Novel Principle Component Analysis (PCA) to Assess Gait in Chronically Exercised vs Unexercised MDX Mice Shows Both Exacerbation and Amelioration of the Underlying Phenotype

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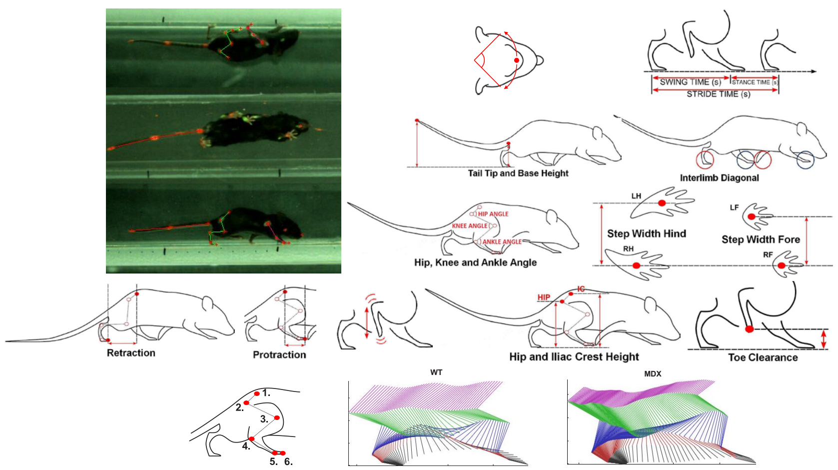
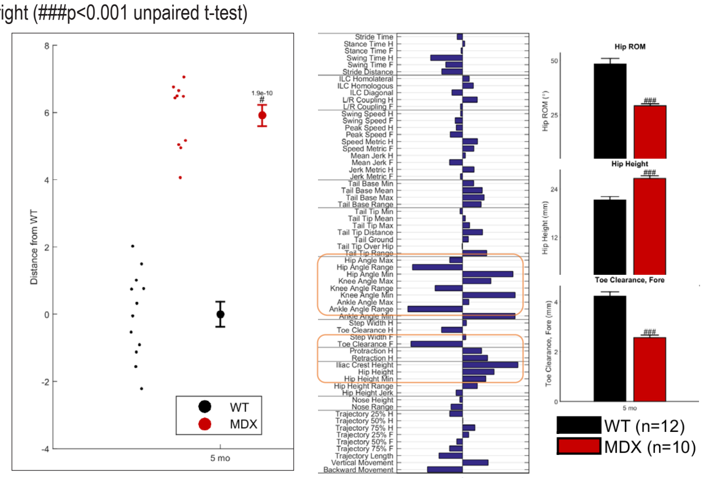
1 INTRODUCTION

- Kinematic analysis is the process of measuring the kinematic quantities to describe motion, or movements. Gait is a cyclic pattern of animal movement during locomotion, and is the most common movement activity.
- Kinematic gait analysis is a systematic and quantitative study of locomotion in quadrupeds and measures the motion in underlying muscle, joints and bones.
- Kinematic analysis process is based on marker based motion capture, using high speed cameras in a two step fashion:
  1) Trajectories of anatomical landmarks are marked and tracked from multiple views.
  2) Then, kinematic model of gait is computed using trajectory data from 3 different views.



3 MEASURABLE COMPONENTS

- 5 month old MDX male mice (C57BL/10ScSn-Dmdmdx/J) with progressive muscular dystrophy show strong alterations in lower body posture, which can be seen in increased hip, knee and ankle extensions, and also in increased overall hip height and decreased fore limb toe clearance, when compared to control mice (C57BL/10ScSnJ).
- The overall "distance from WT" score separates the groups with a clear margin (on left).
- The kinematic "fingerprint" (discriminant vector) of an MDX is shown right (most distinct alterations marked)
- Individual parameters of Hip range of movement (ROM), hip height and toe clearance (fore) are shown far right (###p<0.001 unpaired t-test)



