1 Peak Interval Timing

1.1 Mouse Numbers

There are 16 Nrxn1$^{+/+}$ mice, 16 Nrxn1$^{+/-}$ mice, and 16 Nrxn1$^{\Delta S5/-}$ mice in the peak interval analysis. All mice were males and started testing at 2 months of age.

1.2 Well Timed Trials

During the final block of testing, there was no significant effect of genotype on the number of poorly timed trials ($F_{(2,45)} = 1.34$, $p = 0.273$, $\eta^2_G = 0.056$).

Both well timed and poorly timed trials are included in the following analysis.

1.3 Single Trial Analysis

The single trial parameters were analyzed using ANOVAs and planned comparisons (Nrxn1$^{+/+}$ vs Nrxn1$^{+/-}$ and Nrxn1$^{+/-}$ vs Nrxn1$^{\Delta S5/-}$). There was an effect of genotype on stop times ($F_{(2,45)} = 4.26$, $p = 0.02$, $\eta^2_G = 0.159$), with the Nrxn1$^{\Delta S5/-}$ mice (28.6 ± 2.78) having a later start time than the Nrxn1$^{+/-}$ mice (25.9 ± 2.24; $t_{(45)}$ = -2.92, $p = 0.00548$, $d = 1.05$). There was also an effect of genotype on middle times ($F_{(2,45)} = 3.86$, $p = 0.028$, $\eta^2_G = 0.147$), with the Nrxn1$^{\Delta S5/-}$ mice (19.4 ± 2.63) having a later middle time than the Nrxn1$^{+/-}$ mice (17.1 ± 1.97; $t_{(45)}$ = -2.76, $p = 0.00843$, $d = 0.989$). While there was no main effect of genotype on start times ($F_{(2,45)} = 2.68$, $p = 0.079$, $\eta^2_G = 0.107$), the planned comparisons showed that the Nrxn1$^{+/-}$ mice (8.25 ± 2.03) had a earlier start time than the Nrxn1$^{\Delta S5/-}$ mice (10.2 ± 2.85; $t_{(45)}$ = -2.22, $p = 0.0315$, d = -0.782). There was no effect of genotype on spread ($F_{(2,45)} = 1.03$, $p = 0.366$, $\eta^2_G = 0.044$; Figure 1).

There was an effect of genotype on the coefficient of variation of the start times ($F_{(2,45)} = 4.09$, $p = 0.023$, $\eta^2_G = 0.154$), with the Nrxn1$^{+/+}$ mice (0.802 ± 0.117) having a lower coefficients of variation than the Nrxn1$^{+/-}$ mice (0.956 ± 0.214; $t_{(45)}$ = -2.57, $p = 0.0136$, d = -0.894), and the Nrxn1$^{+/-}$ mice (0.956 ± 0.214) having greater coefficients than the Nrxn1$^{\Delta S5/-}$ mice (0.814 ± 0.164; $t_{(45)} = 2.37$, $p = 0.022$, $d = 0.747$), but not on the stop times ($F_{(2,45)} = 0.865$, $p = 0.428$, $\eta^2_G = 0.037$; Nrxn1$^{+/+}$: 0.271 ± 0.0743; Nrxn1$^{+/-}$: 0.28 ± 0.0585; Nrxn1$^{\Delta S5/-}$: 0.298 ± 0.0367).

