narkotische Wirkung des letzteren auf. Jedoch kommt die bei alleiniger Pyridostigmingabe induzierte psychomotorische Erregung nicht zustande. 16–20 min nach der Injektion von Pyridostigmin ist der Hund bereits völlig wach, während sonst die zentrale Adrenalinnarkose bei dieser Dosierung 2–2½ h dauert. Ab und zu ist zwangsweises Kopfschütteln zu beobachten, zu einem Umherlaufen kommt es nicht.

Eine ähnliche, die zentrale Adrenalinnarkose aufhebende Wirkung konnte für D-Tubocurarin nachgewiesen werden[3].

Wir nehmen an, dass die beobachteten Phänomene über eine Wirkung auf diencephalische Zentren entstehen (wofür die parasympathischen Erregungszeichen während der Pyridostigminwirkung sprechen) und dabei die Folge einer entsprechenden Synapsenhemmung bzw. -entladung sind. Es wäre hier dem «central inhibitory state» (SHERRINGTON), wie er beispielsweise bei intrazisternaler Adrenalininjektion entsteht, ein «central excitatory state» entgegenzusetzen. Das ganze Bild der zentralen Pyridostigminwirkung erinnert stark an psychomotorische Erregungszustände beim Menschen, wie sie im Ablauf anderweitiger Erkrankungen vorkommen, zum Beispiel bei Epilepsie, agitierter Schizophrenie usw. In der Tat lässt sich in Umkehrung unseres Modellversuches der katatone Stupor bei schizophrenen Kranken durch intraventrikuläre Injektion von Cholinesterase unterbrechen[4].

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Summary

By injection of cholinesterase-inhibitor and vagotonic pyridostigmine into the *cisterna cerebello-medullaris* in dogs, it is possible to evoke a state of psychomotoric excitement resembling that seen in various human diseases. On the other hand, intracisternally injected epinephrine (central anesthesia) and pyridostigmine each inhibit the other's action.

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Membrane Potential of a Ranvier Node Measured After Electrical Destruction of its Membrane[1]

In the last few years, methods have been developed to measure the absolute value of membrane potential changes produced by treating nerve fibre bundles or single Ranvier nodes with solutions of variable ionic concentration[2]. These methods and the more accurate compensating method used by HUXLEY and STÄMPFLI[3] had the disadvantage that zero membrane potential could not be determined except by the assumption that isotonic KCl solutions depolarize the membrane completely. Thus all these methods, using external electrodes as compared with intracellular micropipette-measurements, had the disadvantage of giving relative values instead of absolute ones. The newly developed method of the «circulated node»[4] has, however, given a new possibility of measuring the absolute value of the membrane potential (despite external electrodes) by destroying electrically the membrane of the circulated node at the end of an experiment. We had in fact confirmed the observation of FRANKENHAEUSER and WIDÉN[5], showing that anode break excitation in myelinated nerve can be elicited by strong positive pulses. We were able to show[6] that such pulses produce a breakdown of membrane resistance and potential, if they increase the membrane potential by 70 to 110 mV, which corresponds to a

