Serial Reversal in 3xTg-AD Mice

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Subjects

Due to the small number of male mice, sexes are lumped together in this analysis. There are 29 mice included in this study. There was no significant difference in age between the 3xTg-AD and B6129 mice (t_{27} = -1.6, p = 0.126; Table 1).

Training

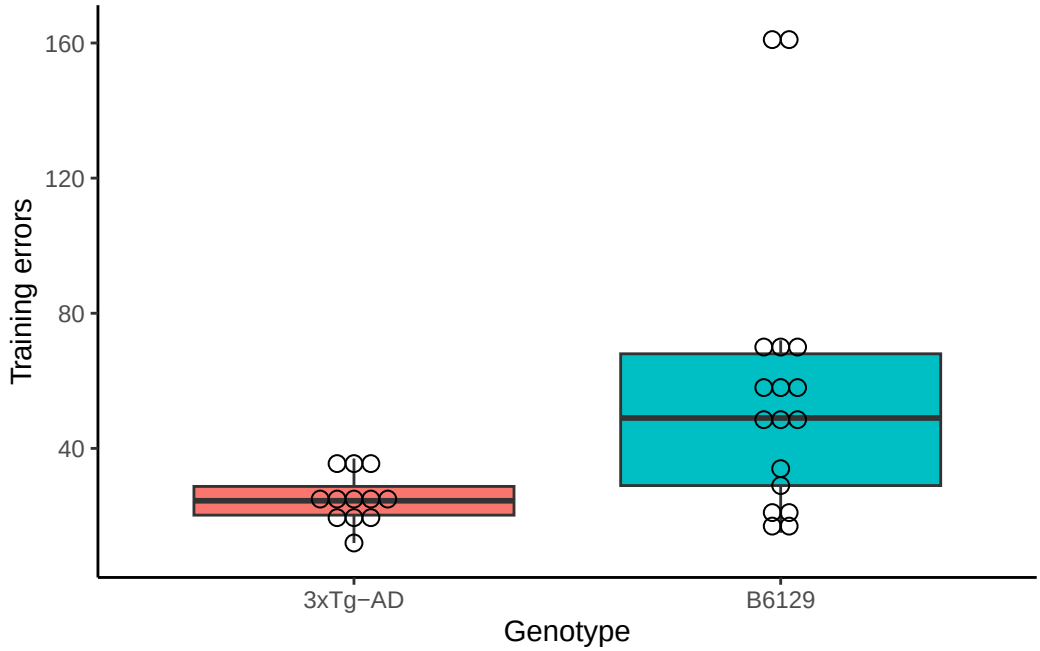

Figure 1: Errors madeduring training.

Table 1: Demographics of mice tested.

Genotype	Sex	Mean age (days)	Minimum age (days)	Maximum age (days)	N
3xTg-AD	Female	296.27	154	558	11
3xTg-AD	Male	366.00	366	366	1
B6129	Female	403.00	172	756	13
B6129	Male	373.00	298	574	4

A t-test was used to compare the number of errors made during training. The B6129 mice (58 ± 43) made more errors than the 3xTg-AD mice (58 ± 43; t_{17} = -3.1, p = 0.0059, Figure 1).

