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THE EFFECTS OF TAURINE ON Ca^{2+} UPTAKE BY THE SARCOPLASMIC RETICULUM AND Ca^{2+} SENSITIVITY OF CHEMICALLY SKINNED RAT HEART

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SUMMARY

1. Caffeine (10 mM) induced a transient contracture in saponin-treated cardiac trabeculae as a result of Ca^{2+} release from the sarcoplasmic reticulum (SR). Regular cycles of uptake and release were repeated to stabilize responses. The SR accumulated Ca^{2+} during the period prior to the addition of caffeine and this was reflected in the size of the caffeine contracture. Increasing the time for Ca^{2+} loading between successive caffeine exposures resulted in an increase in the amplitude of the contracture. Similarly, the size of the contracture was a function of the calcium ion concentration ($[Ca^{2+}]$) in the preceding loading period.

2. Taurine (10 μM–40 mM), when included in both loading and caffeine solutions, markedly potentiated the caffeine-induced contracture. The effect occurs even if taurine was included only in the loading solutions. The potentiating effect was ascribed to a direct action of taurine on the SR, since taurine did not significantly change the $[Ca^{2+}]$ in the loading solutions.

3. The maximal effect of taurine was produced at approximately 5 mM; higher taurine concentrations caused a lesser potentiation of the caffeine contracture. If the solutions were balanced with respect to osmolarity the effect of taurine did not decline at high concentrations.

4. If the $[Ca^{2+}]$ in the loading solutions was increased to produce a caffeine-induced contracture that peaked close to maximal Ca^{2+}-activated force, taurine caused a fall in the size of contracture and a more variable response. This result could be explained by an increase in the spontaneous release of Ca^{2+} from the SR in the presence of taurine.

5. In Triton-skinned trabeculae, taurine (1 mM–40 mM) increased the Ca^{2+} sensitivity of the contractile proteins in a dose-dependent manner but had little effect on maximum Ca^{2+}-activated force. The increase in Ca^{2+} sensitivity was small: in a typical experiment 30 mM-taurine reduced the $[Ca^{2+}]$ necessary for half-maximal activation from 3·02 to 2·56 μM, with no significant change in the shape of the relationship.

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INTRODUCTION

Taurine (2-aminoethansulphonic acid) is the most common free amino acid found in mammalian cardiac muscle. The intracellular concentration of taurine is species dependent, commonly about 10–20 mM (Jacobson & Smith, 1968), but in rat may be as high as 40 mM. These intracellular levels are maintained despite a much lower plasma concentration of about 60 μM (Perry & Hansen, 1969). Higher than normal taurine levels have been found in heart tissue from patients with congestive heart failure and in experimental models of cardiac hypertrophy (Huxtable & Bressler, 1974), while the taurine content of the heart decreases during ischaemia (Crass & Lombardi, 1977). The role of taurine in cellular function is unknown, but it has been suggested that taurine may modulate Ca^{2+} transport in cardiac muscle (Schaffer, Chovan, Kramer & Kulakowski, 1981).

Many previous studies on the action of taurine on cardiac muscle have been carried out by superfusing intact preparations with taurine at concentrations ranging from 1 to 50 mM. These studies have shown that in the presence of normal extracellular [Ca^{2+}] the addition of taurine will (i) increase Ca^{2+} binding to sarcolemma (Chovan, Kulakowski, Sheakowski & Schaffer, 1980) and (ii) increase Ca^{2+} content and twitch tension (Franconi, Martini, Stendardi, Matucci, Zilletti & Giotto, 1982). If extracellular [Ca^{2+}] is raised to values above normal, extracellular taurine has the opposite effects on these variables. Interpretation of these results is difficult since the concentrations of taurine used are unphysiologically high (see above), and it is unclear whether taurine's primary action is on the external surface of the sarcolemma or as a result of increased intracellular taurine levels.

Reports of the effect of taurine on isolated sarcoplasmic reticulum (SR) have been contradictory. Taurine has been found to increase the Ca^{2+} content of skeletal SR (Huxtable & Bressler, 1973). Other studies found no effect of taurine on cardiac SR Ca^{2+} content and uptake (Whelty & Whelty, 1981), but instead taurine appeared to increase Ca^{2+} binding to sarcolemmal and mitochondrial fractions of cardiac muscle (Entman, Bornet & Bressler, 1977; Chubb & Huxtable, 1978; Whelty, 1981; Khatter, Soni, Hoeschen, Alto & Dhalla, 1981).

This study has investigated the influence of taurine on cardiac sarcoplasmic reticulum and contractile proteins, using chemically skinned rat ventricular trabeculae. The experiments show that taurine causes a small increase in myofilament Ca^{2+} sensitivity but a marked increase in the ability of the SR to accumulate calcium. This may explain some of the apparently disparate effects of taurine previously reported in intact cardiac muscle. Preliminary results have been reported to the Physiological Society (Miller, Smith & Steele, 1989).