Pearson's correlations between the start and stop times, the start time and the spread, and the spread and the middle time were also examined. Genotype differences in correlation coefficients were analyzed with ANOVAs. Start and stop time correlations (Nrxn1$^{+/+}$: $r_{(629)} = 0.7$, $p < 0.0001$; Nrxn1$^{+/-}$: $r_{(611)} = 0.72$, $p < 0.0001$; Nrxn1$^{\Delta S5/-}$: $r_{(576)} = 0.69$, $p < 0.0001$) and start time and spread correlations (Nrxn1$^{+/+}$: $r_{(629)}$ = -0.31, $p < 0.0001$; Nrxn1$^{+/-}$: $r_{(611)}$ = -0.43, $p < 0.0001$; Nrxn1$^{\Delta S5/-}$: $r_{(576)}$ = -0.32, $p < 0.0001$) were significant for all genotypes, and mice did not differ on start - stop time correlations ($F_{(2,45)} = 1.26$, $p = 0.293$, $\eta^2_G = 0.053$; Figure 2A), nor start - spread correlations ($F_{(2,45)} = 2.21$, $p = 0.122$, $\eta^2_G = 0.089$; Figure 2B). While the middle - spread correlations were significant for the Nrxn1$^{+/+}$ mice ($r_{(629)} = 0.1$, $p = 0.0106$) and the Nrxn1$^{\Delta S5/-}$ mice ($r_{(576)} = 0.094$, $p = 0.0234$), they were not significant for the Nrxn1$^{+/-}$ mice ($r_{(611)}$ = -0.079, $p = 0.052$), resulting in a significant difference in the middle - spread correlations between genotypes ($F_{(2,45)} = 3.27$, $p = 0.047$, $\eta^2_G = 0.127$), with the Nrxn1$^{+/-}$ (-0.0996 ± 0.259) mice showing lower correlations than both the Nrxn1$^{+/+}$ mice (0.0909 ± 0.224; $t_{(45)} = 2.23$, $p = 0.0309$, d = -0.787) and the Nrxn1$^{\Delta S5/-}$ mice (0.0885 ± 0.242; $t_{(45)}$ = -2.2, $p = 0.033$, d = -0.751 Figure 2C).

