GAIT IMPAIRMENT IN MOUSE MODEL OF TUBEROUS SCLEROSIS COMPLEX (TSC)

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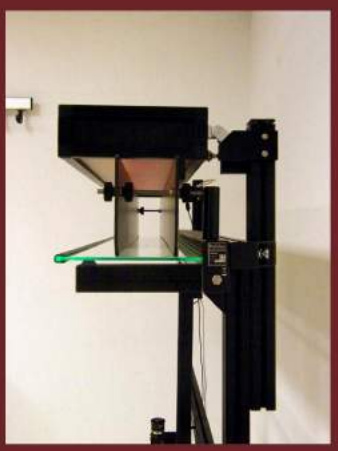
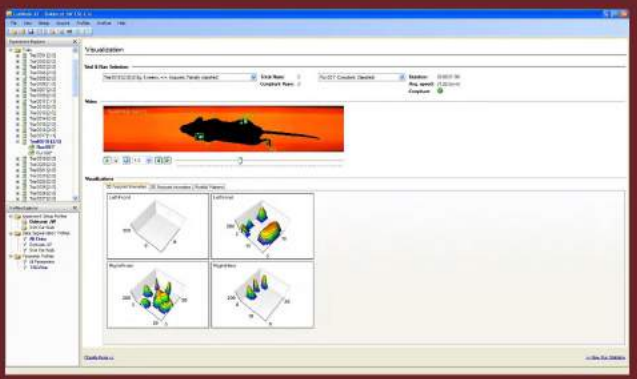
Introduction

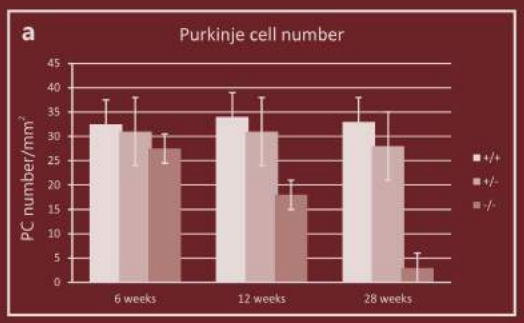
Tuberous sclerosis complex (TSC) is an autosomal dominant disease, mostly present in pediatric patients, and one of the most frequent neurocutaneous disorders. TSC patients typically develop neuropsychiatric signs with symptoms of epilepsy, mental retardation, and autism. Molecular mechanism of TSC involves two genes TSC1 and TSC2, both linked to pathway of mammalian target of rapamycin (mTOR). Expression of both genes results in two proteins tuberin and hamartin negatively regulating mTOR signaling pathway. Mutations in TSC1 or TSC2 disturb their inhibitory function, what impairs the proliferation machinery downstream of mTOR. As the result we can observe tumors (tubers) in many organs including brain structure and neurological symptoms characteristic for autism spectrum disorders (ASD). Mouse mutants for TSC1 or TSC2 gene are suitable model of autism spectrum disorders (ASD).
One of the symptoms specific for autistic-like traits is impaired gait, which is one of the early symptoms of autism. Here we present data on gait analysis in mouse with Purkinje-cell specific knockout of TSC1.

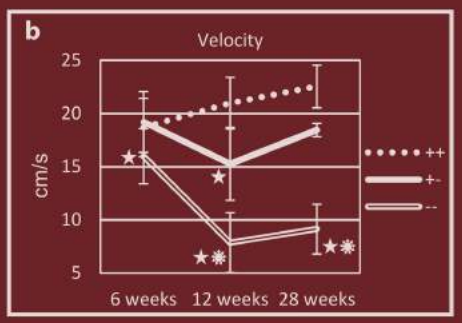


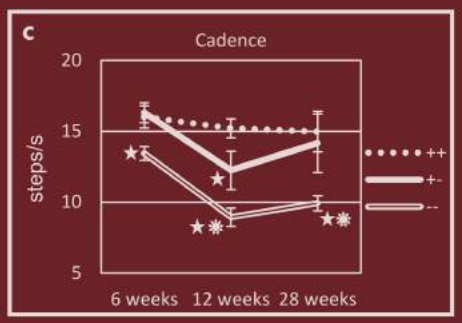


Methods

All animals used for the experiments were bred in the animal facility of the Center for Experimental Medicine. Gait analysis was performed on the Catwalk XT system (Noldus Information Technology, The Netherlands) comprised of a glass floor, illuminated with green LEDs, with a high speed (100 fps) camera mounted beneath the floor that records the footsteps of each animal walking across the glass and sends its data to a computer. Each animal performed two habituation runs for two consecutive days prior to footstep acquisition. Footstep analysis was conducted using Catwalk XT version 9.



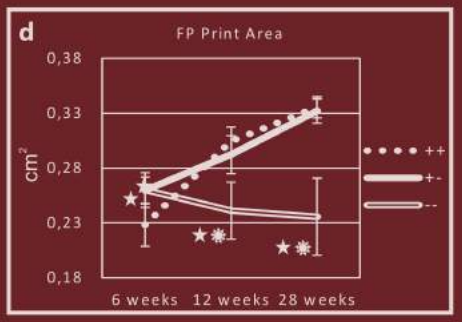


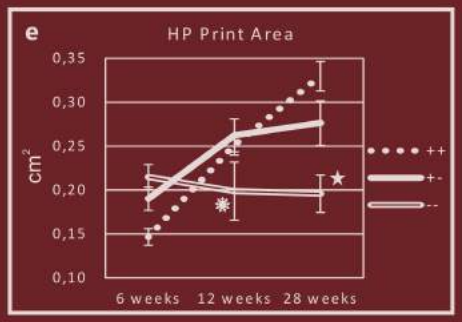


Preliminary results

a. Loss of PC after mTOR activation

b - g. Graphic presentation of selected gait parameters subjected to analysis in the experiment





Conclusions

- Gait parameters are differently affected by loss of PC
- Impairment of some gait parameters preceds significant loss of PC.