Neurochemical Research, Vol. 18, No. 4, 1993, pp. 437–444

β-Adrenergic-Agonist Stimulated Taurine Release from Astroglial Cells is Modulated by Extracellular [K^+] and Osmolarity*

David L. Martin[1,2] and William Shain[1,2]

(Accepted August 6, 1992)

Astroglial cells are known to release taurine in response to stimulation by a variety of stimuli including β-adrenergic receptor agonists such as isoproterenol (IPR). The effects of changing osmolarity and extracellular [K^+] on IPR-stimulated taurine release were studied with LRM55 cells, a continuous astroglial cell line. IPR-stimulated taurine release decreased almost 8% for each 1% increase in osmolarity, indicating that IPR-stimulated release is highly regulated by the osmolarity of the medium. IPR-stimulated taurine release was greatly enhanced when external [K^+] was increased isosmotically by substituting KCl for NaCl but was strongly suppressed when external [K^+] was increased hyperosmotically by adding KCl to the medium. Both IPR-stimulated and K^+-stimulated taurine release depended on external [Cl^-]; IPR-stimulated release declined approximately in parallel to K^+-stimulated release as [Cl^-] in the medium was reduced. The high sensitivity of IPR-stimulated release to factors that change cell volume (osmolarity, external [K^+], external [Cl^-]) is consistent with the idea that IPR, elevated [K^+], and reduced osmolarity all elicit taurine release via a single tension-controlled mechanism.

KEY WORDS: Astrocyte; β-adrenergic agonist; isoproterenol; K^+-stimulated release; taurine; taurine release.

INTRODUCTION

Neuroactive amino acids, such as taurine and γ-aminobutyric acid, play key roles in nervous system function. Claude Baxter began to study these compounds not long after their presence in brain was discovered, and he and his colleagues have made fundamental contributions to the development of our understanding of the functions of these compounds in the central nervous system. Although GABA is now a well established neurotransmitter, taurine's function is far less certain. One possibility is that taurine plays on osmoregulatory role in brain, a problem to which Claude Baxter has made unique contributions (e.g. ref 1). The relationship of taurine to osmoregulation and the sensitivity of taurine release to cell-volume changes are now important foci of current work on brain taurine.

Astrocytes release taurine in response to a variety of stimuli including neurotransmitters and receptor agonists (such as β-adrenergic agonists), elevated $[K^+]_o$, and reduced osmolarity (2-11). An important issue is the relationship among the release processes that are activated by the various stimuli. Adenosine and β-adrenergic agonists such as isoproterenol (IPR) each stimulate release through a cAMP-mediated mechanism that is independent of internal and external Ca^{2+} (3,4,12-14). Current evidence indicates that K^+-stimulated taurine release is a consequence of K^+-induced cellular swelling and, therefore, occurs by the same process as release

[1] Wadsworth Center for Laboratories and Research, New York State Department of Health, Albany, NY 12201-0509
[2] Department of Environmental Health and Toxicology, School of Public Health, State University of New York at Albany.
* Special issue dedicated to Dr. Claude Baxter.

0364-3190/93/0400-0437$07.00/0

induced by the application of low-osmolarity medium (8,11). Aside from reports of Ca^{2+} involvement in K^+-stimulated release (6), there is no evidence that second messengers are involved in K^+- or osmotically-stimulated release.

We have proposed that release is controlled by a tension-mediated mechanism that may operate through the membrane or submembrane cytoskeletal structures (8,15). According to the tension hypothesis, any factor that increases tension on a "tension sensor" will increase release while any factor that reduces tension will reduce release. Thus, reduced osmolarity and isosmotically elevated [K^+] each cause cellular swelling, increase tension, and induce release. Elevated osmotic pressure, which would be expected to shrink cells and reduce tension, suppresses baseline release and K^+-stimulated release (8). Agents such as β-adrenergic agonists and adenosine stimulate the phosphorylation of cytoskeletal and membrane proteins (16-18) which may lead to an increase in tension and thereby induce release or, alternatively, may change the threshold of the tension mechanism, and thereby stimulate release without actually changing tension. In either case, this theory predicts that IPR-stimulated release should be strongly affected by elevated external [K^+] and the osmolarity of the medium, as these factors will change the tension on the system and thus change sensitivity to agents such as IPR. We have investigated these possibilities in the work presented here.

EXPERIMENTAL PROCEDURE

LRM55 glial cells are derived from a single cell clone obtained from a rat spinal tumor and possess a number of glial cell properties such as carbonic anhydrase and Cl^- transport (19,20). Cells are routinely grown in mass cultures in 100 mm dishes in modified Ham's F12 medium supplemented with 5% fetal bovine serum. To prepare for release experiments LRM55 cells were subcultured onto plastic strips (Cell Support film, Bellco Glass) and allowed to grow to confluence.

Release experiments were conducted with a modified Hepes-buffered Hanks' saline with ascorbate (HHA) that contained 128.7 mM NaCl, 4.09 mM KCl, 1.125 mM $CaCl_2$, 0.49 mM $MgCl_2$, 0.21 mM $MgSO_4$, 0.93 mM Na_2HPO_4, 0.45 mM KH_2PO_4, 11 mM glucose, 0.5 mM sodium ascorbate, and 10 mM Hepes and was adjusted to pH 7.3 with NaOH. Ascorbate was included to prevent the oxidation of isoproterenol when it was used. Modified media containing elevated [K^+] were prepared by substituting KCl for an equimolar amount of NaCl (isosmotic replacement) or by dissolving solid KCl in HHA (hyperosmotic addition). Low-osmolarity media were prepared by adding deionized water to HHA, if the change was less than 10%; otherwise the media were prepared by omitting an appropriate amount of NaCl. The osmolarity of the media was checked routinely with a Wescor vapor-pressure osmometer. The calculated osmolarity was 300 mosM and the measured osmolarity was about 272 mosM.

