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ISOLATED LIVING HEART SLICES FROM ADULT RATS AND GUINEA PIGS AS A MODEL FOR DRUG TESTING

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Living tissue slices from the brain have been extensively used in neuropharmacological and toxicological research throughout the past 30 years. Comparable studies on tissue slices from the heart are rarely encountered. Here we describe the preparation and maintenance of slices from heart tissue of adult rats and guinea pigs.

Experiments were carried out according to the guidelines for animal welfare. The heart was carefully removed under deep anesthesia. After perfusion with oxygenated physiological solution containing 10-15 mM BDM, tissue blocks (4 mm x 6-8 mm) were prepared from the left ventricle. A tissue block was glued to the cutting stage of a precision vibratome (Integraslice, Campden, UK) and 300 µm thick transmural longitudinal, transverse slices as well as sagittal slices were cut .

Up to 4 slices were transferred into a 4-channel chamber (Synchroslice System, LRE, Germany; superfusion rate 2ml/min) for simultaneous electrophysiological examination. A concentrical bipolar electrode was positioned centrally into each slice for application of biphasic stimulation pulses (200-300 µs duration). Extracellular potentials were recorded with quartz glass isolated platinum/tungsten wires (Thomas Rec., Germany). Alternatively, heart slices were positioned on a multielectrode array (MEA, MCS, Germany).

Extracellular monophasic action potentials (MAP) and local electrograms (ECG) after electrical stimulation could be recorded from any region of the heart slice. The AP size and shape strongly depended on the heart subregion and species used.

Frequency dependent adaptation of action potential duration could be determined and the effect of the I_{Kr} selective inhibitor E-4031 revealed an AP prolongation effect in the same concentration range as in previous reports in papillary muscles. In addition 4-aminopyridine, lidocaine and flecainide were tested to validate the model. Multielectrode experiments demonstrated AP conduction velocities of about 0.5 m/s but a non-isotropic spatial distribution.

Our results show that acute heart slices with normal physiology and pharmacology can be prepared in a standardized manner from adult rat and guinea pig hearts and maintained for up to 30 hours. Therefore, the living heart slice will be a valuable new tool in heart research including risk assessment of QT prolongation.

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