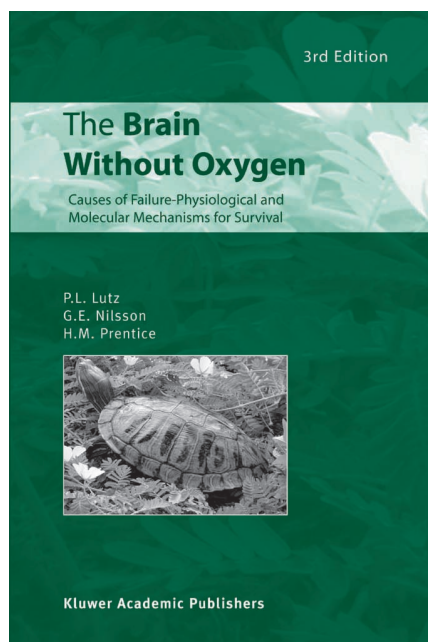


## HOW BRAINS HANDLE HYPOXIA



### The Brain Without Oxygen: Causes of Failure-Physiological and Molecular Mechanisms for Survival

P. L. Lutz, G. E. Nilsson and H. M. Prentice

Kluwer Academic Publishers (2003)  
pp. 260. ISBN 1-4020-1165-2  
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The search for the understanding and treatment of hypoxic or ischemic brain injuries is a formidable physiological and biomedical challenge. The lack of effective treatment for these conditions has greatly frustrated medical research: billions of dollars and hundreds of large clinical trials have yielded no significant neuroprotective treatments. A central thesis of Lutz, Nilsson and Prentice's 3rd edition of *The Brain Without Oxygen* is that a comparative approach to understanding the hypoxic brain may provide new opportunities to solve this problem.

The leading characters of the book are anoxia-tolerant fish, turtles and a few other organisms that possess the capacity to endure long periods of hypoxia and hypothermia. The book compares and contrasts the responses of their brains with that of typical mammals. It describes two main brain survival strategies: a metabolic and functional shutdown characterized by

freshwater turtles (*Chrysemys*) and a switch to sustainable anaerobic metabolism based on ethanol by the crucian carp. Because Lutz and Nilsson have authored numerous papers on these two organisms, their review is authoritative and comprehensive.

The authors face a challenge in that they set out to review multiple aspects of some of the most rapidly evolving research in biomedical science. The book includes chapters on normal brain neurotransmitter function, anoxic brain failure mechanisms, mechanisms of hypoxia tolerance, and adaptations of animals to high altitude, diving and dormancy. New additions to this edition include material on the molecular basis of oxygen sensing, the role of the mitochondrion in delayed neuron death following hypoxia, and the role of hypoxia inducible factor (HIF-1 $\alpha$ ) in gene expression. Hypoxia-activated intracellular signal transduction mechanisms are also included. In many cases, it is difficult to know whether a signaling event is part of an injury mechanism or part of a survival adaptation. This, and the daunting complexity of ischemic neuropathology, can make for a challenging read. In particular, the chapter on molecular aspects of brain ischemia in mammals presents conflicting information on the survival or injury potential of several processes. For example, Lutz et al. initially state that the MAPK p42/44 signaling cascade is associated with injury, only later to list it among protective processes. The beneficial *versus* injurious effects of nitric oxide is another example where there is equivocation. It should be noted that significant controversy does surround these issues. Importantly, these cases illustrate very clearly the advantage of using anoxia-tolerant organisms to study neuroprotection and to separate defense and injury mechanisms. More could be said concerning the vast opportunities offered by hypoxia-tolerant neurons to solve this kind of dilemma.

The book presents a good review of the state of knowledge concerning the adaptations of hypoxia-tolerant fish and turtles. Despite this and other strengths, there are some areas that could be improved in the next edition. For one, the surviving chapters from earlier editions need updating and revision. The references in Chapter 1 are nearly 10 years old, and so a new student of brain neurotransmitter systems would be advised to look elsewhere for this information. In addition, Kluwer Academic Publishers have not taken care in editing and typesetting this book or in providing high-quality

reproduction of the figures. Some comments are also in order concerning the chapter on 'Clinical perspectives'. Here, the protective potentials of concepts that have actually failed in large clinical stroke trials, including NMDA receptor antagonism, GABA-ergic potentiation, and block of voltage-gated calcium channels are presented as still viable concepts. Also, the authors state that hypothermia is not

used to care for neurosurgical patients because functional impairment may result. Actually, hypothermia is used routinely in neurosurgical care, a concept adopted directly from hibernating mammals, cold fishes and chilly turtles!

This book will be a good resource both for beginning graduate students and experienced researchers who desire a

comprehensive review of brain hypoxia and its consequences.

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