Additional File 1

Remodeling the light-adapted electroretinogram using a Bayesian statistical approach

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1 Remarks

Here we have used a Highly robust (outlier-resistant) modeling of the ERG signal done for each of the four eye-flash strength combinations separately. Our proposal was to use a heavy tailed observation distribution (t-distribution with a low number (3) degrees of freedom) to produce that were resistant to occasional large outliers.

This was important since in the data, there were occasional wild individual curves that might bias the results.

1.1 Multivariate t (3 df) model, LKJ correlation regularization (eta=1), no regularization on mean trajectories, Bayesian approach

We used the robust (only 3 degrees of freedom) multivariate t model that works with independent individuals and independent measurements for different combinations of eye and flash strength (logcd) but correlated ERG values within one measurement session (for a given individual and given eye, logcd combination). The shape of this correlation was taken as unknown *a priori* so it was learned from the data.

We constructed a 100 x 100 matrix at 100 equidistant time positions (obtained via the GAM-t-distribution model of the original data and evaluated the 100 time points that were the same for every individual), thus generating a 100-dimensional distribution. This also means a 100x100 covariance matrix with the covariance matrix estimate regularized (because of one part of the Bayesian model used) via the so called LKJ prior (with eta parameter 1).

The following sections provide plots for each group and eye at 0.6 and 1.2 log cd.s.m^{-2} flash strength.

1. Posterior Mean ERG amplitude vs time.
2. Posterior Standard Deviation of the ERG amplitude vs time.
3. 95% CI of mean of the ERG amplitude vs time.
4. Eigenvalue of the posterior mean *covariance* matrix vs rank (1-100)
a. Mean posterior *covariance* for the 1st, 50th and 100th rows.
5. Eigenvalue of the posterior mean *correlation* matrix vs rank (1-100)
a. Mean posterior *correlation* for the 1st, 50th and 100th rows.

1.2 Medications

In the ADHD group n=10 were using: methylphenidate (Concerta slow-release n=2, Ritalin n=1); dexamphetamine (n=1), lisdexamfetamine (Vyvanse n=4), risperidone (n=1) and sertraline (n=1). All participants abstained from medication use on the day of testing. Three of the ADHD group had a co-diagnosis of dyslexia.

2 Posterior Mean values of the a- and b-wave

Table 1 presents the posterior mean from the 100 equidistant times for the a- and b-wave for each eye and

	Right Eye		Left Eye	
0.6 log cd.s.m^{-2}	ADHD	Control	ADHD	Control
a-wave	6.48 (5.64 - 7.31)	7.18 (6.51 - 7.86)	5.83 (5.06 - 6.59)	6.95 (6.41 - 7.47)
b-wave	18.52 (16.41 - 20.42)	18.91 (16.45 - 21.34)	17.79 (15.47 - 19.93)	17.24 (14.88 - 19.55)
1.2 log cd.s.m^{-2}				
a-wave	**7.64 (6.58 - 8.71)**	**9.70 (8.97 - 10.41)**	**7.51 (6.64 - 8.43)**	**8.83 (8.03 - 9.60)**
b-wave	12.39 (10.73 - 14.03)	16.00 (14.08 - 17.83)	12.66 (11.11 - 14.21)	12.59 (10.69 - 14.55)

flash strength combination for the two groups with the credible confidence intervals. The only notable and consistent difference is that the a-wave is reduced in the ADHD group compared to the Control group.

Table 1. Posterior Mean values of the a- and b- waves from equidistant time series. The a-wave amplitude shows a small reduction at the 1.2 log cd.s.m^{-2} strength for the ADHD group. All other values are equivalent or not replicated between eyes.

3 Left Eye: log 0.6 cd.s.m^{-2}

Figure 1 shows the posterior mean, standard deviation and robust Bayesian modelled 95th centiles for the groups at 0.6 log cd.s.m^{-2}. Note that the mean and the posterior deviation varies beyond the time point of 70 msec from flash onset. The lower panel shows the eigenvalues and here the *covariance* for the 50th and 100th rows.