Difference scores

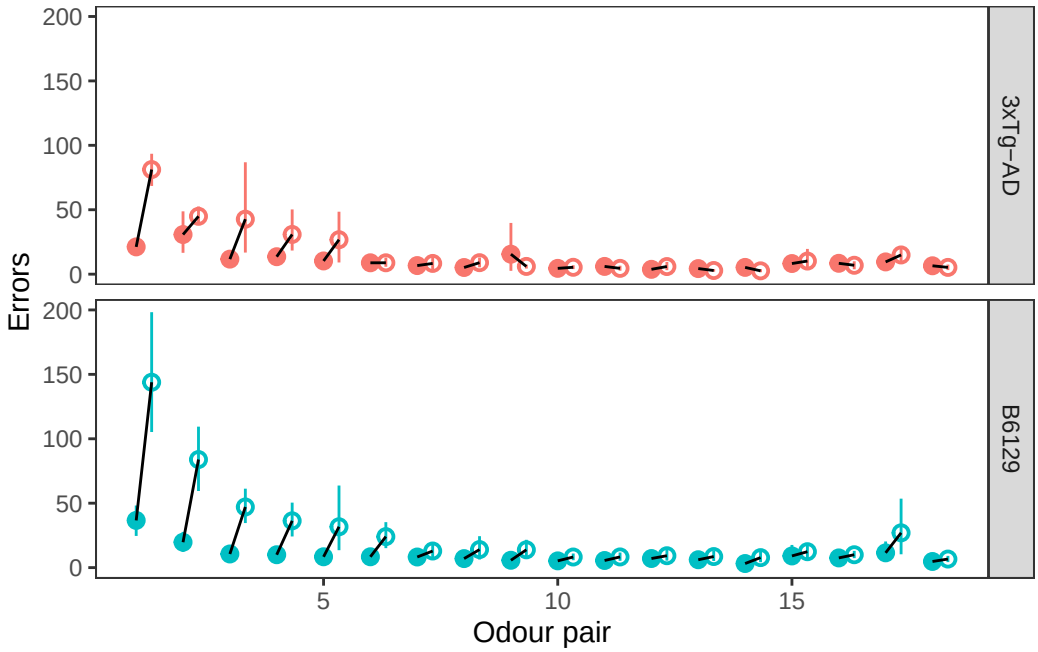

Figure 2: Errors (±95% CI) made by the mice at on each odour pair.

The sequence of odour pairs was divided into thirds, and ANOVAs examining the differences between the errors on the discrimination trials and the reversal trials were run on each third. Greenhouse-Geisser corrections were applied when Mauchly's test for sphericity detected that within-subjects factors violated sphericity.

In the first third of odour pairs, there were significant effects of genotype ($F_{(1,19)}$ = 12, p = 0.003, , η^2_G = 0.08) and odour pair ($F_{(2.2,42)}$ = 8.5, p < 0.001, η^2_G = 0.28; Figure 2). There was no significant interaction ($F_{(2.2,42)}$ = 0.74, p = 0.5, η^2_G = 0.032)). Post-hoc Tukey HSD tests found that there was a significant difference between the B6129 and 3xTg-AD mice on the second odour pair (p = 0.0178).

On the second and last thirds there were no significant effects (p's >= 0.076).

Discrimination

The sequence of odour pairs was divided into thirds, and ANOVAs examining the the errors on the discrimination trials were run on each third (Figure 3). Greenhouse-Geisser corrections were applied when Mauchly's test for sphericity detected that within-subjects factors violated sphericity.

In the first third of trials there was a significant effect of odour pair ($F_{(2.8,71)}$ = 10, p < 0.0001, η^2_G = 0.24), but no effect of genotype ($F_{(1,25)}$ = 0.003, p = 0.96, η^2_G = 2.6e-05), nor an interaction ($F_{(2.8,71)}$ = 2.3, p = 0.09, η^2_G = 0.064).

There were no significant effects in the second or last thirds of trials (p's >= 0.11).

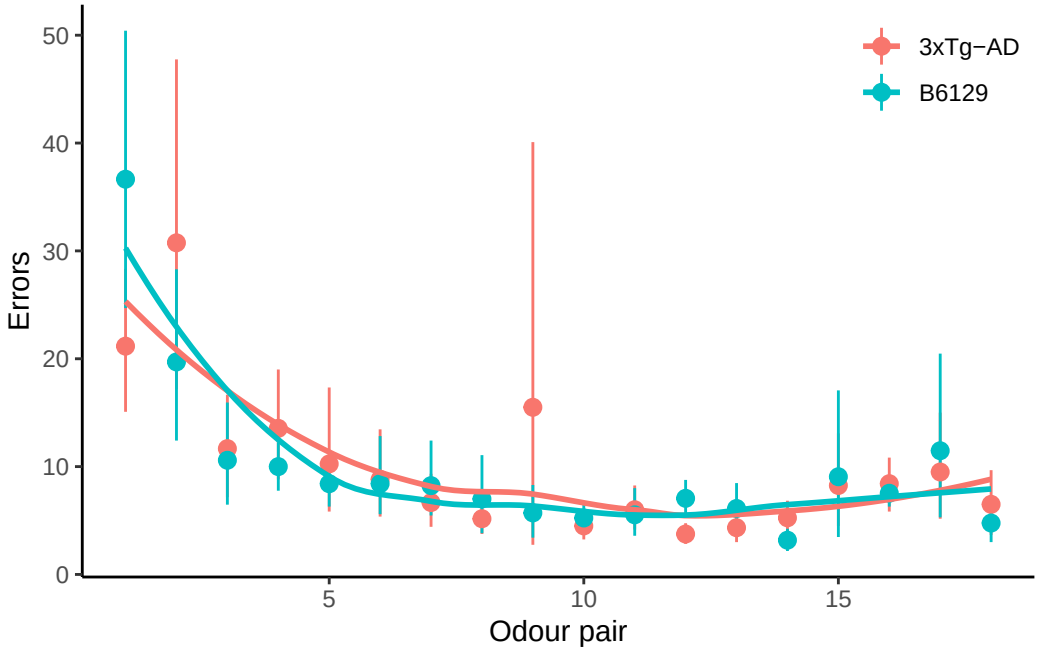

Figure 3: Errors (±95% CI) made by the mice at on each odour pair during the discrimination stages.

