Behavioral Characterization of the PS19 Mouse Model of Alzheimer's Disease

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BACKGROUND

Tau is a microtubule-associated protein and a primary component of neurofibrillary tangles – one of the major pathological hallmarks of Alzheimer´s disease. PS19 transgenic mice overexpressing the disease-associated P301S tau mutation, are shown to present strong tauopathy-related brain pathologies.
The aim of this study was to characterize the PS19 mice behaviorally and electromyographically for their cognitive and motor deficits, activity, and compound muscle action potential (CMAP), that can be successfully employed to test novel drug agents and therapeutic treatments.

MATERIAL & METHODS

For this study, 80 PS19 mice of mixed sex and 80 wild type (WT) littermates at the age of 2 to 6 months were included in a cross-sectional experiment.
Animals at the age of 2 to 4 months were evaluated in a behavioral test battery for cognitive deficits including the Y-maze, Morris water maze and fear conditioning test. Activity and motor deficits were evaluated in the open field and wire hanging test. Additionally, electromyography (EMG) was performed to measure CMAP.
Behavioral tests using 6 months old animals are still in progress.

RESULTS

Cognitive Deficits – Morris Water Maze

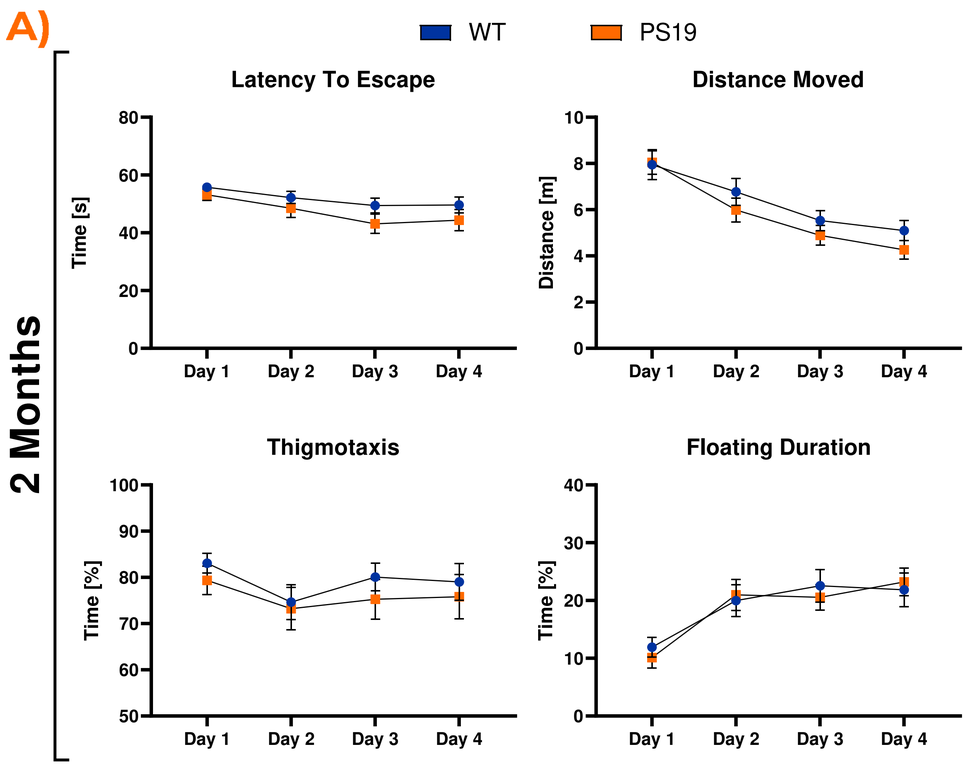
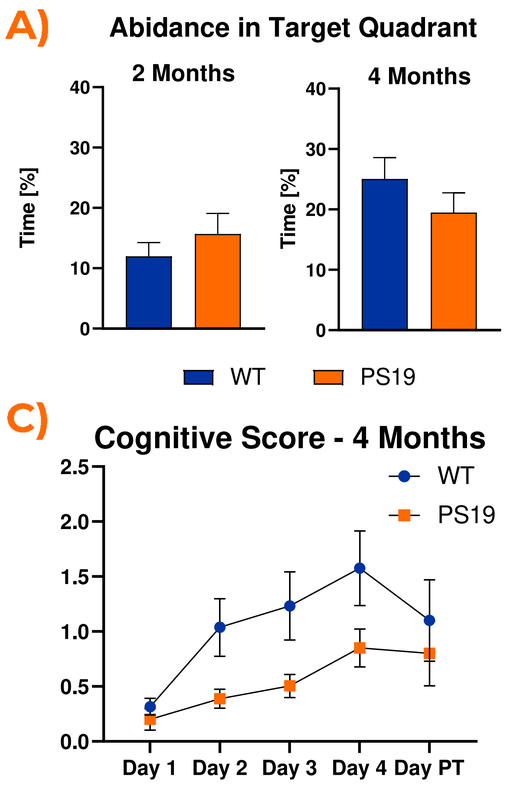


Figure 1. Morris water maze test of PS19 mice: Latency to escape (s), distance moved (m), thigmotaxis (%) and floating duration (%) in (A) 2 months old PS19 mice and (B) 4 months old PS19 mice compared to WT littermates.. n=20 / group. Two-way ANOVA followed by Bonferroni's *post hoc* test. Mean ± SEM. WT: wild type.

