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9. Taurine and neurotransmission

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1.1. Introduction

Taurine is enriched in electrically excitable tissues such as brain, retina, heart and skeletal muscles. Since the 1960s it has been envisaged to act in the central nervous system as a neurotransmitter, neuromodulator, neuroprotector, membrane stabilizer, endogenous antiepileptic agent, cell volume regulator, and thought to maintain calcium homeostasis and membrane integrity [1]. Of the many proposed functions we here review the role of taurine in neurotransmission and endeavor to draw inferences as to whether it could qualify as a neurotransmitter or neuromodulator. The neurotransmitter function implies the existence of specific taurine receptors and the neuromodulatory role an interference with the functions of other transmitter systems. There is but scant evidence to corroborate the first assumption, but ample for the latter [2, 3].

1.2. Occurrence of taurine in the central nervous system

Taurine is abounds in the central nervous system, its concentration being generally exceeded only by glutamate, though interspecies differences are

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prominent [4, 5]. For instance, in the guinea pig the brain concentration is rather low but high in the rat [6]. The regional distribution is heterogeneous [7, 8]. In adults, the cerebral cortex, cerebellum, olfactory bulbs, striatum and hypothalamus contain more taurine than the ponsmedulla and spinal cord. The amount of taurine gradually decreases during postnatal development in most animal species [4, 5, 9]. This decrease is several times greater in the spinal cord and medulla than, for example, in the cerebellar and cerebral cortex [10]. In aged animals, the levels of taurine further decrease but less than during development [11-14]. Taurine distribution in the rat spinal cord and thalamus is fairly even, whereas the canine spinal cord shows segmental differences [15]. Of individual brain nuclei, taurine is enriched in the lateral geniculate and inferior colliculus, the posterior region of the latter has the highest and the anterior region the lowest taurine concentration in the cat [16]. In the cerebellum, the stellate cells contain more taurine than the other cerebellar cortical cells [17,18].

All brain cells seem to contain taurine. Immunostaining has made possible to map taurine's localization in the cells and cellular organelles. In the dorsal cochlear nucleus, the taurine concentration diminishes from superficial to deep layers [19]. In the olfactory bulb there is much taurine in primary olfactory neurons, in their axons in particular [20]. Taurine immunoreactivity has also been seen in the axons of cerebellar Purkinje cells [21], as well as in their somata and dendrites [22]. In the cerebellar cortex taurine immunoreactivity is present also in mossy fibers and Golgi axons [23]. The concentration of taurine, however, is generally higher in glial cells than in neurons. In cultured astrocytes the intracellular taurine concentration may even exceed 20 mM [24, 25]. In keeping with these in vitro studies taurine immunoreactivity is intense in glial cell bodies in the ventral glial lamina and in the glial processes surrounding magnocellular neurons in the rat supraoptical nucleus [26] and in glial cells in the cat perihypoglossal nuclei [27].

1.2.1. Taurine as neurotransmitter

Characteristic of a neurotransmitter is the heterogeneous distribution within the central nervous system. The above brief overview of the occurrence of taurine in the brain is not at variance with this criterion but the distribution pattern does not either unequivocally support the neurotransmitter role of taurine. On the opposite, the predominant location of taurine in glial structures does not bespeak such an assumption. If taurine could function as a classical-type of neurotransmitter, it should be localized in synaptic vesicles. In the bovine brain, taurine is in fact enriched by

synaptic vesicles [28]. However, it remains open whether it resides in the vesicular fluid, since taurine has an inherent tendency to bind relatively tightly to synaptic membranes [29-31]. Other neurotransmitter criteria include the release from neurons upon depolarization, existence of specific membrane receptors to mediate the effects to other cells and efficient mechanism to terminate the extracellular actions. Furthermore, the binding to receptors should generate manifest effects in the targeted cells.

1.2.2. Taurine release

Taurine release from nervous cells can be mediated by simple leakage through membranes, reverse action of taurine transporters, flux through anion channels and exocytosis [32-35]. Depolarization by high extracellular K^+ significantly enhances taurine release from many neural preparations [12, 35-40]. These findings have been interpreted not to result from neuronal depolarization but being due to potassium-induced swelling of cells [41-44]. The swelling-induced release is a prominent phenomenon in many cases associated with cell volume alterations, particularly with isolated neurons and astrocytes, but in the preparations in which the tissue integrity is reserved the high-K^+ evoked release manifests itself irrespective of cell volume alterations [45, 46]. Electrical stimulation [47, 48], veratridine [49] which opens the voltage-dependent Na^+ channels and the selective Na^+, K^+-ATPase inhibitor ouabain [50-53] have also been shown to induce taurine release from a number of neural preparations. The basal extracellular concentration of taurine is already under resting conditions in vivo about one magnitude greater than the concentration of the established neurotransmitters [54-60]. Correspondingly, the molar amounts of taurine released upon excitation are significantly higher that those of the established neurotransmitters both in vivo [61] and in vitro, in preparations from the developing brain in particular [37, 62-64].

The activation of all ionotropic glutamate receptors have been shown to evoke taurine release from different brain preparations in vitro [35, 55, 66-71] and in vivo [56, 72-76]. The N-methyl-D-aspartate (NMDA) receptor antagonists have been shown to block these enhancements [35, 66, 71, 73, 77, 78]. NMDA receptor activation leads to activation of the nitric oxide (NO)/cyclic GMP (cGMP) cascade with the subsequent induction of neurotransmitter release. Taurine release is also enhanced by this pathway both in vitro preparations [79-81] and in vivo [76, 82], as already reviewed by us [83]. In keeping with these results, cGMP alone is able to potentiate taurine release in the hippocampus [84] and the NO synthase blockers inhibit the K^+-evoked [85] and NMDA-mediated [76] release. The effects of

metabotropic glutamate receptors have been markedly variable, both enhancing and attenuating effects being seen, depending of the receptor group and brain preparations subjected to studies [35, 71, 86]. On the other hand, activation of adenosine A_1 receptors has enhanced taurine release in the rabbit hippocampus [87], the mouse hippocampus and brain stem [88-90] and adenosine A_2 receptors the release from cultured astroglial cells [91].

Calcium dependency is assumed to witness the exocytotic release of neurotransmitters from synaptic vesicles. The question of calcium dependency of stimulated taurine release is not yet settled. In a number of studies the K^+-evoked release has been found to be Ca^{2+}-independent [38, 73, 92], but some other more recent investigators have reported Ca^{2+} dependency [93, 94]. In fact, only part of the release may require external Ca^{2+} ions, while there also occurs simultaneously release independently of external Ca^{2+} [35, 36, 51, 63, 95]. The stimulated taurine release may originate from Ca^{2+}-dependent emptying of synaptic vesicles or directly from cytoplasma [96]. Intracellular Ca^{2+} stores may also sustain apparently Ca^{2+}-independent release [55].

The depolarization-induced and glutamate receptor-activated Ca^{2+}-dependent release of taurine are absolute prerequisites for consideration of its transmitter role. However, these matters do not witness that taurine is a transmitter. The release of neuromodulators can be likewise enhanced by depolarization and activation of excitatory receptors.

1.2.3. Taurine receptors?

If taurine were a neurotransmitter, it is mandatory that there are specific taurine receptors. In the past several investigators tried to test the binding of taurine to neural membranes, but only we initially succeeded to demonstrate its binding to mouse brain synaptic membranes [97]. It appeared that the membranes had to be subjected to several freezing-thawing cycles and detergents to get rid of endogenous taurine tightly bound to them [30]. The binding was Na^+-independent and exhibited a sigmoidal dependence on the ligand concentration [98, 99]. The binding was effectively displaced by the proposed taurine antagonist 6-aminomethyl-3-methyl-4H-1,2,4-benzothiadiazine-1,1-dioxide hydrogen maleate (TAG) [100], but also by the glycine receptor antagonist strychnine and GABA antagonists. Since TAG is the only compound to have any selectivity to these taurine binding sites, it remained open whether the binding tested truly represented taurine binding to the receptors of its own or whether it was binding to GABA receptors or strychnine-sensitive glycine receptors.

Taurine also binds to washed and detergent-treated membranes from the rabbit brain [31]. This binding is displaced by TAG, 2-aminoethylarsonate, 2-hydroxyethanesulfonate and (±)cis-2-aminocyclohexanesulfonate which do not interfere with the $GABA_A$ or $GABA_B$ receptors, but the glycine receptor agonists and antagonists were not tested in these studies. In the frog spinal cord, two taurine receptors have been claimed to exist with different pharmacological properties [101] and a taurine receptor has been reported to exist in the lobster olfactory organ [102]. The few studies cited above show that taurine binding is discernible only to thoroughly washed and detergent-treated membrane preparations. All scattered pieces of information on putative taurine receptors still wait to be corroborated or refuted by further studies.

