Slow Pulse Due to Calcium Current Induces Phase-2 Reentry in Heterogeneous Tissue

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Phase-2 reentry is thought to underlie many causes of idiopathic ventricular arrhythmias as, for instance, those occurring in Brugada syndrome. Reexcitation due to phase-2 reentry needs two conditions to be met: first, that a heterogeneous loss of dome is produced in tissue and, second, that the spike-and-dome regions are able to reexcitate the loss-dome areas.

We analyze the conditions that lead to very short APs, as well as possible mechanisms for reexcitation in a cable. Provided the system is in a state close to the loss of dome, very small gradients of electrophysiological properties, for instance, of the transient outward current, are enough to result in big dispersion of repolarization, giving rise to reexcitations and, eventually, reentry. The origin of reexcitation is based on the existence (often transiently) of a slow pulse (due to the calcium inward current) that propagates into the region of short action potentials (APs) until it reaches excitable tissue. We calculate the speed of the slow pulse, and also give an estimate of the minimal tissue size necessary for reexcitation. Depending on parameters this minimum tissue size may be very small, of the order of 0.5-1 cm. We then study the induction of reentrant waves (spiral waves) in simulations of AP propagation in the heart ventricles.

Drugs that increase the strength of the calcium current may eventually help recovering the dome, thus decreasing dispersion of repolarization, but until this happens, they increase the probability that a reexcitation occurs. This happens because an increase in calcium strength stabilizes the slow calcium pulse, that then is able to reexcitate adjacent tissue. Thus, drugs that decrease the transient outward current would seem more suitable candidates to avoid dispersion of repolarization while maintaining a low probability of reexcitation.