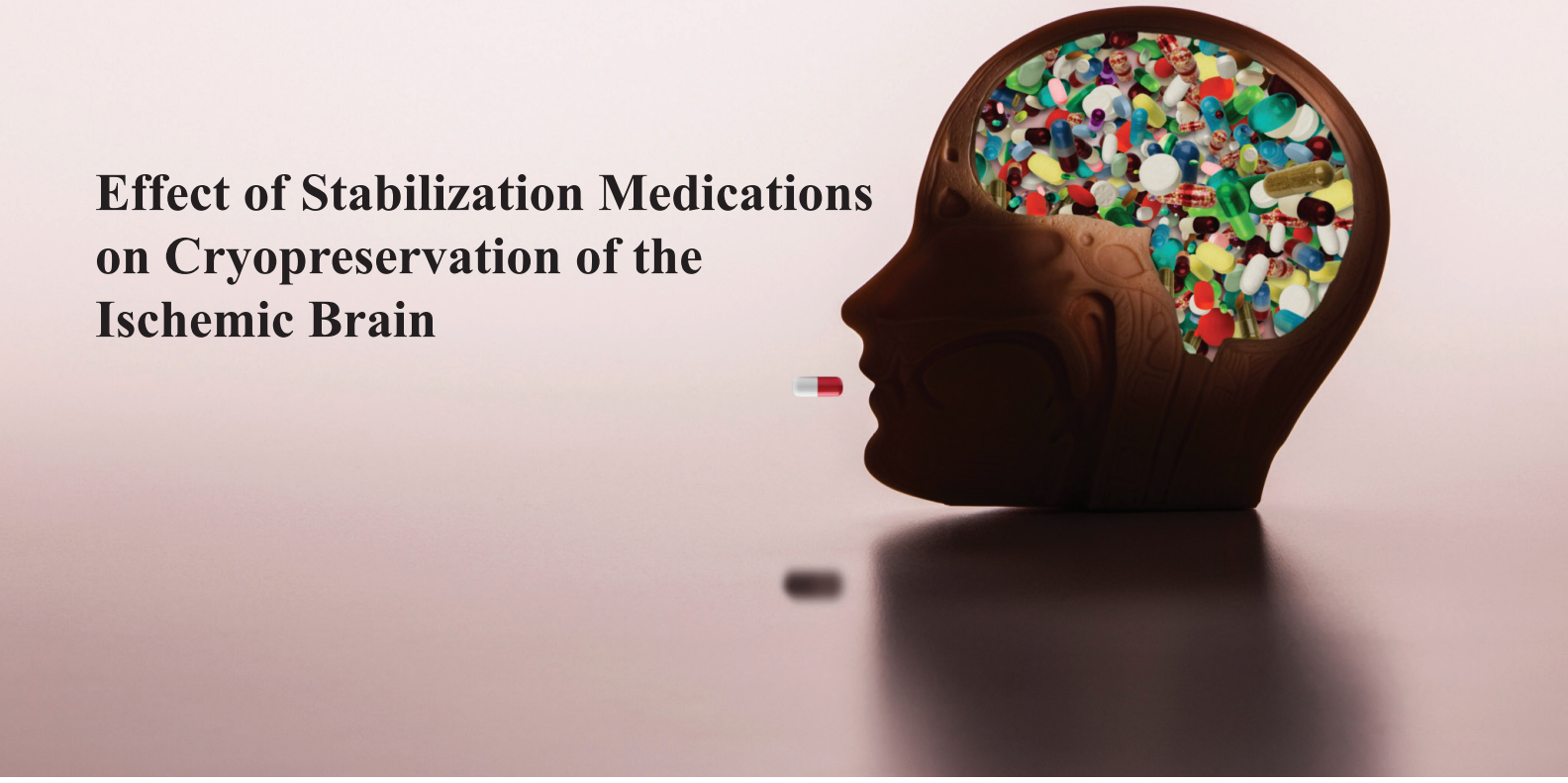
Effect of Stabilization Medications on Cryopreservation of the Ischemic Brain



INTRODUCTION

During the period of 2014-2016 Advanced Neural Biosciences, Inc. (ANB) collaborated with the Alcor Life Extension Foundation to investigate the effects of Alcor's stabilization medications protocol on the cryopreservation of the brain. This work builds on prior work at ANB to characterize the effects of ischemia on perfusion and cryopreservation of the brain.

Experimental validation of Alcor's medications protocol is important because: a) these protocols have not been validated using ice formation after cryopreservation of ischemic animals as an endpoint, b) the current number of medications in Alcor's protocol mandates a sensible cost-benefit analysis, and c) improvements to Alcor's medications protocol might be feasible.

To keep the scope of this project reasonable and practical, ice formation after cryoprotective perfusion and cooling to -130° Celsius was used to evaluate the efficacy of the drugs. The guiding hypothesis was that administration of Alcor's transport medications should make an observable difference in terms of ice formation in normothermic and cold ischemic patients. While the limitations of the rat model, and using ice formation as an end-point should be recognized, these experiments can guide further research in large animal models and contribute to a greater understanding of the efficacy of Alcor's stabilization medications protocol.

BACKGROUND

ANB has conducted experiments into the effects of cerebral ischemia since its inception in 2008 and has reported on its findings in a prior article for this magazine[1]. In short, in our research we established (or further corroborated) that:

- The degree of perfusion impairment and ice formation after cryopreservation is a function of the duration of ischemia.
- Cryoprotective perfusion times increase as the duration of ischemia increases
- Rapid cooling after circulatory arrest reduces perfusion impairment and ice formation after cryopreservation.
- Blood brain barrier breakdown (absence of CPA-induced dehydration) is substantial after 24 hours of cold ischemia and complete after 48 hours of cold ischemia.
- Blood substitution with an organ preservation solution permits ice-free cryopreservation up to at least 48 hours of cold ischemia.
- Composition of the organ preservation matters. The "extracellular" organ preservation solution named MHP-2 produces the best results.
- High perfusion pressure negatively affect outcomes in cryoprotection of the ischemic brain and lower perfusion pressures improve outcome.
- High viscosity cryoprotectants and loading protocols with sharp increases in osmolality improve perfusion of the ischemic brain and reduce ice formation.
- Ischemia-induced whole body edema cannot be mitigated by blood substitution, pharmaceutical treatment, or cryoprotectant carrier solution formulation.
- Blood substitution remains advantageous up to 1 hour of normothermic ischemia.