1.2.4. Taurine actions

Taurine has been shown to inhibit neuronal firing to produce neuronal hyperpolarization by altering membrane permeability to ions in many brain areas [4, 5, 103]. Taurine has been shown to increase Cl^- conductance in the cerebellum [104], substantia nigra [105] and olfactory bulb [106]. It is typical that the effects of taurine are slow at the outset. For example, the currents evoked by GABA in the relay neurons of the rat olfactory bulb are fast and the currents induced by taurine slow [107]. Taurine may cause in these cells prolonged reduction in the input resistance and sustain a prolonged and modest inhibition. Furthermore, at low concentrations taurine inhibits GABA-induced Cl^- fluxes into synaptic membrane microsacs prepared from different brain areas, but at higher concentrations enhances the fluxes, apparently due to the activatory properties of its own [108]. It also induces single-channel currents by opening Cl^- channels in cultured rat cerebellar granule cells in patch-clamp experiments [109]. These actions of taurine are in most cases blocked by antagonists of GABA and/or glycine receptors, the effects depending on the brain area. The effects of taurine are difficult to demarcate from those mediated via GABA or glycine receptors, because of the lack of taurine agonists and antagonists specific enough. These matters will be dwelled therefore more below when the neuromodulatory role of taurine is discussed.

1.2.5. Taurine uptake

Taurine is not broken down in the mammalian organisms. The only manner to get rid of extracellular taurine is the uptake into surrounding cells or removal into blood or cerebrospinal fluid. Taurine uptake is a saturable, concentrative and energy-, Na^+- and Cl^--dependent process. It is specific for ω (or β) -amino acids in which the acidic and basic groups are separated by a

straight two- or three-carbon-atom backbone [4, 110]. These structural requirements have been later confirmed by studies on cloned taurine transporters [111-113]. The molecular structure of the two cloned taurine transporters, TAUT-1 and TAUT-2, show marked homology with the other neurotransmitter transporters [114]. TAUT-1 and TAUT-2 are universally distributed in the brain. Of them, TAUT-2 is probably predominantly localized in glial cells [115, 116]. The affinity of the transporters to taurine is high and their transport capacity of the same order of magnitude or even greater than that of GABA transporters [117-119].

1.3. Taurine as neuromodulator

The release and uptake of taurine overviewed above also apply to the criteria whether taurine acts as neuromodulator. The classical view is that a neuromodulator should not act at any receptors of its own but affect only the function and responses generated by proper neurotransmitters. It is somewhat a matter of taste whether taurine could be called a neuromodulator. It definitely has own effects in the brain which are not associated with the concomitant actions of transmitters, but in other occasions it clearly modifies the neurotransmitter responses. By far the strongest evidence bespeaks taurine's interference with glycine receptors, but also both main classes of GABA receptors, A and B, are involved to some extend [3, 120]. There are also some more scattered data of the mutual interactions of taurine with other transmitter systems in the brain.

1.3.1. Interactions with glycine receptors

Taurine displaces glycine from its strychnine-sensitive binding sites in the mouse brain stem [121]. It acts as an agonist at glycine receptors cloned in Xenopus oocytes [122] and inhibits the glycine responses in oocytes injected with rat $\alpha 1$ subunits of the glycine receptor or spinal cord poly$(A)^+$ RNA [123]. Taurine acts at glycine receptors in the rat supraoptic magnocellular neurons [124] and in dopaminergic neurons in the ventral tegmental area in young rats [125]. In acutely isolated rat basolateral membranes taurine alters in a strychnine-sensitive manner the resting potential [126] and activates in sacral commissural neurons strychnine-sensitive currents [127]. In the central nucleus of the rat inferior colliculus taurine depresses the spontaneous and current-evoked firing of neurons [128]. It activates glycine-gated chloride channels. These effects were blocked by strychnine but not bicuculline. In neurons of the rat nucleus accumbens the responses to taurine and glycine are antagonized by strychnine but not by the

$GABA_A$ receptor antagonist bicuculline [129]. Taurine may not always act on synaptic glycine receptors. For example, it activates excitatory non-synaptic glycine receptors on dopamine neurons in the ventral tegmental area of young rats [130]. In the mammalian receptors glycine is more effective than taurine, but in Hydra vulgaris glycine and taurine are almost equipotent [131].

Taurine is a full agonist of the glycine receptors in the ventral tegmental area [130]. Taurine more efficiently gates glycine α1 receptors than α2 receptors, but glycine is more effective than taurine in both receptor subtypes [132]. Only minor alterations in the glycine receptor structure result in their markedly different sensitivity to taurine. Human and rat α2 and α3 glycine receptors respond only slightly to taurine [132-134]. The glycine receptor α1 subunit of the zebrafish (αZ1) is very similar to the rat α1 receptor in both length and amino acid residue composition, but the homomeric αZ1 receptor exhibits exceptionally high sensitivity for taurine, almost comparable to glycine sensitivity [135, 136]. The cloned homomeric α4 subunit from chicks is also potently activated by taurine [137]. Two separate point mutations at the same base pair in the gene encoding the human glycine receptor α1 subunit have been observed to convert taurine from a full agonist to a competitive antagonist [138-140]. These mutations may either simply disconnect the binding site of taurine from the Cl^- channel activation site or selectively disrupt a common agonist recognition subsite and thereby unmask the antagonist subsite for taurine [139-141]. On the other hand, three other mutations in the α1 subunit of the human glycine receptor GlyRA1, which cause hyperekplexia, greatly reduce Cl^- currents elicited by taurine [142].

Taurine may sometimes affect both $GABA_A$ and glycine receptors simultaneously. To date, it controls hormone release from the rat neurohypophysis [143] and prevents the ammonia-induced accumulation of cGMP in the rat striatum in this manner [144]. Taurine activates glycine receptors at low concentrations in CA1 neurons in the immature rat hippocampus, whereas at high concentrations both glycine and GABA receptors are activated [145]. The neuroprotective effect of taurine against focal cerebral ischemia in rats is likewise mediated by activation of both $GABA_A$ and glycine receptors [146]. In mice, the target of taurine shifts from glycine receptors to GABA receptors during postnatal development [147].

1.3.2. Interactions with $GABA_A$ receptors

A number or all of the taurine actions dealt with before may result from its interactions with $GABA_A$ receptors. There are numerous reports on the direct interference of taurine with $GABA_A$ receptors. Taurine displaces GABA

binding to the GABA-benzodiazepine receptor complex and interferes allosterically with the ligand binding to its benzodiazepine site [148-152]. Taurine has been reported to be a full agonist of receptors in rat brain synaptic membranes [153]. On the other hand, in the rat nucleus accumbens taurine has been reported to be only a partial agonist [129]. The efficacy of taurine in synaptic $GABA_A$ receptors is less than that of GABA itself [154]. However, GABA acts only as a partial agonist in some atypical $GABA_A$ receptors, depending on their subunit composition [155]. Taurine is a potent activator of extrasynaptic $GABA_A$ receptors, acting already at physiologically relevant concentrations in the mouse ventrobasal thalamus [156]. Such extrasynaptic $GABA_A$ receptors are thought to mediate tonic or so called volume transmission in the central nervous system [157, 158]. Taurine responses are slow at outset and prolonged which could well fit to the assumption that its actions at these $GABA_A$ receptors were responsible for tonic conductances.

The neurotoxicity of β-amyloid is also blocked by taurine activating $GABA_A$ receptors in rat hippocampal and cortical neurons [159]. Due to the binding of taurine to $GABA_A$ receptors it can also inhibit the effects mediated by these receptors [105]. The $GABA_A$ receptor antagonists bicuculline and picrotoxin block taurine effects on solubilized rat brain $GABA_A$ receptors [151] and on receptors in the mitral and tufted cells of the rat main olfactory bulb [107]. In taurine-transporter gene knockout mice reduced taurine levels are associated with increased $GABA_A$, kainate and (±)-2-amino-3-hydroxy-5-methylisoxazole-4-propionate (AMPA) receptors in various brain regions [160].

The efficacy of taurine in $GABA_A$ receptors may depend on their molecular structure. It has been reported to act only in the β2 subunit-rich areas in the receptors enriched in certain brain areas [161], although, no regional differences in its efficacy have been found in other studies [162]. Tests on recombinant $GABA_A$ receptors have also indicated that taurine can interact with receptors composed of different subunits [164, 164]. Taurine desensitizes $GABA_A$ receptors only after a prolonged exposure and its interactions with $GABA_A$ receptors are not sensitive to neurosteroids [164-165]. In keeping with this, chronic taurine supplementation to mice causes a down-regulation of expression of the $GABA_A$ receptor β subunit, the key subunit present in virtually all $GABA_A$ receptors [166], though in cultured cerebellar granule cells taurine induces low-affinity GABA receptors [167].

