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Characterization of a sodium-dependent taurine transporter in rabbit choroid plexus

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Abstract

Taurine, a β-amino acid, plays an important role as a neuromodulator and is necessary for the normal development of the brain. Since de novo synthesis of taurine in the brain is minimal and in vivo studies suggest that taurine does not cross the blood-brain barrier, we examined whether the choroid plexus, the blood-cerebrospinal fluid barrier, plays a role in taurine transport in the central nervous system. The uptake of [^{3}H]taurine into ATP-depleted choroid plexus from rabbit was substantially greater in the presence of an inwardly directed Na^+ gradient, whereas in the absence of a Na^+ gradient taurine accumulation was negligible. A transient inside-negative potential gradient enhanced the Na^+-driven uptake of taurine into the tissue slices, suggesting that the transport process is electrogenic. Na^+-driven taurine uptake was saturable with an estimated V_{max} of 111 ± 20.2 nmol/g per 15 min and a K_m of 99.8 ± 29.9 μM. The estimated coupling ratio of Na^+ and taurine was 1.80 ± 0.122. Na^+-dependent taurine uptake was significantly inhibited by β-amino acids, but not by α-amino acids, indicating that the transporter is selective for β-amino acids. Na^+-dependent taurine uptake showed some selectivity for anions: the accumulation was comparable in the presence of Cl^-, Br^- and thiocynate whereas I^-, SO_4^{2-} and gluconate did not stimulate the uptake significantly. Collectively, our results demonstrate that taurine is transported in the choroid plexus via a Na^+-dependent, saturable and apparently β-amino acid selective mechanism. This process may be functionally relevant to taurine homeostasis in the brain.

Key words: Taurine; Taurine transport; Sodium dependence; Central nervous system

1. Introduction

Taurine, a β-amino acid, is essential for normal development and function of the cerebellum and visual cortex, as well as the retina [1–4]. Also, taurine has been shown to alter the release of neurotransmitters such as acetylcholine and norepinephrine [5], and, thus, it is generally accepted to be a neuromodulator [5,6].

Biosynthesis of taurine is minimal in brain [6,7] so that a systemic source is essential. Since taurine is zwitterionic at physiologic pH, it is unlikely that taurine diffuses passively through biological membranes. Therefore, its transport into or out of the brain must involve carrier-mediated process(es) at the blood-brain barrier and/or the blood-cerebrospinal fluid (CSF) barrier. In general, such membrane-associated transport system(s) at the barriers of the central nervous system (CNS) functions to provide a protected environment for the brain by selectively excreting certain substances and reabsorbing others. However, the site and underlying mechanism for taurine's entry into or exit from the CNS is currently unknown.

In experiments using the Oldendorf carotid injection technique, the brain uptake index of taurine ranged from 4.1% to 6.8% [8,9], values which were not significantly different than that for sucrose, a compound which does not cross the blood-brain barrier. These in vivo studies suggest that taurine is not directly transported across the blood-brain barrier, since the brain uptake index presumably reflects the first pass uptake of a substance through the barrier.

Although few data are available specifically for taurine, an important role for the choroid plexus in maintaining homeostasis of α-amino acids in the brain has been suggested by both in vitro [10,11] and in vivo

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[12,13] studies. For example, it has been documented that isolated choroid plexus tissue slices accumulate α-amino acids against a concentration gradient via saturable and energy-dependent mechanism [10,11]. Also, in the perfused choroid plexus of the sheep [14], Preston and Segal noted that the net flux for several α-amino acids between blood and the CSF could be directed into or out of the CSF depending on the amino acid concentrations in the biological fluids [12]. These observations suggest that the choroid plexus plays a significant role in regulating the concentrations of α-amino acids in the CSF and in maintaining the low CSF to plasma concentration ratios [14,15]. However, there are no available data in the literature to explain the low CSF-to-plasma ratio of taurine.

Based on the study in the isolated perfused sheep choroid plexus [12,13] for α-amino acids and on the low brain uptake index for taurine [8,9], we hypothesized that the choroid plexus is a site for the transport of taurine via the CSF. Thus, the objectives of this study were to determine whether taurine is transported in the choroid plexus and to characterize the mechanism responsible for its transport. We describe a Na^+-dependent transport system for taurine in rabbit choroid plexus which may be important in maintaining homeostasis of taurine in the CSF and, ultimately, the extracellular fluid of the brain.

