REVIEW

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Taurine, energy drinks, and neuroendocrine effects

ABSTRACT

Taurine is an amino acid found abundantly in brain, retina, heart, and reproductive organ cells, as well as in meat and seafood. But it is also a major ingredient in popular "energy drinks," which thus constitute a major source of taurine supplementation. Unfortunately, little is known about taurine's neuroendocrine effects. The authors review the sparse data and provide a basic background on the structure, synthesis, distribution, metabolism, mechanisms, effects, safety, and currently proposed therapeutic targets of taurine.

KEY POINTS

Energy drinks are widely consumed in the United States, with an estimated 354 million gallons sold in 2009, or approximately 5.25 L/year per person over age 10.

Taurine has been reported to have anti-inflammatory action. Supplementation has been proposed to have beneficial effects in epilepsy, heart failure, cystic fibrosis, and diabetes, and has been shown in animal studies to protect against neurotoxic insults from alcohol, ammonia, lead, and other substances.

Taurine is an inhibitory neurotransmitter and neuromodulator. It is structurally analogous to gamma-aminobutyric acid, the main inhibitory neurotransmitter in the brain.

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Taurine—an amino acid found in abundance in the human brain, retina, heart, and reproductive organs, as well as in meat and seafood—is also a major ingredient in "energy drinks" (**Table 1**).[1,2] Given the tremendous popularity of these drinks in the United States, it would seem important to know and to recognize taurine's neuroendocrine effects. Unfortunately, little is known about the effects of taurine supplementation in humans.

This paper reviews the sparse data to provide clinicians some background on the structure, synthesis, distribution, metabolism, mechanisms, effects, safety, and proposed therapeutic targets of taurine.

TAURINE'S THERAPEUTIC POTENTIAL

Taurine has been reported to have widespread anti-inflammatory actions.[3,4] Taurine supplementation has been proposed to have beneficial effects in the treatment of epilepsy,[5] heart failure,[6,7] cystic fibrosis,[8] and diabetes[9] and has been shown in animal studies to protect against neurotoxic insults from alcohol, ammonia, lead, and other substances.[10–16]

In addition, taurine analogues such as homotaurine and *N*-acetyl-homotaurine (acamprosate) have been probed for possible therapeutic applications. Homotaurine has been shown to have antiamyloid activity that could in theory protect against the progression of Alzheimer disease,[17] and acamprosate is approved by the US Food and Drug Administration (FDA) for the treatment of alcohol use disorders.[18]

TAURINE CONSUMPTION

Energy drinks are widely consumed in the United States, with an estimated 354 million

TABLE 1

Taurine content of common energy drinks

Brand (can size)	Taurine per can (mg)	Taurine per 8 oz
Cocaine (8.4 oz)	788	750
Go Girl Sugar-Free (12 oz)	1,200	800
Monster (16 oz)	2,000	1,000
Red Bull (8.3 oz)	1,038	1,000
Rockstar (16 oz)	2,000	1,000
Tab Energy (12 oz)	1,178	785

Based on information from reference 91.

gallons sold in 2009, or approximately 5.25 L/year per person over age 10.[1] In 2012, US sales of energy drinks exceeded $12 billion,[19] with young men, particularly those in the military deployed in war zones, being the biggest consumers.[20–22] Analyses have found that of 49 nonalcoholic energy drinks tested, the average concentration of taurine was 3,180 mg/L, or approximately 750 mg per 8-oz serving.[23,24] Popular brands include Red Bull, Monster, Rockstar (**Table 1**), NOS, Amp, and Full Throttle.

Vegans take in much less taurine and have lower circulating levels

Taurine is plentiful in the human body, which contains up to 1 g of taurine per kg.[25] Foods such as poultry, beef, pork, seafood, and processed meats have a high taurine content (**Table 2**).[26–29] People who eat meat and seafood have plentiful taurine intake, whereas vegetarians and vegans consume much less and have significantly lower circulating levels[30] because plants do not contain taurine in appreciable amounts.[26,29]

The typical American diet provides between 123 and 178 mg of taurine daily.[26] Consumption of one 8-oz energy drink can increase the average intake 6 to 16 times. A lacto-ovo vegetarian diet provides only about 17 mg of taurine daily, and an 8-oz energy drink can increase the average intake by 44 to 117 mg.[26] And since a vegan diet provides essentially no taurine,[30] energy drink intake in any amount would constitute a major relative increase in taurine consumption.