METHODS

Sprague-Dawley rats weighing 200–250 g were killed by a blow to the head and cervical dislocation. Their hearts were rapidly removed and bathed in Tyrode solution. Free-running trabeculae 50–100 μm in diameter and 2–3 mm in length were dissected from the right ventricle. Experiments were performed at room temperature (22–23 °C).

Apparatus

Full details of the measurement of sarcomere length and isometric tension and the solution exchange system have been published recently (Harrison, Lamont & Miller, 1988). In summary, a trabecula was attached between a force transducer (Akers AE875) and a fixed end by means of snares. This arrangement was used to hold the trabecula in one of a series of chambers

TABLE 1. Composition of solutions (in mM except where stated)

Solution	K^+	Na^+	Mg^{2+}	Total Ca^{2+}	$[Ca^{2+}]$ (μM)	ATP	PCr	EGTA	HDTA	HEPES
A	130	40	7	10·0	57·5	5	15	10·0	—	25
B	130	40	7	0·02	0·001	5	15	10·0	—	25
C	130	40	7	0·02	0·051	5	15	0·2	9·8	25
D	130	40	7	10·1	100·0	5	15	10·0	—	25
E (Tyrode)	5	150	1	2·0	—	—	—	—	—	5

All solutions contain 25 i.u./ml creatine kinase (Sigma) at pH (activity) 7·00. Free $[Mg^{2+}]$ was 2·1 mM in all solutions. Total chloride concentration varies from 110 to 120 mM. Caffeine (10 mM) was added to solution C.

containing 4·6 ml of fluid. The chambers were switched under microcomputer control to effect the solution change. Initially, the preparation was incubated in either saponin or Triton X-100 and then transferred for viewing in a modified Vickers microscope with differential interference contrast optics. This system was arranged to allow the sarcomere pattern of the trabecula to be observed and the sarcomere length to be set at 2–2·2 μm. The mounted preparation was returned to the automated bath-change system for the experiment.

Chemical skinning procedure

The preparation was initially exposed to a 'relaxing' solution including either 50 μg/ml saponin (Sigma Chemicals Ltd) in solution C (Table 1) or 1% (v/v) Triton X-100 in solution B (Table 1) for 30 min. The skinning agent was removed by washing the preparation in solution C. In some experiments measurements were carried out after saponin treatment, then the SR membranes were removed by exposure to Triton X-100 before completing the experiment.

Solution composition

The Ca^{2+} buffer EGTA was used to control $[Ca^{2+}]$. The solutions contained ATP and PCr (phosphocreatine) to support contraction of the skinned muscle. Experiments were carried out at a pH (activity) of 7·00. The complete composition of the solutions used is shown in Table 1. Solutions with a range of $[Ca^{2+}]$ were created by mixing solutions A and B in different proportions when the Triton-treated preparation was studied. Solution D was used to provide the highest $[Ca^{2+}]$. Caffeine-induced contractures were evoked in 0·2 mM-EGTA (solution C); higher concentrations of EGTA would tend to buffer the Ca^{2+} ions released from the SR too strongly and inhibit the caffeine-induced contracture. Calcium chloride (1 M titration standard, BDH) was added to solution C to provide a range of $[Ca^{2+}]$ from 0·051 to 0·470 μM. The equilibrium concentrations of metal ions were calculated using a computer program with the affinity constants for H^+, Ca^{2+} and Mg^{2+} for EGTA taken from Smith & Miller (1984). The affinity constants used for ATP and PCr were those quoted by Fabiato & Fabiato (1979). Corrections for ionic strength, details of pH measurement, allowance for EGTA purity and the principles of the calculations are detailed elsewhere (Smith & Miller, 1984; Harrison *et al.* 1988).

Taurine was added in powder form to the solutions and the pH adjusted to 7·00 with KOH. Sucrose was used as an osmotically active substitute for taurine. The $[Ca^{2+}]$ was checked in solutions using the fluorescent indicator Fura-2 (1 μM) in a fluorometer (Perkin Elmer). In the range of solutions used in the study, taurine (up to 50 mM) did not alter the $[Ca^{2+}]$ significantly. The

curve-fitting procedure for the $[Ca^{2+}]$ *vs.* tension relationship (Fig. 8) is described in Harrison *et al.* 1988.

