Apoptosis of mouse hippocampal cells induced by *Taenia crassiceps* metacestode factor

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INTRODUCTION

Human neurocysticercosis is an infection of the central nervous system (CNS) caused by oral ingestion of *Taenia solium* eggs. Among the most frequently reported symptoms in human neurocysticercosis are seizures, headaches and neurological deficits. However, the neurological deficits caused by *T. solium* in humans have not been fully examined, particularly depression syndromes; moreover, cognitive impairments may be much more prevalent than previously thought in patients with neurocysticercosis. Previously it has been reported that both *T. crassiceps* infection and a low molecular weight fraction (metacestode factor (MF)) isolated from secretions of *T. crassiceps* metacestodes induced severe histopathological damage, mainly extensive apoptosis, in mouse testis, ovary and spleen cells (Zepeda et al., 2011a, b, 2015; Solano et al., 2015). However, given that human neurocysticercosis appears to be associated with cognitive deficits, including memory impairments, studies that investigate the involvement of memory-related areas in neurocysticercosis are needed. The purpose of the present research was to study the effects of intraperitoneal infection of mice with *T. crassiceps* metacestodes and of the subcutaneous inoculation of mice with *T. crassiceps* MF on hippocampal cells, as a model of human cysticercosis. We hypothesized that the cellular death (apoptosis) induced by the *T. crassiceps* MF would occur in regions involved in some forms of learning and memory, and other hippocampal functions, which would provide new insight into the neurological deficits observed in human neurocysticercosis.

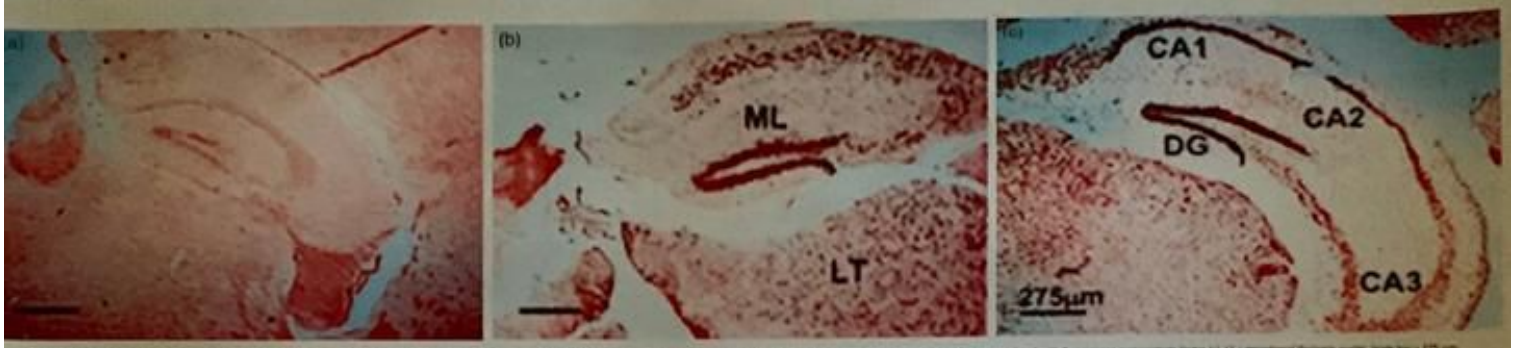

Fig. 1. TUNEL/FOD stained brain sections that contain the dentate gyrus (DT), CA1, CA2, CA3, and hippocampal molecular layer (ML) from control mice (a), mice infected with *Taenia crassiceps* metacestodes (b), and mice inoculated with *T. crassiceps* metacestode factor (c). LT, Lateroventral thalamic nuclei. Scale bar = 275 μm.