2. Materials and methods

2.1. Preparation of ATP-depleted choroid plexus

Choroid plexus was obtained from male New Zealand White rabbits (2–3 kg) and ATP-depleted by the method of Carter-Su and Kimmich [16], modified by Suzuki et al. [17] and our laboratory [18]. Briefly, rabbits were anesthetized with ketamine (5 mg/kg) and then quickly decapitated. The choroid plexuses were immediately isolated from the lateral ventricles and placed in either of the following buffers (mM): KCl (120), mannitol (40), Hepes (25), or NaCl (120), mannitol (40), Hepes (25), pH 7.4 with 1 M Tris. The choroid plexuses were cut into 2–3 mm pieces and then placed into buffer containing 250 μM 2,4-dinitrophenol (DNP) for 20 min at 37°C to deplete the tissue of ATP. When it was necessary to prevent the development of an electrical potential gradient, the tissue slices were initially equilibrated in either (mM) choline chloride (120), KCl (40), Hepes (15) (pH 7.4, adjusted with 1 M Tris) or NaCl (120), KCl (40), Hepes (15) (pH 7.4, adjusted with 1 M Tris) and the K^+ ionophore, valinomycin (10 μM), was added along with DNP.

In all studies, after ATP depletion, the tissue slices were stored in buffer on ice, until the experiments were performed (< 2 h after the DNP treatment). For the initiation of uptake, the tissue slices were removed from the preloading buffer, blotted lightly on a tissue paper and added to the appropriate reaction mixture (see 2.3).

2.2. Electrical potential gradient studies

To test whether Na^+-dependent taurine uptake is electrogenic, the Na^+-dependent taurine uptake in the presence of inside negative potential gradient was compared to that under voltage clamped condition. In these studies all buffers contained 15 mM Hepes (final pH 7.4). Valinomycin (10 μM) was present in the DNP treatment (i.e., preloading) buffer. When an inside negative potential was created, DNP treatment buffers contained 40 mM KCl and uptake was carried out in K^+-free buffer with 40 mM mannitol. In the voltage clamped condition, preloading and uptake buffers contained an equal concentration of KCl (i.e., 40 mM). When a Na^+ gradient was tested, preloading buffers contained choline chloride (100 mM) and uptake mixtures contained NaCl (100 mM). When taurine uptake in equal Na^+ or no Na^+ was tested, equal concentrations of either NaCl (100 mM) or choline chloride (100 mM) was present in both preloading and uptake buffers.

2.3. Uptake studies

The uptake of taurine into the choroid plexus was examined by incubating the tissue slices at 37°C with 140 μl of uptake mixture that contained [^{3}H]taurine (0.0391 μM), [^{14}C]mannitol (17.9 μM) and unlabeled taurine (25 μM) in an appropriate buffer (see figure legends). DNP (250 μM) was present to ensure continued depletion of ATP. Under the voltage clamped condition, Na^+-dependent taurine uptake was linear and reproducible at 15 min (Fig. 2). Therefore, uptake at 15 min was determined in subsequent studies.

For inhibition studies, the uptake (at 15 min) was studied in the presence of [^{3}H]taurine and test compounds (2 mM). For all studies, uptake was terminated by removing the tissue from the uptake mixture and blotting it on laboratory tissue paper. The blotted tissue was placed on a pre-weighed piece of aluminum foil, dried under an IR-lamp heater for 1 h, and then weighed to calculate the net dried tissue weight. The tissue was carefully detached from the foil with a forceps and digested in 50 μl of 3 M KOH solution in a liquid scintillation counting vial. After the tissue was completely dissolved, the identical volume of 3 N HCl solution was added to neutralize the KOH. After the corresponding aluminum foil piece was added to the vial, the tissue-associated radioactivity was determined by liquid scintillation counting. In addition, the uptake mixture (50 μl) was sampled and added to separate

vials for liquid scintillation counting. ^{14}C and ^{3}H were determined by a dual isotope liquid scintillation counting on a Beckmann Model 1801 liquid scintillation counter (Beckmann Instruments, Fullerton, CA). Counting efficiency of ^{3}H ranged from 45% to 47% and that of ^{14}C ranged from 92% to 94%.