1.3.3. Interactions with $GABA_B$ receptors

An interaction of taurine with $GABA_B$ receptors has also been documented [168, 169]. In some instances it has proved to be an even more potent displacer

at $GABA_B$ than at $GABA_A$ receptors [150]. Taurine has been suggested to act as an agonist of $GABA_B$ receptors in the rat cerebellum where their subcellular localization is unrelated to GABAergic inputs [170]. In the frog olfactory bulb in vivo, taurine likewise acts mainly on $GABA_B$ receptors, suppresses the spontaneous firing of mitral cells and increases the signal-to-noise ratio [171]. Taurine may also regulate GABA release from rat brain olfactory bulb synaptosomes via activation of presynaptic $GABA_B$ receptors [172, 173]. In the rat, taurine has suppressed olfactory nerve-evoked monosynapic responses of mitral and tufted cells and has blocked chloride conductance, possibly due to the $GABA_B$ receptor-mediated inhibition of glutamate release even though $GABA_A$ receptor antagonists also attenuated taurine effects in this area [107]. Furthermore, taurine has markedly potentiated the ability of NMDA to stimulate phosphaditylinositol hydolysis in the developing rat cerebellum, but not in adults. This effect was mediated by $GABA_B$ receptors since it was mimicked by an agonist of these receptors, baclofen, and blocked by the corresponding antagonist [174]. In many other occasions taurine responses have also been shown to be more marked in the developing brain [35, 37, 63, 66, 84].

So far, studies on the interactions of taurine with $GABA_B$ receptors are relatively scant and therefore reliable interferences are not yet possible. The few reports available are intriguing, though. Further investigations are thus needed. If taurine finally emerges to be an endogenous ligand of either $GABA_A$ or $GABA_B$ receptors, then the concept of taurine as a neuromodulator should possibly be replaced by a definition that taurine is a neurotransmitter in this true notation.

1.3.4. Interference with other neurotransmitters

Intranigrally injected taurine reduces extracellular dopamine [175, 176] and modulates striatal dopaminergic transmission [177-179]. The age-related decline in taurine in the striatum is correlated with a loss of dopaminergic markers [180]. Intracerebroventricularly [181] and intraperitoneally [182] injected taurine and taurine administered directly into the striatum [183] have significantly increased extracellular dopamine [184]. However, in other studies direct administration of taurine into the rat striatum has not markedly altered extracellular dopamine, but has reduced the extracellular concentration of dopamine metabolite dihydroxyphenylacetic acid [185, 186]. Taurine has inhibited the synthesis and release of serotonin in rat rostral, but not in caudal, rhomboencephalic raphe cells [187]. It also affects noradrenaline uptake and release in rat cerebral cortical slices [188] and interferes with the binding of labeled spiperone (serotonin 5-HT_{2A} and dopamine D_2 receptor antagonist) to

cerebral cortical membranes [189]. Taurine interferes with the binding of phencyclidine (which blocks NMDA receptor activation) in the mouse cerebral cortex [190]. Finally, taurine reduces K^+-stimulated adenosine release in slices from the hippocampus in the developing but not in adult mice [191].

Taurine initiates a long-lasting enhancement of glutamatergic transmission in the hippocampus [192] and dorsal striatum [193, 194] and enhances corticostriatal transmission as well [195]. Under in vivo conditions it is often difficult to define which transmitter system is the primary target of taurine's action since the neural networks form a complex functional system. The effects on excitatory transmission may be mediated by GABA and/or glycine receptors. For example, the unilateral injection of taurine into the rat substantia nigra induced a dose-dependent contralateral circling behavior. It was interpreted that, besides the dopaminergic nigrostriatal pathway, the nondopaminergic nigral output pathways were also involved in this taurine-induced behaviour [196]. Local taurine perfusion into the rat nucleus accumbens also increased the dopamine content which effect was antagonized by strychnine, indicating the involvement of glycine receptors [197]. The data on the interactions of taurine with other transmitter receptors and systems is still rather fragmentary and no definite conclusions can be drawn from them. It only seems certain that it affects dopaminergic neurotransmission but the exact mechanisms are not yet settled.

1.3.5. Effects on calcium levels

A mechanism by which taurine could interfere with the function of neurotransmitters is the regulation of calcium homeostasis. Taurine has inhibited NMDA-evoked Ca^{2+} accumulation in brain slices [198] and attenuated Ca^{2+} influx into slices from developing mice [199]. It protects cultured rat astrocytes against reperfusion injury [200]. Taurine efficiently counteracts the glutamate-induced Ca^{2+} uptake in cerebellar granule cells [201, 202]. It has also prevented or reduced the glutamate-induced increase in intracellular Ca^{2+} [203] and protected in this manner neurons from glutamate-induced excitotoxicity [204]. Taurine inhibits the reverse mode of the Na^+/Ca^{2+} exchangers and the glutamate-induced release of Ca^{2+} from the internal pools [205]. It regulates cytoplasmic and mitochondrial calcium homeostasis [206]. It possibly may not be directly affecting the rate of Ca^{2+} uptake but rather the duration of the maximal response to glutamate [207]. Taurine has been shown to inhibit the glutamate-induced Ca^{2+} influx through L-, P/Q-, and N-types of voltage-gated calcium channels and the NMDA receptor-governed calcium channel in whole-brain primary neuronal cultures

[208]. On the other hand, taurine increases the accumulation of $^{45}Ca^{2+}$ in mitrochondria of the rat cerebral cortex. In this manner it can reduce the cytosolic free Ca^{2+} concentration, which, in turn, inhibits specific protein posphorylation and phosphoinositide turnover [209].

In brain slices taurine forestalls cell damage evoked by overactivation of ionotropic glutamate receptors [210]. Overactivation of NMDA receptors leads to mitochondrial damage associated with Ca^{2+} influx, which results in the generation of free radicals, including superoxide. It is thought that a part of the neuroprotective action of taurine depends on its anti-oxidant properties [211]. Taurine has been shown to antagonize the Ca^{2+} overload induced by glutamate and hypoxia in cultured rat hippocampal neurons [212]. Taurine may thus have an essential role in the modulation of intracellular calcium homeostasis under both normal and cell-damaging conditions [203, 213].

1.4. Conclusion

Present data of the possible role of taurine as a neurotransmitter are inconclusive. The most pivotal piece of knowledge still missing is to prove or disprove the existence of specific taurine receptors. Isolation and possible cloning of such receptors would be essential. Taurine is not a neuromodulator in the classical notation, because it has actions of its own and does not only interfere with the functions of established neurotransmitters. Glycine and GABA receptors from various species and brain areas with differing molecular structures and mutations show differing responses to taurine, glycine and GABA. Do specific taurine receptors underlie some of these actions? It is open whether or not all taurine actions in neurotransmission are attributable to its interactions with GABA and glycine receptors.

1.5. References

1. Oja SS, Saransaari P. Taurine. In Handbook of Neurochemistry and Molecular Neurobiology, vol 6, 3rd edn, S.S. Oja, A. Schousboe and P. Saransaari (eds), Springer, New York 2007, pp 155-206.
2. Oja SS, Saransaari P. Pharmacology of taurine. Proc West Pharmacol Soc 2007, 50:8-15.
3. Saransaari P, Oja SS. Taurine in neurotransmission. In Handbook of Neurochemistry and Molecular Neurobiology, 3rd edn, vol 2, Neurotransmitter Systems, E. S. Vizi (ed.), Springer, New York 2008, pp 325-342.
4. Oja SS, Kontro P. Taurine. In Handbook of Neurochemistry, A. Lajtha (ed.), 2nd edn, vol. 3, Plenum Press, New York 1983, pp 501-533.
5. Huxtable RJ. Taurine in the central nervous system and the mammalian actions of taurine. Prog Neurobiol 1989, 32:471-533.

