

## Extreme Survivor: The physiology of living through the winter without oxygen

Most vertebrate brains are highly susceptible to the damage resulting from a lack of oxygen, with brain damage and death occurring within only a few minutes. Several turtle species, however, have the remarkable ability to survive days (at room temperature) to weeks or months (at 3°C) in the complete absence of oxygen (anoxia). The physiology of anoxia tolerance has been well studied, and depends on the turtles' ability to decrease basal metabolic rate to such an extent that energy needs can be met entirely by anaerobic metabolism (lactate production). Adaptations to decrease metabolism in the brain include a reduction in ion flux, decreased release of excitatory neurotransmitters, and an increase in neuroprotective compounds like GABA and adenosine. These adaptations reduce energy expenditure and electrical activity and allow the turtle to enter what is essentially a "reversible coma". At the molecular level there is an upregulation of protective pathways that both promote cell survival and block cell death. Remarkably, the turtle brain is also able to survive reoxygenation. In mammals, the influx of oxygen after a period of anoxia results in the overproduction of oxygen free radicals like superoxides and hydrogen peroxide, which magnify brain damage over hours to days. The turtle avoids this damage through a combination of antioxidants and the suppression of free radical formation. The ability to survive without oxygen allows the turtles to overwinter under frozen ponds, with survival time in the winter apparently related to energy stores (glycogen) and the ability to buffer the resulting lactic acid produced by anaerobic metabolism. First year hatchlings, on the other hand, may either supercool or freeze to survive the winter in shallow natal nests. The remarkable adaptations that allow freeze tolerance and life without oxygen also have potential implications for the medical field.