2.4. Data analysis

The uptake of taurine into the choroid plexus was expressed as volume of distribution (V_d)[18] by the following equation:

$$V_d = \frac{\text{dpm}[^3\text{H}]\text{taurine in choroid plexus/g of choroid plexus}}{\text{dpm}[^3\text{H}]\text{taurine in media/ml of media}} - \frac{\text{dpm}[^{14}\text{C}]\text{mannitol in choroid plexus/g of choroid plexus}}{\text{dpm}[^{14}\text{C}]\text{mannitol in media/ml of media}}$$

For the Michaelis-Menten studies, the initial rate of uptake was expressed as nmol/g of choroid plexus per 15 min and plotted against the initial concentration of taurine. The data were fit to the following equation:

$$\text{Rate} = \frac{V_{max} \cdot C_{\text{taurine in uptake mixture}}}{K_m + C_{\text{taurine in uptake mixture}}}$$

where V_{max} is the maximal uptake rate and K_m is the concentration of taurine when the rate is 50% of the maximal rate. The data were fit to this equation using a non-linear regression program on Kalidagraph® (version 2.0, Synergy Software, Reading, PA) on a Macintosh SE computer.

To determine the stoichiometric coupling ratio of Na^+ and taurine, the Hill equation was used:

$$\text{Rate} = \frac{V_{max} \cdot C^n_{Na^+ \text{ in uptake mixture}}}{K^n_m + C^n_{Na^+ \text{ in uptake mixture}}}$$

where V_{max} is the initial rate at the saturating concentration of Na^+, K_m is the concentration of Na^+ at half maximal rate, and n is Hill's coefficient [19]. However, since we could not achieve the saturating concentration of Na^+ in the physiological osmolarity range (i.e., up to 250 mosM), the data were fit to a simplified version of Hill's equation:

$$\text{Rate} = a \cdot C^n_{Na^+ \text{ in uptake mixture}}$$

where a is essentially V_{max}/K^n_m when $K^n_m \gg C^n_{Na^+ \text{ in uptake mixture}}$. The data were transformed with a logarithm and linearly regressed to obtain a and n.

In general, each data point was determined in triplicate and a minimum of three experiments was carried out. Data are expressed in terms of mean ± standard deviation (S.D.) of all determinations. Means were compared using unpaired Student's t-test or one-way ANOVA and $P < 0.05$ was accepted as denoting statistical significance.

2.5. Materials

[^{3}H]Taurine was obtained from Du Pont-New England Nuclear (Boston, MA). [^{14}C]Mannitol was obtained from Moravek Biochemicals (Brea, CA). All other chemicals were purchased from Sigma (St. Louis, MO). New Zealand White rabbits were purchased from Nitabell Rabbitry (Hayward, CA). Cytocint ES scintillation fluid was obtained from ICN (Irvine, CA).

3. Results

3.1. Time-course of taurine uptake

The uptake of taurine into ATP-depleted choroid plexus slices was examined in the presence and absence of an inwardly directed Na^+ gradient (120 mM) (Fig. 1). The uptake of taurine was significantly greater ($P < 0.001$, except at 2 min) in the presence of a Na^+ gradient, compared to the uptake when Na^+ was present at equal concentrations inside and outside the tissue slices. Also, in the absence of Na^+ (i.e., equal K^+ concentration inside and outside), the accumulation was depressed further than that in the presence of equal Na^+ concentration ($P < 0.01$, except 2 and 90 min).