The release of labelled amino acids was measured as previously described (2,4). Briefly, the cells were incubated for about one hour with labelled amino acid (generally at a concentration of 10 μCi/ml in HHA, ca. 300 nM) to load the cells with label. The cell support film with adherent cells was then transferred to the superfusion chamber and superfused with HHA at 0.5 ml/min. Drugs or modified medium were applied to the cells at appropriate times with a system of valves controlled by a computer. In some experiments, the superfusate was collected at 1-min intervals with a fraction collector, and the radioactivity in each sample determined by liquid scintillation counting. In other experiments, the radioactivity in the superfusate was measured for 1-min intervals with an in-line, flow-through scintillation counter (Radiomatic Instruments).

For release profiles, the amount of taurine release was expressed as fractional release, i.e. the amount of [^{3}H]taurine in each sample was expressed as a percentage of the [^{3}H]taurine remaining in the cells at that time. This was accomplished by a series of calculations starting with the amount of labeled taurine remaining in the cells. To measure the total release in response to a stimulus we summed the radioactivity in the samples comprising the peak (e.g. in response to an application of IPR) and then subtracted the estimated baseline release.

[1,2-^{3}H]Taurine (35 Ci/mmol) was from Amersham and L-[U-^{14}C]lysine (300 mCi/mmol) was from Research Products International (Mount Prospect, Il). (-)Isoproterenol was from Sigma. Solvents were HPLC grade. Other compounds were analytical grade or the highest purity available.

RESULTS

The tension-controlled release hypothesis predicts that any factor that increases tension on the release mechanism will stimulate release and any factor that reduces tension will reduce release. Since the tension-sensing mechanism is the common point of interaction of all of the stimuli with the release mechansim, each of the stimuli should affect the response of the system to the other stimuli. Thus, elevated osmotic pressure should relax the system and inhibit the effect of IPR, because the IPR-mediated mechanism would have to "take up the slack" of the relaxed system before it could achieve the threshold tension required to elicit release. Similarly, reduced osmotic pressure and isosmotically-elevated [K^+] (which causes cell swelling) should enhance IPR-stimulated release, because the IPR-mediated mechanism is adding tension to an already activated system. Exactly these effects were observed when the osmolarity of the medium was altered. The data in Figure 1 demonstrate that IPR-stimulated taurine release is greatly enhanced when IPR is added in the presence of hyposmotic medium. This effect was clearly evident even when the osmolarity was reduced by only 2.5% (−7 mosM; Figure 1A). IPR-stimulated release was suppressed when the osmolarity was increased by raising the concentration

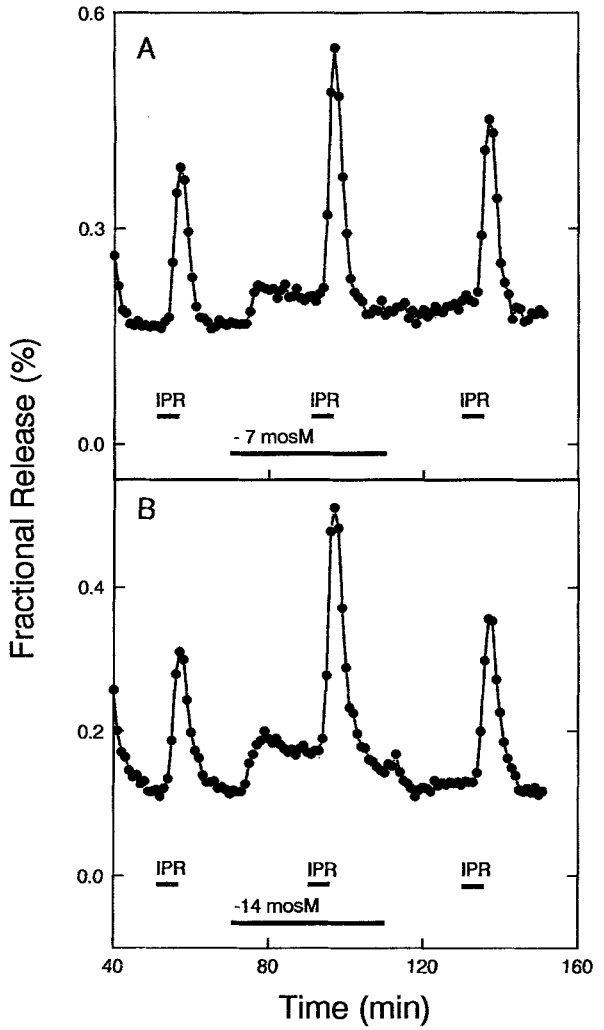

Fig. 1. IPR-stimulated taurine release is greater when the osmolarity of the medium is reduced. IPR (0.1 μM) was applied for three-minute intervals as indicated by the short bars. Medium having reduced osmolarity was applied as indicated by the long bar. The osmolarity was reduced by 2.5% (panel **A**) and 5% (panel **B**). Notice that reduced osmolarity significantly increases the baseline rate of release. To measure release, LRM55 cells were preloaded with [^{3}H]taurine and superfused as described under Experimental Procedures.

