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MYOTONIA AND BLOCK OF CHLORIDE CONDUCTANCE BY IODIDE IN AVIAN SKELETAL MUSCLE. K.A. Gráive*, R.K. Entrikin* and S.H. Bryant Dept. Pharmacology, Col. of Med., Univ. of Cincinnati, Cincinnati, Ohio 45219

Adult pigeons within 7 days after addition of potassium iodide (3%) to the drinking water develop a severe myotonia characterized by stiffness upon movement and abnormal repetitive firing of skeletal muscle fibers. Following a suggestion by Mayberry and Lambert (J.Lab.& Clin.Med.72:995,1968) we investigated the possibility that the myotonia was due to a specific block of membrane chloride conductance by iodide ion. Cable parameters, component conductances, excitability and membrane potentials were measured with microelectrodes in fibers of isolated biventer cervicis muscles. Measurements in normal muscles were made at 39° C and in the presence of myotonia-inducing concentrations of iodide (15 to 120 mM) and in chloride-free (methylsulfate) physiological solution. Myotonic muscles from chronically treated birds were similarly studied in normal and chloride-free solution. Iodide conductance of the membrane was found to be low, and an acute application of 15 mM iodide reduced the chloride conductance of control fibers to one half or less. Similar reductions of chloride conductance were found in muscles from chronically treated birds. Reduced chloride conductance leading to repetitive firing, and twitch potentiation due directly to iodide ion appear to be sufficient to account for the observed myotonic behavior. Supported by USPHS, NIH Grant NS-03178 and HL-05280 .

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EARLY TRANSIENT CALCIUM CURRENTS DURING VOLTAGE CLAMP IN SQUID GIANT AXONS. Robert E Taylor, Clay M. Armstrong and Francisco Bezanilla*. Laboratory of Biophysics, NINDS, NIH, Bethesda, Md. 20014, and Dept. Physiology, University of Rochester, School Med. Dent., Rochester, N.Y. 14642.

Axons internally perfused with 290mM CsF + 400 mM sucrose were immersed in either 120mM $CaCl_2$ + 391mM TrisCl or 367 $CaCl_2$ + 7mM TrisCl. From a holding potential of -70mV, alternate pulses of ±70mV, of 3 msec duration, were applied and currents averaged. This was repeated with 300nM TTX and the TTX insensitive component (mostly gating current) subtracted. The resultant inward ionic current had a time course similar to sodium current in 444mM NaCl artificial sea water. The peak inward current was -2.4μAmp/cm^2 in 120mM $CaCl_2$ and -19.2μAmp/cm^2 in 367mM $CaCl_2$ (10°C). On the assumption that the total current is calcium plus cesium and that the calcium current is proportional to external calcium concentration one obtains +5.8μAmp/cm^2 for peak cesium and -8.2μAmp/cm^2 for peak calcium current in 120mM $CaCl_2$ and -25μAmp/cm^2 in 367mM $CaCl_2$. Peak sodium current was about -1.5mAmp/cm^2 in the 444mM NaCl ASW. These preliminary results clearly confirm that the early calcium current flows through the "sodium" channels. Supported in part by NIH grant No. NS-08951-05.

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ACTIVITIES OF POTASSIUM AND SODIUM IN RABBIT HEART MUSCLE. Chin O. Lee* and Harry A. Fozzard, Univ. of Chicago, Chicago, Ill. 60637

In rabbit ventricular papillary muscles, potassium (a_K) and sodium (a_{Na}) activities, which are important for understanding electrophysiological properties of the cells, were measured with cation-selective glass microelectrodes. The intracellular potassium (C_K) and sodium (C_{Na}) concentrations of the same muscle were also determined with flame photometry. The C_K and a_K (in millimoles per liter H_2O) were 134.9±3.1 (mean value ± S.E.) and 82.6 respectively for 8 muscles immersed in Tyrode's solution at 25°C. The corresponding C_{Na} and a_{Na} (in millimoles per liter H_2O) were 32.7±2.7 and 5.7 respectively. The apparent intracellular activity coefficients for K^+ (γ_K) and Na^+ (γ_{Na}) (expressed as the ratios, a_K/C_K and a_{Na}/C_{Na}) were 0.612 and 0.175 respectively. Similar results were obtained from the muscles immersed at 35±1°C in Tyrode's solution. The γ_K was substantially lower than the activity coefficient (0.745) of extracellular fluid (Tyrode's solution) and the γ_{Na} was much lower than that of extracellular fluid. Under the assumption that the intracellular ionic activity coefficient is equal to that of extracellular fluid, 24mM and 26mM for sequestered K^+ and Na^+ were obtained. These results suggest that about 18% of the C_K and about 79% of the C_{Na} were sequestered somewhere in the cells and not detected by the microelectrodes. Several possibilities and some physiological significance for the sequestered K^+ and Na^+ will be discussed. (Supported by USPHS HL 11665 and MIRU Contract NO1-HL-81334).

