Longitudinal Characterization of the Cln6nclf Mouse Model of CLN6 Batten Disease - Characterization of Fine Motor Performance, Brain Pathology and Metabolic Changes

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1 INTRODUCTION

CLN6-Batten disease is a progressive rare disease characterized by neurodegeneration, motor and cognitive impairments, and the accumulation of autofluorescent storage material in lysosomes. In this study, we use a technique called kinematic gait analysis (KGA) to look for changes in gait associated with CLN6-Batten disease and advanced imaging technology to monitor changes in the brain in a mouse model of CLN6-Batten disease over time.

2 STUDY DESIGN AND METHODS

Cohort of 20 CLN6nclf and 20 WT mice (10 females + 10 males/group; number mice used for each modality stated in data figures). Fiducial Mark Extraction, – Motionize, TurboRARE: 78 µm in-plane, 0.45 mm slices, PRESS: Prefrontal Ctx, TE/TR 10/2000 ms, EPI-DTI: 30 diff dirs, 0-970 s/mm2, 80 µm in-plane resolution and 0.6 mm slices. TurboRARE: 78 µm in-plane, PRESS: Prefrontal Ctx, TE/TR 10/2000 ms, 2D-3D, 0.06-0.3 mm slices, 30 sec. resolution and 0.3 mm slices.

3 RESULTS

3.1 FDG PET shows widespread glucose uptake deficits in the 12 month CLN6nclf brain. At 12 months, we observed the most severe alterations in brain anatomy and metabolism, we found that FDG standard uptake values (SUV) were significantly compromised in all regions examined. CLN6nclf n = 16 (7f + 9m), WT n = 13 (7f + 6m). Data are mean ± SEM; unpaired t-test. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

3.2 Changes presented here are captured in reduced parameter setting which eventually can be translated to clinics.

4 CONCLUSIONS

- Cln6nclf mice show progressive and profound changes in brain anatomy, brain metabolism, and gait.
- These techniques here are able to reveal unique features about the CLN6-Batten disease mouse model that have not been previously described.
- All changes presented here are captured in reduced parameter set using contrastive PCA to produce a highly significant and non-invasive score of disease progression; see linked poster 031.14 for detailed description.
- Our findings provide robust and reliable tools in preclinical setting which eventually can be translated to clinics.

Acknowledgements – this work was supported by the National Institutes of Health (R01NS082283); JB, T2, DT and JW