

Serial Reversal in 3xTg-AD Mice

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Subjects

Due to the small number of male mice, only females are included in this analysis. There are 24 female mice included in this study. There was no significant difference in age between the 3xTg-AD and B6129 mice ($t_{20} = -1.5$, $p = 0.149$; Table 1).

Discrimination

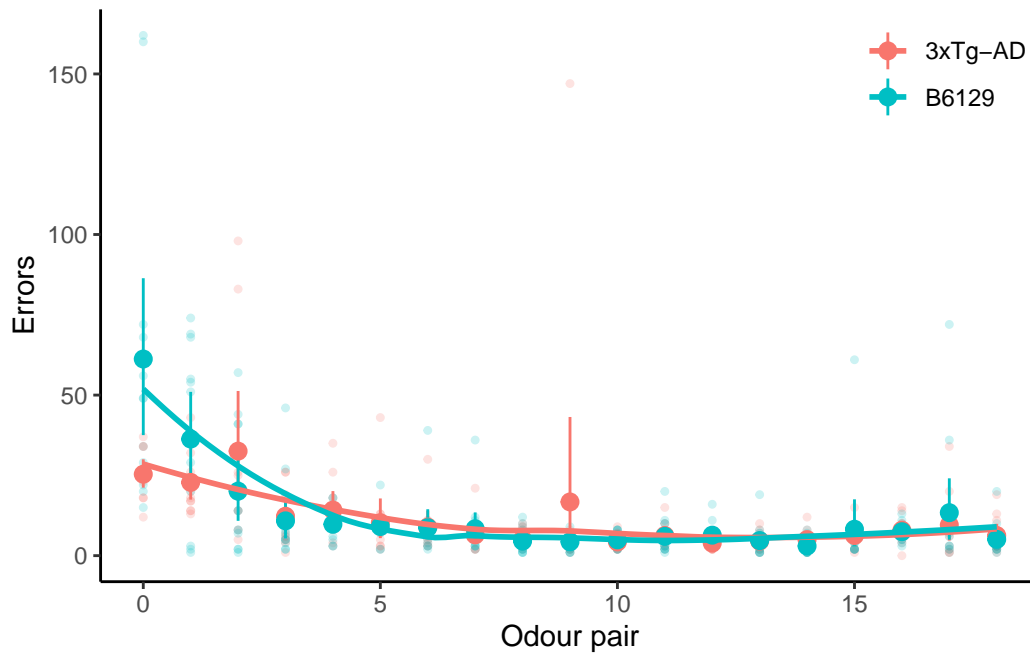


Figure 1: Errors ($\pm 95\%$ CI) made by the mice at on each odour pair during the discrimination stages.

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

Table 2: AICc model table for discrimination.

geno	op	geno:op	df	logLik	AICc	delta	weight
	-1.28		4	-1922.91	3853.92	0.00	0.46
+	-1.01	+	6	-1921.19	3854.57	0.65	0.33
+	-1.28		5	-1922.69	3855.52	1.60	0.21
			3	-1959.86	3925.78	71.86	0.00
+			4	-1959.62	3927.33	73.41	0.00

Table 3: AICc model table for near errorless learning during discrimination.

geno	df	logLik	AICc	delta	weight
+	3	-108.20	222.46	0.00	0.54
	2	-109.36	222.75	0.29	0.46

The discrimination trials were assessed with linear mixed effects models on the number of errors made on each odour pair. The errors made decreased as the mice advanced through the odour pairs (Figure 1). The model with just an effect of odour pair best explained the data (Table 2), this model differed from the null model ($\chi^2_1 = 74, p < 0.0001$).

Near errorless learning

There were 29 instances of mice making a single error on the initial discrimination of the odour pair, and 1 instance of a mouse making zero errors. With 17 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.

During the second half of the experiment, odour pairs 10 through 18, the B6129 made an average of 6.6 ± 9.3 errors, while the 3xTg-AD mice made 6 ± 4.9 errors. This difference was not significant ($t_{181} = -0.58, p = 0.565$).

Generalized linear mixed effects models were used to examine the proportion of mice making one or zero errors on each odour pair. The model with an effect of genotype best explained the data (Table 3), but did not differ from the null model ($\chi^2_1 = 2.3, p = 0.128$).

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 2). The correlations were not significant for either the B6129 ($r = -0.023, p = 0.94$), nor the 3xTg-AD ($r = 0.34, p = 0.309$) mice.

