strate the electrical activity of acetylcholine at a phase boundary, which may explain the electrical phenomena in cholinergic nerves. These findings have theoretical interest and suggest that acetylcholine is more than a "chemical mediator" or "synaptic transmittor." Acetylcholine is capable of producing variations of electrical potential differences in the nervous system of a size and sign (invariably negative) similar to the electrical currents associated with the "nerve impulses."

Conclusion The addition of acetylcholine to saline solution in contact with cholesterol dissolved in an inert solvent (benzyl alcohol) gives rise to a negative electrical potential difference. It is suggested that this electrical negativity may play an important role in the origin of the negative variation associated with the nerve impulse.

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Locomotor Reactions of Fundulus Embryos with Abnormal Mauthner's Neurones.

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Some *Fundulus heteroclitus* embryos have been prepared in which the central nervous system is characterized by various deviations from normal in both the number and arrangement of Mauthner's neurones. In view of the divergent opinions expressed in the literature[1-3] concerning these cells, it has seemed desirable to investigate the behavior of these embryos for information concerning the function of the giant neurones.

The operations, which involved the implantation of grafts into the prospective brain region of gastrula stages, were performed by methods already described.[4] The operated embryos were allowed to develop through to swimming stages, and their reactions were observed at least twice daily during the progress of development. The embryos were fixed in Bouin's solution, sectioned at 10 micra, and impregnated with silver by a modification of Bodian's method.

In 7 embryos Mauthner's axones were lacking in the posterior medulla and cord. Four of these embryos, although capable of swimming both spontaneously and in response to artificial stimulation, were abnormally passive and tended to remain immobile, if left undisturbed, for long periods of time. The 3 remaining embryos exhibited vigorous movements. One of these was kyphotic because of disturbance to portions of the brain other than Mauthner's neurones, to such a degree that it was mechanically unable to maintain its normal postural relationships. Yet even in spite of the great mechanical obstacle to normal locomotion, it made continual efforts to produce the swimming reaction.

Four embryos showed one Mauthner's axone coursing posteriorly through the cord, instead of 2. In one of these the fiber extended down the cord only as far as the posterior trunk region, and was located in the dorso-lateral white rather than in its usual ventral position; this embryo, like some of those described above, was abnormally passive and at times immobile. In the 3 remaining embryos the axone ran in its usual position in the cord: one of these

* All operations were performed at the Osborn Zoological Laboratory, Yale University. Part of the histological work was completed in that laboratory during the tenure of a John Simon Guggenheim Memorial Foundation Fellowship.

1 Bartelmez, G. W., *J. Comp. Neur.*, 1915, **25**, 87.

2 Detwiler, S. R., *J. Exp. Zool.*, 1933, **64**, 415.

3 Coghill, G. E., *Psych. en Neur. Bladen*, 1934, **38**, 386.

4 Oppenheimer, J. M., *J. Comp. Neur.*, 1941, **74**, 131.

embryos was abnormally passive and immobile for long periods, although capable of swimming normally when artificially stimulated; the other 2 showed no evidence of atypical suppression of activity.

One embryo, of another category, whose swimming movements were normally sustained and vigorous, had an ectopic Mauthner's neurone whose axone coursed posteriorly only as far as the mid-trunk level; the contralateral axone was normal in the cord. This embryo veered to the left when swimming, but its deviation was accounted for not by changes in the central nervous system but rather by a pathological puckering of the skin in the trunk region which resulted in a contracture of the somites in the region involved.

There were 7 embryos in which the 2 Mauthner's fibers coursed posteriorly on the same side of the cord rather than on opposite sides. One of these was a kyphotic embryo which swam only sporadically; another was an abnormally immobile and passive embryo. The remaining 5 embryos exhibited no irregularities of locomotion attributable to the unusual location of the Mauthner's axones; 2 of them, in fact, were completely normal in behavior despite other structural abnormalities of the brain.

Finally, the cords of 22 embryos were characterized by the presence of axones arising from supernumerary Mauthner's cells. In some cases the extra axones were located dorsolaterally in the cord; in others they were located in their typical position. The arrangement of axones in these embryos was sometimes symmetrical, sometimes asymmetrical. The group included, for instance, among the embryos in which the fibers were in their normal position, 8 in which there was one axone on one side of the cord and 2 on the opposite side. In 2 of these embryos the only detectable abnormality of the brain was a unilateral duplication of Mauthner's cell with all its processes; in both cases the accessory cells and their dendrites were immediately adjacent to their normal counterparts and hence presumably subject to the reception of impulses from all the pathways usually impinging on the neurones. There were 3 embryos with one fiber on one side of the cord and 3 on the opposite side; one in which there were 2 fibers on each side of the cord; one in which there were 3 fibers on one side of the cord and 2 on the other, all in the normal position.