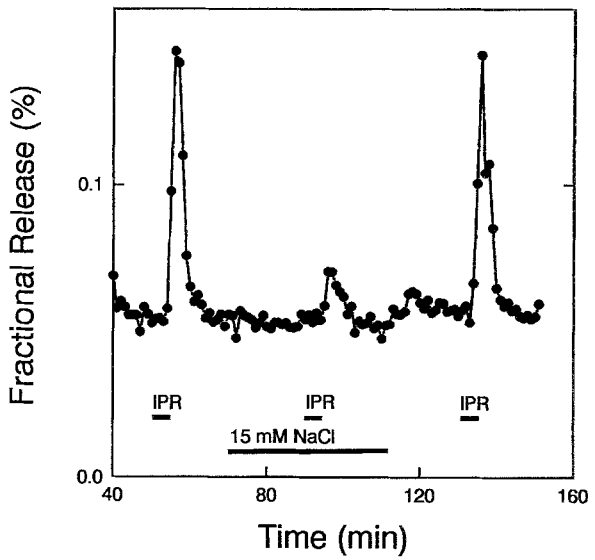

Fig. 2. IPR-stimulated taurine release is suppressed when the NaCl content of the incubation medium is elevated. IPR (0.1 μM) was applied for three-minute intervals as indicated by the short bars. Medium containing 15-mM added NaCl was applied as indicated by the long bar.

of NaCl in the medium by a small amount (Figure 2). This effect is not attributable to changing [Na^+] as we have previously shown that IPR-stimulated release is also suppressed by adding sucrose or $MgCl_2$ (13). To examine the sensitivity of IPR-stimulated taurine release to osmolarity we plotted IPR-stimulated taurine release as a function of osmolarity (Figure 3). Each measurement used in Figure 3 was obtained in an experiment similar to those in Figure 1. Linear regression analysis of the data in Figure 3 showed that IPR-stimulated taurine release is reduced by 2.9% per 1 mosM increase in osmolarity. This corresponds to a 7.6% reduction in release for every 1% increase in osmolarity. Thus, IPR-stimulated release was highly sensitive to osmolarity.

Changing external [K^+] had corresponding effects on IPR-stimulated taurine release. As expected from the hypothesis, the response to IPR was substantially enhanced when the cells were stimulated with IPR in the presence of isosmotically-elevated [K^+] (Figure 4). The enhanced response was observed at external [K^+] as low as 10 mM and was very large when [K^+] was raised to 50 mM. Also, as expected hyperosmotically-elevated KCl inhibited IPR-stimulated taurine release (Figure 5). Inhibition was clearly detectable at 10-mM KCl and was complete at 50-mM KCl. This inhibition is attributable to the osmotic effect of the added KCl, as similar effects have been observed with sucrose, NaCl, and $MgCl_2$ (see above and ref 13). We observed a large increase in release when the hyperosmotic KCl medium was removed (Figure 5). We attribute this effect to the accumulation of KCl and accompanying increase in the osmolarity of the cytoplasm that occurs when LRM55 cells are incubated in high KCl medium (19). Thus when cells are returned to normal medium there is an osmotic pressure difference across the membrane that leads to swelling and taurine release. Depolarization per se did not directly determine the effect of elevated [K^+] on IPR-stimulated

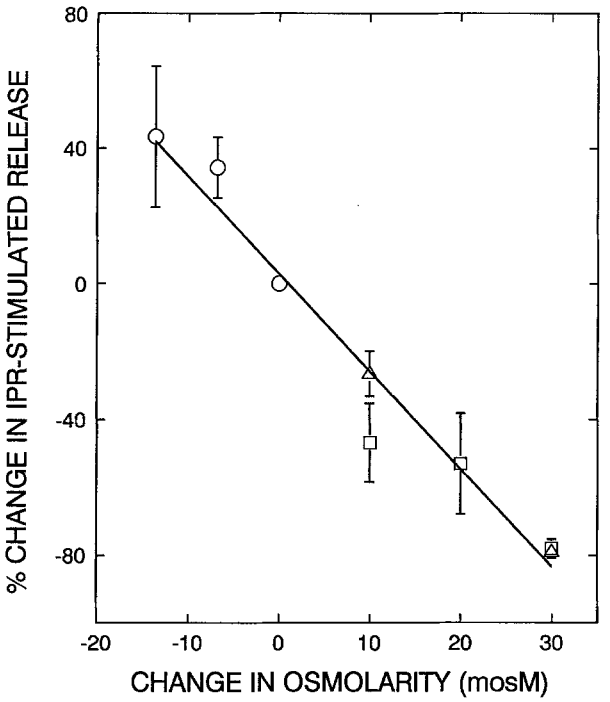

Fig. 3. Aggregate data showing the effect of osmolarity on IPR-stimulated release of [^{3}H]taurine from LRM55 cells. Osmolarity was increased by adding sucrose (□) or NaCl (△) and was reduced (○) as described under Experimental Procedures. The line was fitted by linear regression analysis. The slope of the line (−2.9% change in release/mosM change in osmolarity) gives the sensitivity of IPR-stimulated taurine release to the osmolarity of the medium.

release, as the direction of the effect depends on how [K^+] is raised (isosmotically or hyperosmotically), and because the effect of [K^+] is observed at concentrations that do not appreciably depolarize LRM55 cells (8).

