Comprehensive Behavioral Characterization of Aged Wild Type Mice

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Background

Aging is a process that leads to profound structural and physiological changes in the brain which are often accompanied by behavioral impairments and an increased susceptibility to neuropsychiatric and neurodegenerative diseases. Aged mice thus serve as an important model in biological research offering a powerful instrument for understanding the complex processes of aging. To gain a better understanding of how emotion, motor performance, and cognition affect each other in aged mice, we have set up a comprehensive test battery.

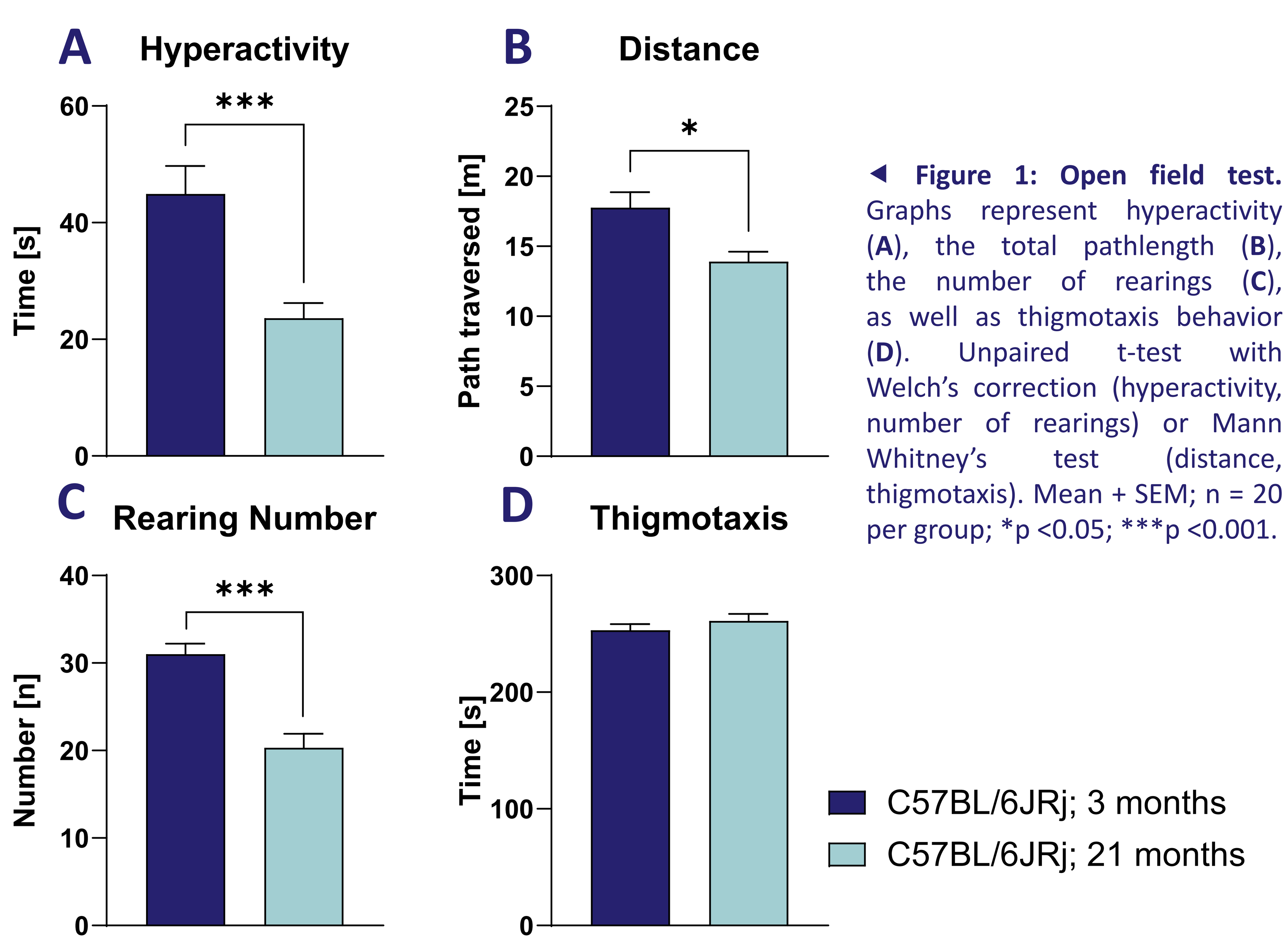
Material and Methods