RESULTS

Protocol for caffeine-induced contractures

The records shown in Fig. 1 were obtained from a saponin-treated trabecula in the presence of 0·2 mM-EGTA. Reproducible caffeine contractures could be obtained by standardizing the $[Ca^{2+}]$ and the time period prior to the addition of caffeine. During this period the SR can actively take up Ca^{2+} from the bathing solution. In the example shown in Fig. 1 the muscle was exposed to a solution with a $[Ca^{2+}]$ subthreshold for tension production (0·12 μM). After 1 min the muscle was switched to a solution with the same $[Ca^{2+}]$ and 10 mM-caffeine. The resultant transient contracture is caused by caffeine-induced release of Ca^{2+} from the SR and the consequent activation of the myofilaments. The contracture is only transient since the Ca^{2+} diffuses out and is buffered by the EGTA within the preparation. Under the conditions chosen here, the peak of the contraction represented approximately 15% of maximal Ca^{2+}-activated force. This sequence of loading and releasing can be continued indefinitely with little variation in the size of the caffeine-induced contractures. As shown in Fig. 1*B* the contractures typically peaked within 0·25 s and relaxed again within 1–2 s. The size and time course of the caffeine-induced contracture was sensitive to the $[Ca^{2+}]$ during the loading period; Fig. 1 shows that raising the $[Ca^{2+}]$ in the loading period to 0·2 μM caused a 240% increase in the size of the tension transient and a prolongation of its time course. As expected, the size to the caffeine-induced contracture is decreased if the period allowed for SR Ca^{2+} loading is reduced. Figure 1 shows that shortening the period from 1 min to 30 s caused 42% reduction in the size of the transient.

The effect of taurine on caffeine-induced contractures

Figure 2 illustrated that taurine (5 mM) will increase the size on the caffeine contracture when it is included in the loading solution. In this experiment the $[Ca^{2+}]$ was maintained at 0·12 μM; this gave a caffeine-induced contracture that was 20% of maximal Ca^{2+}-activated force. Taurine was first added to the caffeine solution. This had no immediate effect on the size of the caffeine contracture. However, taurine was then included in the loading solution which resulted in an enhanced caffeine-induced contracture. The figure shows that the potentiating effect of taurine stabilizes within one or two load-release cycles. The presence of up to 50 mM-taurine did not significantly alter the $[Ca^{2+}]$ in the bathing solutions (see Methods), so it was concluded that taurine was able to increase the ability of the SR to take up Ca^{2+}. Another intracellular site for taurine's action could be the mitochondria (Dolora, Agresti, Giotti & Pasquini, 1973). However, in this study all mitochondrial substrates were absent from the bathing solution. Furthermore, under these loading conditions it is thought that the mitochondria do not contribute to the caffeine-induced responses as they are unaffected by azide or changing the Na^+ concentration of the bathing solution (D. S. Steele, unpublished observations).

The individual contractures shown in Fig. 3 are representative of the steady-state effects of taurine at the concentrations shown. As little as 10 μM-taurine in the

loading solution produced a small but significant potentiation of the contracture. This effect is dose-dependent with the maximum effect seen at about 5 mM. Higher concentrations of taurine caused no further increase in the size of the caffeine-induced contracture and at concentrations above 5 mM the effect apparently decreased. In this preparation 40 mM-taurine caused a small depression of the caffeine-induced contracture relative to the control.

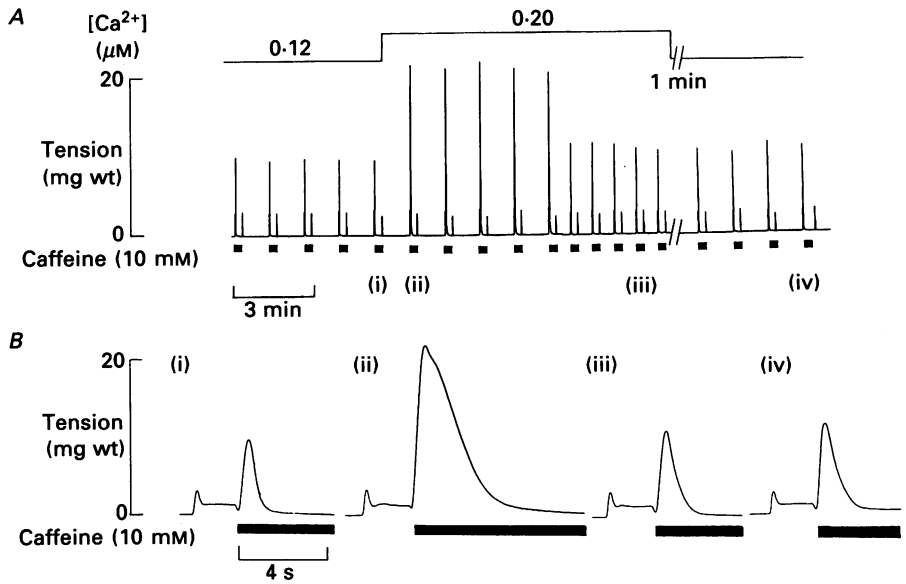

Fig. 1. The effect of $[Ca^{2+}]$ and duration of Ca^{2+} loading on the caffeine-induced contractures from a saponin-treated rat trabecula. Each large upstroke is the caffeine-induced response; each small upstroke is the solution change artifact. Panel *A* shows a continuous record of isometric tension; 10 mM-caffeine was added for 15 s, after a 60 s incubation in caffeine-free solution. At the point indicated the $[Ca^{2+}]$ in both solutions was increased from 0·12 to 0·2 μM (0·2 mM-total EGTA). After several contractures the duration of exposure to the caffeine-free solution was reduced to 30 s. Panel *B* shows example caffeine contractures from the sections indicated in panel *A*, on an expanded time scale. The solution-change artifact precedes the response initiated by caffeine (black bar under trace).