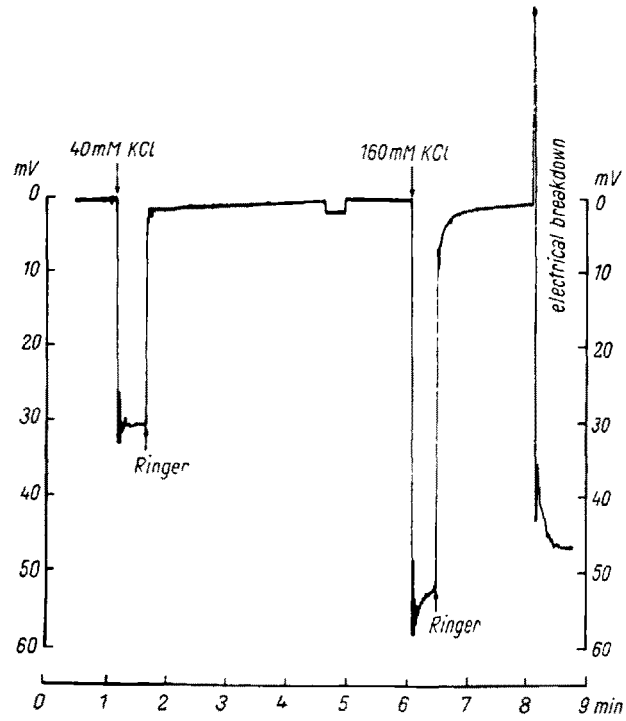

Fig. 1. – Example of electrical breakdown of membrane potential by a short application of 10 V DC to the Ranvier node under investigation. The node had previously been used to determine the equilibrium potential for 40 and 160 mM KCl. Notice that membrane potential zero is only reached after a certain time which may be explained by a junction potential between axoplasm and external fluid which disappears rapidly after removal of membrane. The small rectangular deviation of the base line between the two increases of external KCl concentration (1,9 mV downwards) is due to the application of – 10 mV in the current feeding device, having an external resistance of 70 Megohms. The current flowing during this time was measured with $0{\cdot}6 \times 10^{-10}$ A. The resistance of the nodal membrane was therefore $1{\cdot}9 \times 10^{-3} : 0{\cdot}6 \times 10^{-10}$ = ca. 31·5 Megohms. The ink-writer was not completely aperiodically damped which explains the oscillations after strong potential changes. (Experiment No. 81; February 8, 1957; single motor fibre *Rana esculenta* ♀ 20° C.)

[1] Supported by grants from the Swiss National Foundation for Scientific Research.

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[4] R. STAMPFLI, J. Physiol. (Paris) *48*, 710 (1956).

[5] B. FRANKENHAEUSER and L. WIDÉN, J. Physiol. *131*, 243 (1956).

[6] R. STÄMPFLI and G. RUDOLPH (in preparation).

voltage gradient of approximately half a million volts/cm across the membrane. If only one short pulse is given, the membrane recovers immediately after the breakdown like an electrolytic condenser. If very strong positive pulses of the order of 10 V are applied, the membrane is destroyed irreversibly. This is proved by the sudden appearance of a membrane potential difference of 40 to 60 mV (treated node negative) between the destroyed node and its neighbouring ones and by the impossibility of polarizing this node by feeding positive

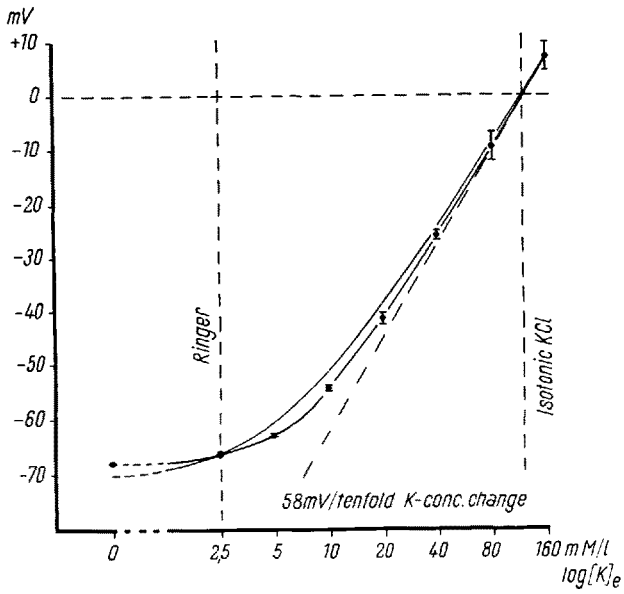

Fig. 2. – Ordinate: Inside potential in mV; Abscissa: External K-concentration (K substituted for Na). Curve without points: Relation between membrane potential and log $[K]e$ as determined by HUXLEY and STÄMPFLI[3] with their compensating method. Curve with black points: Average membrane potential values corrected for short-circuiting factor determined by the 'circulated node' technique after electrical breakdown of membrane and assumption of an average membrane potential of -67 mV (according to[3], Figure 3). Vertical lines: Statistic error of mean. Number of experiments: 6 for all concentrations, except 11 for 20 mM KCl and 12 for 40 mM KCl.