6. Oja SS, Uusitalo AJ, Vahvelainen M-L, Piha RS. Changes in cerebral and hepatic amino acids in the rat and guinea pig during development. Brain Res 1968, 11:655-661.
7. Palkovits M, Elekes I, Lang T, Pathy A. Taurine levels in discrete brain nuclei of rats. J Neurochem 1986, 47:1333-1335.
8. Banay-Schwartz M, Palkovits M, Lajtha A. Heterogeneous distribution of functionally important amino acids in brain areas of adult and aging humans. Neurochem Res 1993, 18:417-423.
9. Oja SS, Kontro P, Lähdesmäki P. Amino acids as inhibitory neurotransmitters. Prog Pharmacol 1977, 1/3:1-119.
10. Cutler RW, Dudzinski DS. Regional changes in amino acid content in developing rat brain. J Neurochem 1974, 23:1005-1009.
11. Banay-Schwartz M, Lajtha A, Palkovits M. Changes with aging in the level of amino acids in the rat CNS structural elements. II. Taurine and small neutral amino acids. Neurochem Res 1989, 14:563-570.
12. Oja SS, Holopainen I, Kontro P. Stimulated taurine release from different brain preparations: changes during development and aging. Prog Clin Biol Res 1990, 351:277-287.
13. Benedetti MS, Russo A, Marrari P, Dostert P. Effect of ageing on the content in sulfur-containing amino acids in rat brain. J Neural Transm 1991, 86:191-203.
14. Dawson RJr, Liu S, Eppler B, Patterson T. Effects of dietary taurine supplementation or deprivation in aged male Fischer 344-rats. Mech Ageing Dev 1999, 107:73-91.
15. Lane JD, Smith JE, Hall P, Campbell RL. Distribution of taurine and putative amino acid neurotransmitters in eight areas of the canine lumbar spinal cord. Brain Res 1978, 152:386-390.
16. Guidotti A, Badiani G, Pepeu G. Taurine distribution in cat brain. J Neurochem 1987, 19:431-435.
17. Nadi NS, McBride WJ, Aprison MH. Distribution of several amino acids in regions of the cerebellum of the rat. J Neurochem 1977, 28:453-455.
18. McBride WJ, Frederickson RC Taurine as a possible inhibitory transmitter in the cerebellum. Fed Proc 1980, 39:2701-2705.
19. Godfrey DA, Farms WB, Godfrey TG, Mikesell NL, Liu J. Amino acid concentrations in rat cochlear nucleus and superior olive. Hearing Res 2000, 150:189-205.
20. Didier A, Ottersen OP, Storm-Mathisen J. Differential subcellular distribution of glutamate and taurine in primary olfactory neurons. Neuroreport 1994, 6:145-148.
21. Walberg F, Ottersen OP, Rinvik E. GABA, glycine, aspartate, glutamate and taurine in the vestibular nuclei: an immunocytochemical investigation in the cat. Exp Brain Res 1990, 79:547-563.
22. Nagelhuis EA, Lehmann A, Ottersen OP, Neuronal-glial exchange of taurine during hypo-osmotic stress: a combined immunocytochemical and biochemical analysis in rat cerebellar cortex. Neuroscience 1993, 54: 615-631.

23. Gragera RR, Muniz E, De Esteban G, Alonso MJ, Martínez-Rodríguez R. Immunochemical demonstration of taurine in the rat cerebellar cortex. Evidence for its location within mossy fibers and Golgi axons. J Hirnforsch 1995, 36:269-276.
24. Holopainen I, Oja SS, Marnela K-M, Kontro P. Free amino acids of rat astrocytes in primary culture: changes during cell maturation. Int J Devl Neurosci 1986, 4:493-496.
25. Wysmyk U, Oja SS, Saransaari P, Albrecht J. Long-term treatment with ammonia affects the content and release of taurine in cultured cerebellar astrocytes and granule neurons. Neurochem Int 1994, 24:317-322.
26. Decavel C, Hatton GI. Taurine immunoreactivity in the rat supraoptic nucleus: prominent localization in glial cells. J Comp Neurol 1995, 354:13-26.
27. Yingcharoen K, Rinvik E, Storm-Mathisen J, Ottersen OP. GABA, glycine, glutamate, aspartate and taurine in the perihypoglossal nuclei: an immunocytochemical investigation in the cat with particular reference to the issue of amino acid localization. Exp Brain Res 1989, 78:345-357.
28. Kontro P, Marnela K-M, Oja SS, Free amino acids in the synaptosome and synaptic vesicle fractions of different bovine brain areas. Brain Res 1980, 184:129-141.
29. Marnela K-M, Kontro P, Pitkänen R, Oja SS. Free amino acids in synaptic subfractions of bovine brain. Acta Univ Ouluensis [A] 97, Biochem 1980, 29:11-16.
30. Kontro P, Oja SS. Taurine and GABA binding in mouse brain: effects of freezing, washing and Triton X-100 treatment on membranes. Int J Neurosci 1987, 32:881-889.
31. Frosini M, Sesti C, Dragoni S, Valoti M, Palmi M, Dixon HBF, Machetti F, Sgaragli G. Interactions of taurine and structurally related analogues with the GABAergic system and taurine binding sites of rabbit brain. Br J Pharmacol 2003, 138:1163-1171.
32. Saransaari P, Oja SS. Release of GABA and taurine from brain slices. Prog Neurobiol 1992, 38:455-482.
33. Saransaari P, Oja SS. Taurine release is enhanced in cell-damaging conditions in cultured cerebral cortical astrocytes. Neurochem Res 1999, 24:1523-1529.
34. Saransaari P, Oja SS. Enhanced taurine release in cultured cerebellar granule cells in cell-damaging conditions. Amino Acids 1999, 17:323-334.
35. Saransaari P, Oja SS. Characteristics of taurine release in slices from adult and developing mouse brain stem. Amino Acids 2006, 31:35-43.
36. Kontro P. Components of taurine efflux in rat brain synaptosomes. Neuroscience 1979, 4:1745-1749.
37. Kontro P, Oja SS. Taurine and GABA release from mouse cerebral cortex slices: potassium stimulation releases more taurine than GABA from developing brain. Devl Brain Res 1987, 37:277-291.
38. Rogers KL, Philibert RA, Dutton GR. K^+-Stimulated amino acid release from cultured cerebellar neurons: comparison of static and dynamic stimulation paradigms. Neurochem Res 1991, 16:899-904.

39. Oja SS, Saransaari P. Chloride ions, potassium stimulation and release of endogenous taurine from cerebral cortical slices from 3-day-old and 3-month-old mice. Neurochem Int 1995, 27:313-318.
40. Zheng L, Godfrey DA, Waller HJ, Godfrey TG, Chen K, Sun Y. Effects of high-potassium-induced depolarization on amino acid chemistry of the dorsal cochlear nucleus in rat brain slices. Neurochem Res 2000, 25:823-835.
41. Pasantes-Morales H, Schousboe A. Release of taurine from astrocytes during potassium-evoked swelling. Glia 1989, 2:45-50.
42. Pasantes-Morales H, Moran J, Schousboe A. Volume-sensitive release of taurine from cultured astrocytes: properties and mechanism. Glia 1990, 4:427-432.
43. Schousboe A, Morán J, Pasantes-Morales H. Potassium-stimulated release of taurine from cultured cerebellar granule neurons is associated with cell swelling. J Neurosci Res 1990, 27:71-77.
44. Oja SS, Saransaari P. Cell volume changes and taurine release in cerebral cortical slices. Adv Exp Med Biol 1992, 315:369-374.
45. Oja SS, Saransaari P. Taurine release and swelling of cerebral cortex slices from adult and developing mice in media of different ionic composition. J Neurosci Res 1992, 32:551-561.
46. Oja SS, Saransaari P. Relations of taurine release and influx to cell volumes in cerebral cortical slices. Adv Exp Med Biol 1994, 359:269-277.
47. Simpson RKJr, Robertson C., Goodman JC. Segmental release of amino acid neurotransmitters from transcranial stimulation. Neurochem Res 1991, 16:89-94.
48. Kubo T, Takano A, Tokushige N, Miyata N, Sato M, Hatakeyama S. Electrical stimulation-evoked release of endogenous taurine from slices of the hippocampus, cerebral cortex and cerebellum of the rat. J Pharmacobiodyn 1992, 15:519-525.
49. Della Corte L, Bolam JP, Clarke DJ, Parry DM, Smith AD. Sites of [^{3}H]taurine uptake in the rat substantia nigra in relation to the release of taurine from the nigrostriatal pathway. Eur J Neurosci 1990, 2:50-61.
50. Basavappa S, Mobasheri A, Errington R, Huang CC, Al-Adawi, Ellory JC. Inhibition of Na+, K+-ATPase activates swelling-induced taurine efflux in a human neuroblastoma cell line. J Cell Physiol 1998, 174:145-153.
51. Saransaari P, Oja SS. Mechanisms of ischemia-induced taurine release in mouse hippocampal slices. Brain Res 1998, 807:118-124.
52. Saransaari P, Oja SS. Characteristics of ischemia-induced taurine release in the developing mouse hippocampus. Neuroscience 1999, 94:949-954.
53. Estevez AY, Song D, Phillis JW, O'Regan MH. Effects of the anion channel blocker DIDS on ouabain- and high K^{+}-induced release of amino acids from the rat cerebral cortex. Brain Res Bull 2000, 52:45-50.
54. Lerma J, Herranz AS, Herreras O, Abraira V, Martín del Río R. In vivo determination of extracellular concentration of amino acids in the rat hippocampus. A method based on brain dialysis and computerized analysis. Brain Res 1986, 384:145-155.
55. Menéndez N, Solís JM, Herreras O, Galarreta M, Conejero C, Martín del Río R. Taurine release evoked by NMDA receptor activation is largely dependent