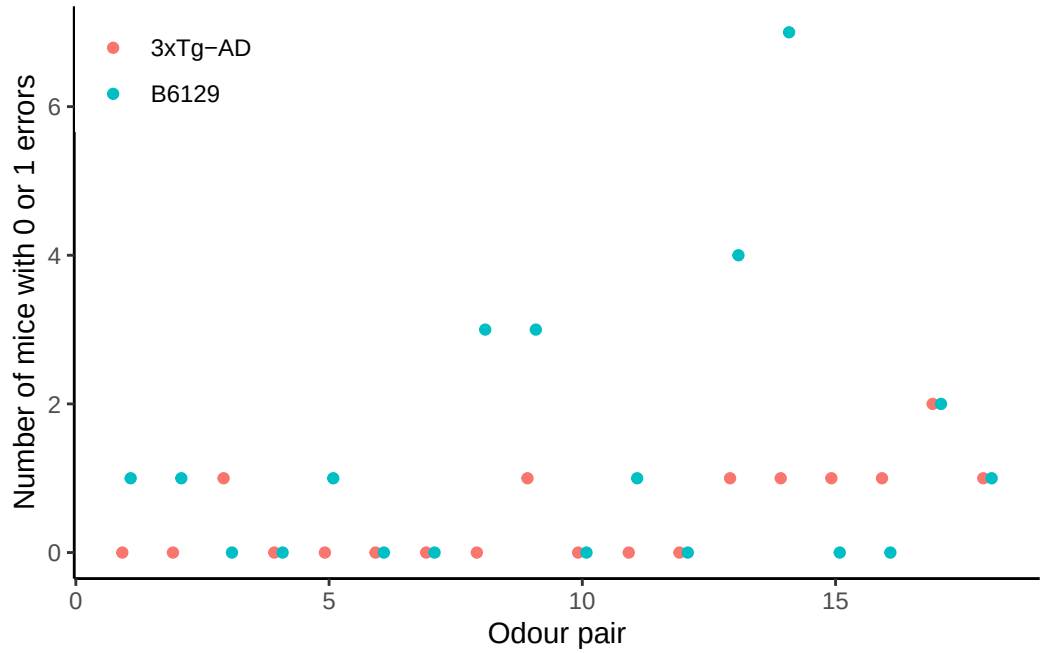

Figure 4: Number of mice showing errorless learning on each odour pair during discrimination.

Near errorless learning

There were 32 instances of mice making a single error on the initial discrimination of the odour pair, and 1 instance of a mouse making zero errors (Figure 4). With 19 mice passing at least one discrimination with just one or zero errors. One mouse, a B6129, had one or fewer errors on the initial discrimination of 6 odour pairs.

Pearson's χ^2 tests with Yate's continuity corrections were run on the number of mice showing errorsless learning. The χ^2 on the effect of odour pair was significant ($\chi^2_{17} = 47$, $p < 0.001$), while the χ^2 on the effect of genotype was not ($\chi^2_1 = 2.2$, $p = 0.136$).

