Taurine Activates GABA Receptors

Study Title:

Taurine is a potent activator of extrasynaptic GABA(A) receptors in the thalamus.

Study Abstract:

Taurine is one of the most abundant free amino acids in the brain. In a number of studies, taurine has been reported to activate glycine receptors (Gly-Rs) at moderate concentrations (> or = 100 microM), and to be a weak agonist at GABA(A) receptors (GABA(A)-Rs), which are usually activated at high concentrations (> or = 1 mM). In this study, we show that taurine reduced the excitability of thalamocortical relay neurons and activated both extrasynaptic GABA(A)-Rs and Gly-Rs in neurons in the mouse ventrobasal (VB) thalamus. Low concentrations of taurine (10-100 microM) decreased neuronal input resistance and firing frequency, and elicited a steady outward current under voltage clamp, but had no effects on fast inhibitory synaptic currents. Currents elicited by 50 microM taurine were abolished by gabazine, insensitive to midazolam, and partially blocked by 20 microM Zn2+, consistent with the pharmacological properties of extrasynaptic GABA(A)-Rs (alpha4beta2delta subtype) involved in tonic inhibition in the thalamus. Tonic inhibition was enhanced by an inhibitor of taurine transport, suggesting that taurine can act as an endogenous activator of these receptors. Taurine-evoked currents were absent in relay neurons from GABA(A)-R alpha4 subunit knock-out mice. The amplitude of the taurine current was larger in neurons from adult mice than juvenile mice. Taurine was a more potent agonist at recombinant alpha4beta2delta GABA(A)-Rs than at alpha1beta2gamma2 GABA(A)-Rs. We conclude that physiological concentrations of taurine can inhibit VB neurons via activation of extrasynaptic GABA(A)-Rs and that taurine may function as an endogenous regulator of excitability and network activity in the thalamus.

From press release:

Taurine is one of the most plentiful amino acids in the human brain, but neuroscientists are still puzzled by just how brain cells put it to use. Now, a team of researchers at Weill Cornell Medical College (WCMC) has uncovered a prime site of activity for the molecule, bringing them closer to solving that mystery.

“We have discovered that taurine is a strong activator of what are known as GABA [gamma-aminobutyric acid] receptors in a regulatory area of the brain called the thalamus,” said study senior author Neil L. Harrison, professor of pharmacology and pharmacology in anesthesiology at WCMC. “We

had discovered these receptors two years ago and showed that they interact with the neurotransmitter GABA—the brain's key inhibitory transmitter—that is also involved in brain development. It seems that taurine shares these receptors."

The finding, reported in the January issue of the Journal of Neuroscience , opens the door to better understanding taurine's impact on the brain.

While the amino acid is made naturally by the body, it's also a much-touted ingredient in such so-called "energy drinks" as Red Bull. "Its inclusion in these supplements is a little puzzling, because our research would suggest ... [that] taurine actually would have more of a sedative effect on the brain," Harrison said.

The prime focus of the study, however, was to find a site for the neurological activity of taurine.

"Scientists have long questioned whether taurine might act on an as-yet-undiscovered receptor of its own," said lead researcher Fan Jia, postdoctoral scientist in anesthesiology. "But after some recent work in our lab, we ended up zeroing in on this population of GABA receptors in the thalamus."

The thalamus, located deep in the brain's center, is involved in what neuroscientists call "behavioral state control," helping to regulate transitions between sleep and wakefulness, for example.

"It's like a railway junction, controlling information traffic between the brainstem, the senses and the executive functions in the cortex," Harrison said. The researchers exposed thin slices of thalamic tissue from the brains of mice to concentrations of taurine that were similar to what might be found in the human brain.

"We found that taurine is extraordinarily active on this population of GABA receptors in the thalamus," Harrison said. "It came as a bit of a surprise that the same receptor was used by both taurine and GABA. Nevertheless, finding taurine's receptor has been like discovering the 'missing link' in taurine biology."

Now, Harrison's group is trying to determine what taurine actually does in the brain; Harrison said that because GABA is important for forging new cell-to-cell connections in the developing brain, "and because taurine shares a receptor with GABA, it, too, may play a role in neurological development."

As for energy drinks, "Remarkably little is known about the effects of energy drinks on the brain," Harrison said. "Assuming that some of [taurine] does get absorbed, the taurine ... may actually play a role in the crash people often report after drinking these highly caffeinated beverages."

The work was funded by the U.S. National Institutes of Health. Co-researchers include Minerva Yue, Angelo Keramidas and Peter A. Goldstein of WCMC as well as Dev Chandra and Gregg E. Homanics of the University of Pittsburgh.

Study Information:

Jia F, Yue M, Chandra D, Keramidas A, Goldstein PA, Homanics GE, Harrison NL. Taurine is a potent activator of extrasynaptic GABA(A) receptors in the thalamus. J Neurosci. 2008 January 2;28(1):106-15.

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Full Study:

http://www.jneurosci.org/cgi/content/full/28/1/106
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Byron J. Richards's Comments:

An important finding that supports the use of supplemental taurine to assist relaxation and sleep via the boosting of GABA nerve transmission.