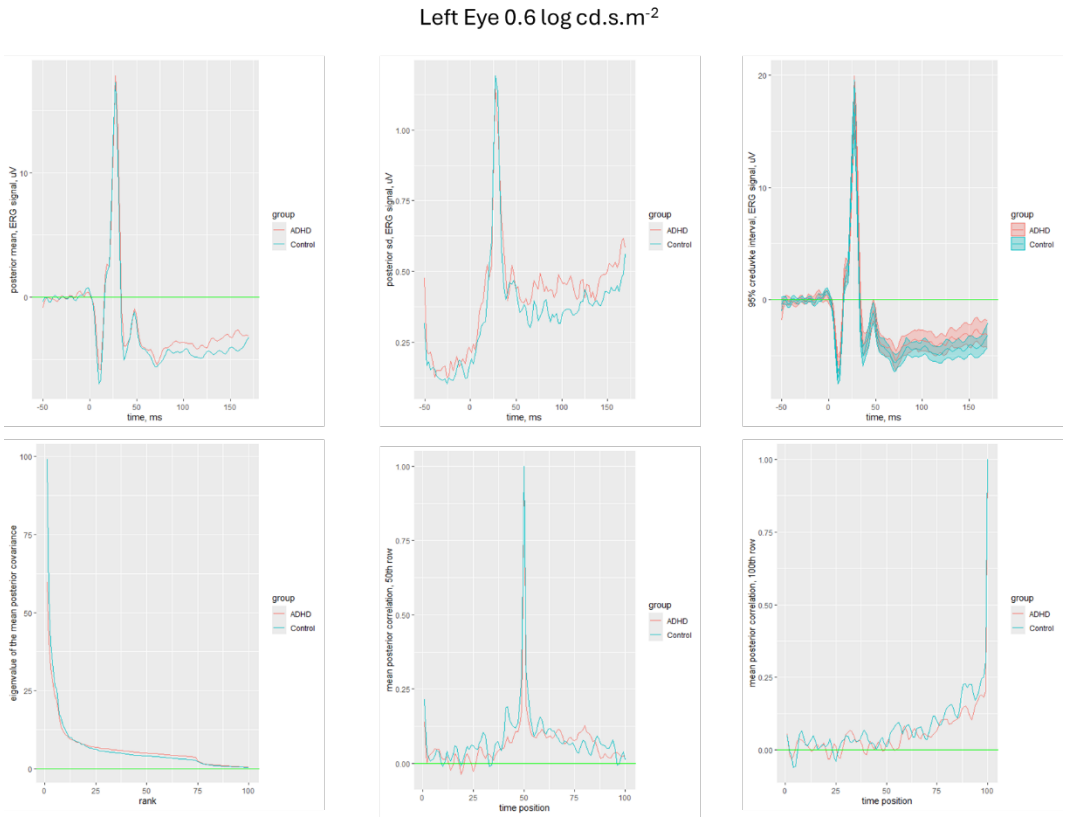

Figure 1 Upper panel the posterior mean and standard deviations for the groups with the Bayesian modelled robust 95th confidence intervals. The lower panels show the covariance for the 50th and 100th rows of the covariance matrix.

4 Right Eye: log 0.6 cd.s.m^{-2}

Figure 2 shows the posterior mean, standard deviation and robust Bayesian modelled 95th centiles for the groups at 0.6 log cd.s.m^{-2}. Note that the mean posterior deviation varies beyond the time point of 70 msec from flash onset. The lower panel shows the eigenvalues and here the *covariance* for the 50th and 100th rows. In this case the posterior standard deviation is similar between groups.

