

NEUROMUSCULAR TRANSMISSION STUDIES IN HUMAN CHRONIC CHAGAS' DISEASE

MARCELA GARCIA ERRO* — O. GENOVESE*
J. CORREALE* — R. E. P. SICA*

SUMMARY — An electrophysiological investigation of the state of the neuromuscular transmission (nmt) was carried out in 58 patients with the diagnosis of chronic Chagas' disease. On repetitive supramaximal nerve stimulation it was found that some patients did not show abnormalities, others had decremental muscle responses, others developed enhancement of the muscle evoked potential amplitudes, while some other patients combined both types of pathological responses. The findings suggest that some patients with chronic Chagas' disease develop impairment of nmt, though data obtained in this study do not give information about neither the type of impairment nor the localization (pre or postsynaptic, or both) of the damage.

Estudio de la transmisión neuromuscular en la enfermedad de Chagas crónica humana.

RESUMEN — Cincuenta y ocho pacientes con edades entre los 1 y 58 años, con diagnóstico de enfermedad de Chagas crónica fueron estudiados para evaluar la transmisión neuromuscular. Se estimuló en forma supramáxima el nervio cubital a nivel de muñeca, con registro de electrodos de superficie en hipotenar. Dicha estimulación se realizó a 3 Hz durante 2 segundos y 10 Hz durante 1 segundo en condiciones basales, tras 4 minutos de ejercicio mecánico, luego de 4 minutos de ejercicio mecánico mas isquemia y tras 2 minutos de liberada la isquemia. Se procedió a medir la amplitud del 3, 5, 6 y 10 potencial, que fueron expresados como variación porcentual con respecto al primero al que se le asignó un valor de 100%. Treinta pacientes no evidenciaron diferencias con respecto a la curva obtenida en 20 sujetos controles, 4 mostraron una caída del potencial evocado muscular, 6 una caída del mismo cuando el estímulo se realizó a bajas frecuencias y un incremento cuanto el estímulo fue a altas frecuencias. En los restantes 18 pacientes se observó un incremento del pem. Estos hallazgos sugieren una posible alteración de la transmisión neuromuscular en algunos pacientes que han alcanzado el estadio crónico de la enfermedad de Chagas de probable localización pré y/o post-sináptica.

In the last years evidences have been accumulated demonstrating the involvement of the peripheral nervous system in the chronic state of human Chagas' disease¹⁶⁻¹⁸. More recently, those findings received support from observations made in a mouse experimental model where the human features could almost be replicated^{6,15}.

The present study has been designed as a complement of earlier investigations looking for the eventual involvement of the neuromuscular transmission (nmt) in patients who have reached the chronic state of the infection. A brief and limited account of these findings has been given elsewhere⁴.

* Sección Electroneurofisiología Clínica, División Neurología, Hospital Ramos Mejía; Departamento Medicina, Orientación Neurología Facultad de Medicina, Universidad de Buenos Aires.

MATERIAL AND METHODS

Patients — Altogether 58 patients were explored, 26 of them were females and 32 were males; their ages ranged between 19 and 58 years. None of them had received any treatment related to the parasitic illness. The diagnosis of Chagas' disease was done at the 'Instituto Nacional de Diagnostico e Investigacion de la Enfermedad de Chagas in Buenos Aires'. For these purposes three serological tests were employed namely: 1. Immunofluorescence; 2. complement fixation; 3. haemoagglutination. Only were accepted for this investigation those patients who showed positiveness of, at the least, two tests. Coincidental causes of peripheral or central nervous system damage were eliminated from the study by rejecting patients over 60 years old¹⁹ and those others who had had toxic, metabolic, genetic or infectious diseases able to develop neurological involvement. Controls — Twenty healthy and non selected people, with negative test for Chagas' disease, were employed as controls. Twelve of them were females and 8 were males. Their ages ranged between 20 and 45 years.

Technique — Electrodes: The recording electrode was a strip of silver foil, 4 cm long and 0.5 cm wide, coated with electrode jelly and fixed with adhesive tapes at the skin of the hypothenar eminence overlying the end-plate area of the adductor digiti minimi muscle. The reference electrode, also a silver strip, was wrapped around the proximal phalanx of the index finger, while the earth electrode was situated at the dorsum of the hand. The stimulating electrode was a pair of silver discs, 0.8 cm in diameter, spaced two cm apart and mounted in a plastic holder which was fixed by a rubber band at the internal border of the ventral aspect of the wrist overlying the ulnar nerve. Once the electrodes were in position, isolated pulses were delivered from a Multistin stimulator and their intensity was gently increased until a maximal M wave could be evoked at the hypothenar muscles. Thereafter, the stimulus intensity was made supramaximal by 20%. **Procedure:** Supramaximal nerve repetitive stimulation was performed at two different frequencies, namely 3 Hz during 2 seconds and 10 Hz throughout 1 second. The time elapsing between both sets of stimulation was, at least, 15 seconds. The ambient temperature was maintained between 24 and 26° C. The procedure was repeated in the following conditions: a) with the muscles at rest; b) immediately after exercising the muscle during 4 minutes by delivering at the ulnar nerve a near-maximal stimulation at 3 Hz frequency; c) immediately after combining during also 4 minutes muscle exercise and muscle ischaemia developed by an over systolic pressure inflated cuff which was positioned at the upper arm; d) after two minutes of interrupting the muscle exercise and releasing the cuff⁵. M wave amplitude was measured pick to pick on the screen of a storage oscilloscope and the amplitudes of the 3rd, 5th, 6th, and 10th potentials were referred as % of the first one.