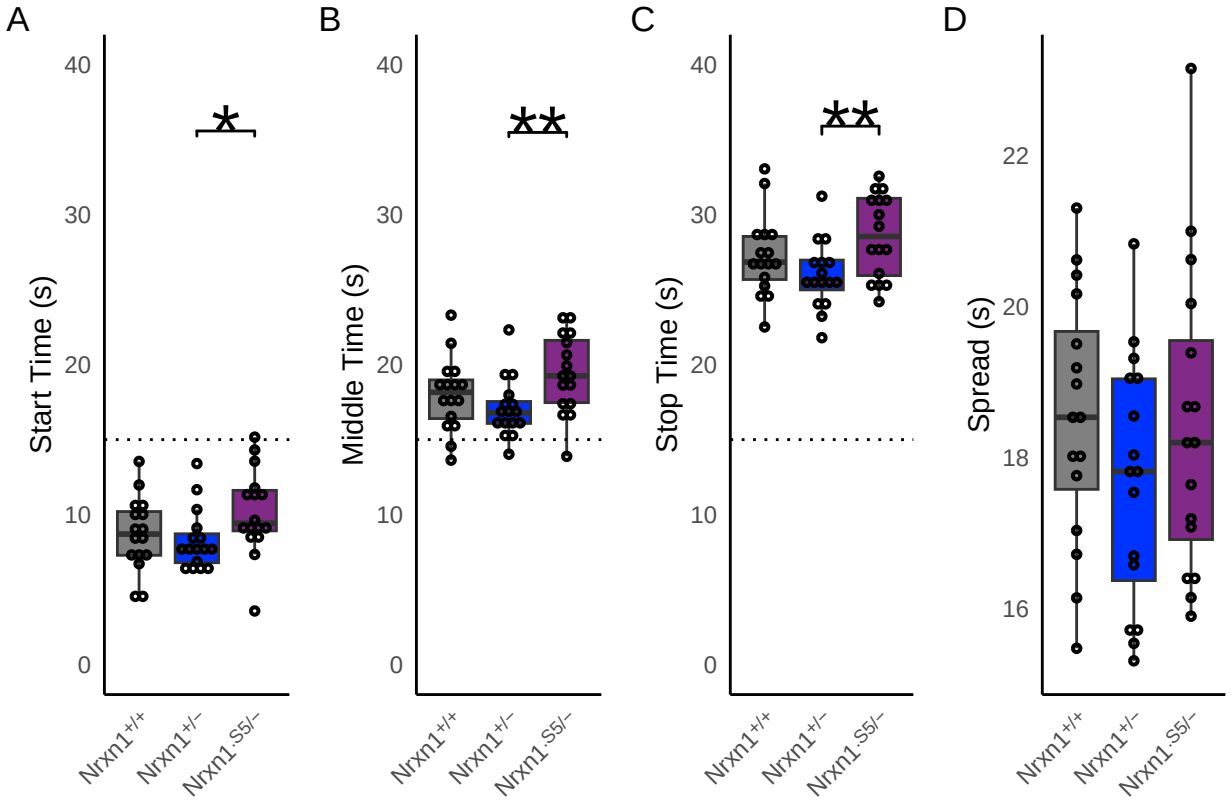

Figure 1: The comparison of single trial analysis between the Nrxn1$^{+/+}$, Nrxn1$^{+/-}$, and Nrxn1$^{\Delta S5/-}$ mice. Bars show the range of data points out to a maximum of 1.5 interquartile ranges (p = .05 * .01 ** .001 *** 0).