160 mM KCl was used instead of isotonic KCl in our experiments. The curves, nevertheless, cross exactly the zero membrane potential level at an external K-concentration corresponding to the one of isotonic KCl (117 mM). The straight line corresponds to a slope of 58 mV per ten-fold concentration change. For explanation of slight difference between the two curves see text.

current into it. We take this as evidence of complete removal of the nodal membrane by electrical breakdown. As seen in Figure 1, the new potential equilibrium is only reached after several seconds. We suppose that this is due to the disappearance of a junction potential between the axoplasm and the external fluid. If the membrane has in fact been destroyed, the sharp limit of concentration difference between the two fluids will rapidly vanish. The residual potentials observed in this way immediately after membrane breakdown are of the order of 10 mV or less, which corresponds to the estimated value[7].

If the membrane potential of the treated node actually drops to zero after electrical breakdown, the true value of any depolarization during the preceding experiment can be calculated by assuming that the measured breakdown potential $[Vm]_{observed} = K\,[Vm]_{true}$ where K is the short-circuiting factor. $[Vm]_{true}$ according to HUXLEY and STÄMPFLI[3] (Fig. 3) has an average value of -67 mV. The absolute values of depolarizations produced by various K-concentrations can then be obtained by dividing the measured potentials by the calculated short-circuiting factor. If the assumptions of an average membrane potential of -67 mV and a zero breakdown potential hold, the average values of absolute membrane potential should fall on the curve for membrane potential plotted against log $[K]e$, published by HUXLEY and STÄMPFLI[3]. As seen in Figure 2, the points fit the original curve quite well. The difference between the two curves is due to the fact that currents flowing along the internodes in the two air-gaps are not compensated with the new method. This would slightly reduce the depolarizations caused by medium $[K]e$ or the polarization caused by K-free Ringer as is actually seen in Figure 2. At high $[K]e$ however, the membrane conductivity becomes high enough to prevent the influence of inward current from adjacent regions. This new procedure of destroying the membrane by a strong positive pulse gives therefore correct values if the new equilibrium after electrical breakdown is taken as zero. This increases, at least for myelinated fibre investigations, the advantages of methods with external electrodes. Attempts are made to measure the total membrane potential without correction for the short-circuiting factor by combining the method of the 'circulated node' with the 'sucrose gap' technique, which brings the short-circuiting factor very nearly to unity.

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Physiological Institute of the Saar-University, Homburg-Saar, March 12, 1957.

Zusammenfassung

Mit Hilfe starker positiver Impulse ist es möglich, durch elektrischen Durchschlag die erregbare Membran eines einzelnen bespülten Ranvier-Knotens vollständig zu zerstören und das Membranpotential zu null zu machen. Auf diese Weise ist es möglich, auch mit Aussenelektroden Anhaltspunkte über die absolute Grösse des Membranpotentials zu erhalten und den Kurzschlussfaktor zu berechnen, falls der Längswiderstand zwischen den Ableitelektroden nicht ohnehin so hoch ist, dass der Kurzschlussfaktor praktisch gleich eins ist und die absoluten Werte direkt gemessen werden können.

PRO LABORATORIO

Über eine einfache russkymographische Methode zur fortlaufenden Blutdruckmessung an Mäusen und Ratten

Für viele pharmakologische Untersuchungen ist es wünschenswert, den mittleren Blutdruck über längere Zeit kontinuierlich zu verfolgen. Da für die kleinen Laboratoriumstiere eine technisch einfache und wenig kostspielige Methode nicht vorliegt, versuchten wir, mit

[7] A. F. HUXLEY and R. STÄMPFLI, J. Physiol. *112*, 490 (1951).