HOROWICZ (1960) to be at a depolarization of about 40 mV, with the maximum tension being reached at a depolarization only about 10 mV greater than threshold. From the results of our a. c. impedance measurements, the time constant C_eR_e by which the action potential would be distorted was, on the average, 1.4 msec and the largest value obtained was 2.1 msec. When RUSHTON's (1937) method of graphical analysis was applied to solve for the potential change which would be produced across C_e by a typical action potential from a frog sartorius fibre (peak amplitude 125 mV) when C_eR_e was 2 msec, it was found that the potential change across C_e reached 60 mV (see Fig. 18 of FALK and FATT 1964) which would be adequate for maximal activation of the contractile system.

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INTERPRETATION OF THE CENTRAL EXCITATORY AND INHIBITORY STATES

by RAGNAR GRANIT

In our scientific vocabulary of today Sherrington's concepts 'central excitatory state' and 'central inhibitory state' no longer play the role they used to do. This being the case it is of some interest, historical as well as theoretical, to inquire into the reasons for it. One might imagine that they finally have been replaced

by more precise concepts or, again, that they simply have been forgotten. In the middle twenties these concepts were important enough to justify a belated inquiry into their fate and present interpretation. And why were they so important? The answer is simply that the two concepts drew attention to the principle of graded excitability as a function of time, and to Sherrington's view that c.e.s. and c.i.s. were capable of algebraic summation. Sherrington's deductions, as formulated in 1925, were rooted in observations over a lifetime including not only reflex work by isometric myography after the first World War, but also experiences from his earlier studies of the scratch reflex, the lengthening and shortening reactions etc.

The c.e.s. was finally analyzed by ECCLES and SHERRINTON (1931) using the technique of a conditioning shock followed by a test shock. A schematic drawing of the rise of c.e.s. as a function of time was produced which figured in most textbooks of that period. It is well known to all students of the central nervous system and need not be reproduced here.

A gradual change of emphasis took place with the introduction of monosynaptic testing by RENSHAW (1940) and LLOYD (1941) because application of the method used by ECCLES and SHERRINGTON then came to imply analysis of transmission at a specific set of synapses activated and tested by a volley in fairly homogeneous, large muscular afferents. This volley was reasonably synchronous, and so the test shock measured the magnitude of remnant excitatory or inhibitory state as a function of time. The concepts c.e.s. and c.i.s. underwent a corresponding purification and lost their general character. This work also shifted the frontier of subsequent analytical efforts to problems of transmission. This line of advance became, as it were, finally codified when ECCLES and his colleagues in 1952 introduced the intracellular approach to reflex work in general and to monosynaptic studies in particular. The monosynaptic EPSP and IPSP then became the 'purified' c.e.s. and c.i.s. respectively. In terms of membrane potential these two processes were antagonistic, and their time course suggested an explanation of the results obtained by monosynaptic testing of an assembly of extensor or flexor motoneurones.

It remained to ask whether the idea of algebraical summation would be valid also in a reflex context and this proposition was tested by GRANIT and RENKIN (1961) whose theoretical reasoning was based on opposite synaptic currents for excitation and inhibition. In their experiments excitation and inhibition cancelled out on the principle of algebraical summation, but it should be realized that the experimental conditions were carefully selected for purity.

It is no criticism of the conclusion drawn from the experiments presented above if one suggests that the original concepts of c.e.s. and c.i.s. may have lost something in the process of purification. This is simply the way science advances: it defines and re-defines its concepts until something precise emerges and in the present case this happened. One is now free to raise the question of whether or