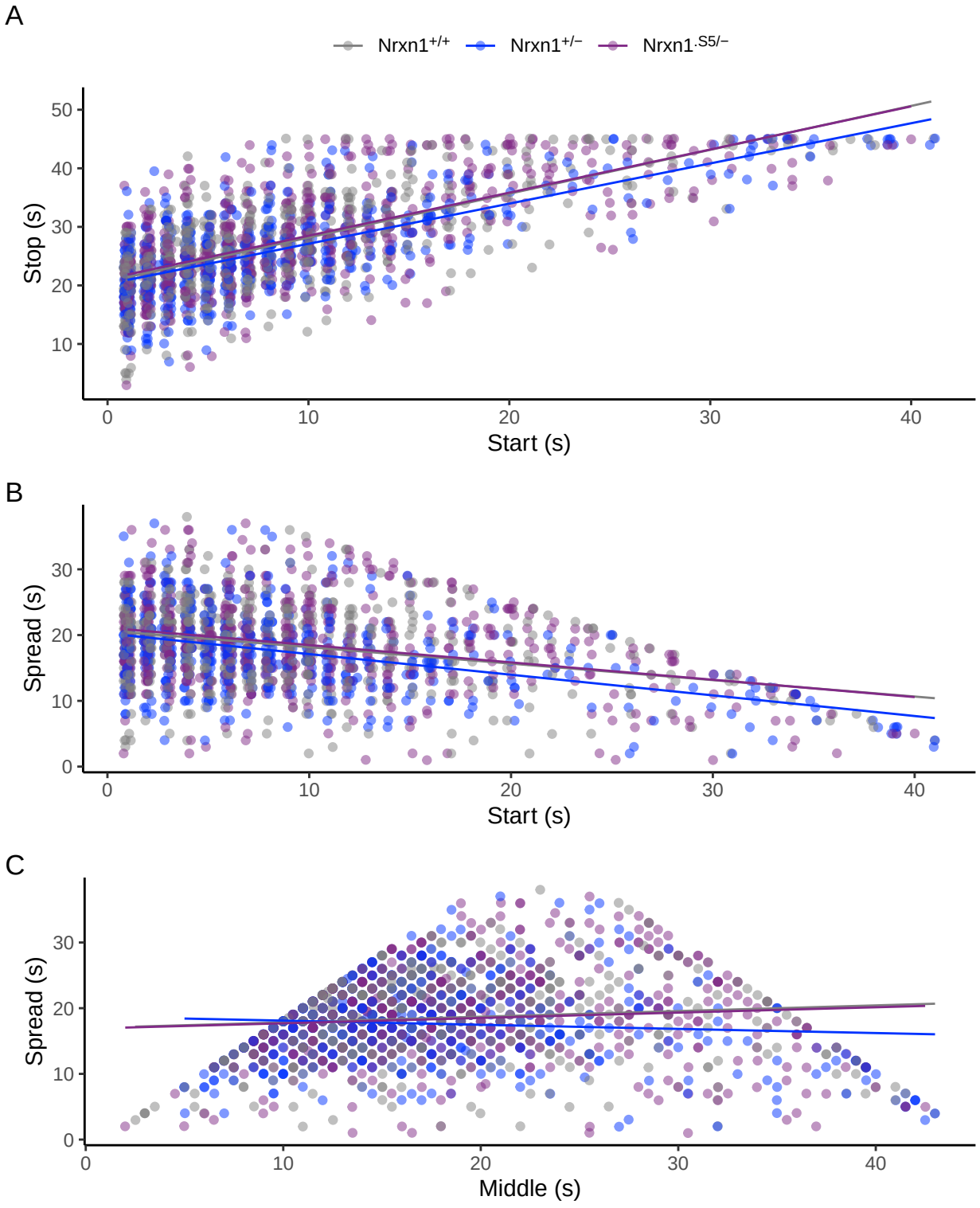

Figure 2: Correlations between A) the start and stop times, B) the start times and the spread, and C) the middle time and the spread.

1.4 Average Response Curve Analysis

The parameters calculated from the average response curves (Figure 3A) were compared between genotypes using ANOVAs. There was an effect of genotype on stop times ($F_{(2,45)} = 3.26$, $p = 0.048$, $\eta^2_G = 0.127$; Figure 3E), with planned comparisons showing the Nrxn1$^{+/-}$ mice (24.3 ± 3.66) had earlier peaks than the Nrxn1$^{\Delta S5/-}$ mice (30.2 ± 8.13; $t_{(45)} = -2.47$, $p = 0.0172$, $d = -0.932$). There was also an effect of genotype on the amplitude at 30s ($F_{(2,45)} = 3.37$, $p = 0.043$, $\eta^2_G = 0.13$; Figure 3G), with planned comparisons showing the Nrxn1$^{+/+}$ mice (0.599 ± 0.249) had a greater amplitude at 30s than the Nrxn1$^{+/-}$ mice (0.407 ± 0.259; $t_{(45)} = 2.18$, $p = 0.0342$, $d = 0.757$), as well as the Nrxn1$^{\Delta S5/-}$ mice (0.61 ± 0.239) having a greater amplitude at 30s than the Nrxn1$^{+/-}$ mice ($t_{(45)} = -2.31$, $p = 0.0258$, $d = 0.815$). No other average response curve measures showed a significant effect of genotype (p's >= 0.202).

1.5 Temporal Differentiation Measures

Temporal differentiation measures were compared with repeated measure ANOVAs. Greenhouse-Geisser corrections were applied to within-subject factors. The Temporal Discrimination Index (TDI) showed significant effects of block ($F_{(1.55,69.6)} = 