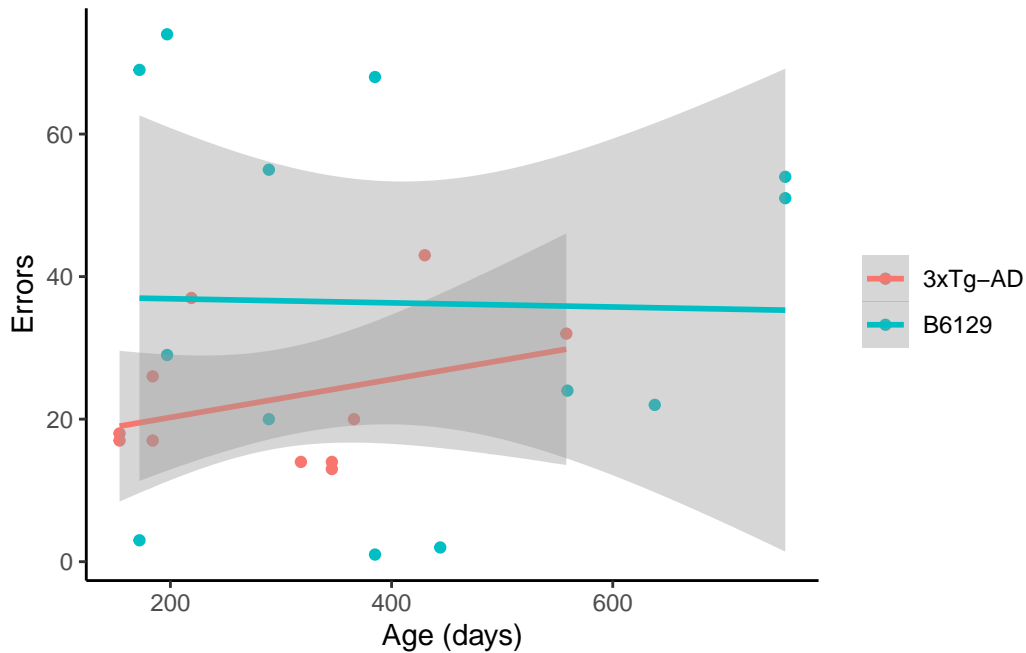


Figure 2: Correlation between age and errors made on odour pair one discrimination.

Table 4: AICc model table for reversal.

geno	op	geno:op	df	logLik	AICc	delta	weight
+	-2.83	+	6	-2121.78	4255.77	0.00	0.76
+	-3.67		5	-2124.06	4258.27	2.51	0.22
	-3.67		4	-2127.30	4262.69	6.93	0.02
+			4	-2171.37	4350.84	95.07	0.00
			3	-2173.80	4353.66	97.90	0.00

Reversal

The reversal trials were assessed with linear mixed effects models on the number of errors made on each odour pair. The errors made decreased as the mice advanced through the odour pairs (Figure 3). The model with effects of genotype, odour pair, and the genotype by odour pair interaction best explained the data (Table 4), this model differed significantly from the null model of just an effect of odour pair ($\chi^2_3 = 104, p < 0.0001$).

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. 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.

Table 5: AICc model table for near errorless learning during reversal

geno	df	logLik	AICc	delta	weight
	2	-113.06	230.15	0.00	0.57
+	3	-112.33	230.71	0.56	0.43