ATTEMPTS TO STUDY TAURINE'S EFFECTS

Since most clinical trials to date have looked at the effects of taurine in combination with other ingredients such as caffeine, creatine, and glucose[31–35] in drinks such as Red Bull, these studies cannot be used to determine the effects of taurine alone. In the few clinical trials that have tested isolated taurine consumption, data are not sufficient to make a conclusion on direct effects on energy metabolism.

Rutherford et al[36] tested the effect of oral taurine supplementation (1,660 mg) on endurance in trained male cyclists 1 hour before exercise, but observed no effect on fluid intake, heart rate, subjective exertion, or time-trial performance. A small increase (16%) in total fat oxidation was observed during the 90-minute exercise period. Since mitochondria are the main location of fatty acid degradation, this effect may be attributed to taurine supplementation, with subsequent improvement in mitochondrial function.

Zhang et al[37] found a 30-second increase in cycling energy capacity after 7 days of 6 g oral taurine supplementation, but the study was neither blinded nor placebo-controlled.

Kammerer et al[38] tested the effect of 1 g of taurine supplementation on physical and mental performance in young adult soldiers 45 minutes before physical fitness and cognitive testing. This double-blind, placebo-controlled randomized trial found no effect of taurine on cardiorespiratory fitness indices, concentration, or immediate memory, nor did it find any effect of an 80-mg dose of caffeine.

In sum, the available data are far from sufficient to determine the direct effect of taurine consumption on energy metabolism in healthy people.

PHARMACOLOGY OF TAURINE

Chemical structure

Taurine, or 2-aminoethane sulfonic acid, is a conditionally essential amino acid, ie, we can usually make enough in our own bodies. It was first prepared on a large scale for physiologic investigation almost 90 years ago, through the purification of ox bile.[39] It can be obtained either exogenously through dietary sources or endogenously through biosynthesis from methionine and cysteine precursors, both essential sulfur-

containing alpha-amino acids.[40] Both sources are important to maintain physiologic levels of taurine, and either can help compensate for the other in cases of deficiency.[41]

The structure of taurine has two main differences from the essential amino acids. First, taurine's amino group is attached to the beta-carbon rather than the alpha-carbon, making it a beta-amino acid instead of an alpha-amino acid.[42] Second, the acid group in taurine is sulfonic acid, whereas the essential amino acids have a carboxylic acid.[43] Because of its distinctive structure, taurine is not used as a structural unit in proteins,[43] existing mostly as a free amino acid within cells, readily positioned to perform several unique functions.

Synthesis

De novo synthesis of taurine involves several enzymes and at least five pathways,[44] mostly differing by the order in which sulfur is oxidized and decarboxylated.[45]

The rate-limiting enzyme of the predominant pathway is thought to be cysteine sulfinate decarboxylase (CSD), and its presence within an organ indicates involvement in taurine production.[44] CSD has been found in the liver,[46] the primary site of taurine biosynthesis, as well as in the retina,[47] brain,[48] kidney,[49] mammary glands,[50,51] and reproductive organs.[52]

Distribution

Taurine levels are highest in electrically excitable tissues such as the central nervous system, retina, and heart; in secretory structures such as the pineal gland and the pituitary gland (including the posterior lobe or neurohypophysis); and in platelets[25] and neutrophils.[53]

In the fetal brain, the taurine concentration is higher than that of any other amino acid,[54] but the concentration in the brain decreases with advancing age, whereas glutamate levels increase over time to make it the predominant amino acid in the adult brain.[54] Regardless, taurine is still the second most prevalent amino acid in the adult brain, its levels comparable to those of gamma-aminobutyric acid (GABA).[55]