on calcium mobilization from intracellular stores. Eur J Neurosci 1993, 5: 1273-1279.
56. Segovia G, Del Arco A, Mora F. Endogenous glutamate increases extracellular concentrations of dopamine, GABA, and taurine through NMDA and AMPA/kainate receptors in striatum of the freely moving rat: a microdialysis study. J Neurochem 1997, 69:1476-1483.
57. Zielińska M, Hilgier W, Borkowska HD, Oja SS, Saransaari P, Goryński P, Albrecht J. Ammonia-induced extracellular accumulation of taurine in the rat striatum in vivo: role of ionotropic glutamate receptors. Neurochem Res 2002, 27:37-42.
58. Molchanova S, Oja SS, Saransaari P. Characteristics of basal taurine release in the rat striatum measured by microdialysis. Amino Acids 2004, 27:261-268.
59. Ahmad S, Fowler LJ, Whitton PS. Lamotrigine, carbamazepine and phenytoin differentially alter extracellular levels of 5-hydroxytryptamine, dopamine and amino acids. Epilepsy Res 2005, 63:141-149.
60. Molchanova SM, Oja SS, Saransaari P. Properties of basal taurine release in the rat striatum in vivo. In Taurine 6, S.S. Oja and P. Saransaari (eds), Springer, New York 2006, pp 365-375.
61. Molchanova S, Kööbi P, Oja SS, Saransaari P. Interstitial concentrations of amino acids during global forebrain ischemia and potassium-evoked spreading depression. Neurochem Res 2004, 29:1519-1527.
62. Oja SS, Kontro P. Release of endogenous taurine and γ-aminobutyric acid from brain slices from the adult and developing mouse. J Neurochem 1989, 52:1018-1024.
63. Saransaari P, Oja SS. Release of endogenous glutamate, aspartate, GABA and taurine from hippocampal slices from adult and developing mice under cell-damaging conditions. Neurochem Res 1998, 23:567-574.
64. Oja SS, Saransaari P. Release of endogenous amino acids from the hippocampus and brain stem from developing and adult mice in ischemia. Neurochem Res 2009, 34:1668-1676.
65. Magnusson KR, Koerner JF, Larson AA, Smullin DH, Skilling SR, Beitz AJ. NMDA-, kainate- and quisqualate-stimulated release of taurine from electro-physiologically monitored rat hippocampal slices. Brain Res 2001, 549:1-8.
66. Saransaari P, Oja SS. Excitatory amino acids evoke taurine release from cerebral cortex slices from adult and developing mice. Neuroscience 1991, 45:451-459.
67. McCaslin PP, Yu XZ. Cyanide selectively augments kainate- but not NMDA-induced release of glutamate and taurine. Eur J Pharmacol 1992, 228:73-75.
68. Saransaari P, Oja SS. Taurine release from mouse hippocampal slices: effects of glutamatergic substances and hypoxia. Adv Med Exp Biol 1994, 359:279-287.
69. Saransaari P, Oja SS. Taurine release from the developing and ageing hippocampus: stimulation by agonists of ionotropic glutamate receptors. Mech Ageing Dev 1997, 99:219-232.
70. Saransaari P, Oja SS, Glutamate-agonist-evoked taurine release from the adult and developing mouse hippocampus in cell-damaging conditions. Amino Acids 1997, 9:323-335.

71. Saransaari P, Oja SS. Modulation of taurine release in ischemia by glutamate receptors in mouse brain stem slices. Amino Acids 2010, 38:739-746.
72. Jacobson I, Hamberger A. Kainic acid-induced changes of extracellular amino acid levels, evoked potentials and EEG activity in the rabbit olfactory bulb. Brain Res 1985, 348:289-296.
73. Sundström E, Mo L-L, Seiger Å. In vivo studies on NMDA-evoked release of amino acids in the rat spinal cord. Neurochem Int 1995, 27:185-193.
74. La Bella V, Piccoli F. Differential effect of β-N-oxalylamino-L-alanine, the Lathyrus sativus neurotoxin, and (±)-α-amino-3-hydroxy-5-methylisoxazole-4-propionate on the excitatory amino acid and taurine levels in the brain of freely moving rat. Neurochem Int 2000, 36:523-530.
75. Scheller D, Szathmary S, Kolb J, Tegtmeier F. Observations on the relationship between the extracellular changes of taurine and glutamate during cortical spreading depression, during ischemia, and within the area surrounding a thrombotic infarct. Amino Acids 2000, 19:571-583.
76. Scheller D, Korte M, Szathmary S, Tegtmeier F. Cerebral taurine release mechanisms in vivo: pharmacological investigation in rats using microdialysis for proof of principle. Neurochem Res 2000, 25:801-807.
77. Katoh H, Sima K, Nawashiro H, Wada K, Chigasaki H. The effect of MK-801 on extracellular neuroactive amino acids in hippocampus after closed head injury followed by hypoxia in rats. Brain Res 1997, 758:153-162.
78. Saransaari P, Oja SS. Characterization of N-methyl-D-aspartate-evoked taurine release in the developing and adult mouse hippocampus. Amino Acids 2003, 24:213-221.
79. Chen D-Z, Ohkuma S, Kuriyama K. Characteristics of nitric oxide-evoked [^{3}H] taurine release from cerebral cortical neurons. Neurochem Int 1996, 28:601-607.
80. Saransaari P, Oja SS. Taurine release modified by nitric oxide-generating compounds in the developing and adult mouse hippocampus. Neuroscience 1999, 89:1103-1111.
81. Saransaari O, Oja SS. Nitric oxide is involved in taurine release in the mouse brain stem under normal and ischemic conditions. Amino Acids 2008, 34:429-436.
82. Guevara-Guzman R, Emson PC, Kendrick KM, Modulation of in vivo striatal transmitter release by nitric oxide and cyclic GMP. J Neurochem 1994, 62:807-810.
83. Oja SS, Saransaari P. Modulation of taurine release by glutamate receptors and nitric oxide. Prog Neurobiol 2000, 62:407-425.
84. Saransaari P, Oja SS. Taurine release in the developing and adult mouse hippocampus: involvement of cyclic guanosine monophosphate. Neurochem Res 2002, 27:15-20.
85. Böckelmann R, Reiser M, Wolf G. Potassium-stimulated taurine release and nitric oxide synthase activity during quinolinic acid lesion of the rat striatum. Neurochem Res 1998, 23:469-475.
86. Saransaari P, Oja SS. Involvement of metabotropic glutamate receptors in taurine release in the adult and developing hippocampus. Amino Acids 1999, 16:165-179.
87. Miyamoto T-A, Miyamoto K-J. Does adenosine release taurine in the A_1-receptor-rich hippocampus? J Anesth 1999, 13:94-98.