31.8$, $p < 0.0001$, $\eta^2_G = 0.302$), but no significant effect of genotype ($F_{(2,45)} = 1.94$, $p = 0.155$, $\eta^2_G = 0.032$), nor a genotype by block interaction ($F_{(3.09,69.6)} = 2.07$, $p = 0.11$, $\eta^2_G = 0.053$; Figure 4A). The Response Initiation Ratio (RIR) showed no significant effects (p's >= 0.142; Figure 4B). The Response Suppression Ratio (RSR) showed significant effects of block ($F_{(2.57,100.1)} = 55.3$, $p < 0.0001$, $\eta^2_G = 0.444$), but not genotype ($F_{(2,39)} = 1.66$, $p = 0.203$, $\eta^2_G = 0.036$), nor a genotype by block interaction ($F_{(5.13,100.1)} = 1.14$, $p = 0.344$, $\eta^2_G = 0.032$; Figure 4C).

1.6 Response Rate and Activity

Response rates and activity were analyzed with ANOVAs. During the final block of testing, all genotypes made a similar number of total nose pokes per session ($F_{(2,45)} = 0.363$, $p = 0.698$, $\eta^2_G = 0.016$). This was true when examining both nose pokes made while the discriminative stimulus was on ($F_{(2,45)} = 0.401$, $p = 0.672$, $\eta^2_G = 0.018$), and during the inter trial intervals ($F_{(2,45)} = 0.296$, $p = 0.745$, $\eta^2_G = 0.013$). The ratio of the number of nose pokes made during the discriminative stimulus to the number of nose pokes during the ITIs was also similar ($F_{(2,45)} = 1.76$, $p = 0.183$, $\eta^2_G = 0.073$). The total number of beam breaks was also similar ($F_{(2,45)} = 1.19$, $p = 0.315$, $\eta^2_G = 0.05$), indicating similar levels of movement in the testing apparatus.