Taurine has also been found in variable amounts in the liver, muscle, kidney, pancreas, spleen, small intestine, and lungs,[56] as well as in several other locations.[45,57]

TABLE 2

Taurine content of meats, seafood, and dairy products

Food	Preparation	Taurine content (mg per 100 g)
Poultry		
Chicken, dark meat	Broiled	132.9–265.1
Chicken, light meat	Broiled	5.20–24.80
Turkey, dark meat	Roasted	161.4–436.6
Turkey, light meat	Roasted	8.4–13.7
Beef	Broiled	8.0–68.0
Veal	Broiled	22.5–71.5
Pork		
Ham	Baked	34.1–65.9
Pork	Roasted	30.2–83.8
Processed meats		
Bologna, pork/beef	Cured	21.2–40.8
Bologna, turkey	Cured	110.8–135.3
Salami	Cured	39.4–78.6
Seafood		
Blue mussels	Cultured	480.6–539.4
Caviar	Raw	63.6–108.4
Clams	Raw	352.0–688.0
Cod, fillet	Wild	64.4–175.6
Mussels	Raw	530.3–779.7
Oysters	Raw	345.8–446.2
Salmon, fillet	Cultured	54.8–133.2
Scallops	Raw	801.0–853.0
Shrimp, medium	Raw	16.5–61.5
Shrimp, peeled	Wild	215.1–224.9
Shrimp, small	Cooked	8.2–13.8
Squid	Raw	191.5–520.5
Tuna, albacore	Canned	10.2–73.8
Tuna, chunk light	Canned	16.5–61.5
Tuna, in water	Canned	20.5–87.5
White fish	Cooked	10.0–334.0
Dairy products		
Cow's milk, whole	Pasteurized	1.4–3.4
Cow's milk, low-fat	Pasteurized	1.6–3.0
Cow's milk, nonfat	Pasteurized	1.6–3.4
Cow's milk yogurt	Pasteurized	0.7–0.9
Goat's milk	Pasteurized	5.3–8.3
Goat's milk yogurt	Pasteurized	5.0–5.5

Taurine is also present in the male and female reproductive organs. In male rats, taurine and taurine biosynthesis have been localized to Leydig cells of the testes, the cellular source of testosterone in males, as well as the cremaster muscle, efferent ducts, and peritubular myoid

cells surrounding seminiferous tubules.[58] More recently, taurine has been detected in the testes of humans[59] and is also found in sperm and seminal fluid.[60] Levels of taurine in spermatozoa are correlated with sperm quality, presumably by protecting against lipid peroxidation through taurine's antioxidant effects,[61,62] as well as through contribution to the spermatozoa maturation process by facilitating the capacitation, motility, and acrosomal reaction of sperm.[63]

In female rats, taurine has been found in uterine tissue,[64] oviducts,[65] uterine fluid (where it is the predominant amino acid),[66] and thecal cells of developing follicles of ovaries, cells responsible for the synthesis of androgens such as testosterone and androstenedione.[65] Taurine is also a major component of human breast milk[67] and is important for proper neonatal nutrition.[68]

Metabolism and excretion

Ninety-five percent of taurine is excreted in urine, about 70% as taurine itself, and the rest as sulfate. Most of the sulfate derived from taurine is produced by bacterial metabolism in the gut and then absorbed.[69] However, taurine can also be conjugated with bile acids to act as a detergent in lipid emulsification.[70] In this form, it may be subjected to the enterohepatic circulation, which gives bacteria another chance to convert it into inorganic sulfate for excretion in urine.[69]

Most studies have focused not on taurine alone, but combined with caffeine and glucose

MECHANISMS AND NEUROENDOCRINE EFFECTS

As a free amino acid, taurine has widespread distribution and unique biochemical and physiologic properties and exhibits several organ-specific functions; however, indisputable evidence of a taurine-specific receptor is lacking, and its putative existence[71] is controversial.[72] Nonetheless, taurine is a neuromodulator with a variety of actions.