The addition of taurine will increase the osmolarity of the solutions. To assess the purely osmotic effects of taurine, its actions were compared with those of similar concentrations of sucrose in a number of experiments. Studies by Kentish (1984) have shown that up to 50 mM-sucrose has no effect on the Ca^{2+} sensitivity or the maximum force production by the myofilaments; these results were confirmed by our own studies. However, at concentrations of 10 mM and above, sucrose was found to decrease the amplitude of the caffeine-induced contracture in a dose-dependent manner. Similar effects were seen with the pH buffer TAPS (tris(hydroxymethyl)methylaminopropanesulphonic acid). An example of the depressive effects of the higher concentrations of sucrose is shown in Fig. 4*B*. A small potentiation obtained with 30 mM-taurine is illustrated for comparison (Fig. 4*C*). Thus the reduced potentiation by high concentrations of taurine may result from an inhibition of SR function by the increased osmolarity of the solutions.

Figure 5 summarizes data accumulated from fourteen saponin-treated pre-

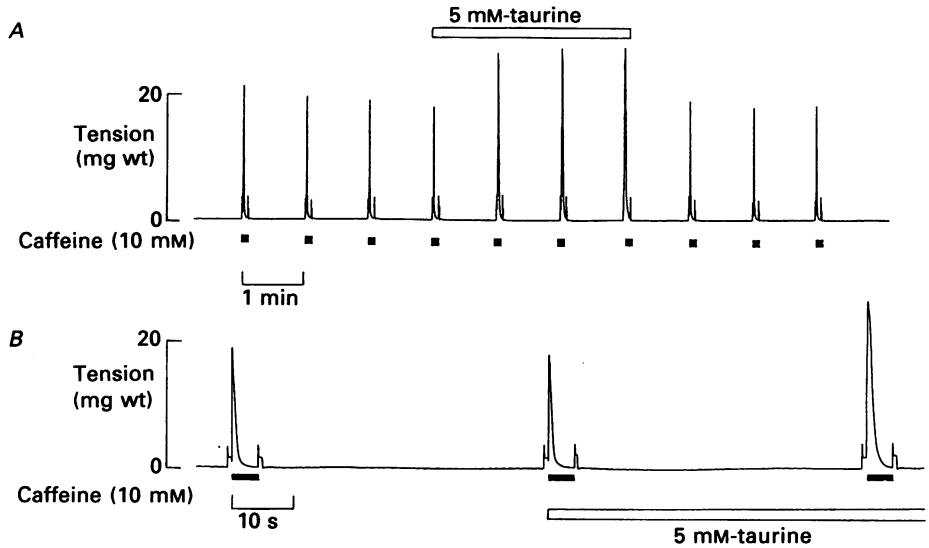

Fig. 2. The effect of taurine (5 mM) on the size of the caffeine-induced contracture. Panel *A* shows a continuous record of isometric tension from a saponin-treated rat trabecula. The [Ca^{2+}] in the solution was 0·12 μM (0·2 mM-total EGTA). At the point indicated taurine was included in the caffeine-containing and caffeine-free solutions. Panel *B* shows a section of this record on a faster time base.

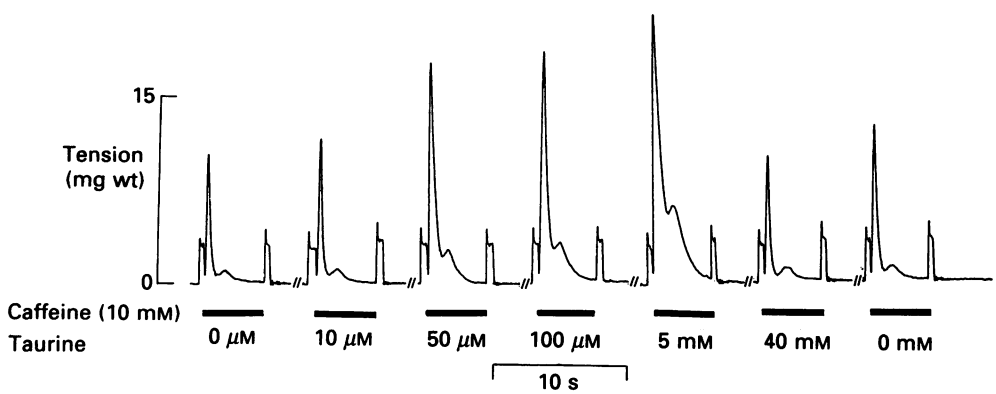

Fig. 3. The effect of a range of taurine concentrations on the caffeine-induced contracture in a saponin-treated rat trabecula (Ca^{2+} and EGTA concentrations as in Fig. 2). The transients represent steady-state caffeine-induced contractures achieved after a range of taurine concentrations had been introduced. The breaks in the record indicate 1 min Ca^{2+} loading periods.

parations. The taurine concentration is shown on a log scale on the abscissa and the peak amplitude of the caffeine contracture, expressed as a percentage of the standard contracture, is plotted on the ordinate. In these experiments the Ca^{2+} loading was chosen so that the standard contracture was close to 20% of maximum Ca^{2+}-activated force. Variation in the size of the standard contracture is small (●).

