Gaucher disease is the most common lysosomal storage disease. The neuronal disease variant is characterized by aggregated protein accumulations in the brain and associated neurological manifestations. The disease is autosomally recessively inherited and modeled by 4L/PS-NA mice that express low levels of prosaposin and saposins, as well as β-glucosidase (GCase) with a point mutation at V394L/V394L. Additionally, the disease can be modeled by treating mice with Conduril-betaxolol-Epoxide (CBE) a specific inhibitor of GCase activity.

To use these models for compound tests against the Gaucher disease a detailed characterization of these mice is needed. We thus analyzed 4L/PS-NA mice for their neuro- and non-neuronopathic features and CBE-treated wildtype mice for their neuronopathic phenotype.

**MATERIALS AND METHODS**

4L/PS-NA mice were tested behaviorally in the Wire Suspension test at the age of 8, 12, and 18 weeks as well as in the Rota Rod test at 12 and 18 weeks of age.

Wildtype mice lacking endogenous α-synuclein (C57BL/6JLibjnsdJ) were treated for 15 days daily intraperitoneally with 100 mg/kg CBE starting at 6 months of age. One day after the last treatment, animals were investigated in the Open Field test and on the second day in the Beam Walk test.

Furthermore, brain tissue of both models was analyzed for neuroinflammation by histological methods. The 4L/PS-NA mouse model was additionally examined for visceral symptoms.

**RESULTS**

**4L/PS-NA mouse model**

**Behavioral Phenotype**

- **Wire Suspension**
  - 4L/PS-NA mice present with a significantly reduced wire hanging time at the age of 18 weeks compared with age-matched controls.
  - Figure 1: Wire Suspension and Rota Rod Impairment in 4L/PS-NA mice.

**Neuroinflammation**

- GFAP (green) and DAPI (blue, merge) in the cortex of 18 weeks old 4L/PS-NA mice.

**CONCLUSION / SUMMARY**

In summary, 4L/PS-NA mice present with highly increased glial activation in the brain that is accompanied by strong motor deficits suggesting that 4L/PS-NA mice are a good model to study chronic neuronopathic type 3 Gaucher disease. Additionally, 4L/PS-NA mice present early alterations in visceral organs and thus further mimicking the non-neuronopathic phenotype of Gaucher disease. Treatment with CBE causes no motor deficits but strong neuroinflammation, suggesting that this induced model has in total a weaker phenotype compared to the 4L/PS-NA model.