Previous work had demonstrated that K^+-stimulated taurine release is virutally eliminated when Donnan-effect-induced swelling is prevented by reducing [Cl^-] in the high-K^+ medium in order to maintain the [K^+]·[Cl^-] equal to that in control conditions (8,11). The induction of taurine release by Donnan-effect-induced swelling suggested that the converse might be true. That is combinations of [K^+] and [Cl^-] that would be expected to cause a Donnan-induced reduction in cell volume would be expected to reduce release. The simplest way to accomplish such changes is to hold [K^+] constant and reduce [Cl^-]. In keeping with this expectation, IPR-stimulated taurine release was reduced when external [Cl^-] was reduced (Figure 6). This effect was observed whether Cl^- was replaced with gluconate or isethionate. Similar experiments were conducted with K^+-stimulated release (Figure 7). In these experiments, low-[Cl^-] normal-[K^+] medium was applied for 20 minutes to allow

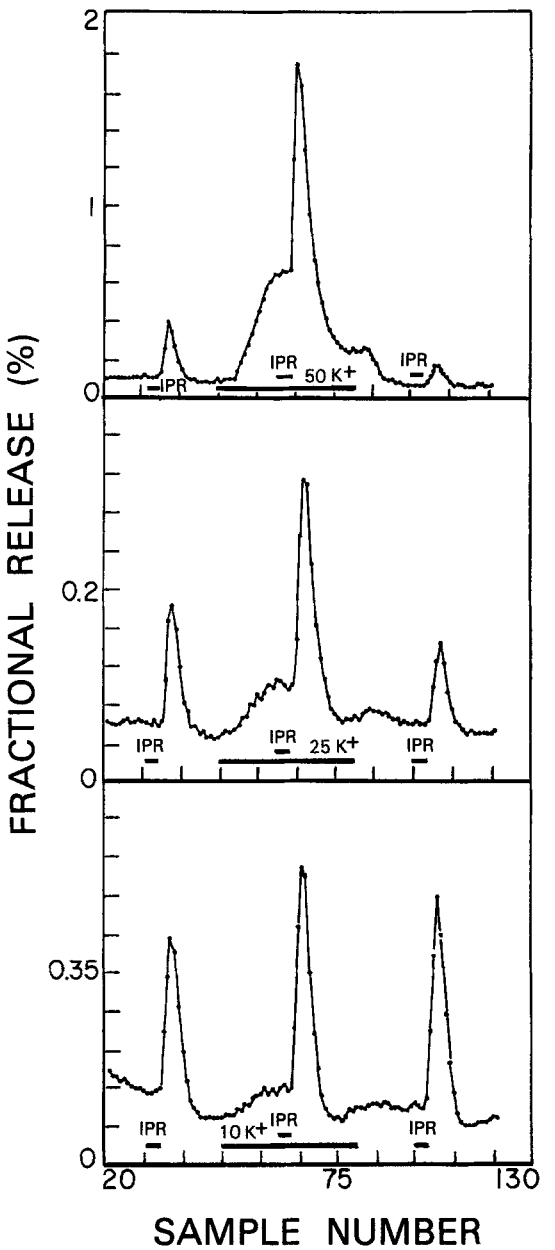

Fig. 4. IPR-stimulated taurine release is enhanced when extracellular [K^+] is increased isosmotically by replacing NaCl with KCl. [K^+] in the perfusion medium was increased to 50 (panel **A**), 25 (panel **B**), or 10 mM (panel **C**), as described under Experimental Procedures. IPR (0.1 μM) was applied for 3 minutes as indicated by the short bars. High-K^+ medium was applied as indicated by the long bars.

the cells to equilibrate osmotically. High-[K^+] medium was then applied (at the same reduced [Cl^-]) to elicit release. Thus, the magnitude of the Donnan-effect was expected to be smaller, and, as expected, K^+-stimulated taurine release was also reduced. It is notable that the

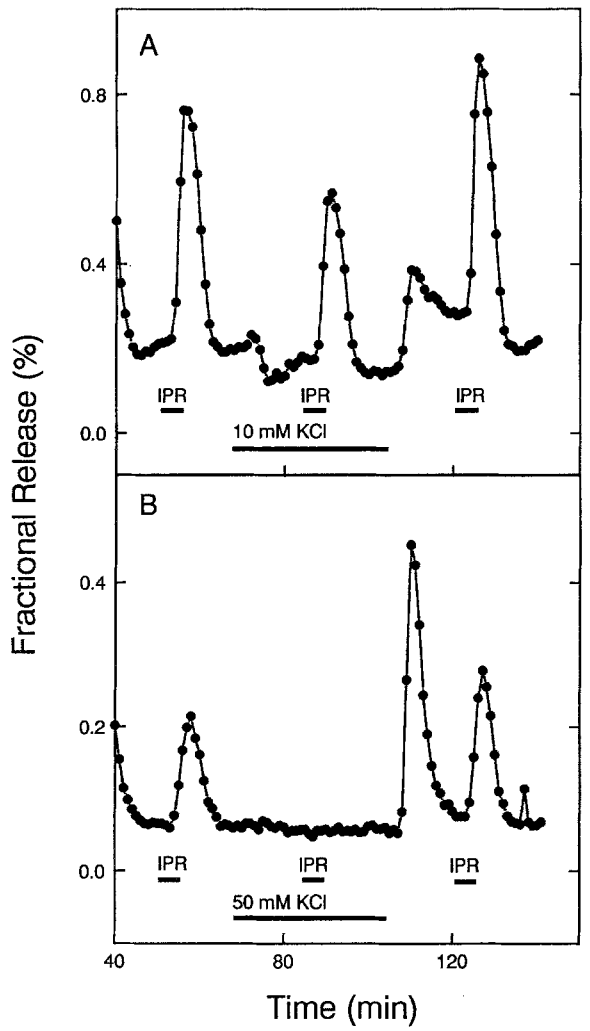

Fig. 5. Hyperosmotically-elevated KCl suppresses IPR-stimulated taurine release from LRM55 cells. The concentration of KCl was increased to 10 (panel **A**) or 50 mM (panel **B**) by dissolving additional KCl in normal medium. IPR (0.1 μM) was applied for 3 minutes as indicated by the short bars. High-KCl medium was applied as indicated by the long bars.

