Neurocognitive Profiles in Adolescence Predict Subsequent Anxiety Trajectories During the COVID-19 Pandemic

Supplemental Information

Methodological Details

Measures

Error Monitoring. At the 13-year assessment, adolescents completed a flanker task while continuous EEG data were acquired using a 128-channel HydroCel Geodesic Sensor Net and EGI software (Electrical Geodesic, Inc., Eugene, OR). The task, data, and preprocessing pipeline have been previously described (Buzzell et al., 2017). In brief, on each trial, five horizontally aligned arrowheads (e.g., < < > < <) were presented. The arrows, which were preceded by a fixation cross (~300–600 ms), were presented for 200 ms and followed by a blank screen (~1860 ms). Participants had to indicate the direction of the central arrow as quickly and accurately as possible. The flanker task consisted of 12 blocks with 32 trials per block. At the end of each block, participants were provided with feedback based on their accuracy to ensure that all participants produced a sufficient number of errors to analyze the EEG activity surrounding erroneous behavior and reduce the likelihood that differences in ERN response were not a result of differing error rates. Participants completed the flanker task twice, once under standard flanker conditions and once under a "social" pressure manipulation. Although there was a larger ERN in the social condition compared to the standard flanker (Buzzell et al., 2017), these manipulations were counterbalanced across individuals, and there was no evidence that manipulation order affected the amplitude of the standard ERN ($t(122)= 0.21$, $p = .834$), nor was there evidence of any significant interaction with order to predict anxiety trajectories (all p's > .496). In the current study, we focus on the ERN data from the standard flanker task because extensive work has documented that it is related with anxiety (Hajcak et al., 2003; Meyer, 2017; Moser et al., 2013) and focusing on the standard (i.e., non-social ERN) allows for comparison with a broader array of literature. A similar approach has been used by previous studies with this sample (Filippi et al., 2020).

EEG data were preprocessed in MATLAB scripts (The MathWorks, Natick, MA) using a combination of the EEGLAB toolbox (Delorme & Makeig, 2004) and custom-made scripts. The preprocessing steps have been described in detail elsewhere (Buzzell et al., 2017; Debnath et al., 2020). In brief, we used independent component analysis (ICA) for artifact removal. Missing channels were interpolated using a spherical spline interpolation and then referenced to the average of all electrodes. Data were epoched to the response markers from -500 to 1000 ms and baseline corrected using the 200-ms period preceding response onset. To isolate error-specific effects, only incongruent trials were analyzed. To determine the minimum number of trials to obtain an ERN estimate with average acceptable reliability (.6), we examined the internal consistency reliability of the ERN and the ERN difference score in our sample in increasing numbers of trials using a Spearman-Brown split-half correlation procedure with multiple iterations (Leach et al., 2020; Morales et al., 2021). Results suggested that participants needed at least 10 trials for a reliable ERN and at least 15 trials for a reliable ERN difference score. Participants with at least 15 artifact-free trials were included. Separate ERPs were calculated for the social and nonsocial conditions of the task, with only the nonsocial ERPs being analyzed in

the current study. Mean amplitudes of ERN and correct-related negativity (CRN) were calculated from a cluster of frontocentral electrodes surrounding FCz (12, 5, 6, 13, 112, 7, and 106) for the first 100 ms following response. The CRN was then subtracted from the ERN for each participant to compute the delta-ERN, which was used for all subsequent analyses. More negative values indicate a larger delta-ERN and increased error monitoring. The ERN showed good reliability (Spearman-Brown r=.84).

Cognitive Control Strategy. At the 13-year assessment, participants completed a standard behavioral AX-CPT to generate a measure of cognitive control strategy (i.e., proactive and reactive control; Braver, 2012). The task, data, and cleaning of these data have been previously described (Troller-Renfree et al., 2019). In short, the AX-CPT is presented as a continuous series of letter pairs composed of 4 trial types—AX, AY, BX, and BY. AX trials were the target trial type and required different response (e.g., "2" after the first stimulus called the cue, "3" after the second stimulus called the probe) than the other 3 trial types (i.e., AY, BX, and BY; "2" after the cue, "2" after the probe). AX trials were presented 70% of the time and each other trial type (AY, BX, BY) was presented 10% of the time. Participants completed a total of 150 trials presented in a pseudorandom order. Each trial began with a centrally located fixation asterisk (200 ms) followed by the presentation of the cue (500 ms) with a 1000-ms response window that displayed the central fixation asterisk. After the response window, a 3900-ms delay was displayed before the presentation of the probe (500 ms), which was followed by a response window (1000 ms).