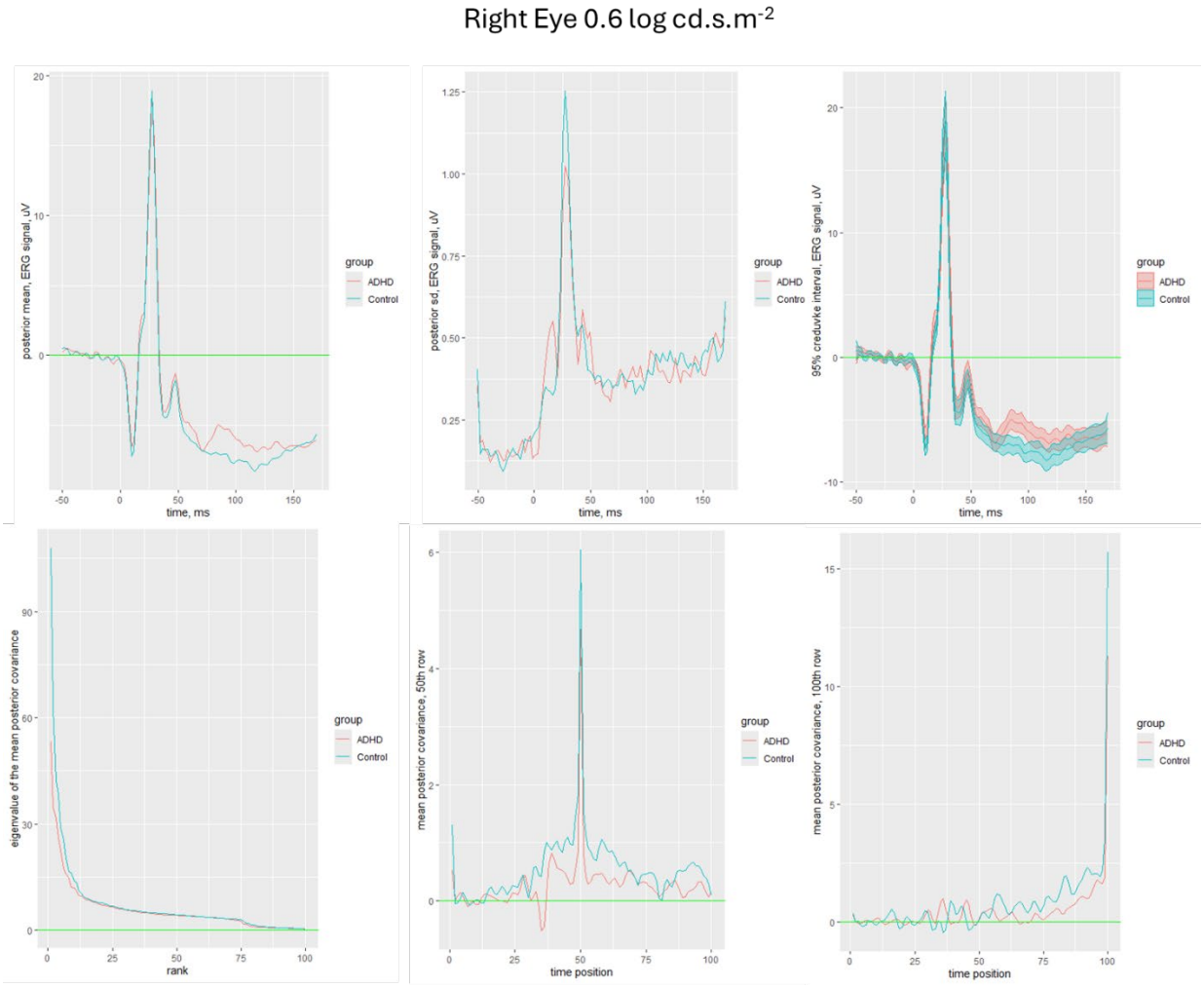

Figure 2 Upper panel the posterior mean and standard deviations for the groups with the Bayesian modelled robust 95th confidence intervals. The lower panels show the covariance for the 50th and 100th rows of the covariance matrix.

5 Left Eye: log 1.2 cd.s.m^{-2}

Figure 3 shows the posterior mean, standard deviation and robust Bayesian modelled 95th centiles for the groups at 1.2 log cd.s.m^{-2}. Note that the mean posterior deviation varies beyond the time point of 70 msec from flash onset. The lower panel shows the eigenvalues and here the *covariance* for the 50th and 100th rows. In this case the posterior standard deviation is similar between groups.