In the presence of an inwardly directed Na^+ gradient, the accumulation of taurine into the tissue reached a maximum at approx. 15 min (5.76 ± 0.619 ml/g), after which the concentration of taurine in the tissue declined with time (at 3 h 3.12 ± 0.356 ml/g, $P < 0.001$

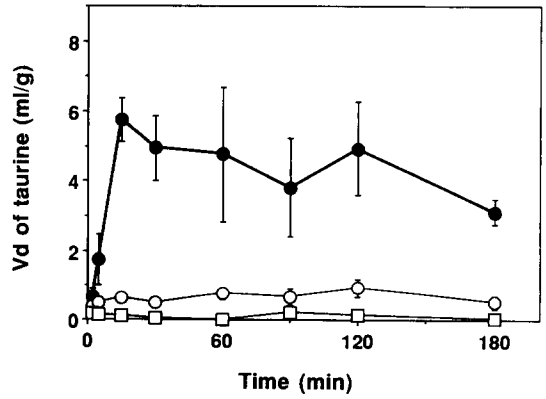

Fig. 1. Temporal profile of taurine accumulation in ATP-depleted rabbit choroid plexus. Uptake (in V_d) of taurine (25 μM) was determined at 37°C. Points represent the means ± S.D. of data from five experiments. Each experiment consisted of triplicate measurements of uptake. Key: 120 mM inwardly directed Na^+ gradient (●); 120 mM equal Na^+ inside and outside of the tissue (○); 120 mM equal K^+ inside and outside of the tissue (□).

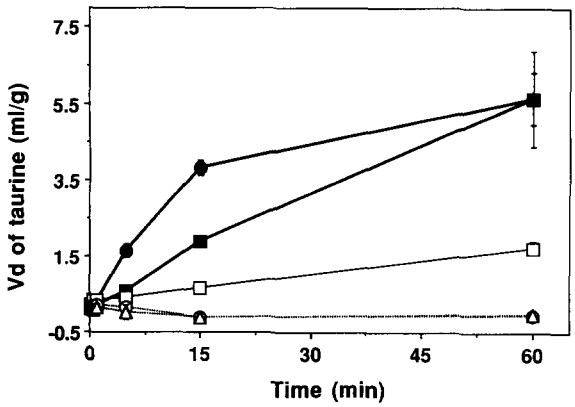

Fig. 2. Effect of potential gradient and Na^+ gradient on the uptake of taurine (25 μM) in ATP-depleted rabbit choroid plexus. Data represent the means ± S.D. of three experiments. Each experiment consisted of triplicate measurements of uptake. Key: 100 mM inwardly directed Na^+-gradient in addition to inside negative potential gradient (●); 100 mM inwardly directed Na^+ gradient under voltage clamp condition (■); 100 mM equal Na^+ concentration inside and outside of tissue with inside negative potential gradient (□); 100 mM equal choline$^+$ concentration inside and outside of tissue with inside negative potential gradient (△); 100 mM equal choline$^+$ concentration inside and outside of tissue under voltage-clamp condition (○).

compared to V_d at 15 min). Although a distinct 'overshoot phenomenon' was not observed, taurine accumulation in the presence of an initial Na^+ gradient was still statistically greater at 3 h that that obtained when the Na^+ concentration was equal inside and outside ($P < 0.001$), suggesting that an equilibrium was not achieved.

3.2. Electrogenicity studies

To determine whether the Na^+-driven transport of taurine in the choroid plexus is electrogenic, we studied Na^+-driven taurine uptake in the presence and absence of an electrical potential difference (Fig. 2). At 1, 5 and 15 min, taurine uptake in the ATP-depleted choroid plexus was enhanced when an inside negative electrical potential gradient was created ($P < 0.05$), suggesting that Na^+-dependent taurine uptake is electrogenic. However, the enhanced accumulation of taurine was no longer apparent at 60 min, most likely because the potential difference had dissipated. Electrical potential alone, however, could not drive taurine accumulation (Fig. 2). Since choline and valinomycin may have affected taurine uptake in ATP-depleted choroid plexus, control studies were performed to test the effects of these compounds. Neither choline nor valinomycin directly affected Na^+-driven taurine uptake (data not shown).