1.7 Non Normalized Response Curve

A non normalized average response curve is provided in Figure 5.

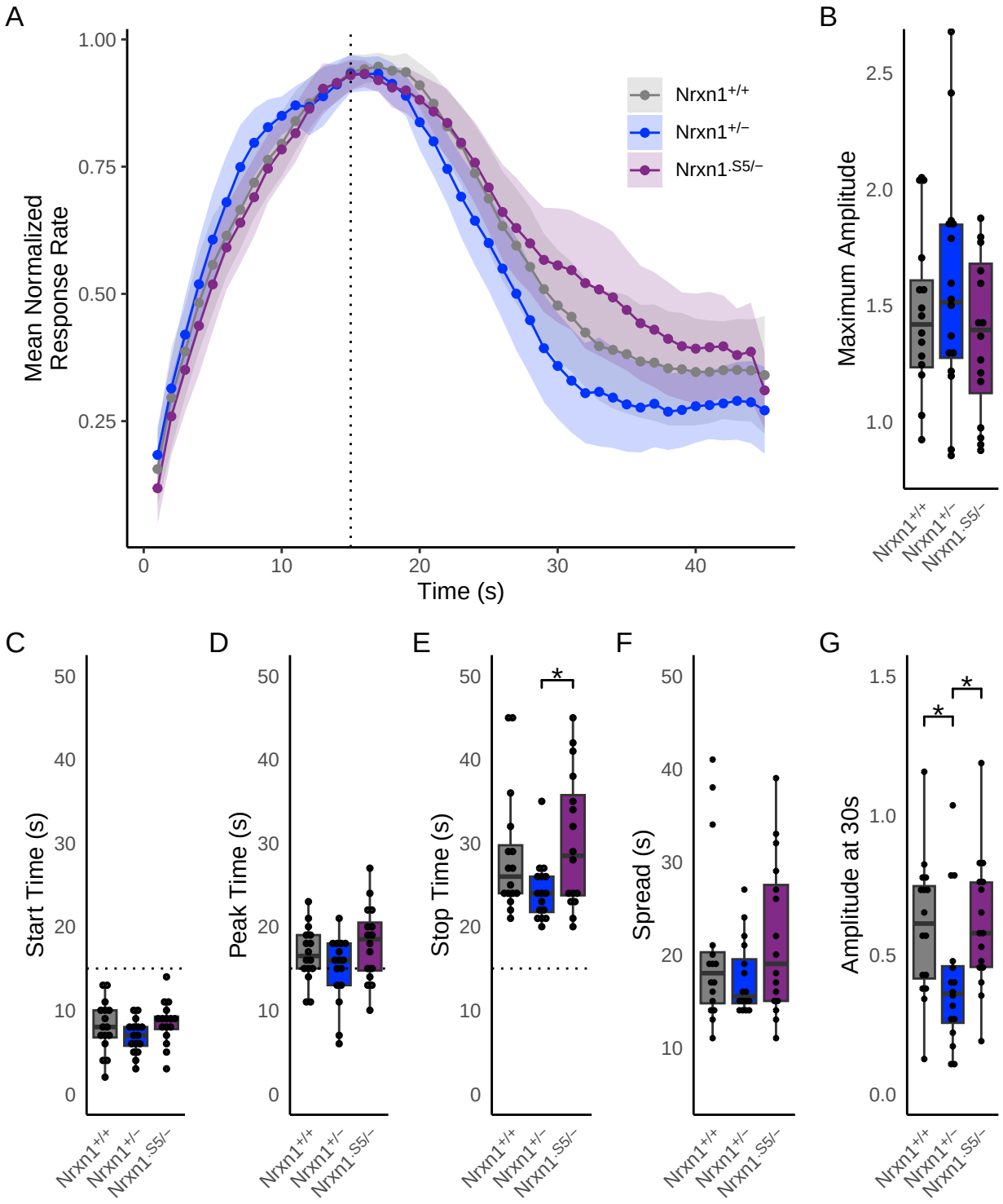

Figure 3: Average peak response curve and the comparison of the indices calculated from the response curve. Bars range of data points out to a maximum of 1.5 interquartile ranges (p = .05 * .01 ** .001 *** 0).

