



The effect of gestational stress on behavioral and physiological phenotypes in the dystrophin-deficient *mdx* mouse

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Patients with Duchenne muscular dystrophy (DMD) suffer from an array of neurocognitive disorders, including a hypersensitivity to stressful stimuli. During gestation, stressful stimuli can impact physical and neuronal development. Therefore, we investigated the long-term effects of gestational stress on dystrophinopathy phenotypes in the *mdx* mouse model of DMD. C57BL/10-*mdx* heterozygous female mice (*mdx*-het) were not stressed (NS) or subjected to a moderate (scruff restraint; SR; 30 s twice/day) or severe stressor (tube restraint; TR; 30 min twice/day) during the last week of gestation. Wildtype (WT) and *mdx* hemizygous male mice born from each stress paradigm were profiled for their behaviour and physiological phenotypes, including anxiety, stress response, mean arterial blood pressure (MAP) during a stressor and *in situ* muscle strength at 6, 12 and 24 weeks of age. Mice were administered 2 – 5% isoflurane for up to 60 min during *in situ* preparations and were humanely killed via cervical dislocation while unconscious. TR stressed *mdx*-het mice had a shorter gestational period relative to NS and SR mice ($p = 0.023$). Male and female WT and *mdx* mice born to TR *mdx*-het mice were lighter in body mass relative to mice born to NS and SR *mdx*-het mice ($p < 0.001$). Gestational stress had some effect on anxiety and the stress response of WT and *mdx*-hemizygous mice at multiple time-points ($p = 0.010$ to 0.866) but had no effect on MAP during a stressor or isometric tetanic force of the tibialis anterior muscle ($p = 0.175$ to 0.958). These data suggest that stress during gestation has minimal impact on behavioural and physiological phenotypes in WT and *mdx* male mice.