88. Saransaari P, Oja SS. Modulation of the ischemia-induced taurine release by adenosine receptors in the developing and adult mouse hippocampus. Neuroscience 2000, 97:425-430.
89. Saransaari P, Oja SS. Interactions of taurine and adenosine in the mouse hippocampus in normoxia and ischemia. Adv Exp Med Biol 2003, 526:445-451.
90. Saransaari P, Oja SS. Adenosine receptor agonists affect taurine release from mouse brain stem slices in ischemia. Amino Acids 2010, 38:1387-1393.
91. Madelian V, Silliman S, Shain W. Adenosine stimulates cAMP-mediated taurine release from LRM55 glial cells. J Neurosci Res 1988, 20:176-181.
92. Solís JM, Herranz AS, Herreras O, Muñoz MD, Martín del Río R, Lerma J. Variation of potassium ion concentrations in the rat hippocampus specifically affects extracellular taurine level. Neurosci Lett 1986, 66:263-268.
93. Kamisaki Y, Wada K, Nakamoto K, Itoh T. Release of taurine and its effects on release of neurotransmitter amino acids in rat cerebral cortex. Adv Exp Med Biol 1996, 403:445-454.
94. García Dopico J, Perdomo Díaz J, Alonso TJ, González Hernández T, Castro Fuentes R, Rodríguez Díaz M. Extracellular taurine in the substantia nigra: taurine – glutamate interaction. J Neurosci Res 2004, 76:528-538.
95. Tuz K, Peña-Segura C, Franco R, Pasantes-Morales H. Depolarization, exocytosis and amino acid release evoked by hyposmolarity from cortical synaptosomes. Eur J Neurosci 2004, 19:916-924.
96. Molchanova SM, Oja SS, Saransaari P. Mechanisms of enhanced taurine release under Ca^{2+} depletion. Neurochem Int 2005, 47:343-349.
97. Kontro P, Oja SS. Sodium-independent taurine binding to brain synaptic membranes. Cell Mol Neurobiol 1983, 3:183-187.
98. Kontro P, Oja SS. Properties of sodium-independent taurine binding to brain synaptic membranes. Prog Clin Biol Res 1985, 179:249-259.
99. Kontro P, Oja SS. Co-operativity in sodium-independent taurine binding to brain membranes in the mouse. Neuroscience 1987, 23:567-570.
100. Yarborough GG, Singh DK, Taylor DA. Neuropharmacological characterization of a taurine antagonist. J Pharmacol Exp Ther 1981, 219:604-613.
101. Kudo Y, Akiyoshi E, Akagi H. Identification of two taurine receptor subtypes on the primary afferent terminal of frog spinal cord. Br J Pharmacol 1988, 94:1051-1056.
102. Sung DY, Walthall WW, Derby CD. Identification and partial purification of putative taurine receptor proteins from the olfactory organ of the spiny lobster. Comp Biochem Physiol Biochem Mol Biol 1996, 115:19-26.
103. Oja SS, Kontro P. Neurotransmitter actions of taurine in the central nervous system. In Taurine and Neurological Disorders, A. Barbeau and R.J. Huxtable (eds), Raven Press, New York 1978, pp 181-200.
104. Okamoto K, Kimura H, Sakai Y. Taurine-induced increase of the Cl^- conductance of cerebellar Purkinje cell dendrites in vitro. Brain Res 1983, 259:319-323.
105. Ye G-I, Tse ACO, Yung W-H. Taurine inhibits rat substantia nigra pars reticulate neurons by activation of GABA- and glycine-linked chloride conductance. Brain Res 1997, 749:175-179.

106. Puopolo M, Kratskin I, Belluzzi O. Direct inhibitory effect of taurine on relay neurons of the rat olfactory bulb. Neuroreport 1998, 9:2319-2322.
107. Belluzzi D, Puopolo M, Benedusi M, Kratskin I. Selective neuroinhibitory effects of taurine in slices of rat main olfactory bulb. Neuroscience 2004, 124:929-944.
108. Oja SS, Korpi ER, Saransaari P. Modification of chloride flux across brain membranes by inhibitory amino acids in developing and adult mice. Neurochem Res 1990, 15:797-804.
109. Linne M-L, Jalonen TO, Saransaari P, Oja SS. Taurine-induced single-channel currents in cultured rat cerebellar granule cells. Adv Exp Med Biol 1996, 403:455-462.
110. Lähdesmäki P, Oja SS. On the mechanism of taurine transport at brain cell membranes. J Neurochem 1973, 20:1411-1417.
111. Liu Q-R, López-Corcuera B, Nelson H, Mandiyan S, Nelson N. Cloning and expression of cDNA encoding the transporter of taurine and β-alanine in mouse brain. Proc Natl Acad Sci USA 1992, 89:12145-12149.
112. Smith KE, Borden LA, Wang CH, Hartig PR, Branchek TA, Weinshank BL. Cloning and expression of a high affinity taurine transporter from rat brain. Mol Pharmacol 1992, 42:563-569.
113. Vinnakota S, Qian X, Egal H, Sarthy V, Sarkar HK. Molecular characterization and in situ localization of a mouse retinal taurine transporter. J Neurochem 1997, 69:2238-2250.
114. Uchida S, Kwon HM, Yamauchi A, Preston AS, Marumo F, Handler JS. Molecular cloning of the cDNA for an MDCK cell Na^+- and Cl^--dependent taurine transporter that is regulated by hypertonicity. Proc Natl Acad Sci USA 1992, 89:8230-8234.
115. Lake N, Orlowski J. Cellular studies of the taurine transporter. Adv Exp Med Biol 1996, 403:371-376.
116. Pow DV, Sullivan R, Reye P, Hermanussen S. Localization of taurine transporters, taurine and [^{3}H] taurine accumulation in the rat retina, pituitary, and brain. Glia 2002, 37:153-168.
117. Kontro P, Oja SS. Taurine uptake by rat brain synaptosomes. J Neurochem 1978, 30:1297-1304.
118. Kontro P. Comparison of the uptake processes of taurine, hypotaurine, and GABA. In Amino Acid Neurotransmitters, F.V. DeFeudis and P. Mandel (eds), Raven Press, New York 1981, pp 161-167.
119. Holopainen I, Kontro P, Frey H, Oja SS. Taurine, hypotaurine and GABA uptake by cultured neuroblastoma cells. J Neurosci Res 1983, 10:83-92.
120. Albrecht J, Schousboe A. Taurine interaction with neurotransmitter receptors in the CNS: an update. Neurochem Res 2005, 30:1615-1621.
121. Kontro P, Oja SS. Glycinergic systems in the brain stem of developing and adult mice: effects of taurine. Int J Devl Neurosci 1987, 5:461-470.
122. Horikoshi T, Asanuma A, Yanagisawa K, Anzai K, Goto S. Taurine and β-alanine act on both GABA and glycine receptors in Xenopus oocyte injected with mouse brain messenger RNA. Brain Res 1988, 464:97-105.

123. Schmieden,V, Grenningloh G, Schofield PR, Betz H, Functional expression in Xenopus oocytes of the strychnine binding 48 kd subunit of the glycine receptor. EMBO J 1989, 8:695-700.
124. Hussy N, Deleuze C, Pantaloni A, Desarménien MG, Moos F. Agonist action of taurine on glycine receptors in rat supraoptic magnocellular neurons: possible role in osmoregulation. J Physiol 1997, 502:609-621.
125. Ye J-H, Wang F, Krnjević K, Wang W, Xiong Z-G, Zhang J. Presynaptic glycine receptors on GABAergic terminals facilitate discharge of dopaminergic neurons in ventral tegmental area. J Neurosci 2004, 24:8961-8974.
126. McCool BA, Botting SK. Characterization of strychine-sensitive receptors in acutely isolated adult rat basolateral membranes Brain Res 2000, 859:341-351.
127. Wang D-S, Xu T-L, Pang Z-P, Li J-S, Akaike N. Taurine-activated chloride currents in the rat sacral dorsal commissural neurons. Brain Res 1998, 792:41-47.
128. Xu H, Wang W, Tang Z-Q, Xu T-L, Chen L. Taurine acts as a glycine receptor agonists in slices of rat inferior colliculus. Hearing Res 2006, 220:95-105.
129. Jiang Z, Krnjević K, Wang F, Ye JH. Taurine activates strychnine-sensitive glycine receptors in neurons freshly isolated from nucleus accumbens of young rats. J Neurophysiol 2004, 91:248-257.
130. Wang F, Xiao C, Ye JH. Taurine activates excitatory non-synaptic glycine receptors on dopamine neurons in ventral tegmental area of young rats. J Physiol 2005, 565:503-516.
131. Pierobon P, Minei R, Porcu P, Sogliano C, Tino A, Marino G, Biggio G, Concas A. Putative glycine receptors in Hydra: a biochemical and behavioural study. Eur J Neurosci 2001, 14:1659-1666.
132. Schmieden V, Kuhse J, Betz H. Agonist pharmacology of neonatal and adult glycine receptor α subunits: identification of amino acid residues involved in taurine activation. EMBO J 1992, 11:2025-2032.
133. Kuhse J, Schmieden V, Betz H. Identification and functional expression of a novel ligand binding subunit of the inhibitory glycine receptor. J Biol Chem 1990, 265:22317-22320.
134. Kuhse J, Schmieden V, Betz H. A single amino acid exchange alters the pharmacology of neonatal rat glycine receptor subunit. Neuron 1990, 5:867-873.
135. David-Watine B, Goblet C, de Saint Jan D, Fucile S, Devignot V, Bregestovski P, Korn H. Cloning, expression and electrophysiological characterization of glycine receptor alpha subunit from zebrafish. Neuroscience 1999, 90:303-317.
136. Imboden M, de Saint Jan D, Leulier F, Korn H, Coblet C, Bregestovski P. Isolation and characterization of an alpha 2-type zebrafish glycine receptor subunit. Neuroscience 2001, 103:799-810.
137. Harvey RJ, Schmieden V, von Holst A, Laube B, Rohrer H, Betz H. Glycine receptors containing the α4 subunit in the embryonic sympathetic nervous system, spinal cord and male genital ridge. Eur J Neurosci 2000, 12:994-1001.
138. Laube B, Langosch D, Betz H, Schmieden V. Hyperekplexia mutations of the glycine receptor unmask the inhibitory subsite for β-amino acids. Neuroreport 1995, 6:897-900.