Neurotransmission

Taurine is known to be an inhibitory neurotransmitter and neuromodulator.[73] It is structurally analogous to GABA, the main inhibitory neurotransmitter in the brain.[45] Accordingly, it binds to GABA receptors to serve as an agonist,[74,75] causing neuronal hyperpolarization and inhibition. Taurine has an even higher affinity for glycine receptors[75] where it has long been known to act as an agonist.[76] GABA and glycine receptors both belong to the Cys-loop receptor superfamily,[77] with conservation of subunits that allows taurine to bind each receptor, albeit at different affinities. The binding effects of taurine on GABA and glycine receptors have not been well documented quantitatively; however, it is known that taurine has a substantially lower affinity than GABA and glycine for their respective receptors.[76]

Catecholamines and the sympathetic nervous system

Surprisingly little is known about the effects of taurine on norepinephrine, dopamine, and the human sympathetic nervous system.[78] Humans with borderline hypertension given 6 g of taurine orally for 7 days[79] experienced decreases in epinephrine secretion and blood pressure, but normotensive study participants did not experience similar results, possibly because of a better ability to regulate sympathetic tone. Mizushima et al[80] showed that a longer period of taurine intake (6 g orally for 3 weeks) could elicit a decrease in norepinephrine in healthy men with normal blood pressure. Other similar studies[81–83] also suggested interplay between taurine and catecholamines, but the extent is still undetermined.

Growth hormone, prolactin, sex hormones, and cortisol

Taurine appears to have a complex relationship with several hormones, although its direct effects on hormone secretion remain obscure. Clinical studies of the acute and chronic neuroendocrine effects of taurine loading in humans are needed.

In female rats, secretion of prolactin is increased by the intraventricular injection of 5 µL of 2.0 µmol taurine over a 10-minute period.[84] Ikuyama et al[85] found an increase in prolactin and growth hormone secretion in adult male rats given 10 µL of 0.25 µmol and 1.0 µmol taurine intraventricularly, yet a higher dose of 4.0 µmol had no effect on either hormone. Furthermore, prolactin receptor deficiency is seen in CSD knockout mice, but the receptor is restored with taurine supplementation.[86]

Mantovani and DeVivo[87] reported that 375 to 8,000 mg/day of taurine given orally for 4 to 6 months to epileptic patients stimulated the secretion of growth hormone. However, in another study, a single 75-mg/kg dose of oral taurine did not trigger an acute increase in levels of growth hormone or prolactin in humans.[88] Energy drinks may contain up to 1,000 mg of taurine per 8-oz serving, but the effects of larger doses on growth hormone, which is banned as a supplement by major athletic organizations because of its anabolic and possible performance-enhancing effects, remain to be determined.

Taurine may have effects on human sex hormones, based on the limited observations in rodents.[89–94]

Although human salivary cortisol concentrations were purportedly assessed in response to 2,000 mg of oral taurine,[95] the methods and reported data are not adequate to draw any conclusions.

Energy metabolism

Mammals are unable to directly use taurine in energy production because they cannot directly reduce it.[25] Instead, bacteria in the gut use it as a source of energy, carbon, nitrogen, and sulfur.[96] However, taurine deficiency appears to impair the cellular respiratory chain, resulting in diminished production of adenosine triphosphate and diminished uptake of long-chain fatty acids by mitochondria, at least in the heart.[97]

Taurine is present in human mitochondria and regulates mitochondrial function. For example, taurine in mitochondria assists in conjugation of transfer RNA for leucine, lysine, glutamate, and glutamine.[98] In *TauT* knockout mice, deficiency of taurine causes mitochondrial dysfunction, triggering a greater than 80% decrease in exercise capacity.[99] Several studies in rodents have shown increased exercise capacity after taurine supplementation.[100–102] In addition, taurine is critical for the growth of blastocytes, skeletal muscle, and myocardium; it is necessary for mitochondrial development and is also important for muscular endurance.[103,104]

Antioxidation, anti-inflammation, and other functions

Taurine is a major antioxidant, scavenging reactive oxygen and protecting against oxidative stress to organs including the brain,[97,105,106] where it increasingly appears to have neuroprotective effects.[107,108]