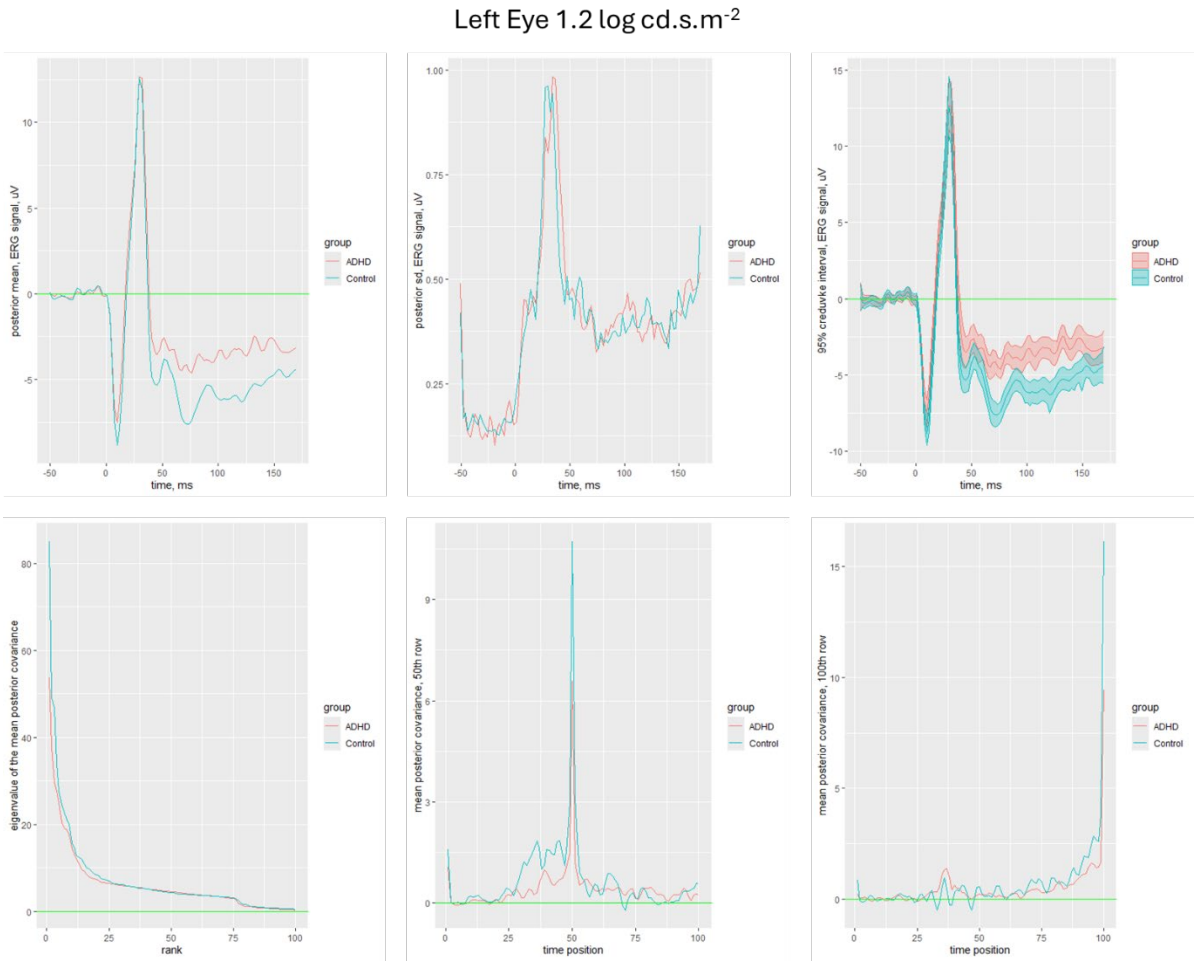

Figure 3 Upper panel the posterior mean and standard deviations for the groups with the Bayesian modelled robust 95th confidence intervals. The lower panels show the covariance for the 50th and 100th rows of the covariance matrix.

6 Right Eye: log 1.2 cd.s.m^{-2}

Figure 4 shows the posterior mean, standard deviation and robust Bayesian modelled 95th centiles for the groups at 1.2 log cd.s.m^{-2}. Note that the mean posterior deviation varies beyond the time point of 70 msec from flash onset. The lower panel shows the eigenvalues and here the *covariance* for the 50th and 100th rows. In this case the posterior standard deviation is similar between groups.