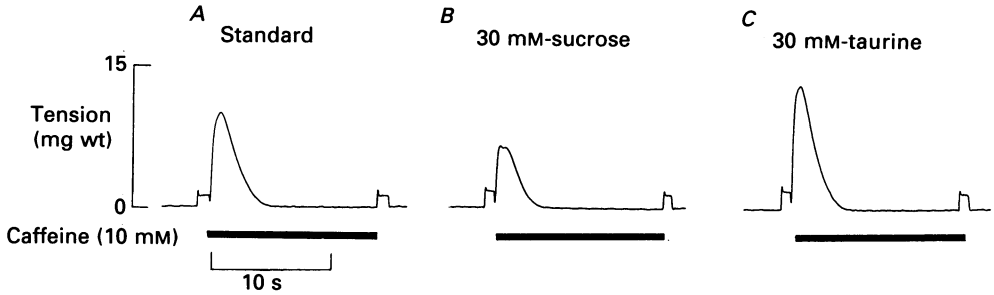

Fig. 4. The effect of sucrose on the caffeine-induced contracture obtained using 1 min, loading periods ([Ca^{2+}], 0·12 μM; [total EGTA], 0·2 mM). Panel *A* shows the steady-state caffeine-induced contracture from a saponin-treated rat trabecula. Panel *B* illustrates the steady-state contracture in the presence of 30 mM-sucrose. Panel *C* is the steady-state contracture in the presence of 30 mM-taurine.

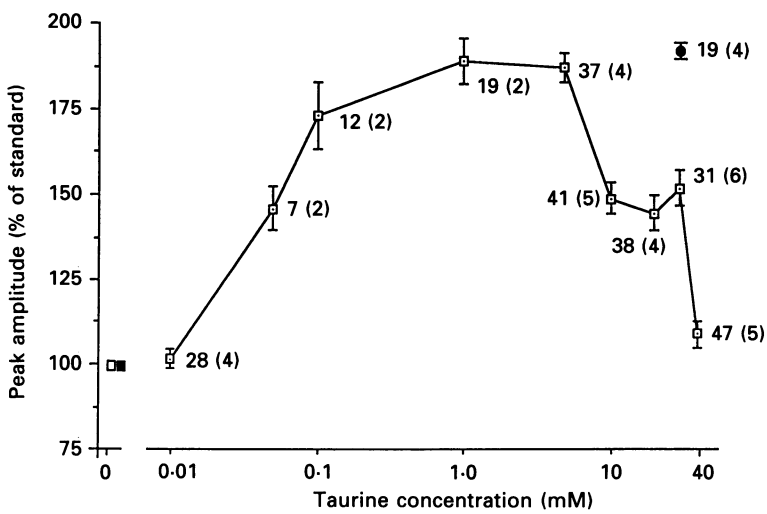

Fig. 5. The effect of taurine on the amplitude of caffeine-induced contractures. The points represent the mean steady-state response at different taurine concentrations as a percentage of the mean standard response (error bars indicate the standard error of the mean). The numbers beside each point indicate the number of observations; the numbers in parentheses are the number of preparations used. The points on the left-hand side of the graph represent the mean standard contracture before (100±0·55%, □) and after (100·65±2·01%, ■) taurine (S.E. is smaller than the points). Results obtained with 30 mM-taurine when compared with those in taurine-free + 30 mM-sucrose solution are also illustrated (●).

The potentiation was typically greatest at 1–5 mM-taurine but the effect was reduced from 10 to 40 mM. However, when the effect of osmolarity was corrected for sucrose substitution no depressive effects were observed at 30 mM-taurine (●), which then potentiated to a similar extent as 1–5 mM-taurine. As illustrated in Fig. 5 (□ and ■), the effects of taurine are completely reversible.