Aged, 21 months old C57BL/6 wild type mice were evaluated for behavioral deficits by comparison to C57BL/6 mice at the age of 3 months. To assess changes in motor performance, general health and activity, the open field test as well as the modified Irwin test battery, including the wire hanging test, were performed. To assess spatial learning abilities, mice were tested in the Barnes maze. Procedural learning was assessed in the T-maze. Finally, emotional learning was measured in the passive avoidance test.

Results

Open Field Test

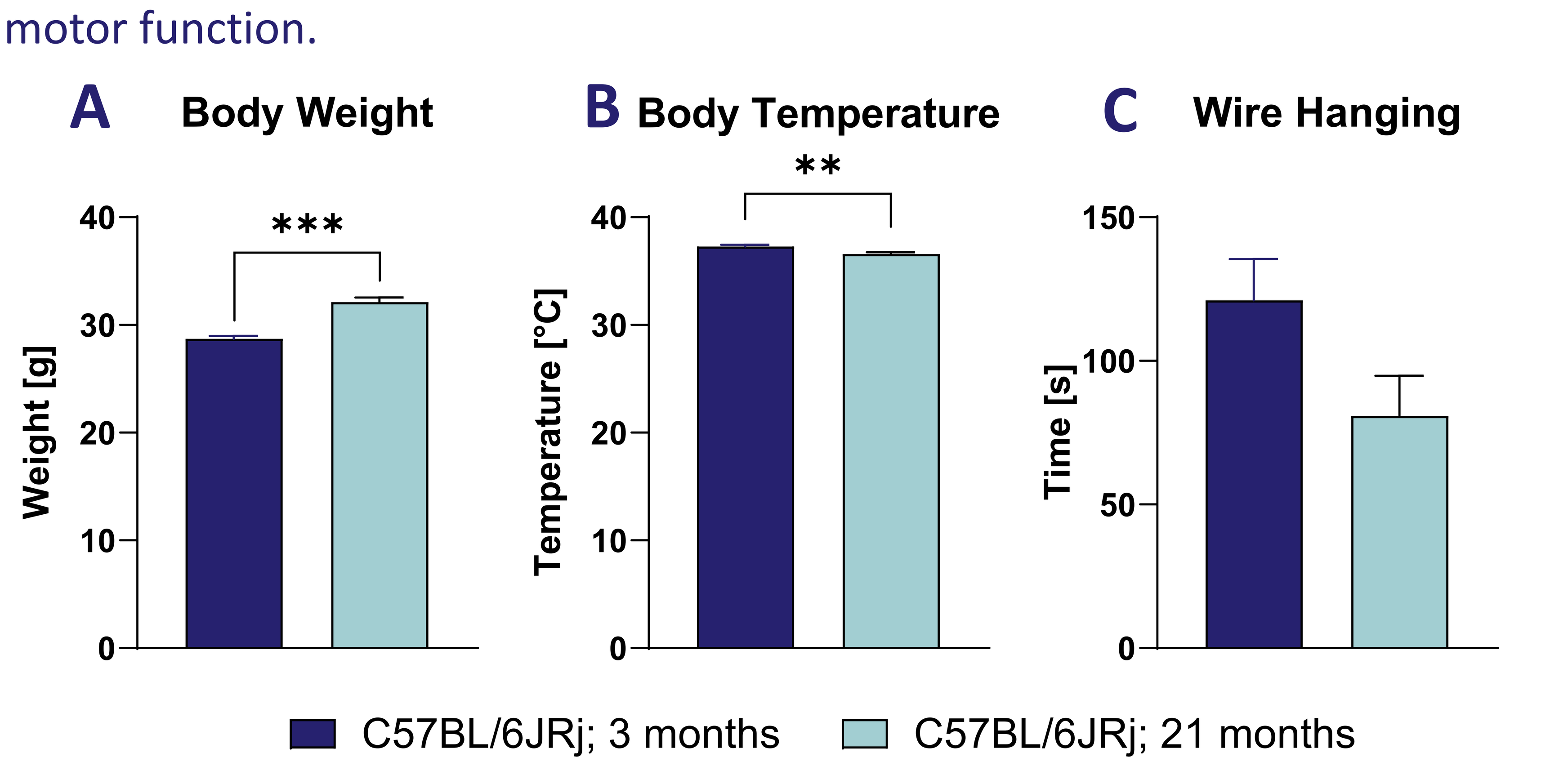
Aged mice exhibited reduced exploratory behavior compared to young control mice, as indicated by reduced general activity, pathlengths and number of rearings (**Figure 1 A-C**). Notably, irrespective of age, all mice spent most time in thigmotaxis, as a measure of anxiety (**Figure 1 D**).