Cellular taurine also has anti-inflammatory actions.[3] One of the proposed mechanisms is taurine inhibition of NF-kappa B, an important transcription factor for the synthesis of pro-inflammatory cytokines.[4] This function may be important in protecting polyunsaturated fatty acids from oxidative stress—helping to maintain and stabilize the structure and function of plasma membranes within the lungs,[109] heart,[110] brain,[111] liver,[112] and spermatozoa.[61,62]

Taurine is also conjugated to bile acids synthesized in the liver, forming bile salts[70] that act as detergents to help emulsify and digest lipids in the body. In addition, taurine facilitates xenobiotic detoxification in the liver by conjugating with several drugs to aid in their excretion.[25] Taurine is also implicated in calcium modulation[113] and homeostasis.[114] Through inhibition of several types of calcium channels, taurine has been shown to decrease calcium influx into cells, effectively serving a cytoprotective role against calcium overload.[115,116]

TAURINE DEFICIENCY

Fetal and neonatal deficiency

Though taurine is considered nonessential in adults because it can be readily synthesized endogenously, it is thought to be conditionally essential in neonatal nutrition.[68] It is the second most abundant free amino acid in human breast milk[117] and the most abundant free amino acid in fetal brain.[118] In cases of long-term parenteral nutrition, neonates can become drastically taurine deficient[119] due to suboptimal CSD activity,[118] leading to retinal dysfunction.[41] Taurine deficiencies can lead to functional and structural brain damage.[118] Moreover, maternal taurine deficiency results in neurologic abnormalities in offspring[120] and may lead to oxidative stress throughout life.[121]

Taurine levels are highest in nerve tissue, retina, heart, pineal gland, and pituitary gland

In 1984, the FDA approved the inclusion of taurine in infant formulas based on research showing that taurine-deficient infants had impaired fat absorption, bile acid secretion, retinal function, and hepatic function.[122] But still under debate are the amount and duration of taurine supplementation required by preterm and low-birth-weight infants, as several

randomized controlled trials failed to show statistically significant effects on growth.[123] Nonetheless, given the alleged detrimental ramifications of a lack of taurine supplementation, as well as the ethical dilemma of performing additional research trials on infants, it is presumed that infant formulas and parenteral nutrition for preterm and low-birth-weight infants will continue to contain taurine.

Age- and disease-related deficiency

Although taurine deficiency is rare in neonates, it is perhaps inevitable with advancing age. Healthy elderly patients ages 61 to 81 have up to a 49% decrease in plasma taurine concentration compared with healthy individuals ages 27 to 57.[124] While reduced renal retention[125] and taurine intake[126] can account for depressed taurine levels, Eppler and Dawson[127] found that tissue and circulating taurine concentrations decrease over the human life span primarily due to an age-dependent depletion of CSD activity in the liver. This effectively impairs the biosynthesis of endogenous taurine from cysteine or methionine or both, forcing a greater reliance on exogenous sources.

Taurine has a variety of neuromodulatory actions

While specific mechanisms have not been fully elucidated, taurine deficiency has also been identified in patients suffering from diseases including but not limited to disorders of bone (osteogenesis imperfecta, osteoporosis),[128] blood (acute myelogenous leukemia),[129] central nervous system (schizophrenia, Friedreich ataxia-spinocerebellar degeneration),[130,131] retina (retinitis pigmentosa),[132] circulatory system and heart (essential hypertension, atherosclerosis),[133] digestion (Gaucher disease),[134] absorption (short-bowel syndrome),[135] cellular proliferation (cancer),[136] and membrane channels (cystic fibrosis),[137] as well as in patients restricted to long-term parenteral nutrition.[138] However, the apparent correlation between taurine deficiency and these conditions does not necessarily mean causation; more study is needed to elucidate a direct connection.

