Taurine modulates expression of transporters in rat brain and heart

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Accepted March 3, 1998

Summary. In pro- and eucaryotic life, cellular and subcellular compartments are separated by membranes and the regulated and selective passage of specific molecules across these membranes is a basic and highly conserved principle.

We were interested whether taurine, a naturally occurring amino acid, would be able to induce or suppress expression of transporters with the Rationale that taurine was shown to detoxify a series of endogenous toxins and xenobiotics of various chemically non-related structures.

For this purpose we used a gene hunting technique, subtractive hybridization, subtracting mRNAs of taurine-treated rat brain and heart from untreated controls. Subtracted mRNAs were then converted to cDNAs, amplified, sequenced and identified by gene bank data.

We found five transporter transcripts, the phosphonate transport ATPase PHNC, multikidrug transporter homolog MTH104, protein-export-membrane protein SECD, oligopeptide transporters oppA and oppD, in the brain and two: ABC-transporter BRAF-2 and cation-transport ATPase PACS, in the heart. Homologies of the sequences found were in any case >50% thus permitting the identification of transporters with high probability.

The biological meaning could be that a naturally occurring amino acid, taurine, modulates complex transport systems. The most prominent finding is the upregulation of a multidrug transporter transcript, explaining a mechanism for the nonselective detoxifying action of taurine.

Keywords: Amino acids – Taurine – Transporter – Rat – Brain – Heart

* C. Y. is supported by a fellowship of the International Society for Amino Acid Research
Introduction

In procaryotes and eucaryotic life, cellular and subcellular compartments are separated by membranes. The regulated and selective passage of specific molecules across these membranes is a basic and highly conserved principle. The importance of membrane transport is exemplified by the fact that almost 20% of the E. coli genes are associated with transport functions (Bachmann, 1990). Transmembrane transport is mediated by specific proteins associated with the membrane and grouped into a number of families, and their members are related to each other in sequence, molecular mechanisms and evolutionary origin.

Transporters are still holding centre stage particularly in biological and medical research, with cystic fibrosis, drug and antibiotic resistance as persistent challenges.

We were interested whether taurine was able to induce or suppress membrane transport with the Rationale, that taurine’s well-documented detoxifying action of endogenous toxins and xenobiotics of various and entirely unrelated chemical structure (Huxtable, 1992) may be due to activation of transport mechanisms pumping the noxae out of the cell; a mechanism described for multidrug resistance phenomena (Higgins, 1992).

For this purpose we selected the gene hunting principle of subtractive hybridization (SH), a method subtracting mRNAs in organs of taurine treated rats from mRNAs in organs of untreated rats and vice versa, thus forming a subtractive library.

Subtracted mRNAs are converted to cDNA by reverse transcription, amplified by PCR and resulting cDNAs are sequenced. The sequences from the SH are compared to gen bank sequences and thus identified.

Using this technique we found a series of up- or downregulated transporter transcripts in brain and heart of taurine treated rats. Our data suggest the modulation of several transport systems by taurine, may help to understand individual action mechanisms of taurine and may explain the detoxification activity, particularly by the upregulation of a multidrug transporter homolog. We are demonstrating a first cue to the understanding of taurine effects on transporters, challenging and providing the basis for further studies at the transcriptional, protein and functional level.

Methods

6 Sprague-Dawley rats, 12 weeks old, female, were fed orally 100mg/kg body weight taurine (Sigma) for a period of three weeks and 6 animals served as controls (Institute of Animal Breeding, Himberg, Austria). They had free access to tap water and rat cake (Altromin®) and were kept under day and night rhythm (Lubec et al., 1996). At the end of the feeding period they were sacrificed by neck dislocation, whole brain and the total ventricular tissue were taken and snap frozen in liquid nitrogen. Gene hunting was performed on pooled brains and hearts of each of the two groups using subtractive hybridization.