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Commentary

Taurine and neuronal resistance to hypoxia

Anders Lehmann, Henrik Hagberg, Peter Andiné and Katarina Ellrén

Institute of Neurobiology, University of Göteborg, POB 33031, S-400 33 Göteborg, Sweden

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In an attempt to explain the high resistance of the immature brain to hypoxic/ischemic damage and the increased resistance of brain tissue repeatedly exposed to hypoxia, Schurr and Rigor [1] propose that production of hypotaurine and taurine is of critical importance. Hypotheses are based on speculation upon established facts. However, in our opinion, the crucial points on which the present hypothesis rests are in conflict with it.

The main feature of the hypothesis is that taurine protects the brain and possibly other organs from ischemic injury by interfering with cellular calcium accumulation. The high levels of taurine in the brain of the neonate would consequently underlie the tolerance to anoxia. Further, it is suggested that cysteine and cysteamine are formed during ischemia and are converted to cysteine sulfinate, cysteate and hypotaurine in the deoxygenation period. These taurine precursors are claimed to scavenge deleterious free oxygen radicals and to be metabolized into taurine, thereby increasing the tissue levels of the amino acid. It is important to point out that the evidence that taurine protects brain tissue against anoxia is at present limited to one single report [2]. However, taurine does not protect the immature rat hippocampal slice against anoxic injury as evaluated morphologically (Ellrén, Andiné, Hagberg and Lehmann, in preparation). There is no evidence for a neuroprotective effect of taurine against ischemia in vivo. Moreover, the literature is not consistent with regard to the preventive effects of taurine on ischemic heart failure [3,4]. It is essential that much more data are acquired on this controversial issue before a meaningful hypothesis can be presented. To support their ideas, the authors list the ample literature on pharmacological effects of taurine on calcium metabolism. It should be noted that there is so far no evidence for a (patho)physiological role for taurine as a calcium modulator.

The key issue of the hypothesis is whether tissue taurine concentrations increase post-hypoxia, and the authors appear to misinterpret our results [5] in this respect. *Extracellular* taurine increases during cerebral ischemia but is normalized upon reperfusion. However, this effect is not a reflection of elevated *intracellular* levels, but rather of conditions that favor an intra- to extracellular shift of taurine distribution, namely depolarization combined with reduced reuptake (intra-/extracellular concentration ratio is approx. 300 for taurine) [5]. Most importantly, tissue taurine levels are remarkably stable in the brain during [5–7] and after [5,6] ischemia which contradicts the proposal of Schurr and Rigor [1]. Taurine is highly concentrated in heart muscle fibers from which it is released during ischemia [8]. In contrast to the situation during cerebral ischemia, cardiac ischemia is accompanied by a net loss of taurine [8], which is in disagreement with the hypothesis. Moreover, mice adapted to hypoxia show no changes in heart levels of taurine [9].

The fact that cerebral taurine decreases postnatally in parallel with increased sensitivity to hypoxia may be coincidental, and a number of similar positive or negative correlations can be

Correspondence address: A. Lehmann, Institute of Neurobiology, University of Göteborg, PO Box 33031, S-400 33 Göteborg, Sweden

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found (e.g. maturation of excitatory amino acid transmitter systems). Moreover, although the developmental pattern of changes in cerebral taurine is well-known, there is a paucity on information on the exact timing of increased sensitivity to ischemia. We are not aware of any reports showing significant elevation of cysteine or cysteamine in the brain during hypoxia. Besides, the cysteamine pathway for taurine biosynthesis has not been found in the central nervous system [10]. Again, these are lateral questions as taurine does not increase in the reperfusion phase. The possibility that an accelerated synthesis is masked by an increased degradation of taurine is unlikely since there is no quantitatively important breakdown of taurine in mammals [11].

In summary, the hypothesis of Schurr and Rigor [1] is not in harmony with established facts and it seems premature to suggest that endogenous taurine has a protective function in ischemic brain damage.

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