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Cardiac arrhythmia induced by hypothermia in a cardiac model in vitro

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Introduction : The neurological damage after cardiac arrest (CA) constitutes a big challenge of hospital discharge since years. The therapeutic hypothermia therapy (34°C-32°C) has shown its benefit to reduce cerebral oxygen demand and improve neurological outcomes after the cardiac arrest. Despite the fact that induced hypothermia after CA has been shown to increase the hospital survival rate, it can have many adverse effects, among which the cardiac arrhythmia generation represents an important part (up to 34%, according different clinical studies). Compared to studies in vivo, cardiac culture in vitro provides a better spatial resolution at cellular level, which could bring some insights of the mechanism of post-hypothermia arrhythmia (PHA) generation.

Method : Monolayer cardiac culture is prepared with cardiomyocytes from new-born rat (1-4 days) directly on the MEA at 37°C. The experiments consist of culture cooling (37°C-30°C) and re-warming (30°C-37°C). The acquired signals are then analyzed with detrended fluctuation analysis (DFA) and phase space reconstruction (PSR).

Results : Both experiments showed that period-doubling phenomena is presented at 35°C, which can be translated as a transit point from normal state to chaos state, from the point view of nonlinear dynamics. Spiral waves are observed in the reconstructed activation map which is commonly considered as a sign of cardiac arrhythmia. Below 35°C, the signals became regular. However, another transit point is found between 30°C-33°C, which agreed with other studies that hypothermia below 32°C could induce arrhythmia. These results are confirmed by methods DFA and PSR.

Conclusion : The general hypothermia therapy uses constant cooling or re-warming. Results in this study showed that a variable speed, especially fast passing 35°C, would help to reduce the rate of post-hypothermia arrhythmia.

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