Tetrahydrobiopterin Improved Clinical Phenotype in a Fatal Model of Krabbe Disease

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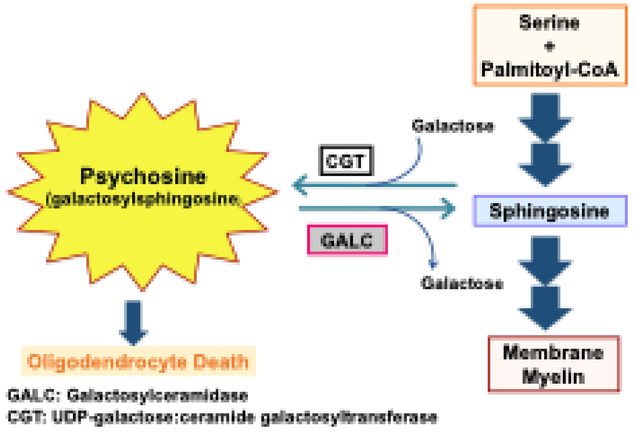
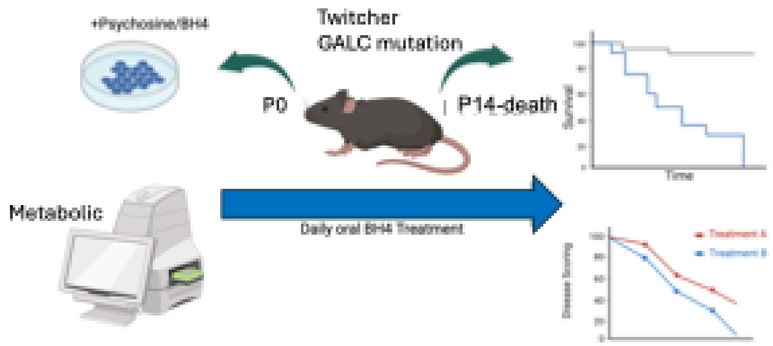
Background

- **Rare autosomal recessive leukodystrophy**
- Caused by **mutations in the *GALC* gene** → deficiency of **galactocerebrosidase (GALC)**
- Leads to accumulation of **psychosine**, a toxic metabolite
- **Incidence:** ~1 in 100,000 live births
- **There is no available treatment except HSPT**
- Different types and onset, infantile form is the most severe type
- Symptoms include weakness, tremor, spasticity, fever
- Mortality by age of 4 (infantile onset)



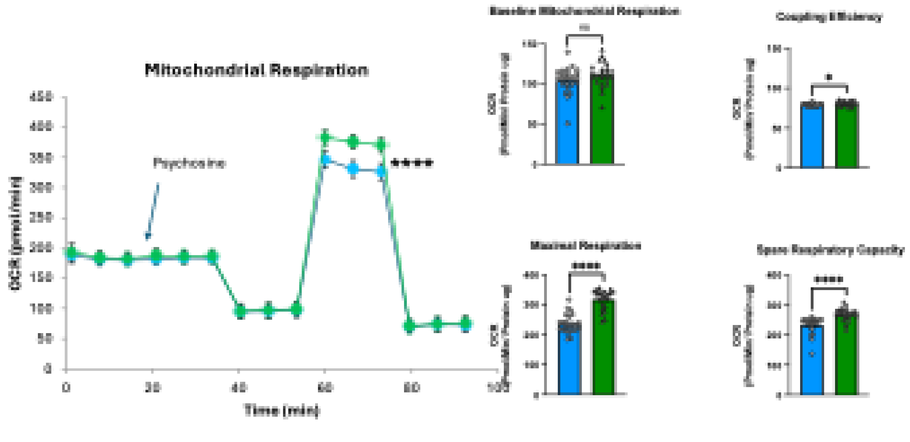
GALC: Galactosylceramidase
CGT: UDP-galactose:ceramide galactosyltransferase

Experimental Approach



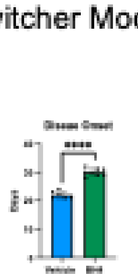
Results

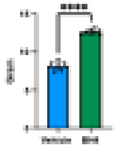
BH4 Reversed Psychosine Induced Mitochondrial Respiration Impairment

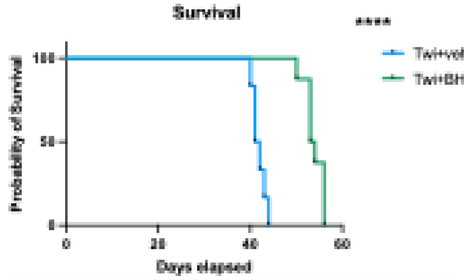


Results

Overall Improvement in Clinical Disease Outcomes in the Twitcher Model







Outcome	Vehicle	BH4	Improvement
Disease Onset (Day) Mean±SD	22±1.27	30±1.3	Delayed
Peak Weight(G) Mean±SD	8.2±0.62	12.6±0.34	Improved 38%
Survival (Day) Median	41.5	53.5	Increased 28%

Conclusion

- **BH4 improved mitochondrial respiration in the presence of inflammation**
- **BH4 Improved survival and overall wellness**
- **Further studies are needed to replicate and expand our current findings**

Acknowledgments

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