Age effects

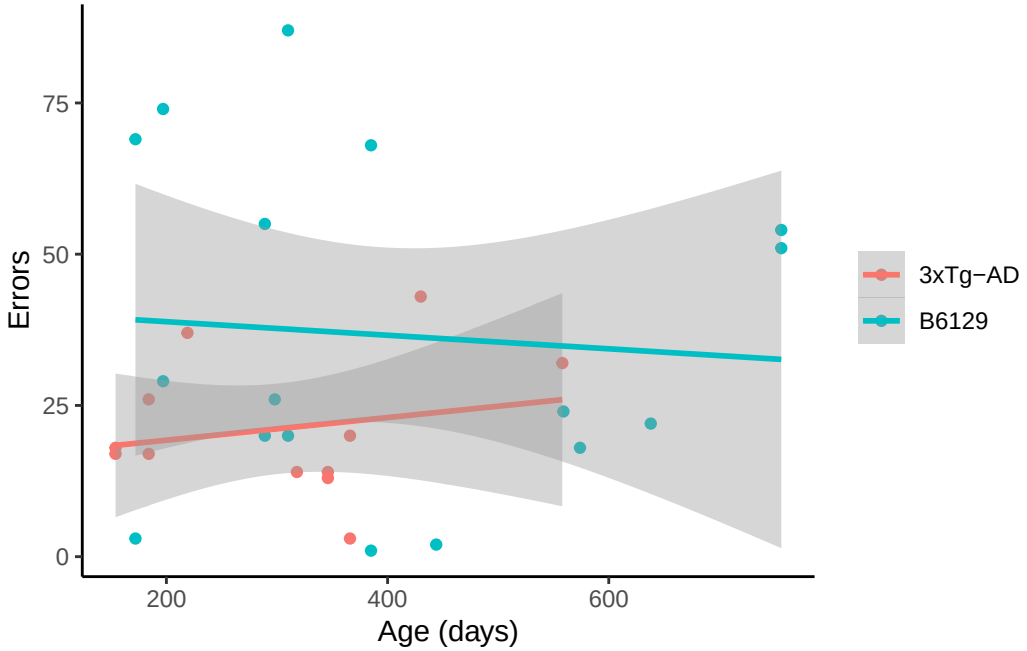

Figure 5: Correlation between age and errors made on odour pair one discrimination.

Pearson correlations were used to compare the number of errors made on odour pair one to the age of the mice for each genotype (Figure 5). The correlations were not significant for either the B6129 ($r = -0.08$, $p = 0.76$), nor the 3xTg-AD ($r = 0.21$, $p = 0.519$) mice.

Reversal

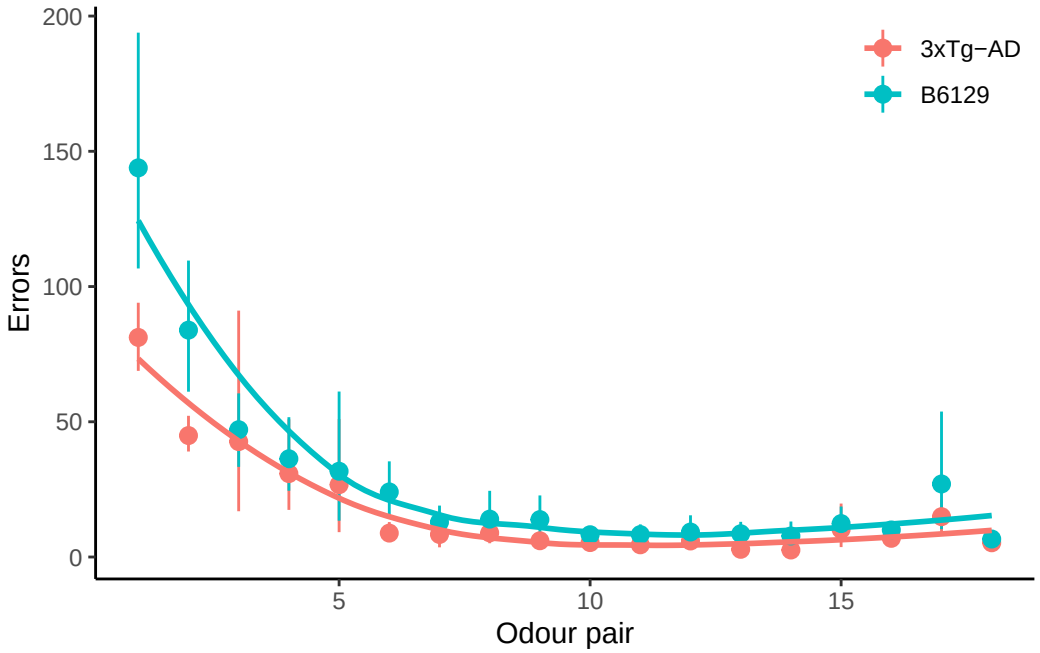

Figure 6: Errors (±95% CI) made by the mice at on each odour pair during the reversal stages.

The sequence of odour pairs was divided into thirds, and ANOVAs examining the the errors on the reversal trials were run on each third (Figure 6). Greenhouse-Geisser corrections were applied when Mauchly's test for sphericity detected that within-subjects factors violated sphericity.

In the first third of trials there were significant effects of odour pair ($F_{(2.5,50)} = 12$, $p < 0.0001$, $\eta^2_G = 0.34$), and of genotype ($F_{(1,20)} = 5.6$, $p = 0.028$, $\eta^2_G = 0.043$), but no interaction ($F_{(2.5,50)} = 1.6$, $p = 0.2$, $\eta^2_G = 0.064$).

Post hoc Tukey HSD tests found that there were significant genotype differences on odour pairs 2 (adjusted $p = 0.0277$) and 6 (adjusted $p = 0.0325$).

There were no significant effects in the second or last thirds of trials (p's >= 0.12).

Near errorless learning

There were 26 instances of mice making a single error on the reversal of the odour pair, and 6 instances of a mouse making zero errors (Figure 7). With 16 mice passing at least one reversal with just one or zero errors. One mouse, the same B6129 mentioned in the discrimination, had one or fewer errors on the reversal of 4 odour pairs.