SAFETY AND TOXICITY OF TAURINE SUPPLEMENTATION

An upper safe level of intake for taurine has not been established. To date, several studies have involved heavy taurine supplementation without serious adverse effects. While the largest dosage of taurine tested in humans appears to be 10 g/day for 6 months,[139] a number of studies have used 1 to 6 g/day for periods of 1 week to 1 year.[140] However, the assessment of potential acute, subacute, and chronic adverse effects has not been comprehensive. The Scientific Committee on Food of the European Commission[141] reviewed several toxicologic studies on taurine through 2003 and were unable to expose any carcinogenic or teratogenic potential. Nevertheless, based on the available data from trials in humans and lower animals, Shao and Hathcock[140] suggested an observed safe level of taurine of 3 g/day, a conservatively smaller dose that carries a higher level of confidence. Because there is no "observed adverse effect level" for daily taurine intake,[141] more research must be done to ensure safety of higher amounts of taurine administration and to define a tolerable upper limit of intake.

Interactions with medications

To date, the literature is scarce regarding potential interactions between taurine and commonly used medications.

Although no evidence specifically links taurine with adverse effects when used concurrently with other medications, there may be a link between taurine supplementation and various cytochrome P450 systems responsible for hepatic drug metabolism. Specifically, taurine inhibits cytochrome P450 2E1, a highly conserved xenobiotic-metabolizing P450 responsible for the breakdown of more than 70 substrates, including several commonly used anesthetics, analgesics, antidepressants, antibacterials, and antiepileptics.[142] Of note, taurine may contribute to the attenuation of oxidative stress in the liver in the presence of alcohol[143] and acetaminophen,[144] two substances frequently used and abused. Since the P450 2E1 system catalyzes comparable reactions in rodents and humans,[142] rodents should plausibly serve as a model for further testing of the effects of taurine on various substrates.

POTENTIAL THERAPEUTIC APPLICATIONS

More analysis is needed to fully unlock and understand taurine's potential value in healthcare.

Correction of late-life taurine decline in humans could be beneficial for cognitive performance, energy metabolism, sexual function, and vision, but clinical studies remain to be performed. While a decline in taurine with age may intensify the stress caused by reactive oxygen species, taurine supplementation has been shown to decrease the presence of oxidative markers[127] and to serve a neuroprotective role in rodents.[145,146] Taurine levels increase in the hippocampus after experimentally induced gliosis[147] and are neuroprotective against glutamate excitotoxicity.[148,149] Furthermore, data in Alzheimer disease, Huntington disease, and brain ischemia experimental models show that taurine inhibits neuronal death (apoptosis).[13,150,151] Taurine has even been proposed as a potential preventive treatment for Alzheimer dementia, as it stabilizes protein conformations to prevent their aggregation and subsequent dysfunction.[152] Although improvement in memory and cognitive performance has been linked to taurine supplementation in old mice,[145,153] similar results have not been found in adult mice whose taurine levels are within normal limits. Taurine also has transient anticonvulsant effects in some epileptic humans.[154]

Within the male reproductive organs, the age-related decline in taurine may or may not have implications regarding sexuality, as only very limited rat data are available.[89–91]

In cats, taurine supplementation has been found to prevent the progressive degeneration of retinal photoreceptors seen in retinitis pigmentosa, a genetic disease that causes the loss of vision.[155]

While several energy drink companies have advertised that taurine plays a role in improving cognitive and physical performance, there are few human studies that examine this contention in the absence of confounding factors such as caffeine or glucose.[36,37,95] Taurine supplementation in patients with heart failure has been shown to increase exercise capacity vs placebo.[156] This supports the idea that in cases of taurine deficiency, such as those seen in cardiomyopathy,[157] taurine supplementation could have restorative effects. However, we are not aware of any double-blind, placebo-controlled clinical trial of taurine alone in healthy patients that measured energy parameters as clinical outcomes.

Although it remains possible that acute supraphysiologic taurine levels achieved by supplementation could transiently trigger various psychoneuroendocrine responses in healthy people, clinical research is needed in which taurine is the sole intervention. At present, the most compelling clinical reason to prescribe or recommend taurine supplementation is taurine deficiency.

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