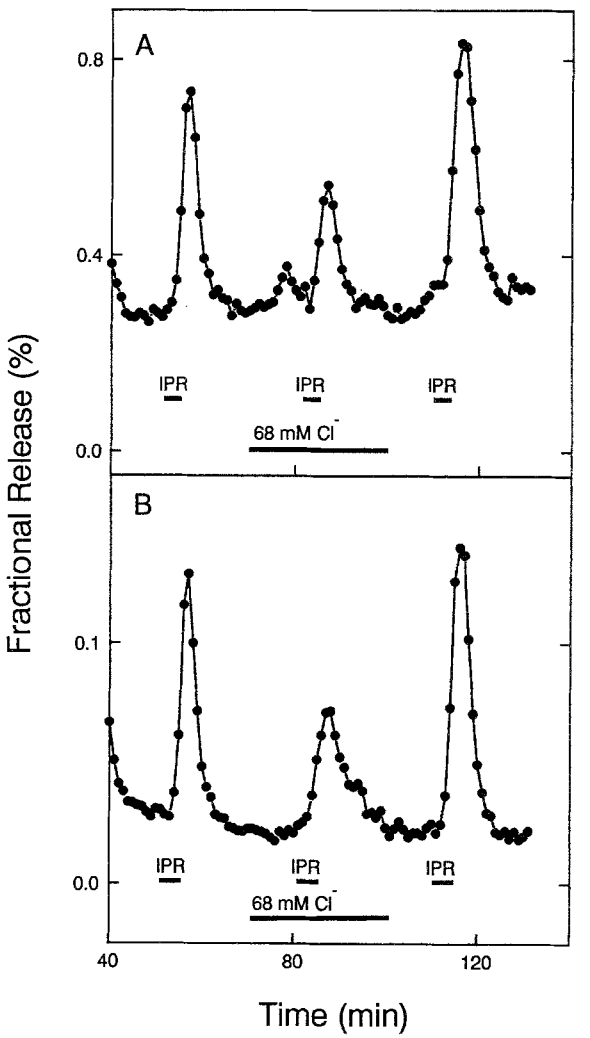

Fig. 6. IPR-stimulated taurine release is Cl^- dependent. Reduced [Cl^-] medium (68 mM) was prepared by replacing NaCl with equimolar amounts of sodium gluconate (panel **A**) or sodium isethionate (panel **B**). IPR (0.1 μM) was applied for three minutes, as indicated by the short bars. Low-Cl^- medium was applied as indicated by the long bar.

[Cl^-]-dependencies of IPR- and K^+-stimulated taurine releases are very similar (Figure 8).

DISCUSSION

Previous studies have demonstrated that reducing the osmolarity of the medium stimulates taurine release while increasing osmolarity suppresses baseline release (8-10,13,21). Similarly, K^+-stimulated taurine release is enhanced by reducing the osmolarity of the medium and is suppressed by increasing osmolarity (8). Furthermore, K^+-stimulated release is only observed under conditions that induce swelling. Thus, astroglial cells release taurine when external [K^+] is raised isosmotically by substituting KCl for NaCl but do not release taurine when external [K^+] is raised hyperosmotically by adding KCl to the medium. Isosmotically-elevated [K^+] also does not stimulate release when Donnan-effect-induced swelling is prevented by lowering extracellular [Cl^-] to maintain the [K^+]·[Cl^-] equal to that of the control medium (11,13,22). The results presented here demonstrate that IPR-stimulated taurine release is highly sensitive to osmolarity and extracellular [K^+] and [Cl^-]. All of these findings are in keeping with idea that taurine release

