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Research Article | Cardiac Excitation and Contraction

The transient outward potassium current plays a key role in spiral wave breakup in ventricular tissue

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Abstract

Spiral wave reentry as a mechanism of lethal ventricular arrhythmias has been widely demonstrated in animal experiments and recordings from human hearts. It has been shown that in structurally normal hearts spiral waves are unstable, breaking up into multiple wavelets via dynamical instabilities. However, many of the second-generation action potential models give rise only to stable spiral waves, raising issues regarding the underlying mechanisms of spiral wave breakup. In this study, we carried out computer simulations of two-dimensional homogeneous tissues using five ventricular action potential models. We show that the transient outward potassium current (I_{to}), although it is not required, plays a key role in promoting spiral wave breakup in all five models. As the maximum conductance of I_{to} increases, it first promotes spiral wave breakup and then stabilizes the spiral waves. In the absence of I_{to}, speeding up the L-type calcium kinetics can prevent spiral wave breakup, however, with the same speedup kinetics, spiral wave breakup can be promoted by increasing I_{to}. Increasing I_{to} promotes single-cell dynamical instabilities, including action potential duration alternans and chaos, and increasing I_{to} further suppresses these action potential dynamics. These cellular properties agree with the observation that increasing I_{to} first promotes spiral wave breakup and then stabilizes spiral waves in tissue. Implications of our observations to spiral wave dynamics in the real hearts and action potential model improvements are discussed.

NEW & NOTEWORTHY Spiral wave breakup manifesting as multiple wavelets is a mechanism of ventricular fibrillation. It has been known that spiral wave breakup in cardiac tissue can be caused by a steeply sloped action potential duration restitution curve, a property mainly determined by the recovery of L-type calcium current. Here, we show that the transient outward potassium current (I_{to}) is another current that plays a key role in spiral wave breakup, that is, spiral waves can be stable for low and high maximum I_{to} conductance but breakup occurs for intermediate maximum I_{to} conductance. Since I_{to} is present in normal hearts of many species and required for Brugada syndrome, it may play an important role in the spiral wave stability and arrhythmogenesis under both normal condition and Brugada syndrome.

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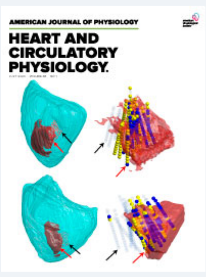

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