Another factor that can limit the effect of taurine on the caffeine contracture is

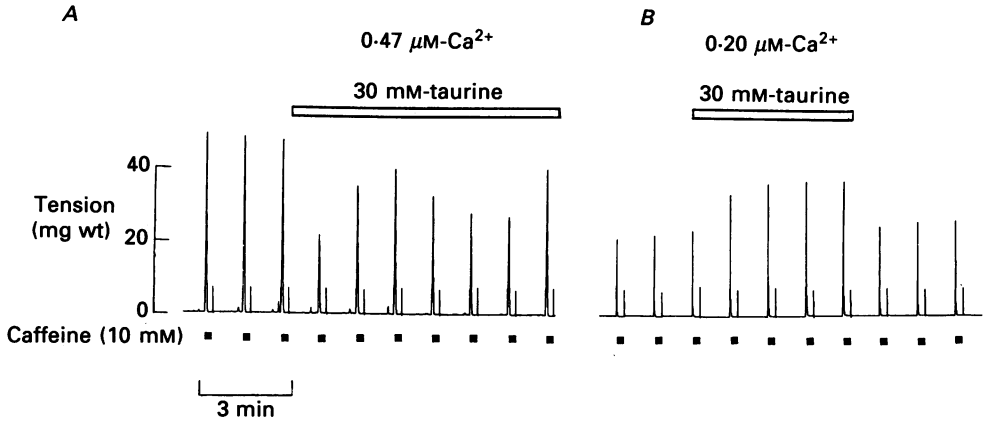

Fig. 6. The effect of taurine on caffeine-induced contractures in a saponin-treated trabecula. In panel *A*, muscle was exposed to 0·47 μM-Ca^{2+} for 1 min prior to each caffeine contracture (in the presence of the same [Ca^{2+}]). Taurine (30 mM) was added at the time indicated. Panel *B*, tension recordings from the same muscle in the presence of 0·2 μM-Ca^{2+}; taurine was added at the time indicated.

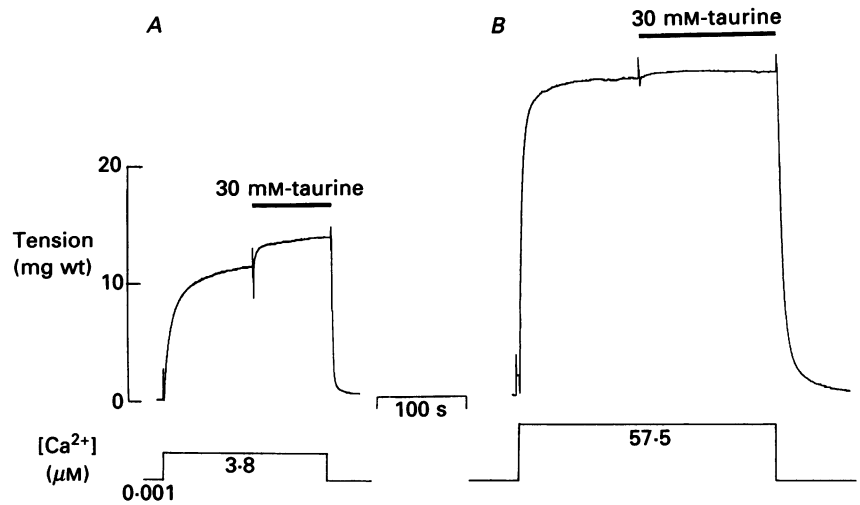

Fig. 7. The effect of taurine on Ca^{2+}-activated force in a Triton-treated trabecula. Panel *A*, tension recording was obtained by raising the [Ca^{2+}] in the bathing solution from 0·001 to 3·7 μM. Taurine (30 mM) was added at the point indicated. Panel *B*, maximum Ca^{2+}-activated force was achieved by raising the [Ca^{2+}] to 57·3 μM; taurine (30 mM) was added at the point indicated on the record (10 mM-total EGTA throughout).

illustrated Fig. 6*A*. Under these circumstances the [Ca^{2+}] in the loading period was increased to 0·47 μM to result in a caffeine-induced contracture that reached approximately 80% of maximal Ca^{2+}-activated force. On addition of 30-mM-taurine, the size of the caffeine-induced contracture decreased and showed a large variation

between successive responses. This variation in the amplitude may result from the spontaneous release of Ca^{2+} from the SR. Evidence for this is provided by the small fluctuations in tension during incubation in the loading solution both before and after the addition of taurine. However, these fluctuations cannot be used as an assay

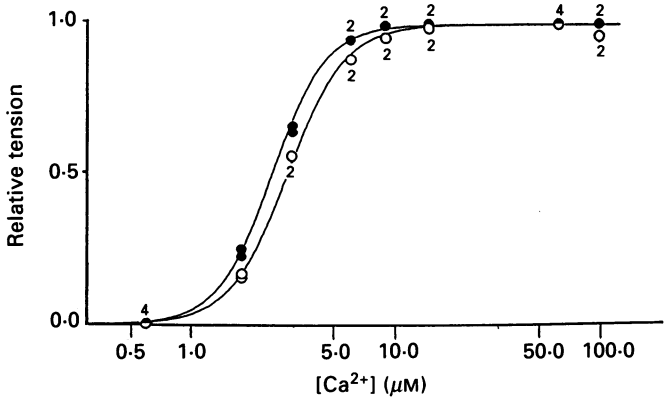

Fig. 8. The relationship between $[Ca^{2+}]$ and tension in a Triton-treated trabecula in the absence (○) and presence (●) of 30 mM-taurine. These results were taken from one preparation; the numbers beside each point represents the number of observations plotted at the point. The continuous lines are best-fit curves to the Hill equation.

