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Rapidly activating delayed rectifier K+ current during post-natal development in mouse ventricle

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Introduction:
The rapidly activating delayed rectifier K+ current (IKr) plays an important role in the repolarization of cardiac action potentials in many mammalian species and is encoded by the ether-a-go-go-related gene (ERG). There is some evidence that IKr is developmentally regulated in mouse heart. However, in these studies, neonatal mouse ventricular myocytes were isolated using the 'chunk' method, which was previously demonstrated to damage the delayed rectifier K+ current. The present study aimed at investigating the developmental changes in IKr in mouse ventricular myocytes isolated from the same Langendorff perfusion method.
Methods:
Single ventricular myocytes were enzymatically isolated from various post-natal stages (day-0 to adult) of C57BL/6 mice using the same Langendorff perfusion method and stored in normal Tyrode solution containing 1.8 mM Ca2+. Appearance of viable day-0 neonate ventricular myocytes was rather rod-shaped, similar to that of adult ventricular myocytes. Whole-cell patch-clamp method was used to record IKr. IKr was identified as an E-4031-sensitive current during various test potentials applied from a holding potential of -50 mV and was expressed as current density (pA/pF). The expression of ERG proteins was also quantitatively assessed using Western blotting.
Results:
IKr was the dominant outward K+ current in day-0 neonatal ventricular myocytes and its amplitude was gradually decreased during the development; IKr amplitude in day-0 and adult myocytes were 3.3±0.2 and 0.5±0.1 pA/pF, respectively. The extent of prolongation of action potential duration at 90% repolarization (APD90) by E-4031 was also progressively decreased from day-0 (30±6%) and day 7 (25±8%) neonatal to adult ventricular myocytes with negligibly small effect. Western blot analysis revealed that ERG protein expression detected at the levels of 130 and 155 kDa was also gradually decreased during development from neonate to adult.
Conclusions:
These data demonstrate that expression of IKr channel and its functional role is developmentally regulated in mouse ventricular myocytes.