Pearson's χ^2 tests with Yate's continuity corrections were run on the number of mice showing errorsless learning. The χ^2 on the effect of odour pair was significant (${\chi^2}_{17} = 39$, $p = 0.00186$), while the χ^2 on the effect of genotype was not (${\chi^2}_1 = 2.7$, $p = 0.101$).

Age effects

Pearson correlations were used to compare the number of errors made on odour pair one to the age of the mice for each genotype (Figure 5). The correlations were not significant for either the B6129 ($r = 0.3$, $p = 0.259$), nor the 3xTg-AD ($r = 0.1$, $p = 0.766$) mice.

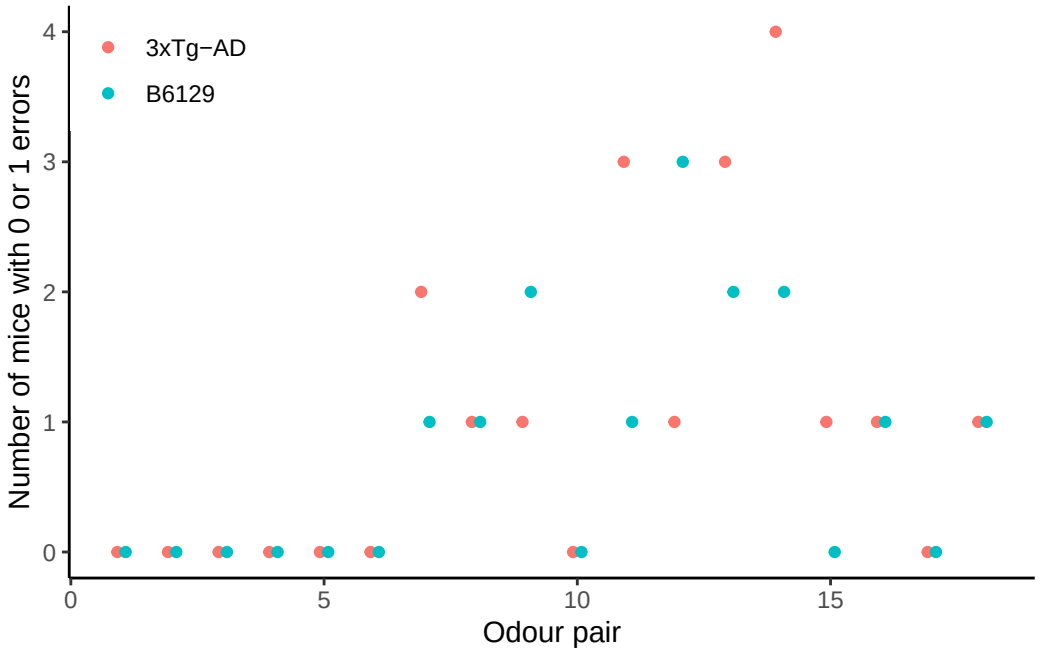

Figure 7: Number of mice showing errorless learning on each odour pair during reversal

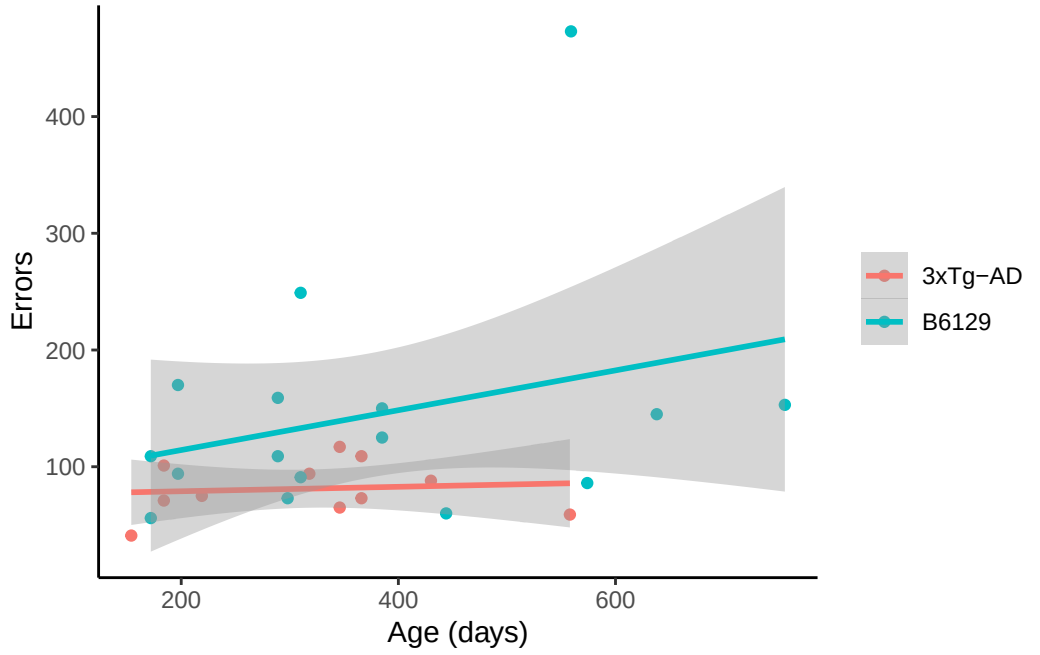

Figure 8: Correlation between age and errors made on odour pair one reversal.