of the spontaneous release of Ca^{2+} from the SR since the fluctuations of $[Ca^{2+}]$ may occur below the threshold for tension. The normal effect of taurine, detailed earlier, was obtained from the same preparation if the $[Ca^{2+}]$ in the loading and caffeine solutions was reduced to 0·2 μM, which gave a caffeine-induced contracture below 50% of maximal Ca^{2+}-activated force (Fig. 6*B*). Under these conditions no spontaneous fluctuation in tension was observed while the preparation was in the loading solution.

The effect of taurine on myofilament Ca^{2+} sensitivity

To investigate the effects of taurine on Ca^{2+} sensitivity, trabeculae were skinned with Triton C-100 to remove the remaining diffusional barriers between the myofilaments and the bathing solution. A typical result is shown in Fig. 7. Taurine (30 mM) produced only a small increase in force when added to a bathing solution with 57 μM-Ca^{2+} (maximal Ca^{2+}-activated force). However, the effect of taurine was greater when applied to a $[Ca^{2+}]$ that evoked approximately 50% of maximal Ca^{2+}-activated force. In general, taurine (30 mM) caused only a slight increase in maximal Ca^{2+}-activated force (0·8 ± 0·4%, $n = 4$).

The overall effect of taurine on myofilament Ca^{2+} sensitivity is illustrated in Fig. 8. Taurine decreased the $[Ca^{2+}]$ required for half-maximal tension from 3·02 to 2·51 μM. In four experiments half-maximal tension was achieved at a range of $[Ca^{2+}]$ from 3 to 8 μM; 30 μM-taurine the $[Ca^{2+}]$ needed for half-maximal tension by an average of 10·5% (±3% S.D.).

The concentration dependence of this effect is shown in Fig. 9. Approximately half Ca^{2+}-activated force was achieved in the presence of 3·8 μM-Ca^{2+}. The addition of

10 μM-taurine had no effect on force, but there was a small increase in force on addition of 1 mM-taurine. The addition of taurine at 20 mM increased Ca^{2+}-activated force by 15%, but the effect of 40 mM-taurine was not significantly greater. A similar effect of taurine on Ca^{2+} sensitivity has been reported for skinned crustacean muscle (Galler & Hutzer, 1988).

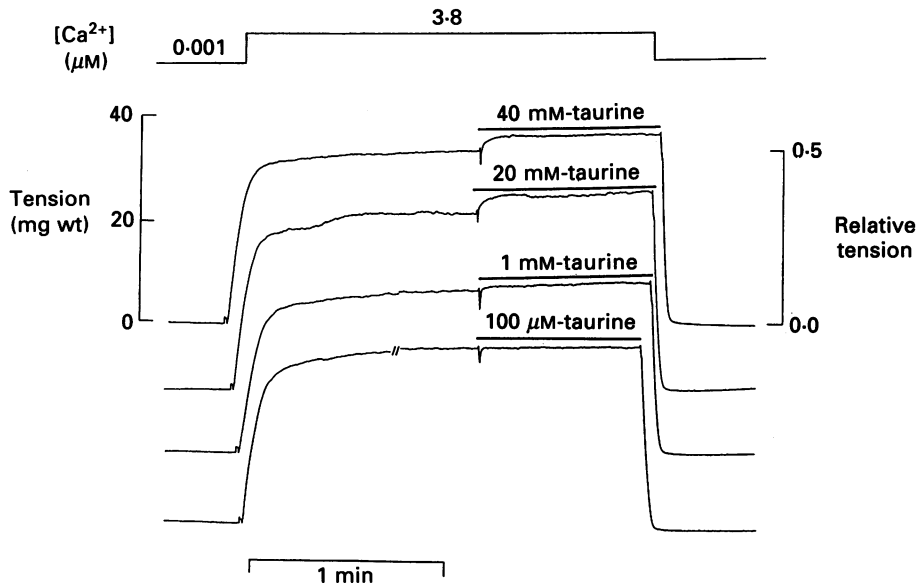

Fig. 9. The effect of taurine on Ca^{2+}-activated force. Each of the four tension records represents the force in response to raising the $[Ca^{2+}]$ from 0·001 to 3·8 μM, which evokes about half-maximal Ca^{2+}-activated force. Taurine concentrations ranging from 40 mM to 100 μM were tested as shown. The tension scale relative to maximal Ca^{2+}-activated force is shown on the right-hand ordinate. A 1 min break in the trace before applying 100 μM-taurine is indicated.