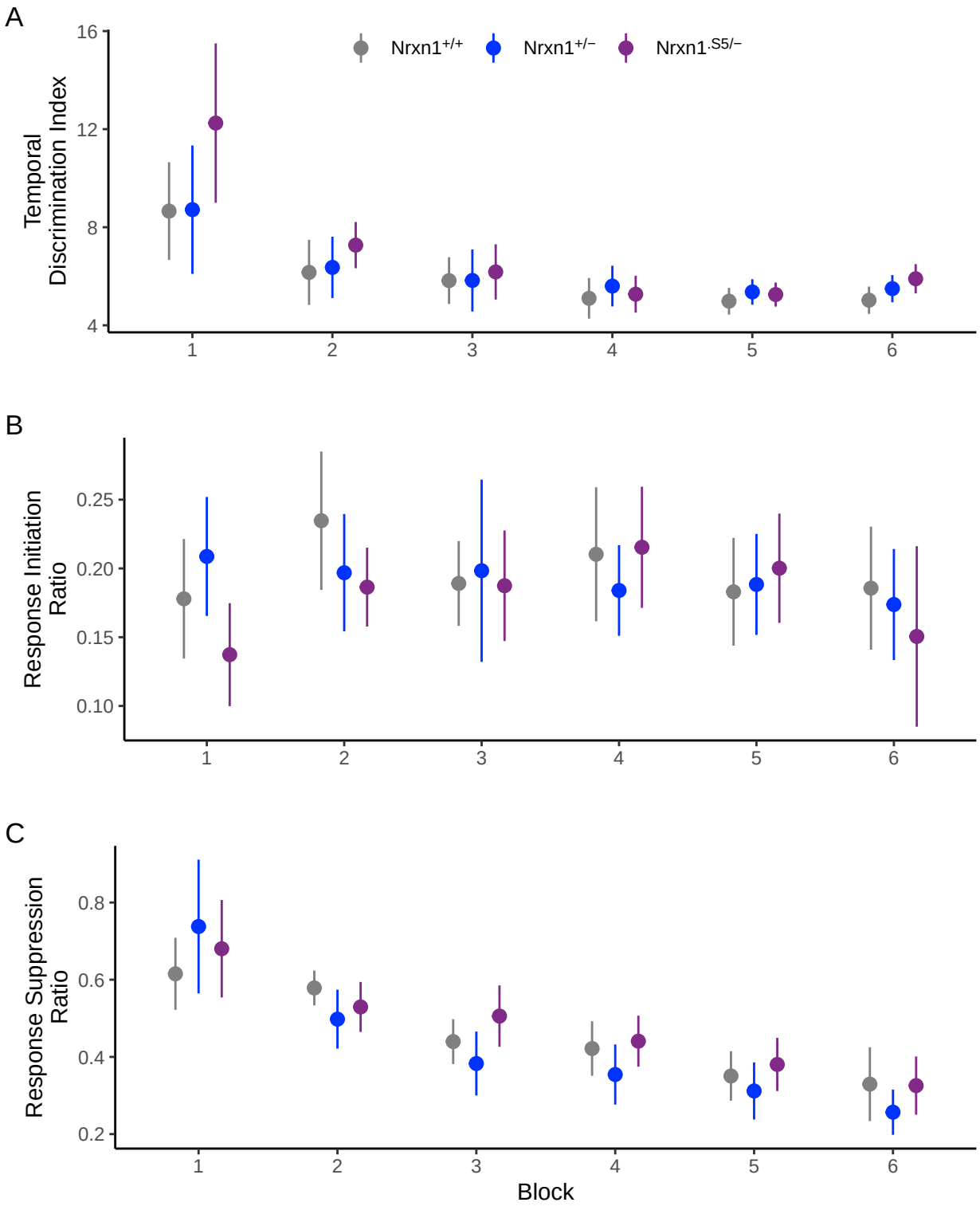

Figure 4: Temporal differentiation measures across the six blocks of trials

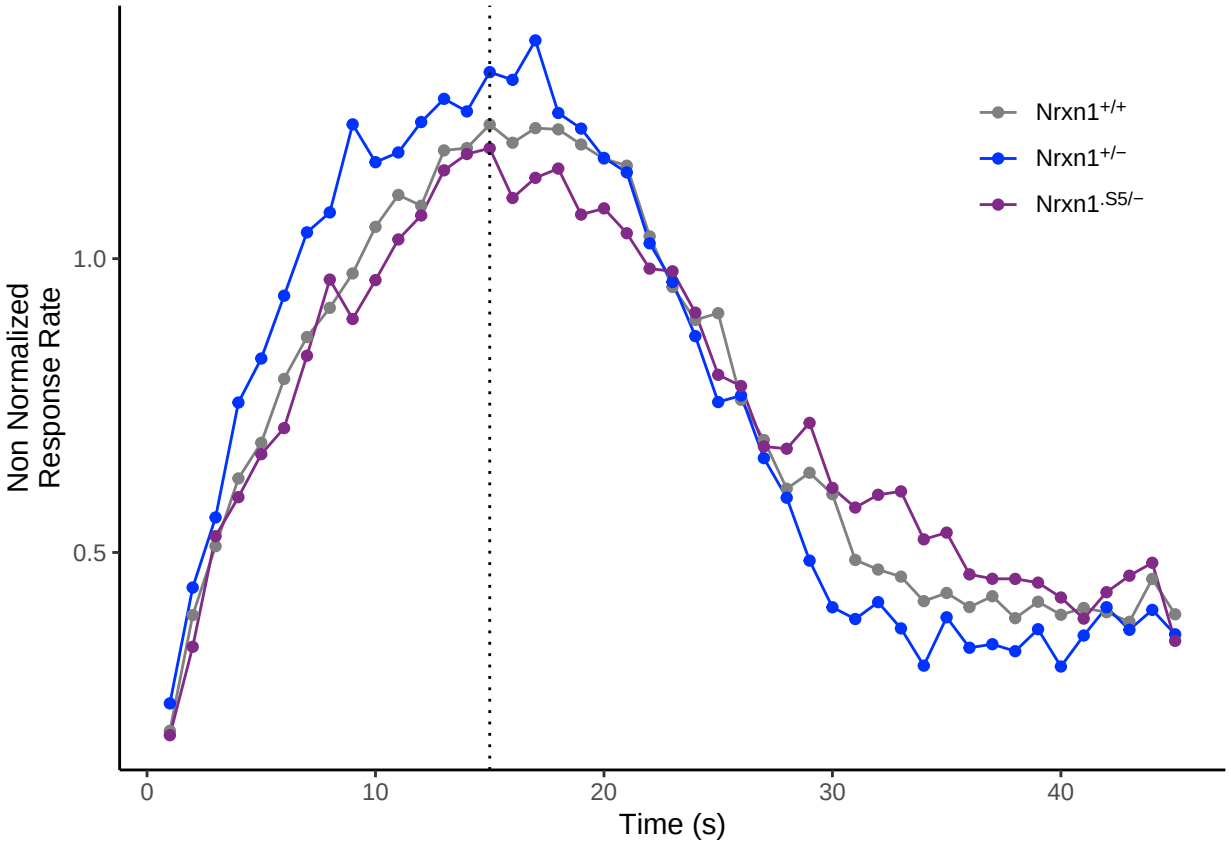

Figure 5: Non normalized average response curve