Real-time optical manipulation of cardiac conduction in intact hearts

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ABSTRACT

Aims: Optogenetics has provided new insights into cardiovascular research, leading to new methods for cardiac pacing, resynchronization therapy and cardioversion. Although these interventions have clearly demonstrated the feasibility of cardiac manipulation, current optical stimulation strategies do not take into account cardiac wave dynamics in real time. Here, we developed an all-optical platform complemented by integrated, newly developed software to monitor and control electrical activity in intact mouse hearts.

Methods and results: The system combines a wide-field mesoscope with a digital projector for optogenetic activation. Cardiac functionality can be manipulated either in free-run mode with sub-millisecond temporal resolution or in a closed-loop fashion: a tailored hardware and software platform allows real-time intervention capable of reacting within 2 ms. The methodology has been applied to restore normal electrical activity after atrioventricular block, by triggering ventricle in response to optically mapped atrial activity with appropriate timing. Real-time intra-ventricular manipulation of the propagating electrical wavefront has been also demonstrated opening the prospect for real-time resynchronization therapy and cardiac defibrillation. Furthermore, the closed-loop approach has been applied to optically induce a re-entry circuit across ventricle demonstrating the capability of our system to manipulate whit high versatility heart conduction even towards arrhythmogenic conditions.

Conclusions: The development of this innovative optical methodology provides the first proof-of-concept that a real-time optical-based stimulation can control cardiac rhythm in normal and abnormal conditions, promising a new approach for the investigation of the (patho)physiology of the heart.