Ultra-structure of the Myoneural Junction in Myasthenia Gravis

In myasthenia gravis the leading abnormality appears to be a disorder of transmission of the nerve impulse from the terminal expansions of the neural component of the end-plate across the myoneural junction to the muscle. The transmission of impulses is promptly restored by administration of anti-cholinesterasic drugs suggesting that the essential structural abnormality, if such there be, is a fine one. For this reason one must feel a reluctance to accord a primary role in the disorder of neuromuscular transmission to the florid and apparently permanent changes in the end-plates demonstrated by vital staining in myasthenic patients by Coërs and Woolf[1], Woolf *et al.*[2] and Bickerstaff and Woolf[3].

An abnormality in the ultra-structure of the synaptic region in such end-plates would, however, be more acceptable as the morphological component of this reversible disorder of transmission. We have, therefore, in our present study of the ultra-structure of the human end-plate in myasthenia and other diseases paid special attention to the synaptic region. Naturally many additional data have been accumulated at the same time, but this will be the subject of a later report when a larger number of cases have been studied and the significance of the variations in structure encountered can be more reliably assessed.

What we wish at this stage to report is : (*a*) that a compound synaptic membrance similar to that described by Robertson[4] in the chameleon lizard also occupies the synaptic troughs of human end-plates both from non-myasthenic and myasthenic patients ; (*b*) that we have been unable to demonstrate until now any significant difference in the structure of the membrane in the two cases.

It will be observed that slightly better preparations were obtained from the non-myasthenic patient (suffering from a peripheral neuropathy following Wernicke's encephalopathy) and in these we are able to see not only the five layers described by Robertson, but two further layers formed by the resolving of the central dense zone into a three-layered structure, two dense layers bordering on an inner lighter layer. This innermost light zone was observed by Robertson only in the depths of the junctional folds. We have also been able to demonstrate in both patients that there appear to be occasional pores in the dense line next to axoplasm, of such a size that the vesicular structures believed to be packets of acetyl choline molecules could pass through the pore from the terminal axoplasmic expansion into the first light layer or zone. Robertson also noted in many regions fragmentation or absence of this line. He was, however, uncertain as to whether such breaks were physiologically significant discontinuities or artefacts. The borders of the pores in our preparations are such as to incline us to regard them as physiologically significant. We have also observed that the central three layers (Robertson's central dense zone) split at the mouth of a junctional fold, so that within the latter the seven-layered arrangement will continue. Our observation that Robertson's central dense zone has a light layer within it suggests that this may be an important channel within which substances may circulate both in the synaptic region and within the troughs.

While we have been unable to demonstrate any significant difference between the synaptic regions in the myasthenic and non-myasthenic patient, this must not be taken to indicate that no such difference exists, rather it provides an indication of the structures to be studied in the course of further investigations.

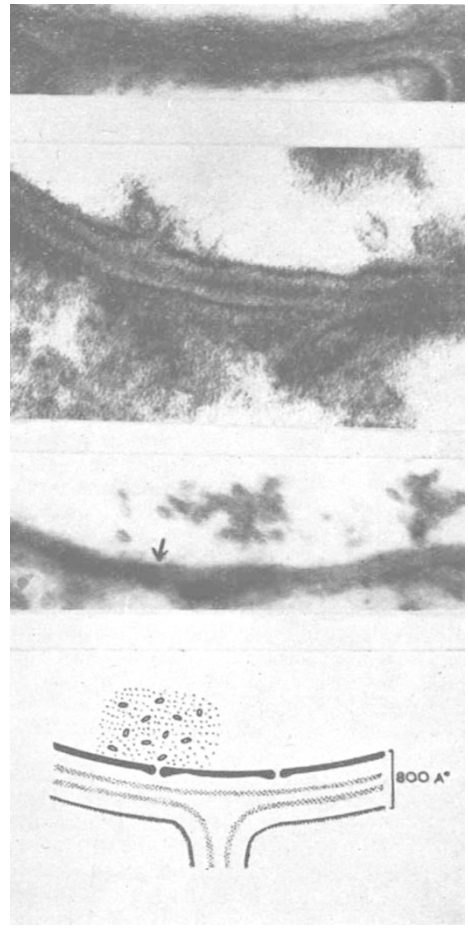

Fig. 1. The compound synaptic membrane in end-plates from non-myasthenic and myasthenic patients. In all the illustrations the neural aspect of the membrane is uppermost. *a*, Non-myasthenic patient—the membrane can be seen, especially to the right, to consist of 7 layers (×86,000) ; *b* and *c*, myasthenic patient. A membrane of at least 5 layers is demonstrated and in (*c*) a pore in the outermost layer (marked with an arrow) can be seen with axonal vesicles in its vicinity (*b* ×100,000 ; *c* ×37,000); *d*, diagrammatic representation of the laminal structure of the synaptic membrane showing the thickness of the layers. This is based on (*a*), and 800 A. is probably a maximum measurement, the synaptic membrane in (*b*) measuring 690 A.

It remains to add that the myasthenic patient whose end-plates are referred to here was a young woman with typical myasthenic weakness and fatiguability affecting the muscle sampled by biopsy, prior to which she had not been treated with anti-cholinesterasic drugs.

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