Reduced long-term depression is recovered in aging mdx cerebellar Purkinje cells

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Duchenne muscular dystrophy (DMD) is characterized primarily by a loss of skeletal muscle and marked CNS and cognitive defects (Anderson *et al*,, 2002). It is known that DMD is due to the mutation of a gene which produces the protein dystrophin, of which there are seven identified isoforms, expressed in a range of tissues including brain. In the cerebellum an isoform of dystrophin is found exclusively in Purkinje neurons and is selectively localised in post-synaptic regions of GABAergic synapses. We have previously demonstrated (Anderson *et al*,, 2004) a deficit in long-term depression (LTD) in cerebellar Purkinje cells in the *mdx* mouse (an animal model of DMD) compared to controls at 3 months of age. mdx mice. --> In the present study we investigated LTD and short-term plasticity at the parallel fibre to Purkinje cell synapse in cerebellar brain slices from ageing (6-12 months) control and *mdx* mice. Mice were anaesthetised with halothane, decapitated, cerebellum removed, bisected, placed in ice-cold aCSF and sagittal slices (250μM) cut. Individual Purkinje cells were visualised using a 40× immersion lens and IR-DIC optics. Intracellular electrodes (~120MΩ) filled with potassium acetate were used and a stimulating electrode was placed in the molecular layer of the slice (<250μM from the cell under study). We found that the deficit in LTD which we reported (Anderson *et al*,, 2004) in *mdx* mice at 3 months of age was no longer evident in aging *mdx* mice, and that these cells showed a long lasting and robust LTD. In addition, there were no differences in short-term plasticity between the ageing control and *mdx* mice.

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