Pharmacologically induced hypothermia with the cannabinoid receptor agonist WIN55, 212-2 improves cardiac function in a rat model of cardiac arrest


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Background
Cannabinoid receptors (CB) located in the preoptic anterior hypothalamus play a major role in thermoregulation. Our previous work demonstrates that the CB antagonist WIN55, 212-2 (WIN) can induce hypothermia in rats post ROSC. However, the effects of pharmacologically induced hypothermia on myocardial function compared to traditional mechanical hypothermia (MH) are not known. We hypothesized that hypothermia produced by WIN results in better post-resuscitation myocardial function as compared to MH.

Methods
Animal Model
Ventricular fibrillation (VF) was induced in 18 Sprague-Dawley rats weighing between 450 and 550g. VF was untreated for 6 min followed by 8 min of CPR. Resuscitation was then attempted with defibrillation.

Experimental Protocol
Animals were randomized into 3 groups five min after resuscitation: Normothermia (N), MH, WIN hypothermia (WH). N and hypothermia (H) were respectively defined as 37˚C and 33˚C. For the WH group, WIN was administered and for the MH and N groups a vehicle (2% Tween-80 in 0.9% NaCl solution) was administered, both at 1.4ml/kg/h for four hours. H in the MH group was induced with ice packs. Ejection fraction (EF), cardiac output (CO) and myocardial performance index (MPI) were measured at baseline, 1, 2, 3 and 4 hours after ROSC with echocardiography.

Results
All animals showed impaired CO, EF, and MPI immediately after resuscitation compared to baseline values. Target core temperature (33˚C) was constant in both groups. Beginning 1 hour after infusion, myocardial function was significantly improved in WIN versus MH treated animals (Fig 1).

Conclusions
Pharmacologic hypothermia induced by WIN improves cardiac function significantly after CPR when compared with MH. The underlying mechanism is unclear and should be a topic of future study.

References

Disclosure
None