

COMUNICAÇÃO

ABSENCE OF HYPERSENSITIVITY TO THE NEGATIVE CHRONOTROPIC EFFECT OF ACETYLCHOLINE IN THE ATRIA OF MICE ACUTELY INFECTED WITH *TRYPANOSOMA CRUZI*, CL STRAIN.

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Cardiac parasympathetic denervation during the acute phase of *Trypanosoma cruzi* infection is believed to play an important role in the pathogenesis of Chagas' cardiopathy⁵. As *Trypanosoma cruzi* infection in mice produces myocarditis with characteristics similar to Chagas' myocarditis in humans^{2,5}, this model was chosen to investigate the sensitivity of atrial muscarinic receptors to exogenously administered acetylcholine (ACh). In a previous study¹⁰ using atria of mice chronically infected with either a reticulotropic (Y) or a myotropic (CL) strain of *Trypanosoma cruzi*, it was reported no significant change in the sensitivity to ACh, a result that might be due to reinnervation processes occurring after the acute phase, as shown in rats^{7,8}. So, it was decided to investigate the atrial reactivity to ACh during the acute phase of *Trypanosoma cruzi* infection in mice. The CL strain was chosen because it induces a more severe myocarditis than the Y strain¹.

Albino mice weighing 24-32 g were inoculated intraperitoneally with 200 trypomastigotes/g of a CL strain of *Trypanosoma cruzi*.

All infected animals exhibited blood parasites after infection, as determined by means of microscopic examination of a drop of blood 14 days after infection. After 30 days of infection (acute phase) the animals were killed for *in vitro* recording of the effects of ACh. Age-matched

noninfected mice were used as controls. Atria (left and right) were mounted in a 7 ml-organ bath (32°C), filled with modified Locke solution (154 mM NaCl, 5.6 mM KCl, 2.2 mM CaCl₂, 0.08 mM NaH₂PO₄, 1.9 mM NaHCO₃ and 5.5 mM glucose) and bubbled with O₂. The atria were attached to a force transducer (Narco F-50) and tension was recorded on a Narco DPM-4B polygraph. An initial tension of 0.1 g was applied to the tissues. An equilibration period of 40 min was allowed before experiments were started. Acetylcholine chloride (from Sigma Co.) was added to the organ bath and a dose-response curve produced. The effect of ACh was expressed as the decrease in beating rate relative to the previous basal value (bpm). Data were expressed as mean \pm S.E.M. and analyzed statistically by the Student's *t*-test, *P* less than 0.05 being considered significant. After the experiments, the atria were fixed in 10% formalin and were paraffin embedded for light microscopy.

Histological examination of the atria from infected mice showed multifocal myocarditis with destruction of some cardiac cells and presence of mononuclear exudate. The atrial ganglia observed in each case showed focal inflammatory lesions, with apparent low level of neuronal destruction. Basal atrial rate was similar in both groups: 250 \pm 11 bpm in chagasic (n=6) and 253 \pm 10 bpm in control (n=6) mice. The dose-response curve to ACh in atria from infected mice did not significantly differ from the control (Figure 1).

These results demonstrate that acute infection of mice with the CL strain of *Trypanosoma cruzi* does not induce cholinergic supersensitivity, as it had already been demonstrated during the chronic phase¹¹. Chagas' disease is still considered to be a natural human model of peripheral autonomic denervation¹⁰, and lesions in cardiac ganglia have

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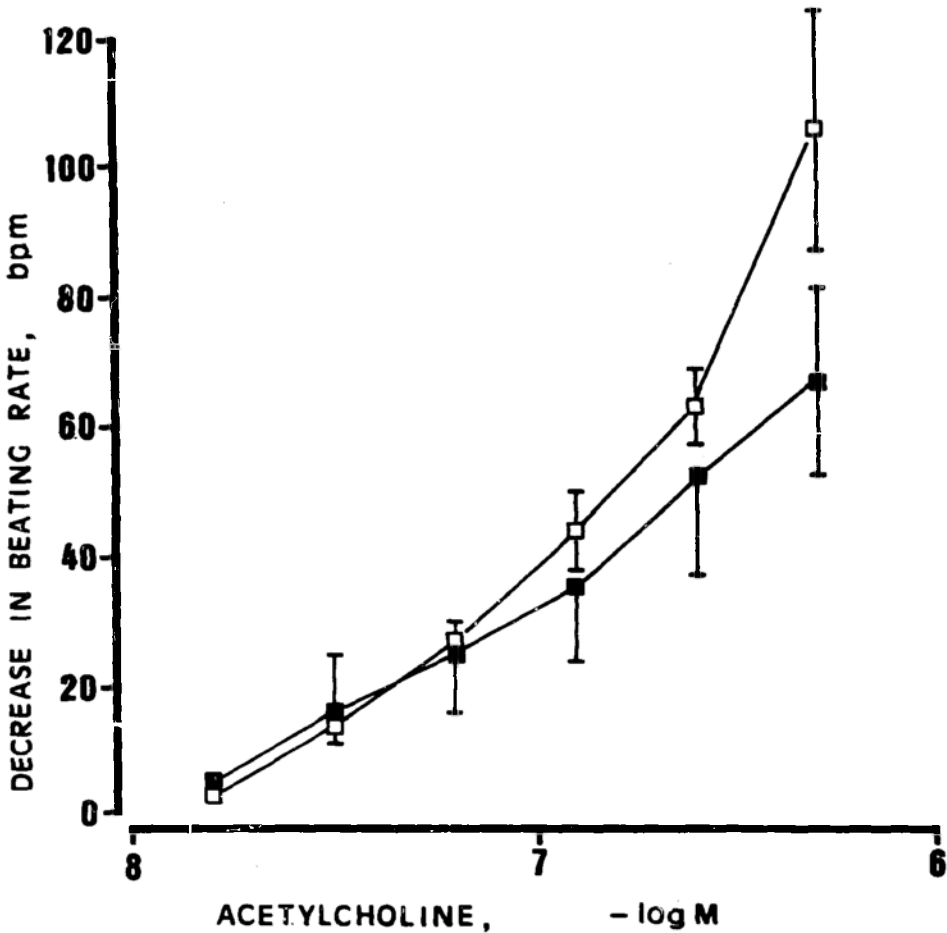


Figure 1 - Dose-response curves for the negative chronotropic effect of acetylcholine on the spontaneous beating of mice atria. Data are reported as means \pm SEM for control (-□-, n=6) and infected (-■-, n=6) animals.

been described in mice acutely infected with *Trypanosoma cruzi*². However, the intensity of denervation in atrial ganglia has not been established in mice with acute *Trypanosoma cruzi* infection. The lesions that we observed in atrial ganglia were focal and do not suggest a severe depletion of nerve cells in those ganglia. Reduction of cardiac neurons has been reported in rats during the acute phase of *Trypanosoma cruzi* infection¹. However, quantitative studies of rats chronically infected with *Trypanosoma cruzi* showed no significant differences in the number of neurons in respect to

age- and sex-matched control rats^{4,9}. Therefore, it is possible that the absence of supersensitivity to ACh that we observed in isolated atria of acutely infected mice would be due to the low intensity of denervation in atrial ganglia.

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