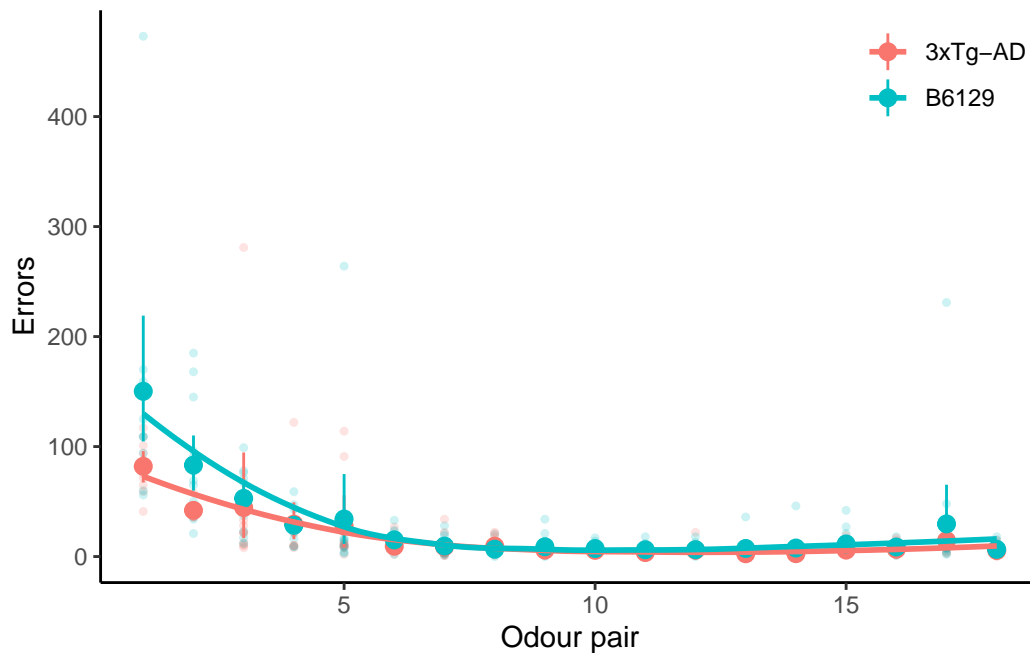


Figure 3: Errors ($\pm 95\%$ CI) made by the mice at on each odour pair during the reversal stages.

During the second half of the experiment, odour pairs 10 through 18, the B6129 made an average of 10 ± 22 errors, while the 3xTg-AD mice made 5.8 ± 6 errors, a significant difference ($t_{136} = -2$, $p = 0.0429$).

Generalized linear mixed effects models were used to examine the proportion of mice making one or zero errors on each odour pair. The null model best explained the data (Table 5).

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 2). The correlations were not significant for either the B6129 ($r = 0.39$, $p = 0.214$), nor the 3xTg-AD ($r = 0.12$, $p = 0.741$) mice.

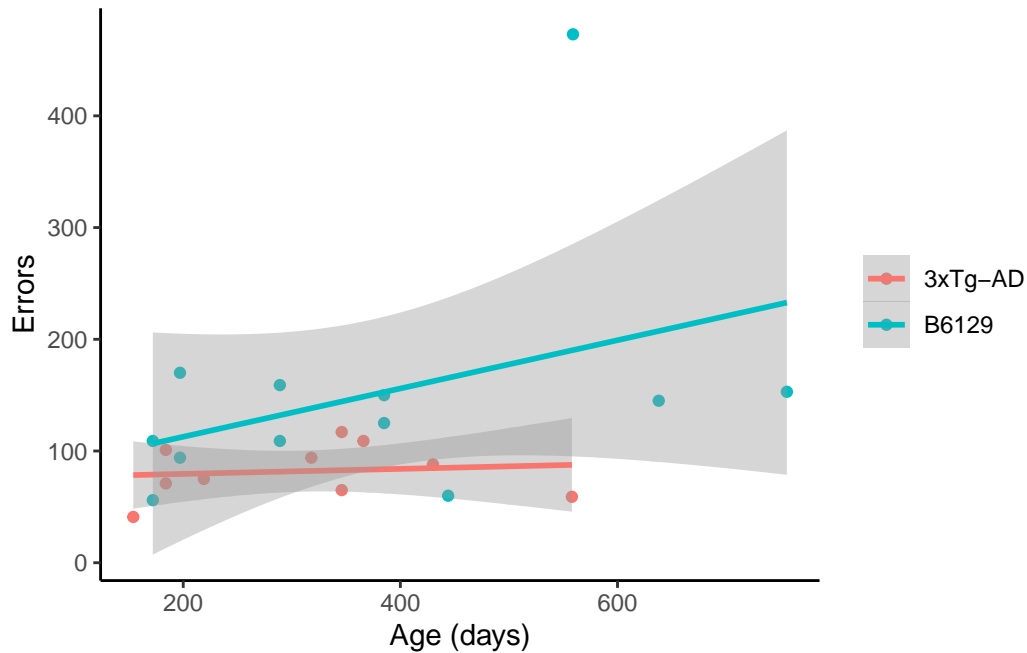


Figure 4: Correlation between age and errors made on odour pair one reversal.

Table 6: AICc model table for total errors.

geno	df	logLik	AICc	delta	weight
+	3	-159.28	325.76	0.00	0.83
	2	-162.15	328.87	3.11	0.17

Total errors

The total errors made were assessed with linear models. The model with an effect of genotype best explained the data (Table 6), this model differed significantly from the null model ($F_1 = 5.9$, $p = 0.0233$; Figure 5).