Total errors

An ANOVA was used to assess the total errors made during the discrimination and reversal trials. There was a significant effect of genotype ($F_{(1,27)} = 6.6$, $p = 0.016$, $\eta^2_G = 0.2$; Figure 9).

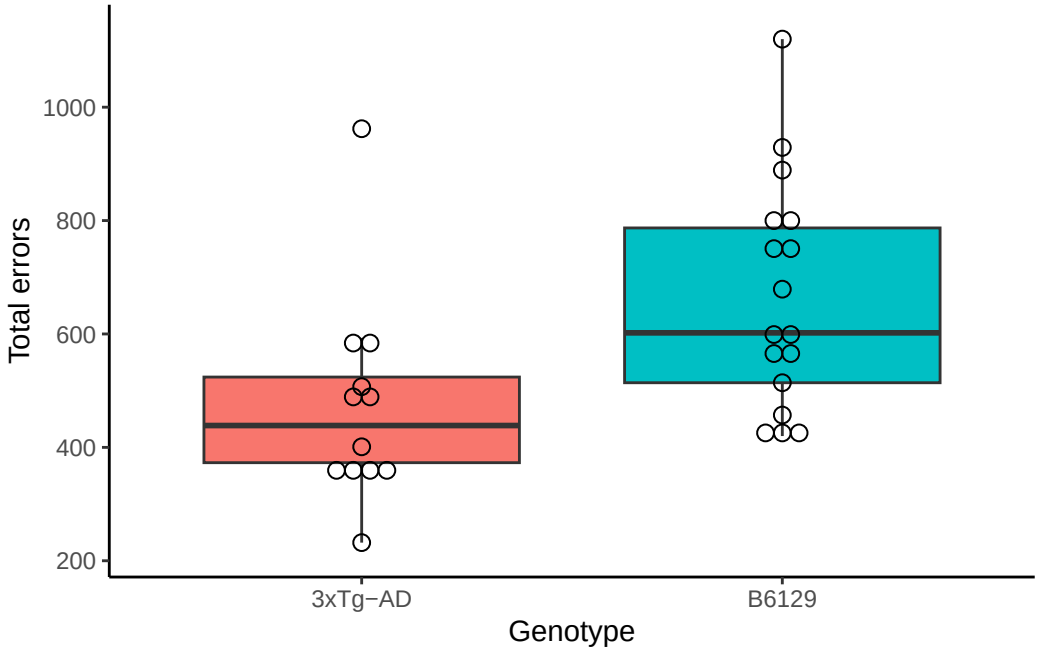

Figure 9: Total errors made, excluding retest.

Age effects

Pearson correlations were used to compare the total number of errors made to the age of the mice for each genotype (Figure 10). The correlations were not significant for either the B6129 ($r = 0.19$, $p = 0.468$), nor the 3xTg-AD ($r = -0.16$, $p = 0.623$) mice.