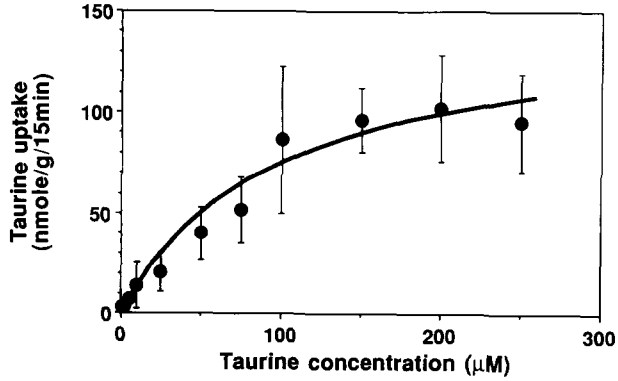

Fig. 3. Concentration dependency of taurine uptake. Uptake in nmol/g per 15 min was measured at 37°C. This study was carried out in the presence of inwardly directed 120 mM Na^+ gradient under voltage clamped conditions. Points represent the means ± S.D. of data from three experiments. Each experiment consisted of triplicate measurements of uptake. Taurine uptakes for the four highest substrate concentrations were not statistically different from each other (one-way ANOVA).

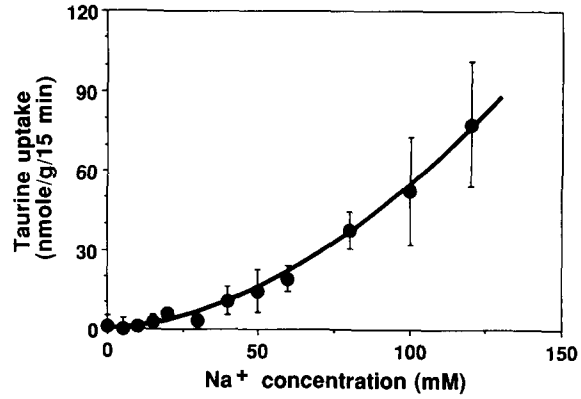

Fig. 4. Effect of Na^+ concentration on taurine uptake. Uptake of taurine (25 μM) in nmol/g per 15 min was measured at 37°C under voltage clamped condition. Points represent the means ± S.D. of data from three experiments. Each experiment consisted of triplicate measurements of uptake. The observed V_d value for taurine is represented by a solid circle. The computer generated fit, estimated by the modified Hill's equation (see Materials and methods), is shown by a solid line.

Table 1
The uptake of taurine (25 μM) in the presence of potential inhibitors

Test condition	V_d of taurine (ml/g)		% of control	P value (by t-test) compared to control
	mean	S.D.		
Control, taurine 25 μM	4.85	0.675	100	–
No Na^+ gradient	0.487	0.189	10.0	< 0.01
Taurine, 2 mM	1.98	0.554	40.9	< 0.05
Hypotaurine, 2 mM	0.593	0.296	12.2	< 0.01
β-Alanine, 2 mM	0.838	0.510	17.3	< 0.01
L-Alanine, 2 mM	5.05	1.18	104	n.s.
Glycine, 2 mM	4.35	1.26	89.7	n.s.
Glutamate, 2 mM	4.41	0.776	90.9	n.s.

Data were obtained from three experiments. Each experiment consisted of triplicate measurements of uptake. Unless specified, values represent taurine uptake (V_d) with a 120 mM inwardly directed Na^+ gradient in the presence of various inhibitors at 15 min at 37°C. n.s., not significant.

3.3. Concentration-dependency and stoichiometry studies

The rate of taurine uptake as a function of concentration was determined at 15 min in the presence of an inwardly directed Na^+ gradient under voltage clamped conditions (Fig. 3). The uptake rate of taurine was saturable, consistent with the Michaelis-Menten kinetics. The data were fit to equations involving one as well as two Michaelis-Menten terms. However, the goodness of the fit was not significantly improved in the more complex kinetic model. Therefore, the simpler kinetic model with a single saturable component was selected. The estimated V_{max} and K_m were 111 ± 20.2 nmol/g per 15 min and 99.8 ± 29.9 μM, respectively. We did not correct for the non-saturable component of taurine uptake, since the uptake values for the four highest concentrations of taurine were not statistically different, indicating that non-saturable taurine uptake is not a major component of the overall taurine transport into the tissue.

