

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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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.

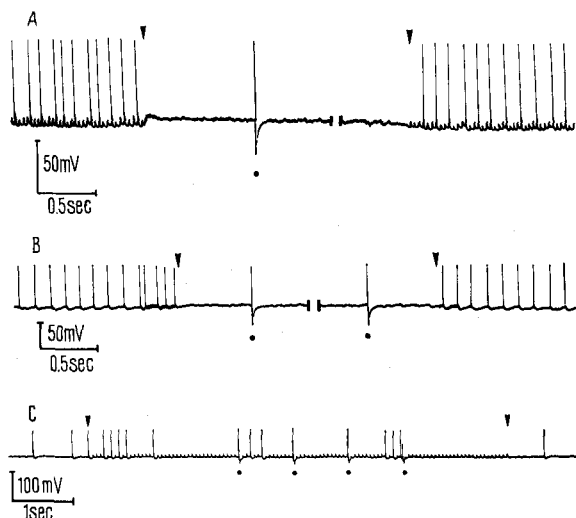
The nerves to the lateral gastrocnemius and soleus muscles (LGS) were stimulated in 7 curarized cats, spinalized under Nembutal anaesthesia; the ventral roots from L6 to S2 were cut. The monosynaptic reflex re-

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.



sponse was recorded by an intracellular micropipette in 23 α motoneurons identified by antidromic stimulation of the central cut end of L7 ventral root. The stimulation frequency of the LGS nerves was kept within values capable of evoking a steady frequency of discharge, which generally ranged from 7 to 12 c/s. Then the stimulation frequency was suddenly raised in order to inhibit the motoneuron response. Threshold intracellular stimuli, previously established when the membrane potential was at resting values, were then applied through the same micropipette⁴ in order to test the motoneuron excitability. Then the stimulation frequency was suddenly lowered to the previous values.

During the reflex inhibition induced by repetitive orthodromic stimulation, no hyperpolarization of the postsynaptic membrane was observed (Figure, A) and the threshold intracellular stimuli were able to evoke a normal response (Figure, A, B, C). When the orthodromic stimulation frequency was decreased to the initial values, the same initial stimulus-response ratio was immediately resumed (Figure, A, B, C).

The lack of the hyperpolarization and the normal excitability of the postsynaptic membrane seem to rule out the possibility that any postsynaptic inhibition is involved in this kind of reflex depression. The peculiarities

of the reflex discharge reappearance, which occurs when the stimulation frequency is lowered, rule out the hypothesis of the 'receptor desensitization' of the postsynaptic membrane⁵.

These experiments support the hypothesis that the reflex discharge suppression observed in the spinal motoneurons during the repetitive orthodromic stimulation is due to a presynaptic mechanism.

Riassunto. La stimolazione elettrica delle fibre afferenti del Gruppo I è in grado di provocare nel singolo motoneurone spinale una depressione della scarica riflessa che è funzione della frequenza di stimolazione. I risultati della presente ricerca sembrano dimostrare che tale depressione riflessa è da attribuirsi ad un meccanismo inibitorio presinaptico.

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Istituto di Fisiologia Umana dell'Università di Milano (Italy), September 11, 1965.

⁴ T. ARAKI and T. OTANI, *J. Neurophysiol.* 18, 472 (1955).

⁵ S. THESLEFF, *J. Physiol.* (London), 148, 659 (1959).

Morphogenetic Field Properties of the Forebrain Area of the Neural Plate in an Anuran

Background. The early amphibian neural plate is known to be, to a large extent, already determined for later regional development, along both the antero-posterior and the medio-lateral axes¹. Thus isolation, transplantation, or reversal of many portions of the early plate fail to prevent their development according to their prospective significance. The presumptive forebrain region, for example, forms in isolation only those structures characteristic of the forebrain². Within this area, however, developmental plasticity is found, since isolated subregions form other forebrain structures in addition to those for which they were specifically fated³. Quantitative differences between the differentiation of the forebrain area *in situ* and *in vitro* also demonstrate that such alterations in the developmental pathways of cells can still take place at the early neural plate stage². Finally, the fact that the experimental 'activation' of neural differentiation from competent ectodermal cells typically results in an isolated but complete forebrain is a further indication of the creation first of a field of 'forebrain' cells, in which only subsequently does a heterogeneous spatial pattern develop⁴. Since most of the experimental analysis of forebrain morphogenesis has been carried out in urodeles, the author's previously cited study of the development of neural plate fragments of the African clawed toad, *Xenopus laevis laevis* (Daudin), offered an opportunity to examine this question in an anuran form.

Experimental. The transparency of the skin in this species made it possible to recognize eye formation in the living explanted tissue by means of the darkly pigmented tapetal outer layer. When examined histologically the tapetum was found to be associated with a fragment of retina, continuous with a neural vesicle or mass. (Retina alone was not encountered under the present experimental conditions, which included the presence of large

amounts of mesodermal cells inside a jacket of ectoderm). In almost 100 preparations of varying size and origin, but all lacking any tissue from the presumptive forebrain area, there were no cases of eye formation. Eye structures were found in 7 out of 8 explants of the entire estimated forebrain area of the early neurula, in 2 out of 4 explants of only the transverse neural fold (presumptive telencephalon) and in all 4 explants of the anterior lateral fold only (future diencephalon roof). When the anterior most region of the neural plate was tested (presumptive eye and ventral forebrain) an eye developed in 8 out of 17 cases. With slightly more caudal plate (mostly diencephalon floor) 4 out of 10 did so. In addition, eye formation occurred in all seven explants made with anterior neural fold tissue excised at the stage of closed neural folds (i.e. late neurula), a region which forms only telencephalon in

¹ H. EYAL-GILADI, *Arch. Biol. (Liège)* 65, 180 (1954). – C. VON WOELLWARTH, *Roux Arch. Entw. Mech.* 145, 582 (1952). – J. GALLERA, *Roux Arch. Entw. Mech.* 145, 143 (1951). – M. A. CORNER, *J. comp. Neurol.* 123, 243 (1964). (For overall surveys of differentiation tendencies in the early plate.) J. C. VAN DE KAMER, Thesis, University of Utrecht (1949). – A. STEFANELLI, *Quart. Rev. Biol.* 26, 17 (1951). – C. O. JACOBSON, *Zoöl. Bidr., University of Uppsala* 36, 73 (1964). (For specific cellular and nuclear development in particular regions of the brain.)

² E. C. BOTERENBROOD, Thesis, University of Utrecht (1962). The total volumes of telencephalon, diencephalon, and eye were measured and compared. Simple spatial patterns were often obtained even in completely disaggregated-reaggregated cell masses.

³ P. D. NIEUWKOOP et al., *Arch. Néerl. Zoöl.* 13, Suppl. 1, 167 (1958); *J. Anim. Morph. Physiol.* 11, 21 (1964). – J. C. VAN DE KAMER¹.

⁴ P. D. NIEUWKOOP, *Develop. Biol.* 7, 255 (1963) for the most recent and precise treatment of this question. This is moreover one of the few experiments where all the future forebrain cells were with certainty exposed to essentially identical conditions during the 'activation'. An anuran form (*Rana pip.*) was studied in addition to a urodele (*Amblystoma punct.*).