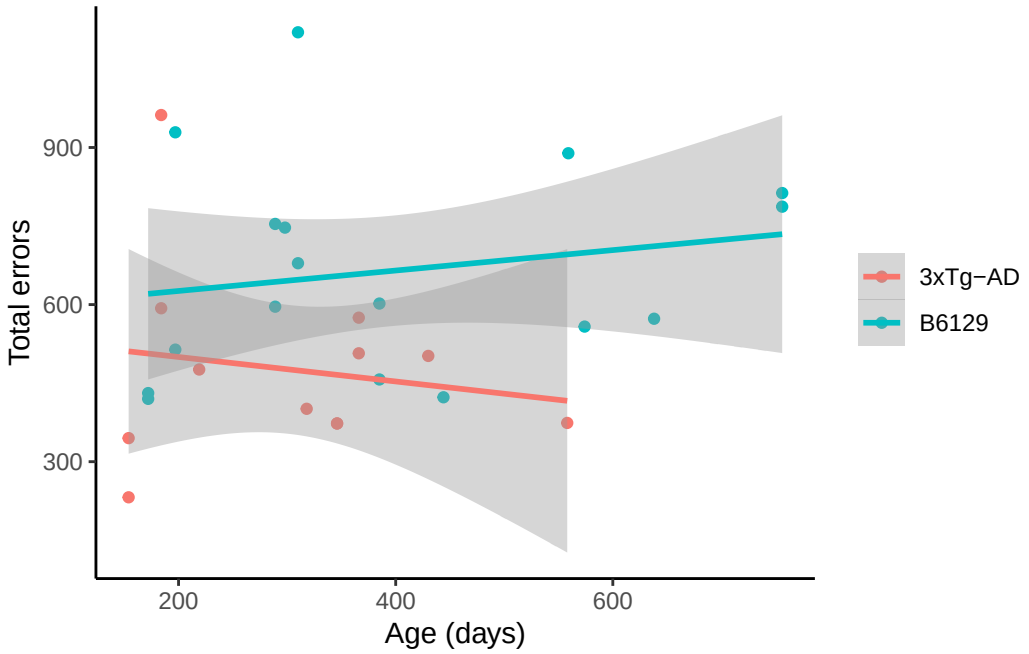

Figure 10: Correlation between age and total errors made.

Retest

Due to mice dying, only 15 B6129 and 8 3xTg-AD mice were given the retest.

The retest occurred between 30 and 94 days after the final reversal. There was no difference between between the days until the retest for the B6129 (55 ± 24) and 3xTg-AD (72 ± 23; $t_{15} = 1.7$, $p = 0.113$).

An ANOVA was used to assess the number of errors made during the retest. There was no significant effect of genotype (($F_{(1,21)} = 0.17$, $p = 0.69$, $\eta^2_G = 0.008$; Figure 11)

A paired t-test was used to compare the number of errors made duringthe retest to the numbers of errors made on the final odour discrimination. The mean number of errors made during the retest (37 ± 18) was significantly higher than the errors made on the final odour discrimination (5.4 ± 5.3; $t_{22} = 8.7$, $p < 0.0001$).

Age effects

Pearson correlations were used to compare the number of errors made on the retest to the age of the mice for each genotype (Figure 12). The correlations was not significant for the B6129 ($r = 0.34$, $p = 0.214$), but was for the 3xTg-AD ($r = -0.72$, $p = 0.0448$) mice.

Time from last test effect

Pearson correlations were used to compare the number of errors made on the retest to the days since the final reversal (Figure 13). There was a significant, positive correlation for the B6129 mice ($r = 0.62$, $p = 0.013$), but not for the 3xTg-AD mice ($r = 0.32$, $p = 0.441$).

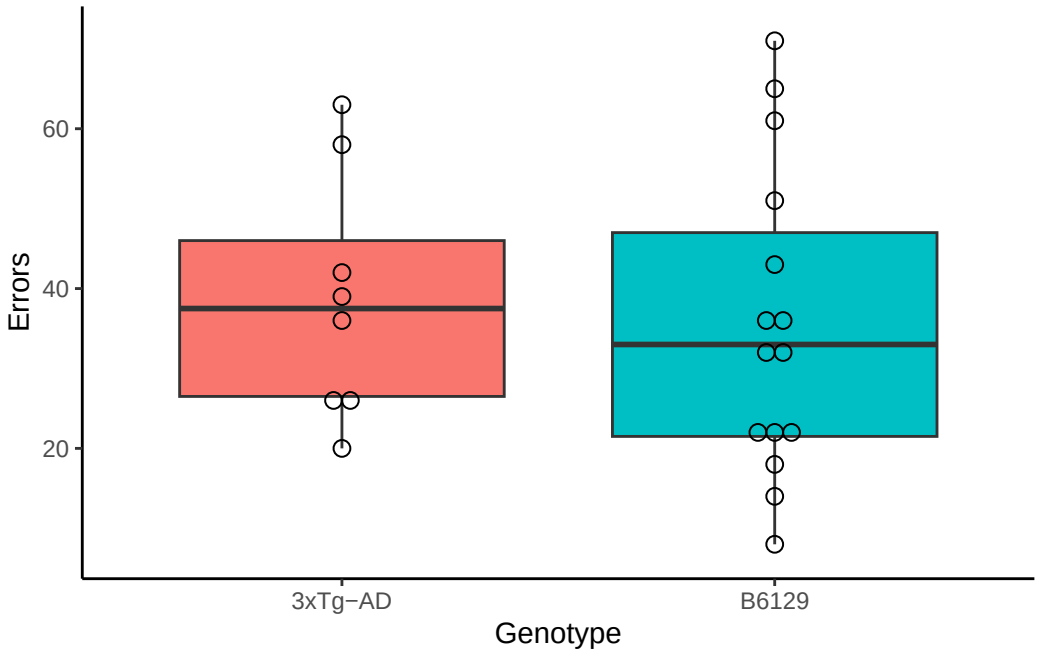

Figure 11: Total errors made during retest.