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ELECTROPHYSIOLOGICAL INVESTIGATIONS OF THE DENERVATED SYMPATHETIC GANGLION. N. Dun* and S. Nishi. Neurophysiology Lab., Dept. of Pharmacology, Loyola Univ. Med. Ctr., Maywood, Illinois 60153.

The cholinergic sensitivities of the superior cervical ganglion (SCG) of the rabbit before and 3-4 weeks after preganglionic denervation were studied by means of sucrose-gap and intracellular recording techniques. Denervation reduced the depolarization of the SCG induced by nicotine or by acetylcholine (ACh) applied after atropinization, while it increased the depolarization caused by methacholine or by ACh applied after curarization. The increased muscarinic depolarization was not entirely due to a reduced cholinesterase activity of the denervated ganglia, for the carbachol induced depolarization of the curarized denervated ganglia was also enhanced. The normal and denervated SCG neurons showed no significant differences in diameter and passive membrane characteristics. The iontophoretic application of ACh to the normal and denervated neurons revealed that the equilibrium potential of the activated nicotinic subsynaptic membrane was only slightly shifted toward the hyperpolarizing direction. The results altogether indicate that the preganglionic denervation depresses the nicotinic sensitivity, whereas it enhances the muscarinic sensitivity. (Supported by USPHS, NIH Grant NS06672).

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THE PROJECTION OF MIDLINE RAPHE NUCLEI TO THE HIPPOCAMPUS OF THE RAT. M. Segal* and F.E. Bloom. Lab of Neuropharmacology, SMR, IRP, NIMH, St. Elizabeths Hospital, Washington, D.C. 20032

Activity of hippocampal pyramidal cells was monitored in anesthetized rats. Bipolar stimulation of dorsal and medial raphe nuclei caused cessation of spontaneous firing of hippocampal cells. This inhibition had a long latency (40-80 msec) and long duration (200-400 msec) and was pronounced when a train of stimuli was used. A similar inhibition was observed as a response to the microiontophoresis of serotonin. These inhibitions were qualitatively different from the responses to stimulation of the fornix or the nucleus locus coeruleus as well as to the iontophoresis of GABA or norepinephrine, all of which are inhibitory with respect to pyramidal spontaneous activity. Iontophoresis of LSD, BOL, methysergide and cyproheptadine as well as picrotoxin antagonized the effects of serotonin. Some of these compounds also antagonized the response to raphe stimulation. A monosynaptic pathway was traced between the raphe and the hippocampus with anterograde and retrograde anatomical techniques. It is suggested that this pathway uses serotonin as a transmitter and that it is inhibitory with respect to hippocampal pyramidal cells.

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THE FUNCTION AND STRUCTURE OF A NONSPIKING INTERNEURON IN THE COCKROACH WALKING SYSTEM. C.R. Fourtner* and K.G. Pearson* (SPON: R.G. Sherman). Univ. of Alberta, Edmonton, Canada.

Several nonspiking interneurons have been found in the metathoracic ganglion of the cockroach. One of these interneurons has the following characteristics. 1) small applied depolarizations of the interneuron excite the leg flexor motoneurons. 2) during rhythmic leg movements there are oscillations in the membrane potential, the depolarizations occurring in phase with the bursts of activity in the flexor motoneurons. 3) short depolarizing pulses applied during these periods of rhythmic activity cause a change in the timing of the subsequent rhythmic activity. This latter observation demonstrates that this interneuron is involved in the generation of the rhythmic motor output. Use of the cobalt iontophoresis technique has shown that the soma of this interneuron is located on the posterior ventral surface of the ganglion and contralateral to the motoneurons it excites. A single process leaves the soma, crosses the ganglion and runs toward the lateral edge of the neuropil where it branches extensively. The terminal branches of the interneuron lie close to the main neurites of the flexor motoneurons. Thus, it is possible that this interneuron monosynaptically excites the flexor motoneuron.