RESULTS

Figure 1 summarizes the findings done in this study. From top to bottom the first row shows the behaviour of control people. The second row comprises 30 patients whose response to repetitive stimulation did not differ from controls. The third row belongs to 4 patients who disclosed a decremental response of at least 15% at 3 Hz stimulation rate and 25% at 10 Hz. The fourth row shows 6 patients who developed a decremental response at lower rates of stimulation and an incremental response at higher rates. Finally, the fifth row is composed by a group of 18 patients who showed an incremental response bigger than 60% at both rates of stimulation.

All patients tested were also submitted to maximal ulnar motor conduction velocity studies. None of them showed values below the lower control limit (50 m/s).

COMMENTS

The findings in the present study point out to the end-plate as a structure which may be functionally impaired in some patients affected by chronic Chagas' disease. With the data obtained, it is hard to decide which is the type of impairment afflicting the neuromuscular transmission. Some patients had a decremental response, as happens with failures at the postsynaptic^{14,21} or presynaptic sides^{1,8,10,11,13,20,22}. Others disclosed enhancement of the amplitude of the muscle evoked potential as has been seen in disorders of the presynaptic side, though not to the extent which may be reached in the Eaton-Lambert syndrome^{3,9}, while a third group had a combined response with decrement of the amplitude of the M wave at low rates of stimulation and increment at higher rates. This last behaviour has also been described in failures of the nmt localized at the pre-synaptic level^{2,7}.

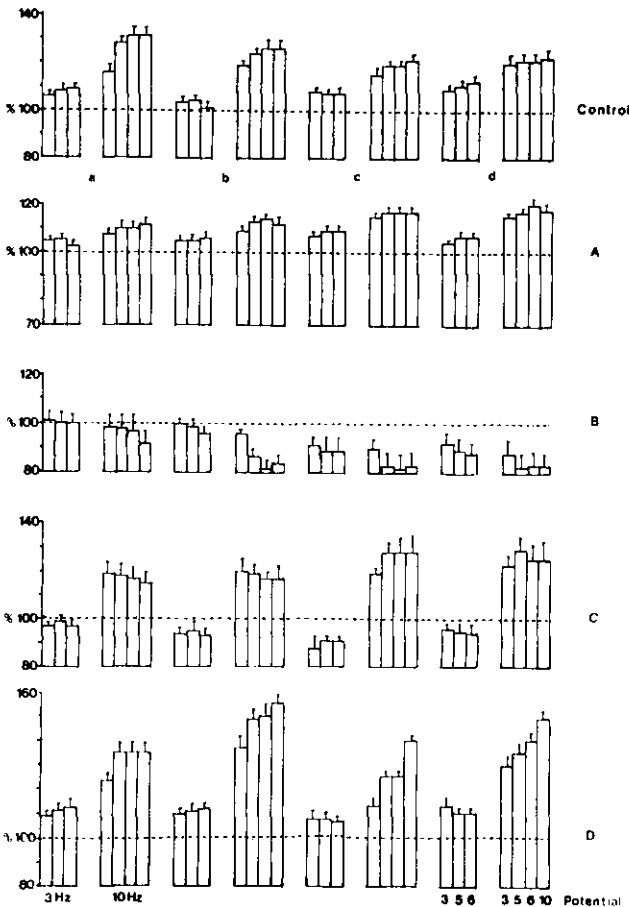


Fig. 1 — Percentage of increment and/or decrement of the amplitude of the third (left hand column on the 3 Hz and 10 Hz histograms), fifth (2nd column on both histograms), sixth (3rd column on both histograms) and tenth (right hand column on both histograms) muscle evoked potential as compared with the first potential. (---), first potential amplitude expressed as 100%. A: patients who do not differ from controls. B: patients with decremental response. C: patients with decremental response at low stimulation rate and incremental response at higher stimulation rates. D: patients with incremental response. a, basal condition. b, exercise. c, exercise combined with ischaemia. d, 2' post exercise and ischaemia.

Based on present observations one is tempted to accept that both sides of the synapsis may be altered, either simultaneously or independently. In fact, Molina et al.¹² recently demonstrated damage of both sides of the end-plate in the mouse infected with trypomastigotes of the Tulahuén strain. However, in man neither we can decide whether this failure means a primary involvement of the end-plate nor if it may represent a damage developed as a consequence of the injury of the neural structures of the motor unit or of the muscle itself. The normal maximal motor conduction velocities found in every patient makes unlikely the possibility that harm of the large motor axons may play some role in the type of responses observed. Perhaps, deeper studies performed in the mouse experimental model⁶ could shed more light on the pathogenesis of these features.

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