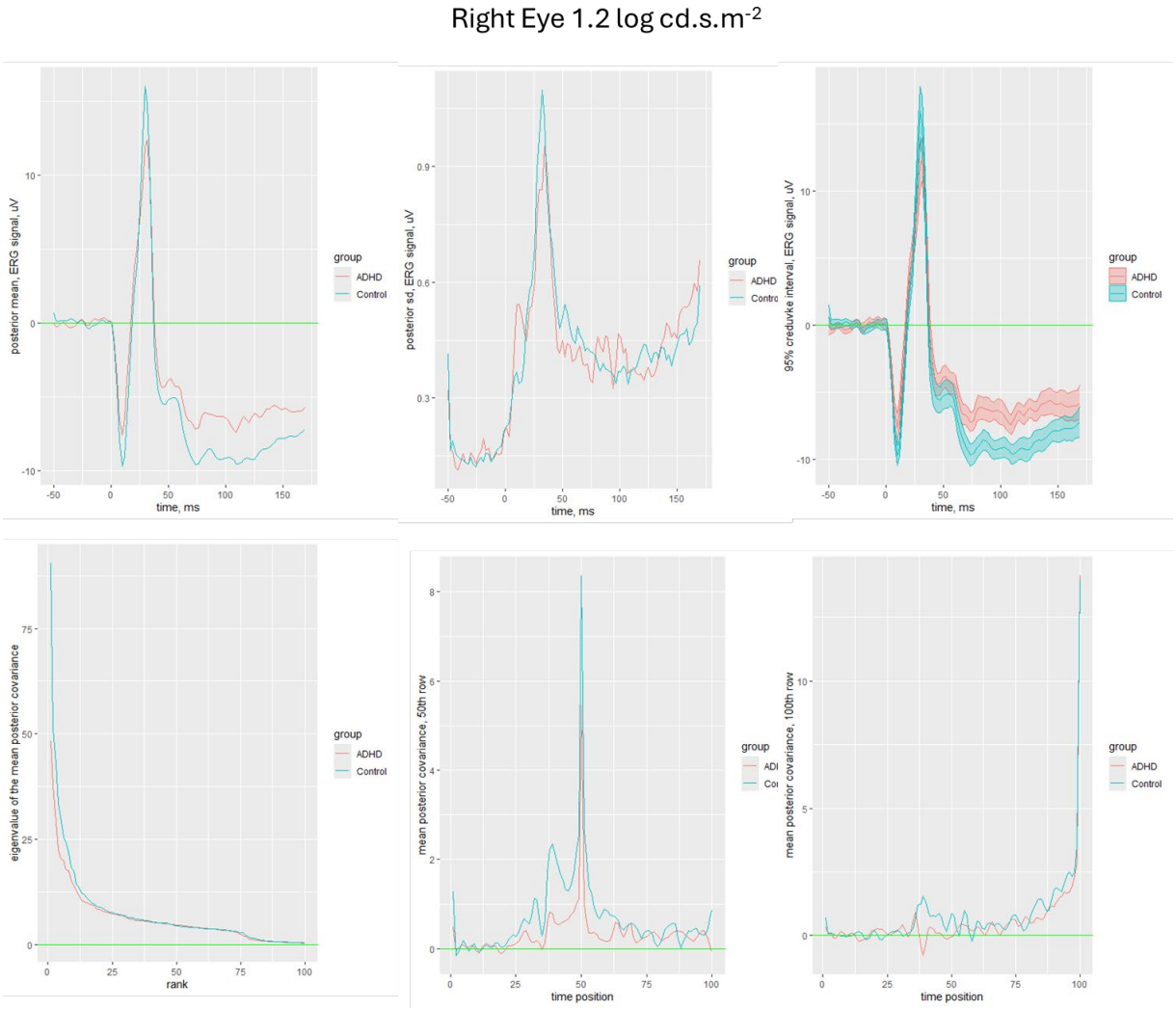

Figure 4 Upper panel the posterior mean and standard deviations for the groups with the Bayesian modelled robust 95th confidence intervals. The lower panels show the covariance for the 50th and 100th rows of the covariance matrix.

7 Correlation Matrices for time points 11.9, 29.6, 71.8 and 124.9 ms

Presented here are the correlation plots at row positions 29, 37, 56, 80 (corresponding to times 11.858941, 29.604114, 71.748901, 124.984422 ms). The times relate to the a- wave peak, b-wave peak, PhNR and at time distant to the PhNR respectively.

7.1 Right and Left Eyes log 0.6 cd.s.m^{-2}

The left and right eye correlation with row for the ADHD and Control groups. The degree of correlation between the equidistant 100-time positions near to the row slice are apparent. Note that in this case there is a divergence between groups for the correlation in the trajectories of the waveforms in the more distant (t=124.98 msec) which highlights a region of difference between the nature of the ERG shape. (Boxed area). See Figure 5.