139. Rajendra S, Lynch JW, Pierce KD, French CR, Barry PH, Scholefield PR. Mutation of an arginine residue in the human glycine receptor transforms β-alanine and taurine from agonists into competitive antagonists. Neuron 1995, 14:169-175.
140. Lynch JW, Rajendra S, Pierce KD, Handford CA, Barry PH, Schofield PR. Identification of intracellular and extracellular domains mediating signal transduction in the inhibitory glycine receptor chloride channel. EMBO J 1997, 16:110-120.
141. Schmieden V, Betz H. Pharmacology of the inhibitory glycine receptor: agonist and antagonist actions of amino acids and piperidine carboxylic acid compounds. Mol Pharmacol 1995, 48:919-927.
142. Castaldo P, Stefanoni P, Miceli F, Coppola G, Miraglia del Giudice E, Bellini G, Pascotto A, Trudell JR, Harrison NL, Annunziato L, Taglialatela M. A novel hyperekplexia-causing mutation in the pre-transmembrane segment 1 of the human glycine receptor α1 subunit reduces membrane expression and impairs gating by agonists. J Biol Chem 2004, 279:25598-25604.
143. Song Z, Hatton GI. Taurine and the control of basal hormone release from rat neurohypophysis. Exp Neurol 2003, 183:330-337.
144. Hilgier W, Oja SS, Saransaari P, Albrecht J. Taurine prevents ammonia-induced accumulation of cyclic AMP in rat striatum by interaction with $GABA_A$ and glycine receptors. Brain Res 2005, 1043:242-246.
145. Wu Z-Y, Xu T-L. Taurine-evoked chloride current and its potentiation by intracellular Ca^{2+} in immature rat hippocampal CA1 neurons. Amino Acids 2003, 24:155-162.
146. Wang H-H, Jiang Z-L, Fan X-J, Zhang L, Li X, Ke K-F. Neuroprotective effect of taurine against focal cerebral ischemia is rats possibly mediated by activation of both $GABA_A$ and glycine receptors. Neuropharmacology 2007, 52:1199-1209.
147. Yoshida M, Fukuda S, Tozuka Y, Miyamoto Y, Hisatsune T. Developmental shift in bidirectional functions of taurine-sensitive chloride channels during cortical circuit formation in postnatal mouse brain. J Neurobiol 2004, 60:166-175.
148. Iwata H, Nakayama K, Matsuda T, Baba A. Effect of taurine on a benzodiazepine-GABA-chloride ionophore receptor complex in rat brain membranes. Neurochem Res 1984, 9:535-544.
149. Medina JH, De Robertis E. Taurine modulation of the benzodiazepine-gamma-aminobutyric acid receptor complex in brain membranes. J Neurochem 1984, 42:1212-1217.
150. Malminen O, Kontro P. Modulation of the GABA-benzodiazepine receptor complex by taurine in rat brain membranes. Neurochem Res 1986, 11:85-94.
151. Malminen, O, Kontro P. Actions of taurine on the GABA-benzodiazepine receptor complex solubilized from rat brain. Neurochem Int 1987, 11:113-117.
152. Quinn MR, Miller CI. Taurine allosterically modulates flunitrazepam binding to synaptic membranes. J Neurosci Res 1992, 33:136-141.
153. Quinn MR, Harris CL. Taurine allosterically inhibits binding of [^{35}S]-t-butyl-bicyclophosphonothionate (TBPS) to rat brain synaptic membranes. Neuropharmacology 1995, 34:1607-1613.

154. del Olmo N, Bustamante J, Martín del Río R, Solís JM. Taurine activates $GABA_A$ but not $GABA_B$ receptors in rat hippocampal CA1 area. Brain Res 2000, 864:298-307.
155. Halonen LM, Sinkkonen ST, Chandra D, Homanics GE, Korpi ER. Brain regional distribution of $GABA_A$ receptors exhibiting atypical GABA agonism: roles of receptor subunits. Neurochem Int 2009, 55:389-396.
156. Jia F, Yue M, Chandra D, Keramidas A, Goldstein PA, Homanics GE, Harrison NI. Taurine is a potent activator of extrasynaptic $GABA_A$ receptors in the thalamus. J Neurosci 2008, 28:106-115.
157. Mody I. Distinguishing between $GABA_A$ receptors responsible for topic and phasic conductances. Neurochem Res 2001, 26:907-913.
158. Wisden W, Cope D, Klausberger T, Hauer B, Sinkkonen ST, Tretter V, Lujan R, Jones A, Korpi ER, Mody I, Sieghart W, Somogyi P. Ectopic expression of the $GABA_A$ receptor $\alpha 6$ subunit in hippocampal pyramidal neurons produces extrasynaptic receptors and an increased tonic inhibition. Neuropharmacology 2002, 43:530-549.
159. Paula-Lima AC, De Felice FG, Brito-Moreira J, Ferreira ST. Activation of $GABA_A$ receptors by taurine and muscimol blocks the neurotoxicity of β-amyloid in rat hippocampal and cortical neurons. Neuropharmacology 2005, 49:1140-1148.
160. Oermann E, Warskulat U, Heller-Stilb B, Häussinger D, Zilles K. Taurine-transporter gene knockout-induced changes in $GABA_A$, kainate and AMPA but not NMDA receptor binding in mouse brain. Anat Embryol 2005, 210:363-372.
161. Bureau MH, Olsen RW. Taurine acts on a subclass of $GABA_A$ receptors in mammalian brain in vitro. Eur J Pharmacol 1991, 207:9-16.
162. Rabe H, Picard R, Uusi-Oukari M, Hevers W, Lüddens H, Korpi ER. Coupling between agonist and chloride ionophore sites of $GABA_A$ receptor: agonist/antagonist efficacy of 4-PIOL. Eur J Pharmacol 2000, 409:233-242.
163. Dominguez-Perrot C, Feltz P, Poulter MO. Recombinant $GABA_A$ receptor desensitization: the role of the $\gamma 2$ subunit and its physiological significance. J Physiol 1996, 497:145-159.
164. Martinez-Torres A, Miledi R. Expression of functional receptors by the human γ-aminobutyric $acid_A$ $\gamma 2$ subunit. Proc Natl Acad Sci USA 2004, 101:3220-3223.
165. Shen W, Mennerick S, Covey DF, Zorumski CF. Prenenolone sulphate modulates inhibitory synaptic transmission by enhancing $GABA_A$ receptor desensitization. J Neurosci 2000, 20:3571-3579.
166. El Idrissi A. Taurine and brain excitability. Adv Exp Biol Med 2006, 583: 315-322.
167. Abraham JH, Schousboe A. Effects of taurine on cell morphology and expression of low-affinity GABA receptors in cultured cerebellar granule cells. Neurochem Res 1989, 14:1031-1038.
168. Kontro P, Oja SS. Interactions of taurine with $GABA_B$ binding sites in mouse brain. Neuropharmacology 1990, 29:243-247.
169. Kontro P, Korpi ER, Oja SS. Taurine interacts with $GABA_A$ and $GABA_B$ receptors in the brain. Prog Clin Biol Res 1990, 351:83-94.