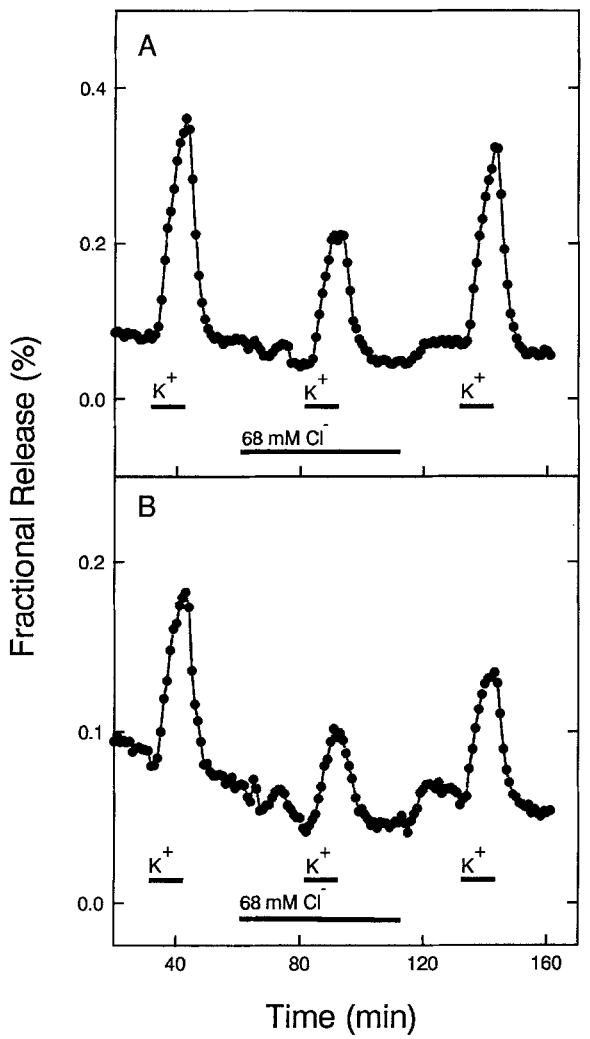

Fig. 7. K^+-stimulated taurine release is Cl^- dependent. Release elicited with 50-mM (panel **A**) or 20 mM (panel **B**) isomotically-elevated [K^+]. Reduced Cl^- medium was prepared by isosmotically replacing NaCl with sodium gluconate. High-K^+ medium was applied for 10 minute as indicated by short bars. Low Cl^- medium was applied (long bar) for 20 minute prior to the second application of high-K^+ medium.

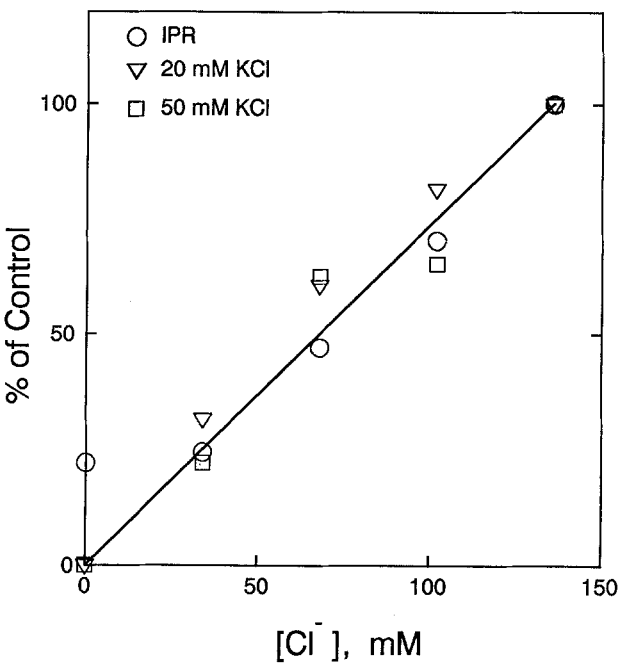

Fig. 8. Cl^- dependence of IPR-stimulated (0.1 μM, ○), and K^+-stimulated (20 mM, ▽; 50 mM, □) [^{3}H]taurine release from LRM55 cells. Each point is the average of 2–5 measurements. Cl^- was replaced by gluconate or isethionate (see Experimental Procedures).

from astroglial cells is mediated by a single, tension-controlled mechanism (8,15).

As predicted by this mechanism IPR-stimulated taurine release was suppressed when the osmolarity of the medium was suppressed by adding sucrose, KCl, or NaCl to the medium (above and refs 13,22). Elevating the osmolarity of the medium would be expected to reduce cell volume and tension on the taurine release mechanism, thus requiring the IPR-mediated mechanism to exert a greater effect on the release mechanism to achieve the same amount of release as observed under control conditions. Reduced osmolarity and isosmotically-elevated [K^+] also affected IPR-stimulated taurine release as predicted by the tension-controlled release hypothesis. Each of these treatments causes astroglia to swell thereby increasing tension on the release mechanism and rendering the system more sensitive to the IPR-stimulated mechanism. The Cl^--dependence of both K^+- and IPR-stimulated release responses are also consistent with the tension controlled release mechanism. Reducing extracellular [Cl^-] while extracellular [K^+] is held constant will lead to Donnan-effect-induced ion shifts and a loss of water from the cell. Thus, as extracellular [Cl^-] is reduced one would expect a reduction of cell volume, a reduction of tension on the membrane, and reduced taurine release whether in response to [K^+] or IPR.

The actual membrane mechanism responsible for taurine release has not been identified. We (15,23) and others (24) have concluded that taurine is not released by reversal of the taurine transport system. It can be argued that stretching the membrane itself cannot activate release because the surface of the astrocyte is highly convoluted, and the initial volume change of the cell involves a deconvolution of the surface with little or no increase in membrane surface area and, therefore, little

or no increase in tension within the membrane (25). However, deconvolution will increase tension between integral membrane proteins and any fixed submembrane cytoskeletal elements to which membrane proteins are attached. Thus, coupling between the cytoskeleton and the membrane proteins may be an essential part of tension-mediated release.

Both β-agonist-stimulated release and K^+-stimulated taurine release may be normal physiological responses of astrocytes in vivo. Extracellular [K^+] is highly dynamic in vivo, rising and falling in concert with neuronal activity (26–28). Extracellular [K^+] can reach 10–12 mM during episodes of extreme neuronal activity such as seizures, and these changes are accompanied by a decrease in the extracellular space, indicating that cells are swelling (29). Astrocytes are thought to be important contributors to the swelling, which has been attributed to osmotic imbalances across the membrane resulting from spatial buffering and changes in HCO_3^-/Cl^- balance (29,30). Cultured astrocytes release taurine under almost identical conditions. Furthermore, taurine is released from brain tissue under a variety of conditions that are accompanied by glial swelling (31–35). β-Agonist stimulated release may be a normal physiological response because astrocytes in vivo possess β-adrenergic receptors (16,36) and satellite glia in the superior cervical ganglion respond to stimulation with IPR by synthesizing cAMP (37,38). We have observed IPR-stimulated taurine release from superfused superior cervical ganglia, and cultured astrocytes release taurine under virtually identical conditions.