Age effects

Pearson correlations were used to compare the total number of errors made to the age of the mice for each genotype (Figure 6). The correlations were not significant for either the B6129 ($r = 0.33$, $p = 0.271$), nor the 3xTg-AD ($r = -0.16$, $p = 0.637$) mice.

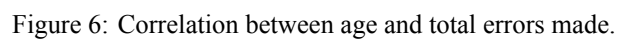
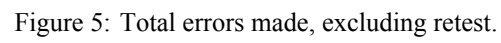


Table 7: AICc model table for retest errors.

geno	df	logLik	AICc	delta	weight
	2	-77.88	160.55	0.0	0.79
+	3	-77.77	163.26	2.7	0.21

Retest

Due to mice dying, only 11 B6129 and 7 3xTg-AD mice were given the retest.

The retest occurred between 30 and 92 days after the final reversal. There was no difference between between the days until the retest for the B6129 (58 ± 21) and 3xTg-AD (74 ± 25 ; $t_{12} = 1.4$, $p = 0.188$).

The number of errors made during the retest was assessed with linear models. The null model best explained the data for the number of errors made during the retest (Table 7), indicating no significant effects of genotype nor sex (Figure 7).

A paired t-test was used to compare the number of errors made during the retest to the numbers of errors made on the final odour discrimination. The mean number of errors made during the retest (37 ± 19) was significantly higher than the errors made on the final odour discrimination (5.6 ± 5.9 ; $t_{17} = 7.2$, $p < 0.0001$).

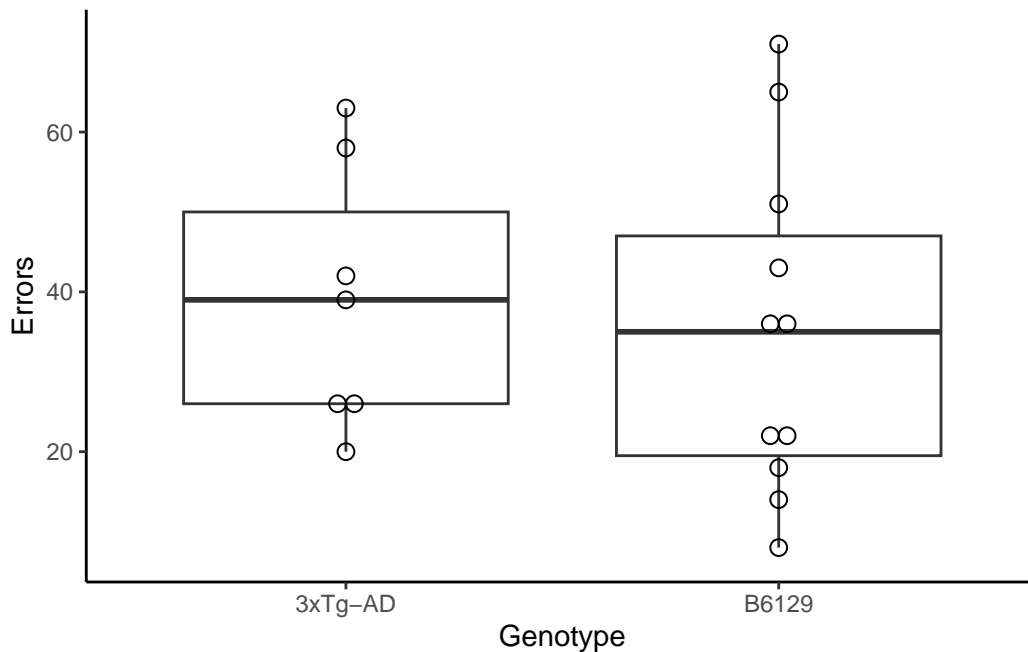


Figure 7: Total errors made during retest.

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 8). The correlations were not significant for either the B6129 ($r = 0.24$, $p = 0.483$), nor the 3xTg-AD ($r = -0.72$, $p = 0.067$) 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 9). There was a significant, positive correlations ($r = 0.48$, $p = 0.0451$).