To assess the stoichiometry of the Na^+-dependent taurine transport, the effect of various concentrations of Na^+ (5 to 120 mM) on the uptake of taurine (25 μM) at 15 min was examined (Fig. 4). The uptake of taurine was dependent on the Na^+ concentration. The estimated slope coefficient, n, was 1.80 ± 0.122 (mean $\pm$ S.E.), consistent with a 2:1 Na^+/taurine ratio.

3.4. Inhibition studies

The effect of various potential inhibitors of taurine transport in choroid plexus was examined (Table 1). At a concentration of 2 mM, the α-amino acids, L-alanine, glycine and glutamate, did not affect taurine uptake. However, β-amino acids (i.e., β-alanine, taurine and hypotaurine) inhibited taurine uptake significantly ($P < 0.05$), indicating that the Na^+-driven taurine transporter in the choroid plexus is selective for β-amino acids.

3.5. Anion requirements

To determine whether Na^+-dependent taurine uptake required specific anion(s), the uptake of taurine (at 15 min) in the presence of various anions was studied under voltage clamped conditions (Table 2). Cl^-, SCN^- and Br^- promoted Na^+-driven taurine uptake comparably. Na^+-dependent taurine uptake was lower in the presence of other anions (i.e., for I^-, 58.1% of Cl^-; for NO_3^-, 37.1% of Cl^-; all statistically different from Cl^-). Gluconate and SO_4^{2-} were unable to support Na^+-dependent taurine uptake. These observations suggest that taurine transport in the rabbit choroid plexus has moderately selective anion requirements.

4. Discussion

Taurine is highly concentrated in the mammalian brain and is known to have important functions in the CNS [1–6]. In particular, it has been suggested that taurine is vital for the normal development of the brain, and deficiency is associated with neurologic dysfunction [1–3]. For example, pediatric patients who develop taurine deficiency while receiving long-term intravenous alimentation have abnormal electroretinograms [20].

Taurine is a polar molecule, and therefore its movement across biological membranes must involve interaction with transport system(s), since simple diffusion should be insignificant. Indeed, Na^+-driven taurine transport has been identified in a variety of tissues [21–23]. However, the specific transport systems at the barriers between the systemic circulation and the brain have not been studied extensively. The physiological significance of such a transport mechanism is further emphasized by the fact that taurine homeostasis in the brain appears to be tightly regulated [24,25]. This regu-

Table 2
Anion requirements for Na^+-driven taurine uptake in ATP-depleted rabbit choroid plexus

Anion tested	V_d of taurine (ml/g)		% of Cl^-	P value (by t-test) when compared to Cl^-	P value (by t-test) when compared to no Na^+
	mean	S.D.			
Cl^-	2.61	0.410	100	–	< 0.001
SCN^-	2.36	0.761	90.3	n.s.	< 0.001
Br^-	2.36	0.531	90.4	n.s.	< 0.001
SO_4^{2-}	0.353	0.159	13.5	< 0.001	n.s.
I^-	1.52	0.466	58.1	< 0.002	< 0.001
Gluconate	0.388	0.133	14.8	< 0.001	n.s.
NO_3^-	0.969	0.228	37.1	< 0.001	< 0.001
No Na^+ gradient	0.256	0.202	9.78	< 0.001	–

In this study, the anions were equilibrated across the membrane. The uptake of taurine (25 μM) was determined in the presence of a 120 mM inwardly directed Na^+ gradient at 15 min at 37°C. The tissue was voltage clamped by the addition of 10 μM valinomycin and equal K^+ concentrations (i.e., 40 mM) inside and outside of tissue. Data were obtained three experiments. n.s., not significant.

lation may occur at a site of a concentrative transport system which mediates taurine's entry into and/or exit from the extracellular fluid of the brain.

Tayarani et al. have described a high affinity Na^+-dependent taurine transport system in isolated brain microvessels of the rat [26]. However, since microvessels are collapsed, the transport system is probably located on the abluminal membrane and mediates taurine transport from brain to blood, not the reverse. Furthermore, the low brain uptake index of taurine argues against the blood-brain barrier as the site of taurine's entry into the brain extracellular spaces. The recent finding that blood vessels in the mouse brain did not contain mRNA encoding a Na^+-and Cl^--dependent taurine transporter [27] also supports the hypothesis that the blood-brain barrier is not primarily responsible for the transport of taurine into the brain.