No significant differences were detected in the contextual fear conditioning and Y-maze test of 2 and 4 months old PS19 mice (data not shown).



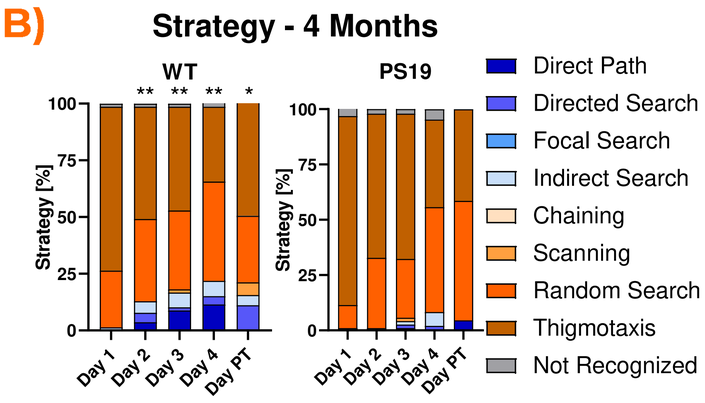


Figure 2. Morris water maze of PS19 mice: (A) Abidance in target quadrant (%) in probe trial of PS19 mice at the age of 2 and 4 months compared to WT littermates. Unpaired t-test, mean + SEM. (B) Strategy (%). Fisher's exact test for hippocampus-dependent and hippocampus- independent strategies of PS19 mice at the age of 4 months. (C) Cognitive scores of PS19 mice at the age of 4 months compared to WT littermates. Two-way ANOVA followed by Bonferroni's post hoc test, mean ± SEM. n=20 / group. WT: wild type.

Motor Deficits

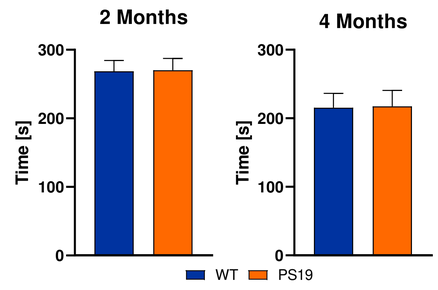


Figure 3 : Wire suspension test of PS19 mice: Hanging time (s) of 2 and 4 months old PS19 mice compared to WT littermates. n=20 / group. Unpaired t-test, mean + SEM.

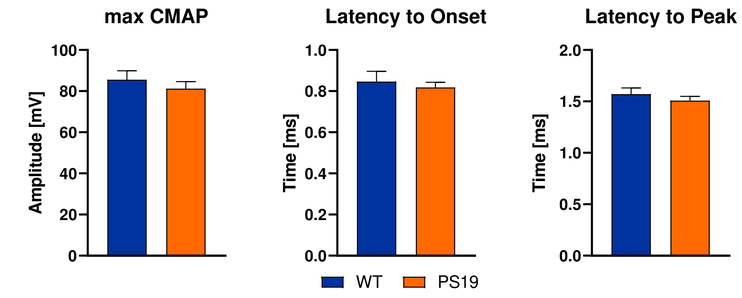


Figure 4 : EMG recordings of 4 months old PS19 mice: Max CMAP (mV), latency to onset (ms) and latency to peak (ms). n=14 / group. Unpaired t-test, mean + SEM.

Activity – Open Field

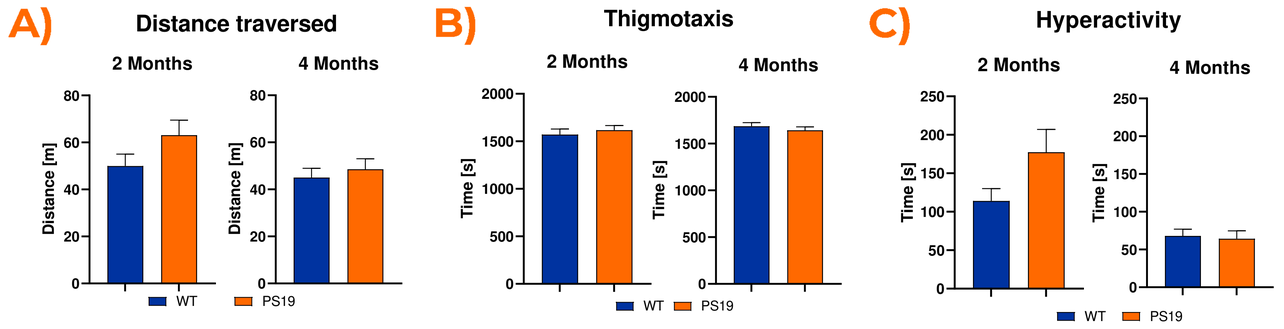


Figure 5 . Open field test of PS19 mice. (A) Distance moved (m), (B) thigmotaxis (s) and (C) hyperactivity (s) of PS19 mice and WT littermates at the age of 2 and 4 months. n=20 per group. Unpaired t-test or Mann-Whitney test, mean + SEM.

CONCLUSION

Our results show that the PS19 mice already start to show cognitive deficits at 4 months of age in the absence of motor deficits or emotional disturbances. Additionally, with a more detailed analysis of strategy learning patterns, we were able to establish a sensitive tool to detect changes in spatial learning. Analysis of 6 months old animals are currently ongoing to complete the characterization of this valuable model to evaluate new compounds against Alzheimer`s disease.

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