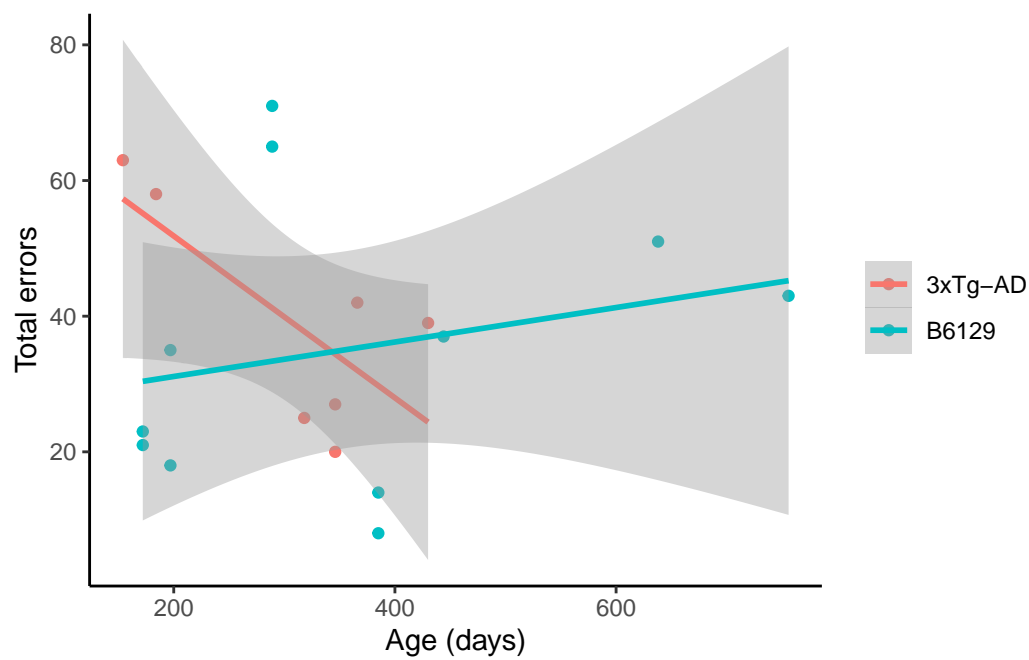


Figure 8: Correlation between age and errors made on the retest.

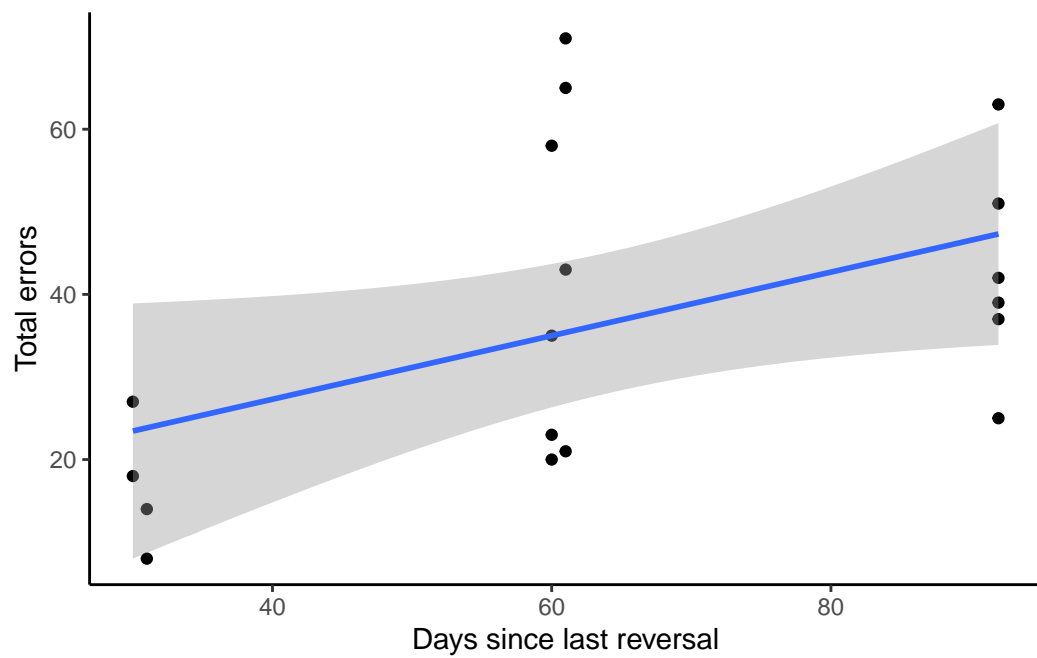


Figure 9: Correlation between days after last reversal and errors made on the retest.