◄ **Figure 1: Open field test.** Graphs represent hyperactivity (**A**), the total pathlength (**B**), the number of rearings (**C**), as well as thigmotaxis behavior (**D**). Unpaired t-test with Welch's correction (hyperactivity, number of rearings) or Mann Whitney's test (distance, thigmotaxis). Mean + SEM; n = 20 per group; *p <0.05; ***p <0.001.

Modified Irwin Test

Aged mice showed significantly higher body weight than young controls; at the same time body temperature was found to be slightly but significantly decreased. Although not statistically significant (3 months vs. 21 months: p = 0.051), aged mice exhibited a reduced latency to fall in the wire hanging test compared to young control mice, indicating an age-dependent decline of motor function.



▲ **Figure 2: Modified Irwin test.** Graphs represent body weight (**A**), body temperature (**B**) and the latency to fall in the wire hanging test (**C**). Unpaired t-test with Welch's correction. Mean + SEM; n = 20 per group; **p <0.01; ****p <0.001.

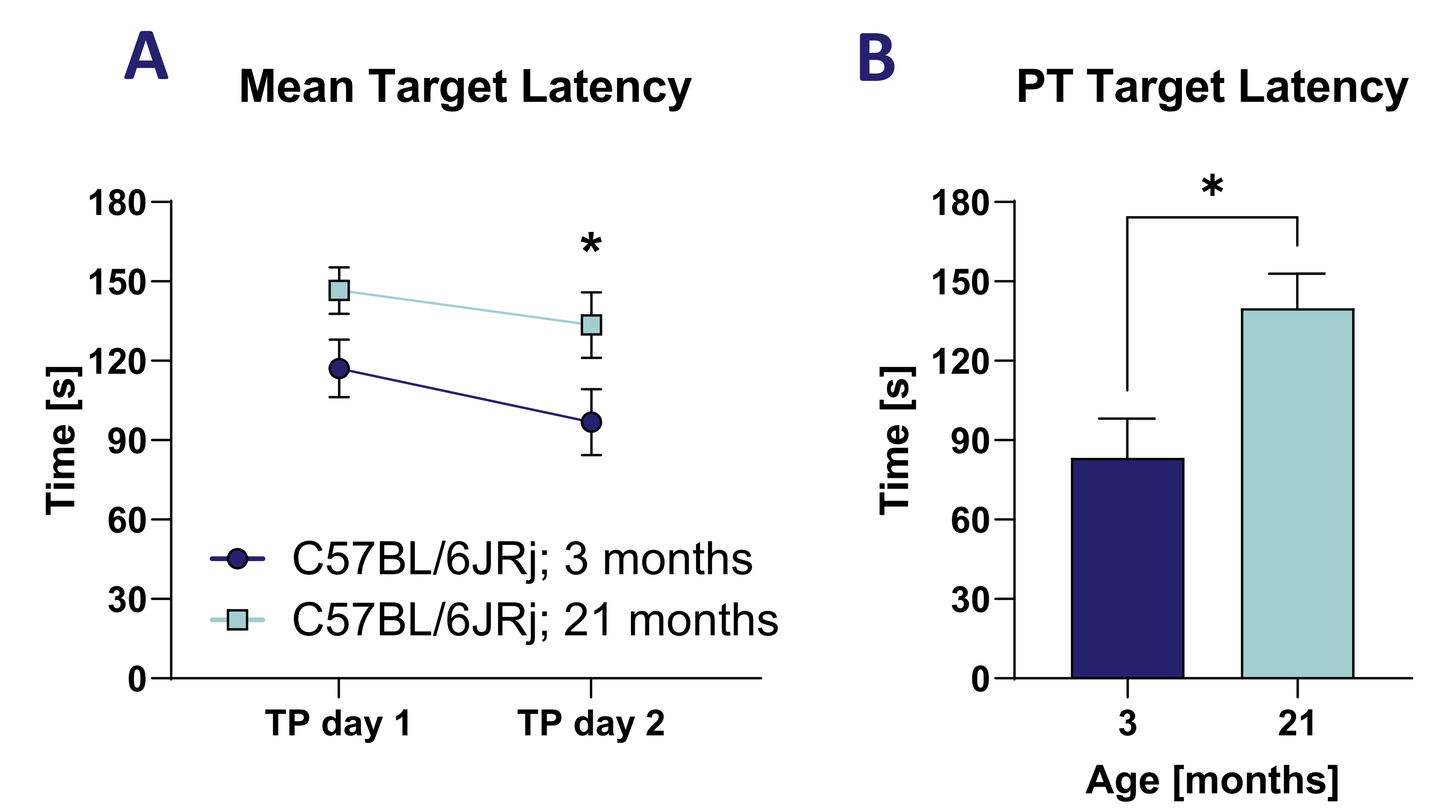
Conclusion

Results from this behavioral characterization study provide extensive insight into different aspects of age-associated cognitive decline in C57BL/6 wild type mice, taking motor disturbances and emotional changes into account. Together with already published data, these results corroborate the value of aged mice in investigating the deleterious effects of aging and for testing of novel drug agents for longevity.

