CHARACTERIZATION OF A-SYNUCLEIN OVEREXPRESSING MICE (PDGF A-SYN, D-LINE): BEHAVIORAL AND HISTOLOGICAL CHANGES THROUGHOUT ADULTHOOD AND AGING

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Introduction: The major feature in the pathology of Parkinson's disease is the Lewy body pathology, accumulations of a-synuclein protein. Transgenic mice overexpressing wild type a-synuclein, such as the D-Line, serve as important models for research and development. Thus, a thorough understanding of the long-term effects of a-synuclein overexpression on both structure and function of the brain is essential for the planning of experiments and the interpretation of results.

Aims: Characterization of the D-Line with regard to age-related expression of a-synuclein (murine and human isoforms) and behavior of transgenic mice and wildtype littermates.

Methods: Behavioral analysis of motor and cognitive function, and quantitative histological analysis of a-synuclein levels and Lewy body-like inclusions.

Results: Animals show an age dependent progression of motoric deficits in the Challenging Beam Walk Test. At 9 months first motor impairments are observed, but cognitive functions are normal until old age. Throughout different regions of the mouse brain expression and distribution of endogenous (murine) and transgene (human) expression of a-synuclein isoforms is changed age-dependently. In addition there is a clear progression in the formation of Lewy body-like inclusions throughout the brain.

Conclusions: Transgenic a-synuclein mice have distinct motoric but no cognitive deficits. Data also indicate that there are alterations in the a-synuclein expression throughout life. This transgenic mouse line is therefore a good tool to study basic mechanisms involved in the development of Parkinson's disease and should be of great help for the testing of new drugs targeting the disease.