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Role of glial dystrophin-associated proteins and perivascular basement membrane in blood brain barrier alteration of mdx mouse

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In this study we have investigated the involvement of the dystrophin–associated proteins (DAPs) and their relationship with the perivascular basement membrane in the brain of two months mdx mice and in the control ones. We have analyzed: 1) The expression of the glial DAPs α-β dystroglycan, -syntrophyn, aquaporin-4 water channel (AQP4), Kir 4.1 and Dp71, by immunocytochemistry, laser confocal microscopy, immunogold electron microscopy, immunoblotting and RT-PCR; 2) The ultrastructure of the basement membrane and the expression of laminin and agrin; 3) The dual immunofluorescence colocalization of AQP4/α-β dystroglycan, and of Kir-4.1/agrin. Results showed in mdx brain as compared to control ones: 1) A significant reduction in protein contents and mRNA expression of DAPs; 2) Ultrastructurally, the basement membrane appeared thickened and discontinuous and showed a significant reduction in laminin and agrin; 3) A molecular rearrangment of the α-β dystroglycan, coupled with a parallel loss of agrin and Kir 4.1 on basement membrane and glial endfeet. These data indicate that in mdx brain the deficiency in dystrophin and Dp71 is coupled with a reduction of the DAPs components coupled with an altered anchoring to the basement membrane.