The physiologic function of taurine release is unclear at present. It has been suggested that taurine may serve as a regulatory osmolyte to reduce cell-volume changes in brain (34,35,39), but this has been questioned because the amount of taurine actually released appears to be small in comparison with the osmolarity of the extracellular and intracellular compartments and with the amount of ion movement that occurs as a result of neuronal activity (22). An alternative possibility is that taurine acts as a messenger or indirect osmoregulatory factor. Our observation that some but not all neurotransmitters stimulate taurine release suggests that astrocytes can respond to the activity of specific groups of neurons via chemical transmission (5). Our data demonstrate that IPR-stimulated taurine release is modulated by physiologically relevant changes in [K^+] ($\leq$ 10 mM) and is highly sensitive to osmolarity (ca. 8% change in release for each 1% change in osmolarity). The ability of astrocytes to respond to a variety of stimuli and the interactions among the stimuli in eliciting taurine release suggest that taurine release is part of an integrated astrocytic response to neuronal activity.

ACKNOWLEDGEMENTS

Supported by contract N0001487J1179 from the U.S. Naval Medical Research and Development Command (to DLM) and grant NS21219 from the USPHS/DHHS (to WS).

REFERENCES

1. Baxter, C. F., Baldwin, R. A., and Oh, C. C. 1990. Acclimation to hyper- and hypo-osmotic changes: The anomalous behavior of taurine in the nervous system and in the blood of vertebrates. Pages 329–336, *in* (H. Pasantes-Morales, D. L. Martin, W. Shain and R. Martin del Rio, eds.) Functional Neurochemistry, Physiology and Cardiology Wiley-Liss, New York.
2. Shain, W. G. and Martin, D. L. 1984. Activation of β-adrenergic receptors stimulates taurine release from glia cells. Cell. Mol. Neurobiol. 4:191–196.
3. Madelian, V., Martin, D. L., Lepore, R., Perrone, M., and Shain, W. 1985. Beta-receptor-stimulated and cyclic adenosine 3′,5′-monophosphate-mediated taurine release from LRM55 glial cells. J. Neurosci. 5:3154–3160.
4. Shain, W., Madelian, V., Martin, D. L., Kimelberg, H., Perrone, M., and Lepore, R. 1986. Activation of beta-adrenergic receptors stimulates release of an inhibitory transmitter from astrocytes. J. Neurochem. 46:1298–1303.
5. Martin, D. L., Shain, W., and Madelian, V. 1988. Receptor-mediated release of taurine from glial cells and signalling between neurons and glia. Pages 183–195, *in* H. K. Kimelberg, (ed.) Glial Cell Receptors Raven Press, New York.
6. Philibert, R. A., Rogers, K. L., Allen, A. J., and Dutton, G. R. 1988. Dose-dependent, K^+-stimulated efflux of endogenous taurine from primary astrocyte cultures is Ca^{2+}-dependent. J. Neurochem. 51:122–126.
7. Tigges, G. A., Philibert, R. A., and Dutton, G. R. 1990. K^+- and temperature-evoked taurine efflux from hypothalamic astrocytes. Neurosci. Lett. 119:23–26.
8. Martin, D. L., Madelian, V., Seligmann, B., and Shain, W. 1990. The role of osmotic pressure and membrane potential in K^+-stimulated taurine release from cultured astrocytes and LRM55 cells. J. Neurosci. 10:571–577.
9. Pasantes-Morales, H. and Schousboe, A. 1988. Volume regulation in astrocytes: A role for taurine as an osmoeffector. J. Neurosci. Res. 20:505–509.
10. Pasantes-Morales, H., Moran, J., and Schousboe, A. 1990. Volume-sensitive release of taurine from cultured astrocytes: Properties and mechanism. Glia 3:427–432.
11. Pasantes-Morales, H., Moran, J., and Schousboe, A. 1990. Taurine release associated to cell swelling in the nervous system. Pages 369–376, *in* H. Pasantes-Morales, D. L. Martin, W. Shain and R. Martin del Rio, (eds.) Taurine: Functional Neurochemistry, Physiology and Cardiology, Wiley-Liss, New York.
12. Madelian, V., Silliman, S., and Shain, W. 1988. Adenosine stimulates cAMP-mediated taurine release from LRM55 glial cells. J. Neurosci. Res. 20:176–181.
13. Martin, D. L., Madelian, V., and Shain, W. 1989. Spontaneous- and beta-adrenergic receptor-mediated taurine release from astroglial cells do not require extracellular calcium. J. Neurosci. Res. 23:191–197.
14. Shain, W., Connor, J. N., Madelian, V., and Martin, D. L. 1989.