2 EXPERIMENTAL SET-UP

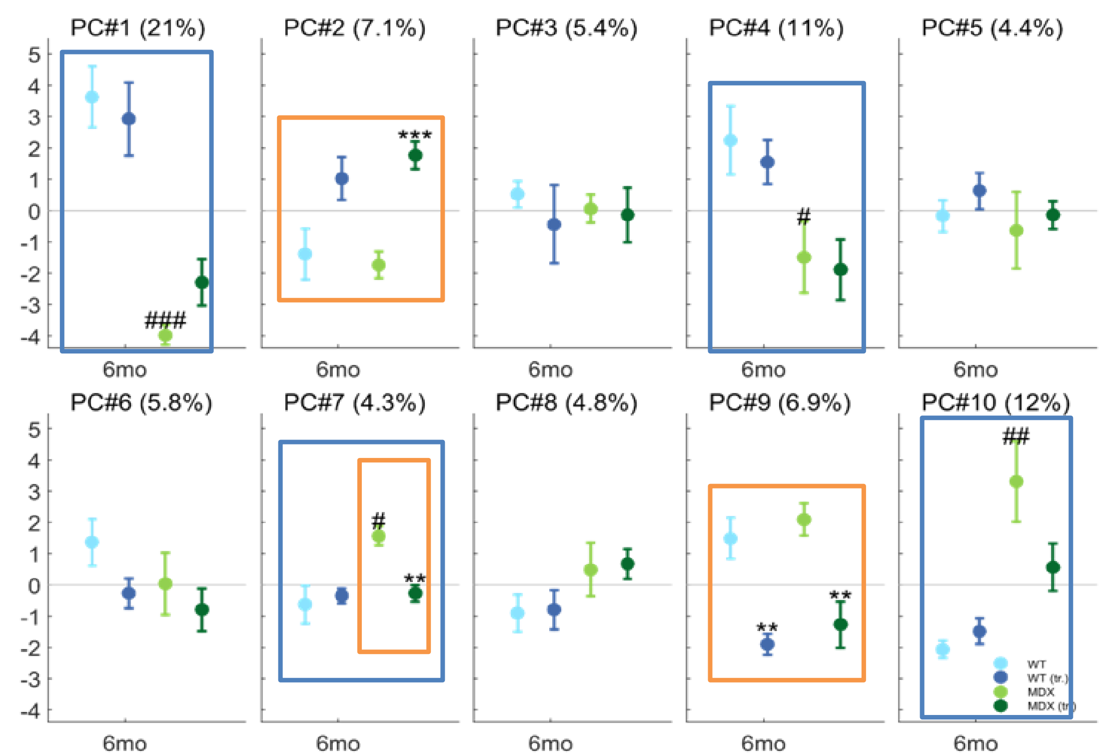
Animals

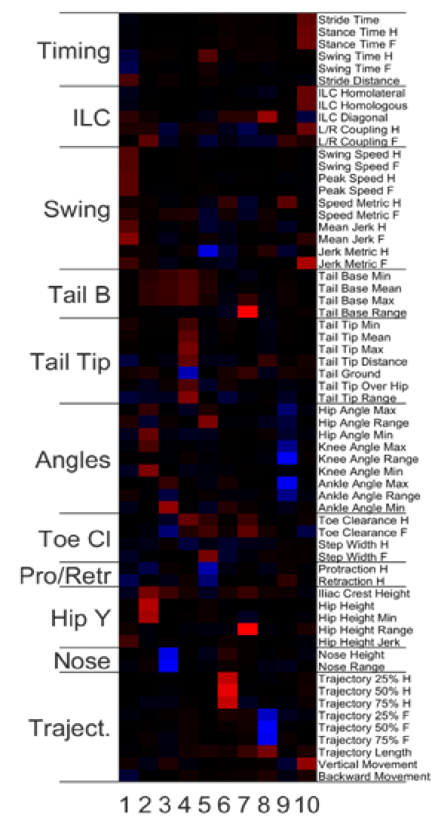
Experiments were conducted at Charles River Discovery Services, Kuopio, Finland. All animal experiments were conducted according to the National Institute of Health (NIH) guidelines for the care and use of laboratory animals, and approved by the State Provincial Office of Southern Finland. Experiments were additionally approved and guided by advisors from the Royal Veterinary College, University of London. MDX (C57BL/10ScSn-*Dmd*^{mdx}/J, stock number 001801) and WT mice (C57BL/6J, stock 000664) were purchased from the Jackson Laboratory (Bar Harbor, ME, USA). All mice were randomized and housed in groups of up to 5 per cage in the controlled environment with ambient temperature of 22 ± 1°C, humidity levels of 30–70% and normal light-dark cycle (7:00–20:00).

Experimental Set-up for Treadmill Exercise

WT and MDX mice were subjected to three 20-min training sessions weekly in a 6-lane treadmill (Exer 3/6 Treadmill; Columbus Instruments, Columbus, OH, USA). The treadmill was set at a 14° decline to facilitate downhill running. Treadmill training began immediately after the acclimatization period at 6 weeks of age. Treadmill was set to a maximal speed of 13 m/min. The number of stops by each mouse as well as the number of prompts were recorded.

4 RESULTS





Genotype effect	Training effect
WT untrained vs. MDX untrained vs. WT trained vs. MDX trained	WT untrained vs. WT trained vs. MDX trained vs. MDX untrained
• PC#1: Swingt Speed • PC#4: Tail tip/Base height • PC#7: Hip Height Range • PC#10: Slowness, decrease in diagonal interlimb coordination	• PC#2: Overall hip height, increased knee and hip angles • PC#7: Hip Height range • PC#9: Decrease in knee and ankle max angle and ranges (of motion) • => *Lower score in both trained groups*
Clear genotypical differences can be picked up	**Trained have greater range of movement and greater min angles**

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