Repurposing of the anti-asthmatic drug Montelukast for the treatment of Parkinson’s disease

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BACKGROUND

Neuroinflammation caused by dysregulated leukotriene (LT) signaling may contribute to the pathogenesis of neurodegenerative diseases including Parkinson’s disease (PD). Montelukast (MTK) is an anti-inflammatory drug originally approved for the treatment of asthma. This study aims to evaluate the potential of MTK as a treatment for PD using the Line 61 o-synuclein transgenic mouse model.

RESULTS

- Improved motor coordination and balance: MTK treatment significantly improved the performance of transgenic mice in the beam walk test as compared to vehicle-treated transgenic mice.
- A significant reduction in the latency to start to traverse the beams from treatment week 5 to 10 suggests an effect of MTK on motivation.

CONCLUSION AND OUTLOOK

This study investigated the effects of a 10-week daily treatment with the anti-asthmatic drug MTK on the behavior of the Line 61 mouse model for PD. Significant genotype effects were detected in many functions, but not in emotional learning, activity, and anxiety. When comparing Tg MTK-treated and Tg vehicle-treated animals, significant improvements were detected in the beam walk test already after 5 weeks of treatment and a non-significant trend towards an improved performance in the Rotarod test was observed. In contrast, both groups showed similar muscle strength results in the wire suspension and grip strength test. This suggests, that MTK treatment has an early effect on motor coordination and balance rather than on muscle strength itself. In conclusion, these findings propose MTK as a possible treatment to alleviate motor impairments in PD.

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METHODS

Starting at an age of 2 weeks, 40 male transgenic (Tg) Line 61 mice and 40 male non-transgenic (nTg) littermates were treated daily orally with either MTK or vehicle for a total of 10 weeks. Behavioral tests were conducted at different time points of the treatment period to assess effects of MTK on motor function, activity and anxiety.

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Future plans: Sampled brain tissue and gastrocnemius muscles will further be analyzed immunohistochemically and biochemically to investigate cellular and molecular changes underlying the effect of MTK treatment on motor coordination and balance.