Reaction times more than 3 SDs from each participant's mean reaction time on correct trials were removed. Accuracy and mean reaction times were then computed for each trial type and d' context was computed. d' context provides a measure of the sensitivity to the differences between target and nontarget trials while controlling for individual differences in response bias. Namely, d' context is a measure of the maintenance of the "A" vs. "B" cue before the presentation of an "X" probe. The d' context was computed by comparing correct responses on AX trials (hits) relative to incorrect responses on BX trials (false alarms). To provide an unbiased estimation, a correction was applied to cases in which there was a hit rate of 1 (hit rate = $2^{-(1/N)}$; where N = target trials) or a false alarm rate of 0 (false alarm = $1–2^{-(1/N)}$; where N = number of non-target trials). Higher d' context scores indicate a more proactive style of cognitive control because the participant was sensitive to cue information and used it to inform future responses. In contrast, lower d' context scores indicate that the participant used a more reactive style of cognitive control because the participant did not use or was not as sensitive to the cue information.

Latent growth curve specification. The latent intercept factor, representing anxiety levels at the first COVID-19 assessment (Month 1), was estimated by constraining the paths of each month to 1. The latent slope factor, representing the linear change in anxiety across the three monthly COVID-19 assessments, was estimated by constraining the paths for each month, Month 1, Month 2, and Month 3, to 0, 1, and 2, respectively. This initial model fit the data well (χ^2 (1) = 0.01, p = .94, RMSEA = 0.00, SRMR = 0.00, CFI = 1.00).

Sensitivity Analyses

Examining the variability in responses and handling of missing data using multilevel modeling

For sensitivity analyses, we examined the impact of the variability in responses during the COVID-19 assessments in the estimation of the anxiety trajectories. For this, we modeled the times of assessment as continuous measures under a multilevel modeling (MLM) framework, as opposed to ordinal in a SEM framework (see Figure S1 for the distribution of the samples).

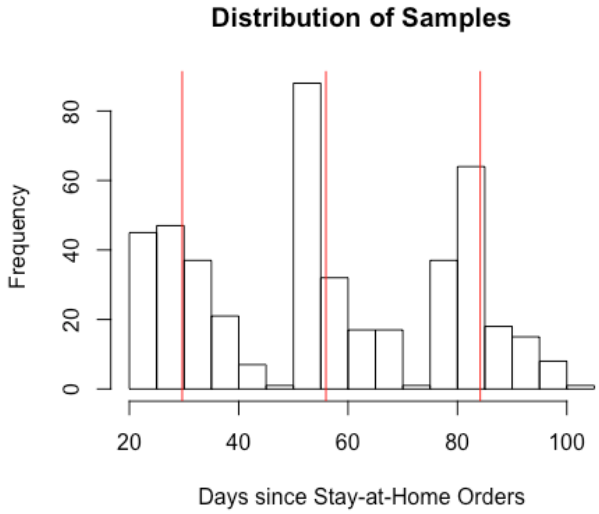

Figure S1. Distribution of anxiety assessments, shown as days since stay-at-home orders were implemented on March 30, 2020.

As in the analyses presented in the main manuscript, on average anxiety decreased across time (b = -.03 SE = 0.007, $p < .001$), suggesting that anxiety was highest at the first assessments and decreased across time as the stay at home orders were lifted and reopening gradually occurred or families adapted to the restrictions (Figure S2).

