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Commentary on: Chick embryo: A preclinical model for understanding Ischemia-reperfusion mechanism.

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Abstract

Research on pertinent, prudently designed, well-characterized, and controlled disease models has been an essential step for fundamental discoveries. The purpose is to understand the disease progression without harming the actual human. In this context, numerous in vitro and in vivo models have been developed and studied to date in ischemia-reperfusion research. However, no in vivo attempts have been made till 2018, till we proposed the recapitulation of ischemia-reperfusion injury in a 72 hours developed chick embryo. The present model is useful in understanding the mechanisms of I/R development, drug screening, and stem cell homing.

Keywords: Ischemia-reperfusion (I/R), Chick embryo, I/R modeling, Doppler blood flow imaging, Oxidative stress, Inflammation, Drug screening, Stem cell homing, Cell death.

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About the Study

In light of the current passion for developing novel therapeutics for ischemic stroke [1-3], we have recently invented a model of ischemia-reperfusion in a 3-day developing chick embryo. The modeling of ischemic events followed by the reperfusion injuries has been provided in the journal Frontiers of Pharmacology entitled "Chick Embryo: A Preclinical Model for Understanding Ischemia-Reperfusion Mechanism" [4]. For more than three decades the biologists, scientists, and clinicians have strived to have a better understanding of mechanisms underlying ischemia-reperfusion (I/R) induced tissue injury, with the expectation for developing therapies to confine the devastating health, social and financial burdens imposed by disorders characterized by organ-specific restriction of blood flow, e.g., ischemic stroke. Several in vitro and in vivo attempts to understand the pathology associated with the I/R has been proposed [5-9]. However, the I/R events have never been mimicked in an in ovo model. Hence, the model proposed by us is the first of its kind.

To brief, the I/R is induced in a fertilized 72 hours White Leghorn chick embryo through an in ovo Hook model – custom made (description in Figure 1) by occluding the right vitelline artery for 5 minutes followed by reperfusion for 5.55 h. The Doppler blood flow imaging system, a technique widely employed for microcirculatory imaging in humans and animals, was used to validate the model. Notably, ours is the first study ever where the Doppler perfusion imaging system is employed to map the chick arteries' blood flow. The current model is efficient enough to study the pathophysiological changes associated with I/R mechanisms such as inflammation, oxidative stress, and cell death: apoptosis and autophagy (Figure 2). Notable is the efficiency of the current model to be used for DNA, RNA, and protein studies. Besides elucidating the pathological mechanisms associated with I/R research, our chick I/R model can also be employed to screen numerous drug types and their receptors, apart from its use in stem cell homing (ongoing studies). To its pros, the model is reproducible, cost-effective, and simple to use with no ethical issues in comparison to the other existing in vitro and in vivo models. Hence, it could be anticipated that our chick-I/R model could become a precious tool for basic science and translational research in the coming years. However, one notable limitation of the current model is its inability to directly measure the infarct, which is a worthy indicator of injuries produced by post- I/R [10-12]. The short time window employed in the study is also a limitation of the present study. Albeit a few limitations associated with it, the model is valuable in parallel with traditional in vitro and in vivo I/R models to understand the mechanisms of I/R development and its treatment.

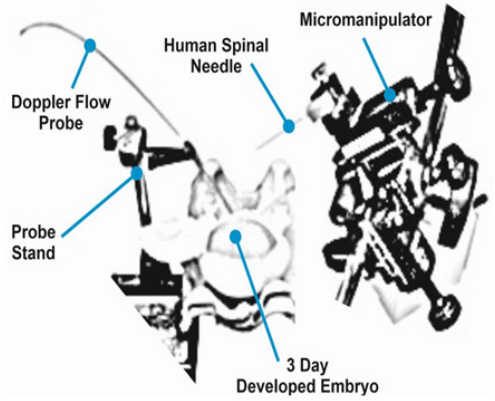

Figure 1. *Represents the sketch of the setup to induce I/R in 72 h developed chick. To measure the changes in the flux, the laser Doppler flow probe is inserted onto the artery to be occluded and reperfused. The sketch also shows the use of a human spinal needle and micromanipulator. For a better description [1].*

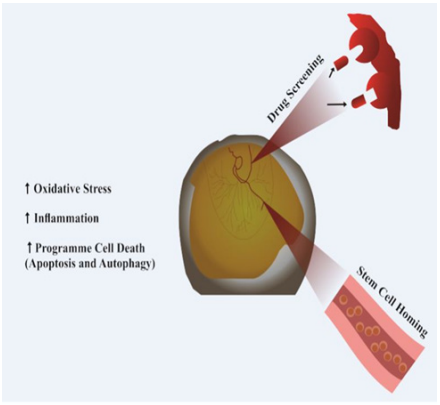

Figure 2. *Reveals the mechanisms associated and induced post- I/R in the embryo. The left part of the egg indicates the pathophysiological events leading to death. To brief, the aftermath of 5 min of ischemia followed by reperfusion induces oxidative and inflammatory stress leading to cell death. The right side indicates the usefulness of the model in drug screening and stem cell homing.*

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