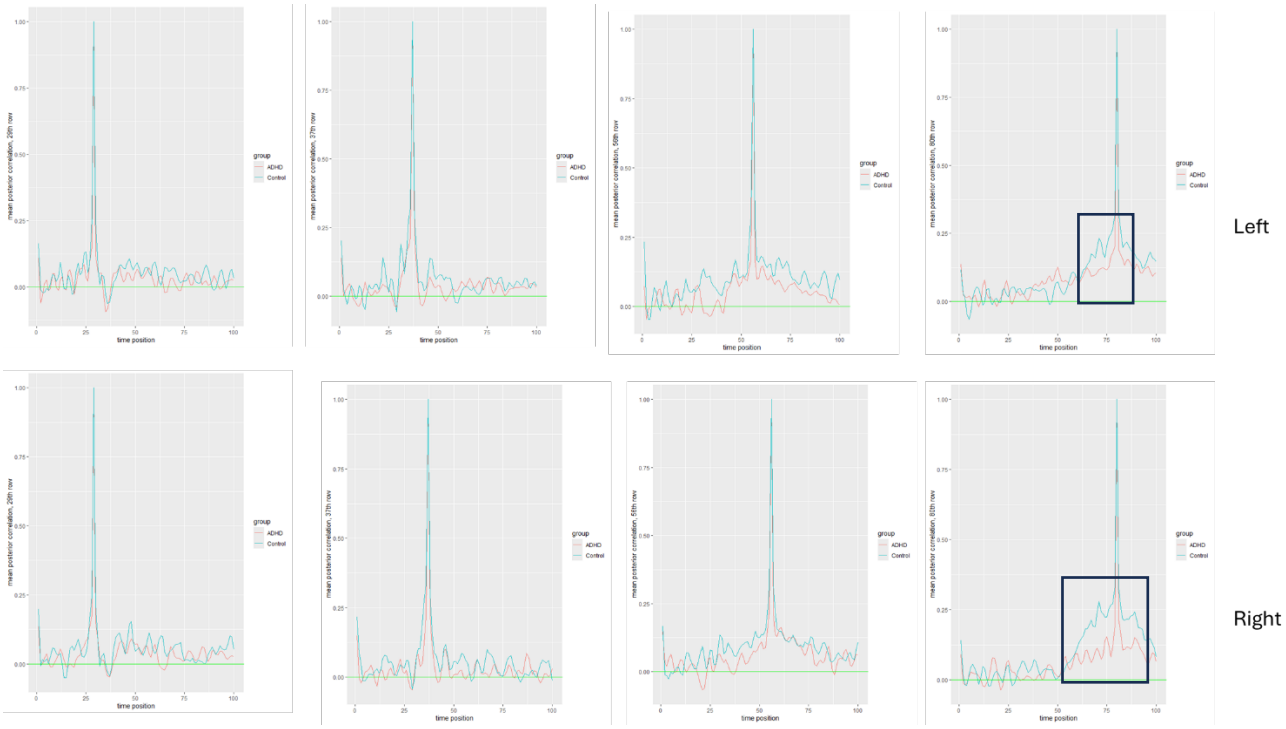

Figure 5 Correlation between groups for the right and left eye at 0.6 log cd.s.m^{-2} at four rows or slices taken (from left to right) at the a-wave, b-wave, PhNR, and distance to the PhNR. In this case the correlations highlight differences between groups in the trajectories of the ERG at regions prior to row 75 corresponding to a time of ~124 msec indicated by the boxed area.

7.2 Left and Right Eye log 1.2 cd.s.m^{-2}

The left and right eye correlation with row for the ADHD and Control groups. The degree of correlation between the equidistant 100-time positions near to the row slice are apparent. Note that in this case there is a divergence between groups for the correlation in the trajectories of the waveforms in the region pf the PhNR at around 75 msec which highlights a region of difference between the nature of the ERG shape. (Boxed area). See Figure 6.