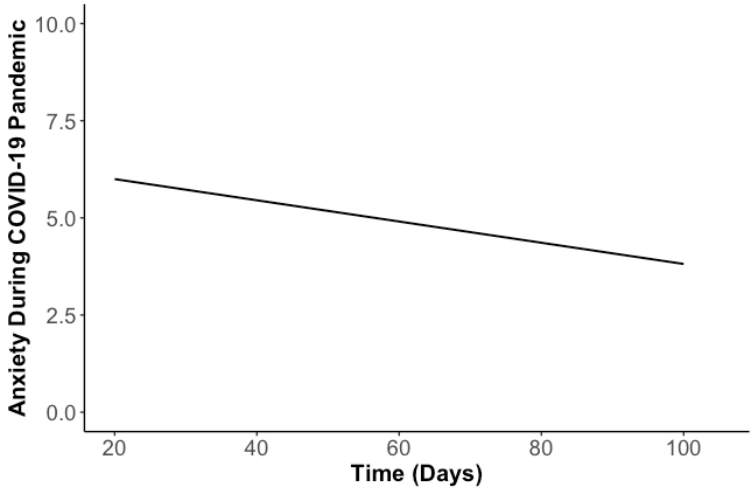

Figure S2. Average trajectory of anxiety (Generalized Anxiety Disorder 7-Item Scale) in days since stay-at-home orders were implemented on March 30, 2020.

When testing the main effect of error monitoring (delta-ERN), results showed that the delta-ERN predicted the intercept (b= -2.41, p = .001) and the slope, (b= 0.02, p = .006), of the anxiety trajectory. As shown in Figure S3, a larger delta-ERN predicted a larger intercept (i.e., greater anxiety at Month 1), but a more negative slope (i.e., greater decreases across time).

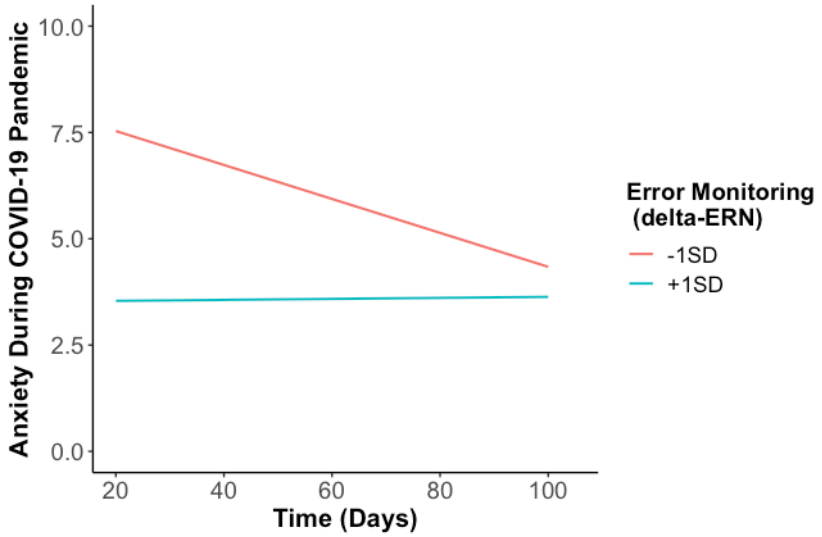

Figure S3. The impact of error monitoring on anxiety trajectories during the COVID-19 pandemic. Note that more error monitoring (a larger delta-ERN) is indicated by a more negative value and more proactive control is indicated by higher d' context values. Lines show the predicted anxiety trajectories at different levels of error monitoring (delta-ERN).

When examining the model with the neurocognitive predictors, results revealed that the interaction between error monitoring (delta-ERN) and cognitive control strategy (d' context) predicted the intercept (b= 2.65, p = .001) and the slope, (b= -0.02, p = .005) of the anxiety trajectory. As shown in Figure S4, probing this interaction by plotting the predicted trajectories for the different levels of delta-ERN and d' context, adolescents with both enhanced error monitoring (more negative delta-ERN) and an increased reliance on more instantaneous (reactive) control (as opposed to planful/proactive control) displayed a larger intercept (i.e., greater anxiety at Month 1), but a more negative slope (i.e., greater decreases across time).