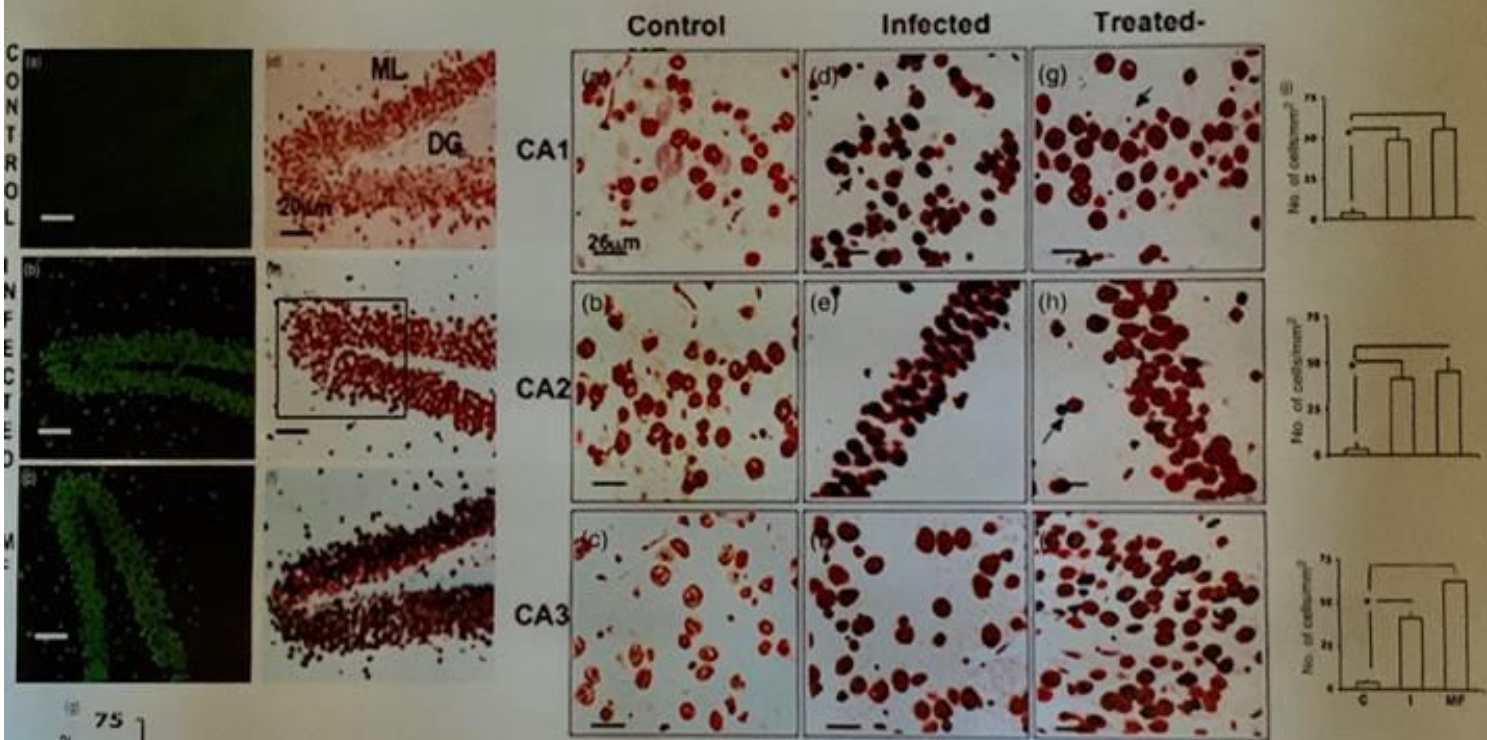

Fig. 2. TUNEL/FOD stained brain sections that contain part of the CA1, CA2 and CA3 regions from control mice (a-c), mice infected with *T. crassiceps* metacestodes (d-f) and mice inoculated with metacestode factor (g-i). Each micrograph has an area of 1mm2. Arrows indicate apoptotic bodies. Scale bars = 26 μm. (j) The bars represent mean ± SD of apoptotic cells/mm2 in CA1, CA2 and CA3 regions from control mice (C), mice infected with *T. crassiceps* metacestodes (I) and mice inoculated with *T. crassiceps* MF (MF). * P < 0.01

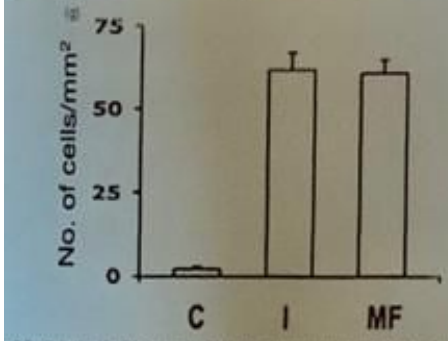

Fig. 3. TUNEL- (a-c) and TUNEL/FOD stained (d-f) brain sections that contain a portion of the glomerular layer of dentate gyri (DG) from control mice (a and d), mice infected with *T. crassiceps* metacestodes (b and e) and mice inoculated with *T. crassiceps* metacestode factor (c and f). Area of rectangle in E = 1mm2. ML, Hippocampal molecular layer. Scale bars = 20 μm. (g) The bars represent mean ± SD of apoptotic cells/mm2 of control mice (C), mice infected with *T. crassiceps* metacestodes (I) and mice inoculated with *T. crassiceps* MF (MF). P < 0.01, I and MF versus C.

CONCLUSION

These results suggest that the intraperitoneally injected metacestodes may have secreted MF into the peritoneal cavity, then MF migrated via the bloodstream and induced the observed unspecific, generalized apoptosis of hippocampal cells and cells in other neighbouring areas. Almost all of the cells in the three layers of the dentate gyrus appeared to be affected, as were many of the cells in the CA1, CA2 and CA3 regions of the hippocampus from both experimental groups. More studies are needed to establish fully the molecular structure of the *T. crassiceps* MF and to determine how it induces apoptosis of several cellular lineages. Future studies should also confirm whether the apoptosis of hippocampal cells that was observed here leads to neurological deficits in learning, memory and behaviour, among others. Additional regions to those observed here (thalamic nuclei) must be studied to determine whether other neurological functions are altered. Also, it will be necessary to carry out studies in male mice to determine whether *T. crassiceps* MF is produced in them and whether this fraction induces the same pathology as that observed in female mice.

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