Spontaneous and beta-adrenergic receptor-mediated taurine release from astroglial cells are independent of manipulations of intracellular calcium. J. Neurosci. 9:2306–2312.
15. Martin, D. L. 1992. Synthesis and release of neuroactive substances by glial cells. Glia 5:81–94.
16. McCarthy, K. D., Salm, A., and Lerea, L. S. 1988. Astroglial receptors and their regulation of intermediate filament protein phosphorylation. Pages 1–22, *in* H. K. Kimelberg, (ed.) Glial Cell Receptors, Raven Press, New York.
17. Browning, E. T. 1988. Hormone and second messenger regulated protein phosphorylation by cultured rat astrocytes: Cytoskeletal intermediate filament phosphorylation. Pages 23–34, *in* H. K. Kimelberg, (ed.) Glial cell receptors, Raven Press, New York.
18. Shain, W., Madelian, V., Martin, D. L., Skolnick, M. M., and Thorbergson, H. 1989. β-receptor stimulation of protein phosphorylation in astroglial cells. J. Neurochem. 52:S107.
19. Wolpaw, E. W. and Martin, D. L. 1984. Cl^- transport in a glioma cell line: Evidence for two transport mechanisms. Brain Res. 297:317–327.
20. Wolpaw, E. W. and Martin, D. L. 1986. Sulfate-chloride exchange transport in a glioma cell line. Biochim. Biophys. Acta 855:302–311.
21. Kimelberg, H. K., Goderie, S. K., Higman, S., Pang, S., and Waniewski, R. A. 1990. Swelling-induced release of glutamate, aspartate, and taurine from astrocyte cultures. J. Neurosci. 10:1583–1591.
22. Martin, D. L., Madelian, V., and Shain, W. 1990. Osmotic sensitivity of isoproterenol- and high $[K^+]_o$-stimulated taurine release by cultured astroglia. Pages 349–356, *in* H. Pasantes-Morales, D. L. Martin, W. Shain and R. Martin del Rio, (eds.) Taurine: Functional Neurochemistry, Physiology and Cardiology, Wiley-Liss, Inc., New York.
23. Shain, W., Madelian, V., Waniewski, R., and Martin, D. L. 1990. Characteristics of taurine release from astroglial cells. Pages 299–306, *in* H. Pasantes-Morales, D. L. Martin, W. Shain and R. Martin del Rio, (eds.) Taurine: Functional Neurochemistry, Physiology, and Cardiology, Wiley-Liss, Inc., New York.
24. Sanchez-Olea, R., Moran, J., Schousboe, A., and Pasantes-Morales, H. 1991. Hyposmolarity-activated fluxes of taurine in astrocytes are medited by diffusion. Neurosci. Lett. 130:233–236.
25. Kimelberg, H. K. and O'Connor, E. 1988. Swelling of astrocytes causes membrane potential depolarization. Glia 1:219–224.
26. Moody, W. J., Futamachi, K. J., and Prince, D. J. 1974. Extracellular potassium activity during epileptogenesis. Exp. Neurol. 42:248–263.
27. Sypert, G. W. and Ward, Jr., A. A. 1974. Changes in extracellular potassium activity during neocortical propagated seizures. Exp. Neurol. 45:19–41.
28. Heinemann, U. and Lux, D. 1977. Ceiling of stimulus induced rises in extracellular potassium concentration in the cerebral cortex of cat. Brain Res. 120:231–249.
29. Dietzel, I., Heinemann, U., Hofmeier, G., and Lux, H. D. 1980. Transient changes in the size of the extracellular space in the sensorimotor cortex of cats in relation to stimulus-induced changes in potassium concentration. Exp. Brain Res. 40:432–439.
30. Kimelberg, H. K. and Ransom, B. 1986. Physiological and pathological aspects of astrocytic swelling. Pages 129–166, *in* S. Federoff and A. Vernadakis, (eds.), Astrocytes, Volume 3, Academic Press, Orlando.
31. Tossman, U., Wieloch, T., and Ungerstedt, U. 1985. γ-Aminobutyric acid and taurine release in the striatum of the rat during hypoglycemic coma, studied by microdialysis. Neurosci. Letts. 62:231–235.
32. Vezzani, A., Ungerstedt, U., French, E. D., and Schwarcz, E. D. 1985. In vivo brain dialysis of amino acids and simultaneous EEG measurements following intrahippocampal quinolinic acid injection: Evidence for a dissociation between neurochemical changes and seizures. J. Neurochem. 45:335–344.
33. Butcher, S. P. and Hamberger, A. 1987. In vivo studies on the extracellular, and veratrine-releasable, pools of endogenous amino acids in the rat striatum: Effects of corticostriatal deafferentation and kainic acid lesion. J. Neurochem. 48:713–721.
34. Solis, J. M., Herranz, A. S., Herreras, O., Lerma, J., and Martin Del Rio, R. 1988. Does taurine act as an osmoregulatory substance in the rat brain? Neurosci. Letts. 91:53–58.
35. Wade, J. V., Olsen, J. P., Samson, F. E., Nelson, S. R., and Pazdernik, T. L. 1988. A possible role for taurine in osmoregulation within the brain. J. Neurochem. 51:740–745.
36. Aoki, C. and Pickel, V. M. 1992. C-Terminal tail of β-adrenergic receptors: Immunocytochemical localization within astrocytes and their relation to catecholaminergic neurons in N. tractus solitarii and area postrema. Brain Res. 571:35–49.
37. Briggs, C. A., Whiting, G. J., Ariano, M. A., and McAfee, D. A. 1982. Cyclic nucleotide metabolism in the sympathetic ganglion. Cell. Mol. Neurobiol. 2:129–141.
38. Ariano, M. A., Briggs, C. A., and McAfee, D. A. 1982. Cellular localization of cyclic nucleotide changes in rat superior cervical ganglion. Cell. Mol. Neurobiol. 2:143–156.
39. Pasantes-Morales, H. and Schousboe, A. 1988. Volume regulation in astrocytes: A role for taurine as an osmoeffector. J. Neurosci. Res. 20:505–509.