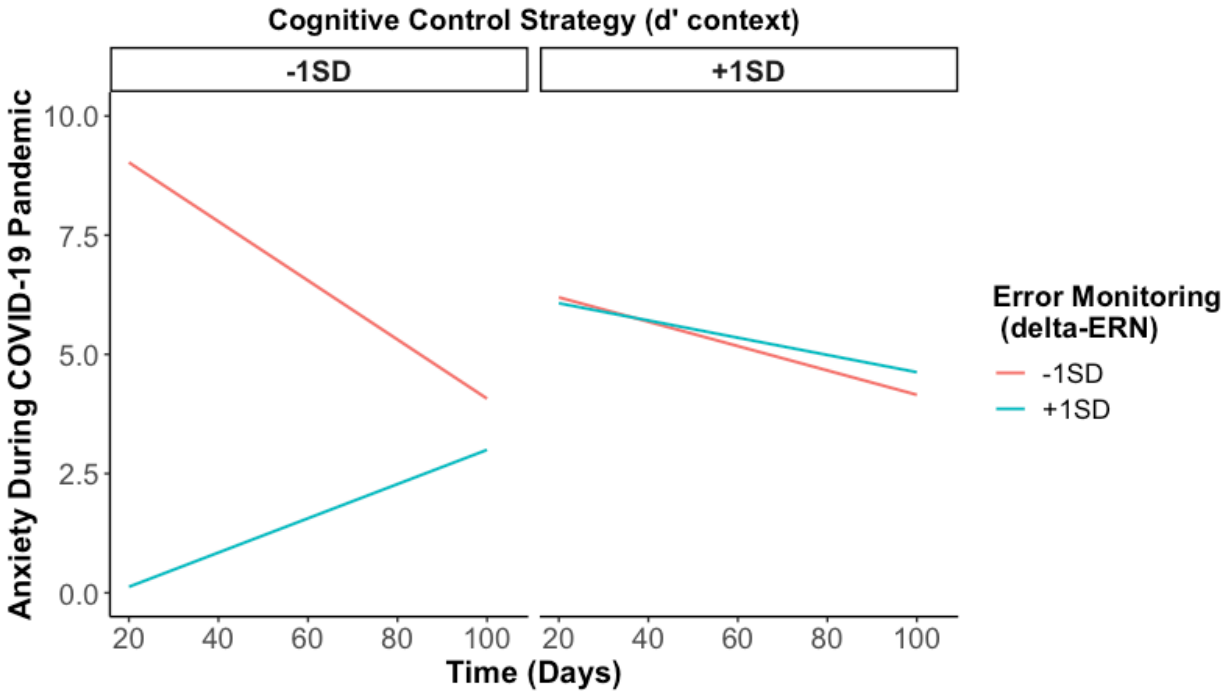

Figure S4. The impact of error monitoring and cognitive control strategy on anxiety trajectories during the COVID-19 pandemic. Note that more error monitoring (a larger delta-ERN) is indicated by a more negative value and more proactive control is indicated by higher d' context values. Lines show the predicted anxiety trajectories at different levels of error monitoring (delta-ERN) and cognitive control strategy.

In sum, these analyses reveal the same pattern of results, yielding the same conclusions as the analyses presented in the main text. Importantly, the MLM approach used maximum likelihood with listwise deletion on the covariates/predictors rather than FIML. As such, these sensitivity analyses also suggest that different ways of handing missing data do not significantly impact the results.