170. Fritschy J-M, Meskenaite V, Weinmann O, Honer M, Benke D, Mohler H. GABAB-receptor splice variants GB1a and GB1b in rat brain: developmental regulation, cellular distribution and extrasynaptosomal localization. Eur J Neurosci 1999, 11:761-768.
171. Chaput MA, Palouzier-Paulignan B, Delaleu JC, Duchamp-Viret P. Taurine action on mitral cell activity in the frog olfactory bulb in vivo. Chem Senses 2004, 29:83-91.
172. Kamisaki Y, Maeda K, Ishimura M, Omura H, Itoh T. Effects of taurine on depolarization-evoked release of amino acids from rat cortical synaptosomes. Brain Res 1993, 627:181-185.
173. Kamisaki Y, Wada K, Nakamoto K, Itoh T. Effect of taurine on GABA release from synaptiomes of rat olfactory bulb. Amino Acids 1996, 10:49-57.
174. Smith SS, Li J. $GABA_B$ receptor stimulation by baclofen and taurine enhances excitatory amino acid induced phosphotidylinositol turnover in neonatal rat cerebellum. Neurosci Lett 1991, 132:59-64.
175. Leviel V, Chéramy A, Nieoullon A, Glowinski J. Symmetric bilateral changes in dopamine release from the caudate nuclei of the cat induced by unilateral nigral application of glycine and GABA-related compounds. Brain Res 1979, 175: 259-270.
176. Ruotsalainen M, Heikkilä M Lillsunde P, Seppälä T, Ahtee L. Taurine infused intrastriatally elevates, but intranigrally decreases striatal extracellular dopamine concentration in anaesthetized rats. J Neural Transm 1996, 103:935-946.
177. O'Neill RD. Effects of intranigral injection of taurine and GABA on striatal dopamine release monitored voltammetrically in the unanaesthetized rat. Brain Res 1986, 382:28-32.
178. Kontro P. Interactions of taurine and dopamine in the striatum. Adv Exp Med Biol 1987, 217:347-355.
179. Kontro P, Oja SS. Release of taurine, GABA and dopamine from rat striatal slices: mutual interactions and developmental aspects. Neuroscience 1988, 24:49-58.
180. Dawson RJr, Pelleymounter MA, Cullen MJ, Gollub M, Liu S. An age-related decline in striatal taurine is correlated with a loss of dopaminergic markers. Brain Res Bull 1999, 48:319-324.
181. Ahtee L, Vahala M-L. Taurine and its derivatives alter brain dopamine metabolism similarly to GABA in mice and rats. Prog Clin Biol Res 1985, 179:331-341.
182. Salimäki J, Scriba G, Piepponen TP, Rautolahti N, Ahtee L. The effects of systemically administered taurine and N-pivaloyltaurine on striatal extracellular dopamine and taurine in freely moving rats. Naunyn-Schmiedeberg's Arch Pharmacol 2003, 368:134-141.
183. Ruotsalainen M, Majasaari M, Salimäki J, Ahtee L. Locally infused taurine, GABA and homotaurine alter differentially the striatal extracellular concentration of dopamine and its metabolites in rats. Amino Acids 1998, 15:117-134.
184. Ruotsalainen M, Ahtee L. Intrastriatal taurine increases striatal extracellular dopamine in a tetrodotoxin-sensitive manner in rats. Neurosci Lett 1996, 212:175-178.

185. Anderzhanova E, Rayevsky KS, Saransaari P, Riitamaa E, Oja SS. Effects of sydnocarb and D-amphetamine on the extracellular levels of amino acids in the rat caudate-putamen. Eur J Pharmacol 2001, 428:87-95.
186. Anderzhanova E, Saransaari P, Oja SS. Neuroprotective mechanisms of taurine in vivo. Adv Exp Med Biol 2006, 583:377-387.
187. Becquet D, Hery M, Francois-Bellan AM, Giraud P, Deprez P, Faudon M, Fache MP, Hery F. Glutamate, GABA, glycine and taurine modulate serotonin synthesis and release in rostral and caudal rhombencephalic raphe cells in primary cell cultures. Neurochem Int 1993, 23:269-283.
188. Kontro P, Korpi ER, Oja OS, Oja SS. Modulation of noradrenaline uptake and release by taurine in rat cerebral slices. Neuroscience 1984, 13:663-666.
189. Kontro P, Oja SS. Taurine interferes with spiperone binding in the striatum. Neuroscience 1986, 19:1007-1010.
190. Saransaari P, Oja SS. Phencyclidine binding sites in mouse cerebral cortex during development and ageing: effects of inhibitory amino acids. Mech Ageing Dev 1993, 68:125-136.
191. Saransaari P, Oja SS. Interactions of taurine and adenosine in the mouse hippocampus in normoxia and ischemia. Adv Exp Med Biol 2003, 526:445-451.
192. Galarreta M, Bustamante J, Martín del Río R, Solís JM. Taurine induces a long-lasting increase of synaptic efficacy and axon excitability in the hippocampus. J Neurosci 1996, 16:92-102.
193. Chepkova AN, Doreulee N, Yanovsky Y, Mukhopadhyay D, Haas HL, Sergeeva OA. Long-lasting enhancement of corticostriatal neurotransmission by taurine. Eur J Neurosci 2002, 16:1523-1530.
194. Sergeeva OA, Chepkova AN, Doreulee N, Eriksson KS, Poelchen W, Monnighoff I, Heller-Stib B, Warskulat U, Haussinger D, Haas HL. Taurine-induced long-lasting enhancement of synaptic transmission in mice: role of transporters. J Physiol 2003, 550:911-919.
195. Chepkova AN, Sergeeva OA, Haas HL. Long-lasting enhancement of corticostriatal transmission by taurine: role of dopamine and acetylcholine. Cell Mol Neurobiol 2005, 25:767-776.
196. Kaakkola S, Kääriäinen L. Contralateral circling behaviour induced by intranigral injection of taurine in rats. Acta Pharmacol Toxicol 1980, 46:293-298.
197. Ericson M, Molander A, Stomberg R, Söderpalm B. Taurine elevates dopamine levels in the rat nucleus accumbens; antagonism by strychnine. Eur J Neurosci 2006, 23:3225-3229.
198. Lehmann A, Hagberg H, Hamberger A. A role for taurine in the maintenance of homeostasis in the central nervous system during hyperexcitation? Neurosci Lett 1984, 52:341-346.
199. Kontro P, Oja SS. Effects of taurine on the influx and efflux of calcium in brain slices of adult and developing mice. Int J Neurosci 1988, 38:103-109.
200. Matsuda T, Takuma K, Kishida Y, Azuma J, Baba A. Protective effect of taurine against reperfusion injury in cultured rat astrocytes. Adv Exp Med Biol 1996, 403:491-497.

201. El Idrissi A, Harris C, Trenkner E. Taurine modulates glutamate and growth factors-mediated signaling mechanisms. Adv Exp Med Biol 1998, 442:385-396.
202. Trenkner E, El Idrissi A, Dumas R, Rabe A. Functional consequences of calcium uptake modulation by taurine in vivo and in vitro. Adv Exp Med Biol 1998, 442:277-284.
203. Chen WQ, Jin H, Nguyen M, Carr J, Lee YJ, Hsu CC, Faiman MD, Schloss JV, Wu J-Y. Role of taurine in regulation of intracellular calcium level and neuroprotective function in cultured neurons. J Neurosci Res 2001, 66:612-619.
204. Tang XW, Deupree DL, Sun Y, Wu J-Y. Biphasic effect of taurine on excitatory amino acid-induced neurotoxicity. Adv Exp Med Biol 1996, 403:499-505.
205. Wu J-Y, Chen W, Tang XW, Jin H, Foos T, Schloss JV, Davis K, Faiman MD, Hsu C-C. Mode of action of taurine and regulation dynamics of its synthesis in the CNS. Adv Exp Med Biol 2000, 483:35-44.
206. El Idrissi A, Trenkner E. Taurine regulates mitochondrial calcium homeostasis. Adv Exp Med Biol 2003, 526:527-536.
207. El Idrissi A, Trenkner E. Growth factors and taurine protect against excitotoxicity by stabilizing calcium homeostasis and energy mentabolism. J Neurosci 1999, 19:9459-9468.
208. Wu H, Jin Y, Wei J, Jin H, Sha D, Wu J-Y. Mode of action of taurine as a neuroprotector. Brain Res 2005, 1038:123-131.
209. Li YP, Lombardini JB. Inhibition by taurine of the phosphorylation of specific synaptosomal proteins in the rat cortex: effects of taurine on the stimulation of calcium uptake in mitochondria and inhibition of phosphoinositide turnover. Brain Res 1991, 553:89-96.
210. Zielińska M, Law RO, Albrecht J. Excitotoxic mechanism of cell swelling in rat cortical slices treated acutely with ammonia. Neurochem Int 2003, 43:299-303.
211. Schaffer SW, Azuma J, Takahashi K, Mozaffari M. Why is taurine cytoprotective? Adv Exp Med Biol 2003, 526:307-321.
212. Zhao P, Huang Y-L, Cheng J-S. Taurine antagonizes calcium overload induced by glutamate or chemical hypoxia in cultured rat hippocampal neurons. Neurosci Lett 1999, 268:25-28.
213. Foos TM, Wu J-Y. The role of taurine in the central nervous system and the modulation of intracellular calcium homeostasis. Neurochem Res 2002, 27:21-26.