Inhalation of nitric oxide prevents ischemic brain damage in experimental stroke by selective dilatation of collateral arterioles.

Stroke is the third most common cause of death in industrialized countries. The main therapeutic target is the ischemic penumbra, potentially salvageable brain tissue that dies within the first few hours after blood flow cessation. Hence, strategies to keep the penumbra alive until reperfusion occurs are needed. To study the effect of inhaled nitric oxide on cerebral vessels and cerebral perfusion under physiological conditions and in different models of cerebral ischemia. This experimental study demonstrates that inhaled nitric oxide (applied in 30% oxygen/70% air mixture) leads to the formation of nitric oxide carriers in blood that distribute throughout the body. This was ascertained by in vivo microscopy in adult mice. Although under normal conditions inhaled nitric oxide does not affect cerebral blood flow, after experimental cerebral ischemia induced by transient middle cerebral artery occlusion it selectively dilates arterioles in the ischemic penumbra, thereby increasing collateral blood flow and significantly reducing ischemic brain damage. This translates into significantly improved neurological outcome. These findings were validated in independent laboratories using two different mouse models of cerebral ischemia and in a
clinically relevant large animal model of stroke. Inhaled nitric oxide thus may provide a completely novel strategy to improve penumbral blood flow and neuronal survival in stroke or other ischemic conditions.