One embryo in the group with supernumerary cells and fibers was abnormally passive and sometimes immobile. In all the other cases, the only variants of behavior recorded were such as could be attributed to abnormalities elsewhere in the brain than in Mauthner's system; in no case was the asymmetry in the arrangement of fibers reflected in asymmetry of reaction.

Discussion. The embryos described as inactive to an abnormal degree may perhaps correspond to the amphibian embryos in which one or both Mauthner's cells were extirpated, or in which the axones of the cells have taken an anterior rather than a posterior course, as described by Detwiler.[2,5,6] The results reported here differ from Detwiler's, however, in that the present embryos lacking one or both axones in the cord were less uniform in behavior than Detwiler's, since only about half of them were abnormally passive or immobile.

This discrepancy may perhaps be explained by the fact that the operations on the Fundulus embryos were performed at earlier stages than were used in Detwiler's experiments. It is conceivable that a greater degree of regulability of function can be attained by a brain abnormal from its earliest formation than by one operated during stages after the neural tube is established. The apparently negative results of the Fundulus experiments in which supernumerary axones are present, and the absence of asymmetry in behavior in both fish and amphibian embryos asymmetrical as to Mauthner's axones in the cord, demonstrate the great regulability of function that can occur in developing brains. Other studies on Fundulus embryos, still in progress, show that brains rendered highly abnormal in structure by operations during gastrula stages can regulate functionally to a surprising extent.

The fact that the unilateral addition of one or more giant axones is not expressed in asymmetry of behavior brings up several other significant issues. Interesting physiological

[5] Detwiler, S. R., *J. Exp. Zool.*, 1927, **48**, 15.

[6] Detwiler, S. R., *J. Exp. Zool.*, 1943, **94**, 169.

problems, hardly germane to the present considerations, are raised by the demonstration of a condition whereby small slowly conducting fibers on one side of the central nervous system can balance the conduction of impulses by larger rapidly conducting contralateral fibers well enough to maintain symmetrical activity of the organism as a whole. The described condition is an important one, however, in relation to future analyses of the function of parts of the developing central nervous system. Any such analyses must take into account the degree to which, and the mechanisms by which, the embryonic brain can successfully compensate for the addition of supernumerary units.

Summary. Locomotor reactions have been observed in *Fundulus heteroclitus* embryos abnormal in number and arrangement of Mauthner's neurones. Five out of 11 embryos lacking Mauthner's axones on one or both sides of the cord were abnormally passive or immobile; the remaining six exhibited vigorous swimming movements. Out of 7 embryos in which the 2 Mauthner's fibers coursed posteriorly both on the same side of the cord, 2 were abnormally passive and 5 exhibited vigorous movements. Axones from supernumerary Mauthner's cells were present in the cord in 22 embryos; one of these embryos was abnormally passive, but the others exhibited no variations of behavior attributable to the altered number of Mauthner's fibers. The apparently negative results of the experiments in which supernumerary axones were added, and the fact that asymmetry in the arrangement of fibers was not reflected in asymmetry of reaction, demonstrate a high degree of regulability of function in the developing brain of Fundulus.

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Activity of Pyridoxine Derivatives in Chick Nutrition.*

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The discovery[1] and confirmation[2] of the existence of pseudo-pyridoxine, which has very high bacterial potency, raises a question regarding its activity in animal nutrition. Carpenter *et al.*[3] reported preparations of pseudo-pyridoxine to be less active for the rat than the original pyridoxine. We wish to report in this paper similar studies on the activity of pseudo-pyridoxine in chick nutrition.

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‡ Called pyracin-5 in this paper to distinguish it from the lactone of 2-methyl-3-hydroxy-4-carboxy-5-hydroxymethylpyridine, which has also been reported to be active.[7] Pyracin-5 has also been termed α-pyracin and pyridoxic acid.

[1] Snell, E. E., Guirard, B. M., and Williams, R. J., *J. Biol. Chem.*, 1942, **143**, 519.

[2] Carpenter, L. E., and Strong, F. M., *Arch. Biochem.*, 1944, **3**, 375.

[3] Carpenter, L. E., Elvehjem, C. A., and Strong, F. M., PROC. SOC. EXP. BIOL. AND MED., 1943, **54**, 123.