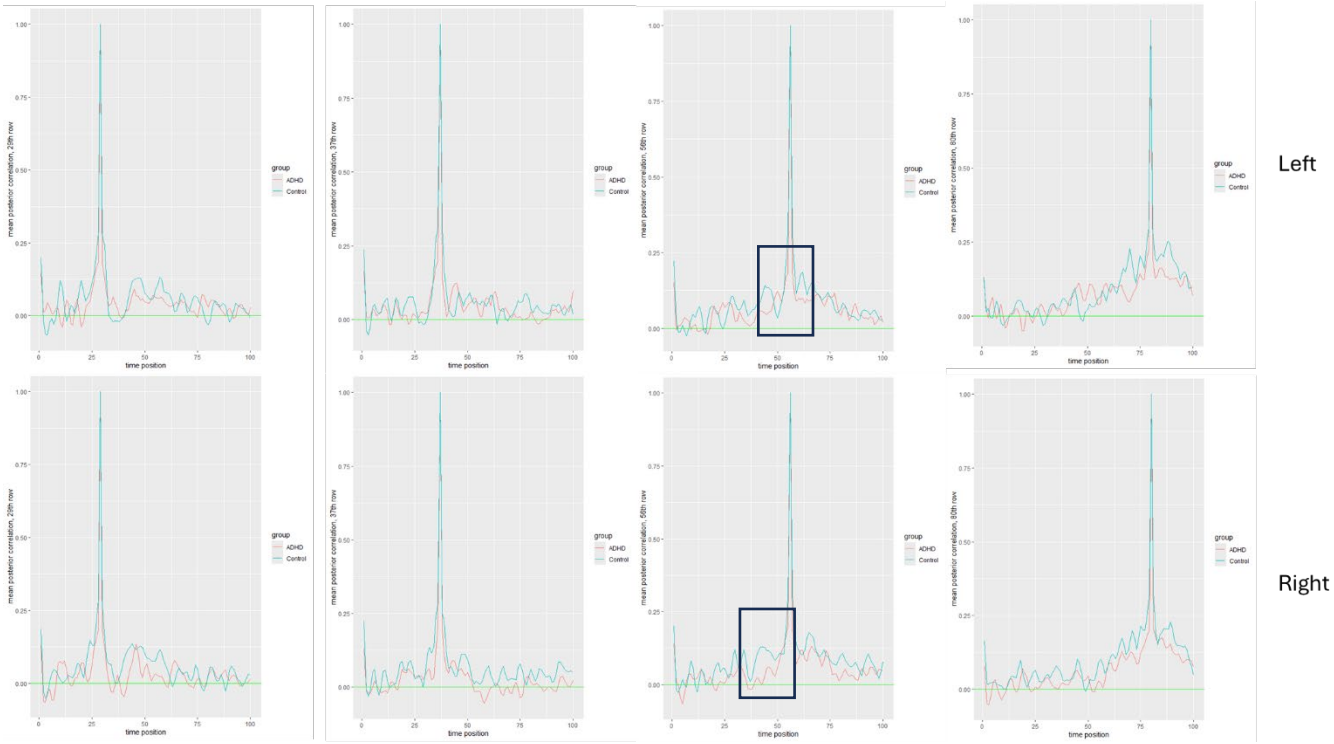

Figure 6 Correlation between groups for the right and left eye at 1.2 log cd.s.m^{-2} at four rows or slices taken (from left to right) at the a-wave, b-wave, PhNR, and distance to the PhNR. In this case the correlations highlight differences between groups in the trajectories of the ERG at regions prior to row 56 corresponding to a time of ~75 msec indicated by the boxed area.

7.3 Time intervals

The 100-time (msec) interval markers used to divide the ERG waveform by row.

Rows [1-17]

-50.249167 -48.031020, -45.812874 -43.594727 -41.376580 -39.158434 -36.940287 -34.722140 -32.503993 -30.285847 -28.067700 -25.849553 -23.631407 -21.413260 -19.195113 -16.976967 -14.758820

Rows [18-34]

-12.540673 -10.322526 -8.104380 -5.886233 -3.668086 -1.449940 0.768207 2.986354 5.204500 7.422647 9.640794 11.858941 14.077087 16.295234 18.513381 20.731527 22.949674

Rows [35-51]

25.167821 27.385967 29.604114 31.822261 34.040407 36.258554 38.476701 40.694848 42.912994 45.131141 47.349288 49.567434 51.785581 54.003728 56.221874 58.440021 60.658168

Rows [52-68]

62.876315 65.094461 67.312608 69.530755 71.748901 73.967048 76.185195 78.403341 80.621488 82.839635 85.057782 87.275928 89.494075 91.712222 93.930368 96.148515 98.366662

Rows [69-85]

100.584808 102.802955 105.021102 107.239248 109.457395 111.675542 113.893689 116.111835 118.329982 120.548129 122.766275 124.984422 127.202569 129.420715 131.638862 133.857009 136.075156

Rows [86-100]

138.293302 140.511449 142.729596 144.947742 147.165889 149.384036 151.602182 153.820329 156.038476 158.256623 160.474769 162.692916 164.911063 167.129209 169.347356