

Brain metabolomics identifies different mild therapeutic hypothermia treatments in an Oxygen-Glucose deprivation rodent model of neonatal asphyxia

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Three large, recent clinical trials have found that some neonates who suffer asphyxia at birth can have greatly improved neurological outcomes if treated immediately for approximately 72 hours with mild, therapeutic hypothermia; specifically, a brain temperature reduction of 4°C. However, hypothermia can also be harmful. Current treatment is by protocol, with beneficial and harmful mechanisms of hypothermia not yet being fully understood. Nuclear Magnetic Resonance (NMR) Spectroscopy (also known as MRS) is capable of *in vivo* detection of brain metabolites in neonates. In many previous clinical and preclinical MRS studies the focus has been on a limited number of metabolites, such as but not limited to lactate, NAA, and ATP; and findings have not been pathognomonic, specific, or rigorously predictive. We decided to start a mechanisms search from scratch, using a rodent brain tissue model of asphyxia, oxygen-glucose-deprivation (OGD), together with 900 MHz ¹H NMR spectroscopy of respiring brain slice extracts, to quantify approximately 40 key metabolites before, during, and after OGD in different hypothermia treatment groups. Because all metabolic reactions are modulated by temperature changes, it seems possible that effective therapies might be distinguishable in multivariate metabolomic analyses. If a 4°C temperature change makes a big difference, such as improved neurologic outcome, one would then thresholds for one or more key chemical reactions might occur in that temperature range, with key metabolic parameters also being discernable. Experimental methods and results by our group and others will be reviewed. Paths to translational research will be discussed.

Biography

Lawrence Litt, PhD, MD, is a Professor of Anesthesia and Radiology. His PhD was in physics from Harvard University in 1971. His research group has had an NIH-supported, NMR spectroscopically-based brain research program for 24 years. (R01 GM34767). He has served on numerous review committees and is an author on 80 peer-reviewed publications.