In this study, we demonstrated that a specific Na^+-driven system for the transport of β-amino acids exists in the choroid plexus of the rabbit. By ATP-depleting the tissue, it was possible to test the role of ion gradients in the transport of a particular substrate [16,18]. In the presence of an initial inwardly directed Na^+ gradient, taurine uptake was greately enhanced. However, only a slight overshoot phenomenon, characteristic of a concentrative uptake, was achieved. This pattern of transport is consistent with an extremely slow efflux of taurine from the tissue. In this study, we did not investigate the mechanisms of taurine efflux in the choroid plexus tissue slices. However, the efflux half-life of taurine from different areas of rat brain ranges from 9 to 240 h [28], supporting the speculation that taurine exits slowly from choroid plexus tissue.

We examined the Na^+-taurine coupling ratio by controlling the Na^+-gradient in the ATP-depleted tissue. The data are consistent with coupling ratio of 2:1 for Na^+-dependent taurine transport. Similar coupling ratios have been reported in renal [22] and placental [21] brush-border membrane vesicles. However, maximal velocity of taurine transport was not achieved even in the presence of a Na^+ concentration of 120 mM. Similarly, maximal taurine transport was not clearly reached at a Na^+ concentration of 200 mM in renal brush-border membrane vesicles [22]. We did not examine taurine uptake in the presence of a higher Na^+-gradient, since extending the Na^+ concentration beyond 120 mM may not be physiologically relevant and hyperosmotic conditions are known to increase taurine uptake in a number of tissues [29–31].

The stoichiometry data are consistent with the finding that a transient inside-negative potential difference could enhance the uptake of taurine in the ATP-depleted choroid plexus (Fig. 2). That is, with a coupling ratio of 2:1, the inward transport of the electrically neutral taurine results in a net uptake of positive charges (i.e., Na^+).

The Na^+-dependent taurine uptake into the ATP-depleted choroid plexus slices was saturable, consistent with the Michaelis-Menten kinetics. The estimated K_m was 99.8 μM, suggesting a high affinity transport system, and is slightly higher than K_m values reported in other tissues (i.e., 4–86 μM) [21–24]. The selectivity of the transport in rabbit choroid plexus also exhibited a similar pattern to that reported in other tissues and species. Only β-alanine and hypotaurine inhibited taurine uptake, while the α-amino acids did not affect taurine transport (Table 2). Therefore, the taurine transporter we characterize in this study appears to be consistent with the previously described system β-amino acid transporter [32,33]. Interestingly, a high concentration of unlabeled taurine (2 mM) did not completely inhibit taurine uptake, suggesting that there may be a low affinity taurine uptake system in the choroid plexus.

Taurine transport in the choroid plexus seems to have broader anion selectivity than that reported in other tissues [22,29,34], in which only Cl^- and Br^- are able to support Na^+-dependent taurine transport. Significant Na^+-dependent taurine uptake occurred in the presence of Cl^-, Br^-, thiocyanate, I^-, and NO_3^-; SO_4^{2-} and gluconate could not promote taurine accumulation.

From this study, we cannot conclude whether the Na^+-dependent taurine uptake system is on the apical (i.e., CSF-facing) or basolateral (i.e., blood-facing) surface, or whether both membranes contain Na^+-dependent taurine transporters. Our data are consistent with the hypothesis that this Na^+-dependent taurine transporter is on the apical membrane, since the taurine CSF to plasma concentration ratio is significantly less than unity [14,15]. Further studies will be necessary to elucidate clearly the location of the transporter and its physiologic significance.

In conclusion, we have characterized the Na^+-dependent taurine uptake in ATP-depleted rabbit choroid plexus. The process appears electrogenic with an estimated coupling ratio of 2 Na^+ to 1 taurine molecule. The accumulation of taurine is saturable with high selectivity for β-amino acids. Anion dependency of the uptake appears to be broader than those described in other tissues. This uptake system may be functionally relevant in maintaining taurine homeostasis in CSF and, ultimately, the extracellular fluids of the brain.

Acknowledgments

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