Results

Barnes Maze

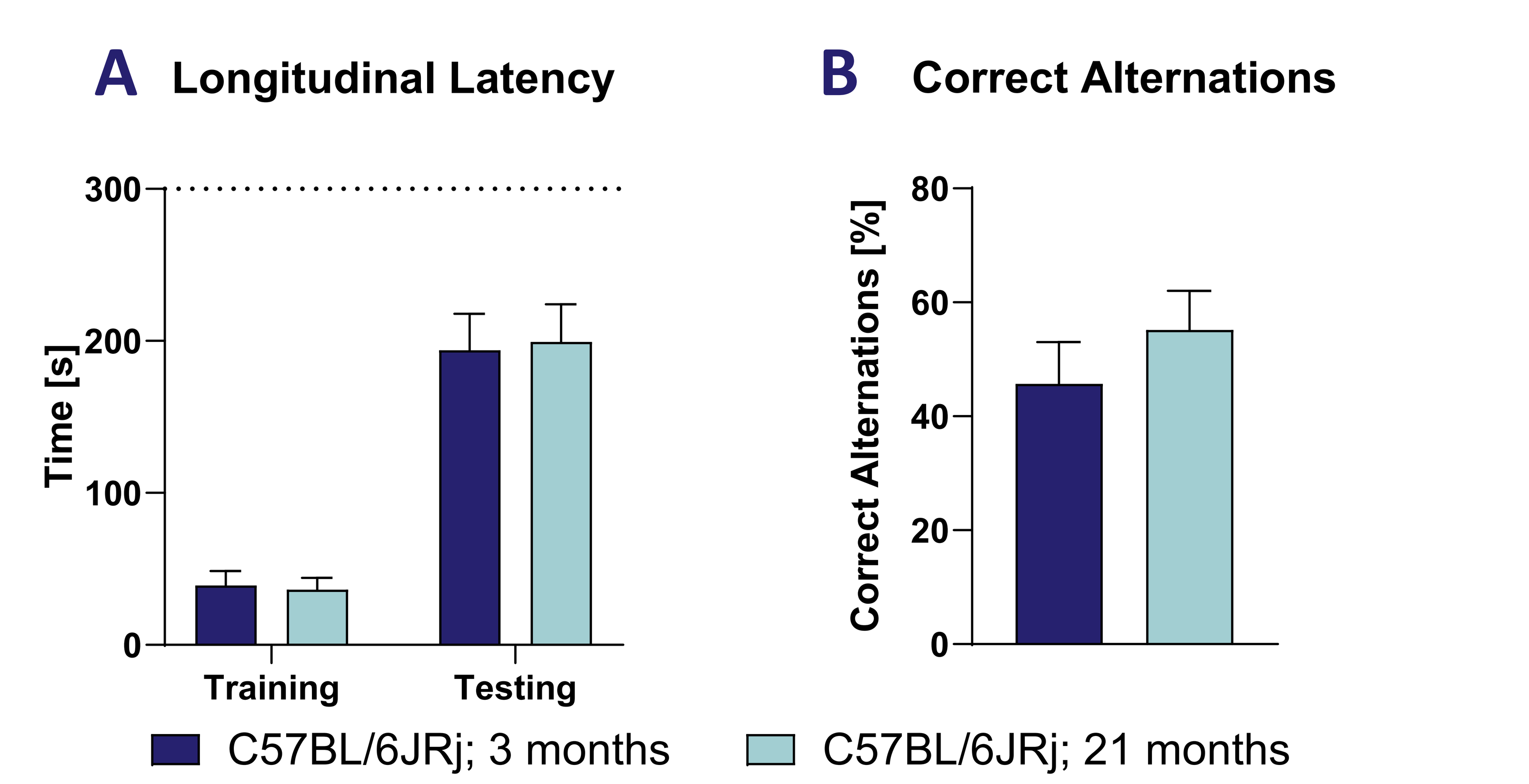
Compared to 21 months old mice, young control animals showed a reduced latency to enter the target hole during the training phase (TP) reaching significance on the second training day (**Figure 3 A**). This effect most prominently occurred also during the final probe trial (PT) on the subsequent testing day 3 (**Figure 3 B**).



▲ **Figure 3: Barnes maze – longitudinal analysis.** Graphs represent the latency to enter the target hole during the training phase (TP) (**A**) and the latency to find the target hole during the probe trial (PT) (**B**). Two-way ANOVA followed by Bonferroni's *post hoc* test (**A**) and Mann Whitney's test (**B**). Mean ± SEM (**A**); Mean + SEM (**B**); n = 20 per group; *p <0.05.

Passive Avoidance Test and T-Maze

While latencies to enter the dark compartment were low on the first training day, vehicle treated young and old mice alike showed significantly increased hesitation to enter the dark compartment on the testing day. No differences could be observed between 3 months old and 21 months old animals (**Figure 4 A**). Both 3 months and 21 months old animals achieved roughly 50-60% of correct alternations in the spontaneous alternation test, indicating close to random entry of the arms of the maze.



▲ **Figure 4: Passive avoidance test and T-maze.** Graphs represent latency to enter the dark compartment in the passive avoidance test (**A**) and correct alternations during T-maze testing (**B**). No statistically significant group differences were detected (**B**). Two-way ANOVA followed by Bonferroni's *post hoc* test (**A**) and unpaired t-test with Welch's correction (**B**). Mean + SEM; n = 20 per group.

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