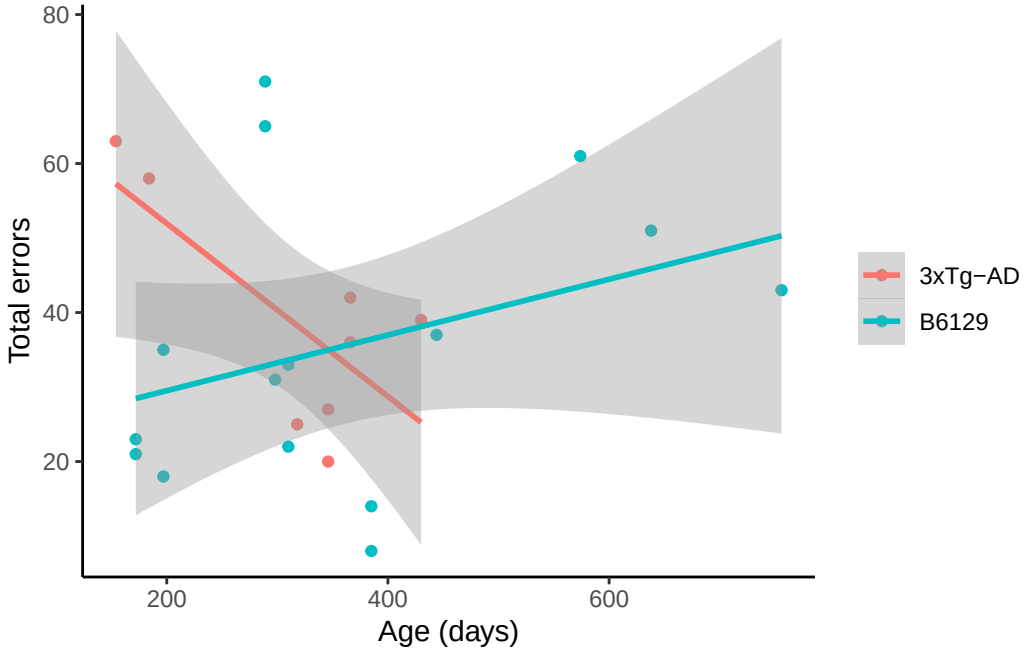

Figure 12: Correlation between age and errors made on the retest.

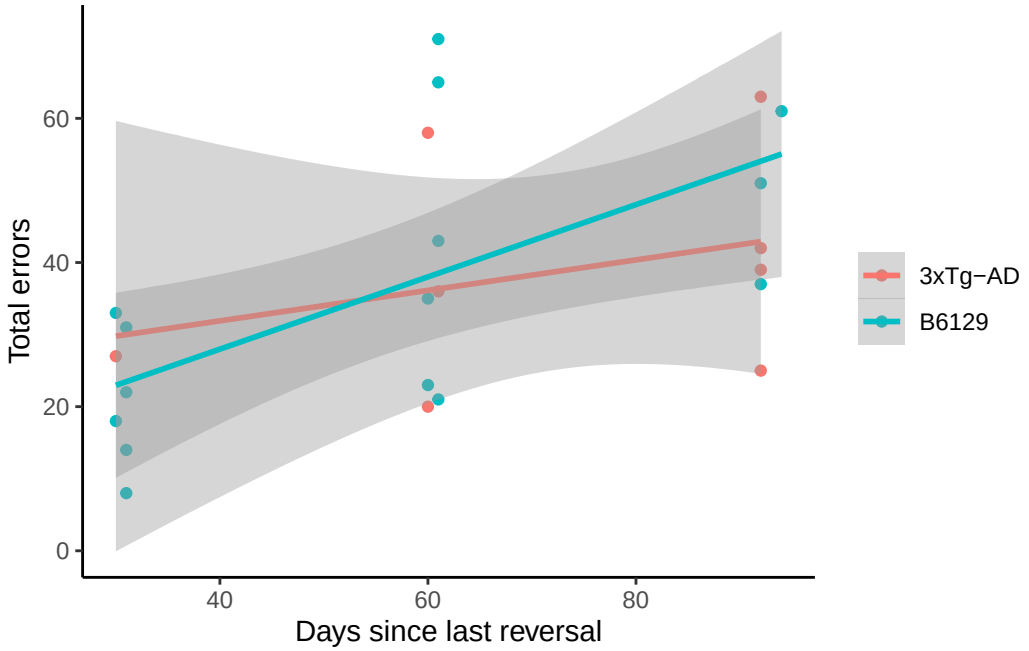

Figure 13: Correlation between days after last reversal and errors made on the retest.