DISCUSSION

This study is the first to show that taurine can have a direct effect on intracellular systems in rat cardiac muscle. Taurine enhanced the ability of rat cardiac SR to take up Ca^{2+} and increased the sensitivity of the myofilaments to Ca^{2+} in chemically skinned cardiac trabeculae. The effect on the SR was evident at 10 μM-taurine, and maximal at 5–10 mM with an apparent K_m of about 50 μM. These values apply strictly to the conditions used in this study; specifically, the SR contained sufficient Ca^{2+} to support a caffeine-induced contracture that reached 10–20% of maximal Ca^{2+}-activated force in the presence of 0·2 mM-EGTA. If the Ca^{2+} loading of the SR was reduced, the dose–response curve for the effect of taurine on the SR would be shifted to the right, resulting in taurine having a maximal effect at higher concentrations. Thus the effect of taurine *in vivo* would depend critically on the Ca^{2+} load of the SR.

Figures 7, 8 and 9 illustrate that taurine increased the Ca^{2+} sensitivity of the

contractile proteins. In the steady-state responses to taurine, this effect may contribute to the larger caffeine-induced contractures seen at concentrations greater than 1 mM. In one experiment, the effect of 30 mM-taurine on the caffeine-induced contraction was measured on a saponin-treated trabecula. The muscle was then treated with Triton X-100 and the change in Ca^{2+} sensitivity due to 30 mM-taurine was measured. The results indicated that taurine caused a doubling of the size of the caffeine-induced contraction (osmotic strength compensated), but if the increased Ca^{2+} sensitivity was taken into account, the amplitude of the caffeine contracture would be increased by a factor 1·76. The complex shape of the relationship of contracture amplitude to taurine concentration (Fig. 5) above 10 mM probably reflects the conflicting influences of increasing Ca^{2+} sensitivity and increasing osmolarity.

Figure 6 illustrates that if the Ca^{2+} load on the SR was sufficiently high, taurine reduced the amplitude of the caffeine contracture, which also became variable in size. Studies on aequorin-injected papillary muscle have shown a very similar change in the amplitude in the Ca^{2+} transient when the extracellular [Ca^{2+}] was raised to well above physiological levels (Allen, Eisner, Pirolo & Smith, 1985). The increased influx of Ca^{2+} is taken up by the SR which quickly becomes overloaded. In this state, the SR releases Ca^{2+} spontaneously, and as a result less is available to be released during a twitch. The highly variable amplitude of the twitch arises from the differing amounts of Ca^{2+} remaining in the SR after spontaneous release (Allen *et al.* 1985). This explanation may apply to the results of Fig. 6*A*; the Ca^{2+} content of the SR was near-maximal due to the raised [Ca^{2+}] in the bathing solution, and the addition of taurine caused a further increase in the Ca^{2+} content of the SR to the extent that spontaneous release occurred and the amplitude of the caffeine response was reduced. Fluctuations in baseline tension are obvious in Fig. 6*A* indicating loss of Ca^{2+} from the SR. This behaviour cannot be properly assessed since there may be Ca^{2+} release that is too small to evoke tension responses; a similar pattern of behaviour is seen in Ca^{2+}-overloaded intact myocardium (Allen *et al.* 1985). Thus taurine can increase the size of caffeine-induced contracture if the Ca^{2+} content of the SR is low, but if the Ca^{2+} content is near-maximal, taurine will cause a fall in the mean caffeine-induced contracture. A similar pattern of responses to taurine is seen in intact cardiac preparations. In guinea-pig ventricle, taurine causes an increase in the size of twitch in a dose-dependent manner, but it has a negative inotropic effect if applied at a high external calcium concentration (Franconi *et al.* 1982). The effect of taurine on rat heart muscle is more complex. At normal external calcium concentrations taurine can cause a negative inotropic response (Dietrich & Diacono, 1971), or a small positive inotropic effect (Schaffer, Chovan & Werkman, 1978). However, in the presence of low external calcium concentrations the addition of taurine causes a marked positive inotropic response (Khatter *et al.* 1981). These results from intact preparations are very similar to those observed in caffeine-induced contractures in this study, which would imply that the major influence of taurine on cardiac muscle is to enhance Ca^{2+} uptake by the SR.

While the results from this study can explain the relationship between contractility and extracellular taurine concentration in intact cardiac preparations, they cannot explain the reported fall in Ca^{2+} content of cardiac preparations in the presence of

taurine (Franconi *et al.* 1982). Results from previous studies have suggested that taurine acts by increasing Ca^{2+} binding to sites on the sarcolemma (Chovan *et al.* 1980). Similar effects on Ca^{2+} binding to SR Ca^{2+}-ATPase and the contractile proteins could explain the results from this study. If the overall effect of taurine is to increase Ca^{2+} affinity for Ca^{2+}-binding sites throughout the muscle cell, the effects of taurine on cardiac contractility will depend on the relative effects of taurine on the various intracellular [Ca^{2+}]-regulating mechanisms.

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