans un labyrinthe en double-T. A 2 et à 5 mois des différences de mêmes sens ont été trouvées entre les deux lignées, mais ces différences ne sont pas significatives.

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(Belgium), September 13, 1965.*

⁶ F. JOHNSON and L. C. STRONG, *J. Geront.* 18, 246 (1963).

⁷ M. J. HEUTS, *Agricultura, N.S.* 4, 346 (1956).

⁸ M. J. HEUTS, in press (1966).

⁹ J. A. AIZENSTAT, *Issledovaniya po Genetike* 1, 122 (1961).

¹⁰ J. M. WATTIAUX and M. J. HEUTS, in *Genetics Today*, Proc. XIth Internat. Congr. Genetics, The Hague (1963), p. 168.

¹¹ C. STERN, *Principles of Human Genetics* (San Francisco 1960), p. 472.

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Motoneurone Excitability During Repetitive Stimulation of Group I Afferent Fibres

In the cat, the evoked monosynaptic reflex response decreases as the repetitive electrical stimulation is raised above 0.3 c/s¹. By recording from single motoneurons, LLOYD² found that the discharge frequency follows the stimulation frequency up to a maximum ranging in the different motoneurons from 0.1 to 10 c/s. When the stimulation frequency is raised above these values, the frequency of discharge is seen to decrease and, eventually, to approach zero.

The nature of this reflex inhibition is not yet well understood. In the present investigation, the membrane potential of the inhibited motoneurone has been measured and the excitability of the postsynaptic membrane has been tested with the procedure of FRANK and FUORTES³. The experimental procedure has also included the re-

cording of the reflex response as the frequency of stimulation was suddenly decreased from the inhibiting values.

The nerves to the lateral gastrocnemius and soleus muscles (LGS) were stimulated in 7 curarized cats, spinalized under Nembutal anaesthesia; the ventral roots from L6 to S2 were cut. The monosynaptic reflex re-

¹ A. A. JEFFERSON and W. SCHLAPP, *CIBA Fdn Symp.* 99 (1953).

² D. P. C. LLOYD, *J. gen. Physiol.* 40, 435 (1957).

³ K. FRANK and M. G. F. FUORTES, *Fed. Proc.* 16, 39 (1957).

Intracellular records from spinal motoneurons monosynaptically excited through electrical stimulation of LGS nerves at various frequencies. Initial stimulation frequencies were 32 c/s in A, 8 c/s in B, and 1.5 c/s in C; inhibition frequencies (between arrows) were 250 c/s in A and B, and 15 c/s in C. Between the initial frequency and the inhibitory, the frequency was 80 c/s for B. Spikes are slightly retouched. The membrane potential, during the inhibition of the reflex discharge, is unchanged (C) or slightly lowered because of the excitatory postsynaptic potential (EPSP) fusion (A and B). The EPSPs are, of course, visible when the orthodromic stimulation evokes intermittent spikes and does not produce the EPSP fusion. Intracellular threshold stimuli (indicated by dots) are effective in producing the motoneurone response; this does not occur, of course, when the intracellular stimulus is applied during the post-hyperpolarization (C). In all records, the initial pattern of discharge is immediately resumed after the inhibition period.