Examining the effects of the ERN and CRN separately

In another set of sensitivity analyses, we examined the independent contributions of the CRN and ERN. The ERN (M = -0.52, SD = 2.66) and CRN (M = 2.01, SD = 2.14) were correlated with each other, $r(122)=.27$, $p=.002$. The ERN and CRN did not significantly predict anxiety at any time point – albeit the ERN marginally predicted the first assessment of anxiety, $r(122)=-.20$, $p=.051$. We tested the same models as the ones tested in the main manuscript predicting the intercept and slope of the anxiety trajectories, but we included both the ERN and CRN as separate predictors (rather than as a difference score). As shown in Table S1, results revealed that only the ERN was predictive of the anxiety trajectories. Moreover, as shown in Table S2, when examining the interaction between error monitoring and cognitive control strategy, the ERN interaction also predicted the anxiety intercept and the slope prediction, albeit a non-significant trend, it was in the same direction as the findings reported with the difference score. Importantly, there were no significant effects of the CRN and its interaction with cognitive control strategy on the anxiety trajectories (Tables S1 and S2). Moreover, although not significant, the effects of the CRN were in the opposite direction. The results from these

sensitivity analyses suggest that the effects are mostly driven by the ERN and that utilizing a difference score is appropriate.

Table S1. *Latent growth curve analysis results for the model including error monitoring, including the ERN and CRN separately, rather than the delta-ERN.*

Predictors/Outcome	***β***	***b***	***p***	**CI Lower**	**CI Upper**
Anxiety Intercept					
Maternal Education	**0.20**	**1.56**	**0.012**	**0.338**	**2.786**
Maternal Ethnicity	0.13	1.57	0.122	-0.419	3.560
Gender	-0.14	-1.56	0.087	-3.358	0.229
Average Age	-0.03	-0.23	0.750	-1.677	1.207
Date of First Assessment	-0.07	-0.07	0.288	-0.189	0.056
Anxiety (13 yrs)	0.20	0.10	0.057	-0.003	0.193
Flanker Task Accuracy	-0.19	-1.04	0.091	-2.240	0.165
CRN	0.20	0.52	0.103	-0.105	1.141
ERN	**-0.35**	**-0.73**	**0.010**	**-1.284**	**-0.175**
Anxiety Slope					
Maternal Education	-0.15	-0.38	0.136	-0.883	0.120
Maternal Ethnicity	0.04	0.17	0.697	-0.702	1.050
Gender	0.12	0.44	0.306	-0.401	1.277
Average Age	0.00	0.00	0.988	-0.616	0.625
Date of Third Assessment	-0.07	-0.02	0.414	-0.080	0.033
Anxiety (13 yrs)	0.06	0.01	0.659	-0.030	0.047
Flanker Task Accuracy	0.08	0.15	0.676	-0.559	0.862
CRN	-0.27	-0.23	0.121	-0.516	0.060
ERN	**0.42**	**0.28**	**0.017**	**0.050**	**0.519**

Note: ERN = Error-related Negativity; Gender is coded as 0 = Females and 1 = Males; Maternal Ethnicity is coded as Non-Hispanic Caucasian = 1 and Other = 0. This model fit the data well, $\chi^2(13) = 13.70$, $p = .40$, RMSEA = .01, SRMR = .02, CFI = 1.00).

Table S2. *Latent growth curve analysis results for final model including neurocognitive predictors, including the ERN and CRN separately, rather than the delta-ERN.*

Predictors/Outcome	***β***	***b***	***p***	**CI Lower**	**CI Upper**
Anxiety Intercept					
Maternal Education	**0.21**	**1.58**	**0.014**	**0.324**	**2.832**
Maternal Ethnicity	0.08	0.99	0.363	-1.142	3.120
Gender	-0.14	-1.46	0.130	-3.358	0.431
Average Age	-0.01	-0.08	0.911	-1.421	1.268
Date of First Assessment	-0.04	-0.03	0.574	-0.156	0.087
Anxiety (13 yrs)	**0.23**	**0.10**	**0.031**	**0.010**	**0.200**
Flanker Task Accuracy	-0.19	-1.03	0.085	-2.193	0.143
ERN	**-0.47**	**-0.96**	**0.000**	**-1.469**	**-0.443**
CRN	**0.28**	**0.71**	**0.022**	**0.101**	**1.320**
AX-CPT d'	0.17	0.94	0.158	-0.364	2.243
ERN x AX-CPT d'	**0.38**	**0.74**	**0.024**	**0.098**	**1.382**
CRN x AX-CPT d'	-0.25	-0.65	0.090	-1.403	0.102
Anxiety Slope					
Maternal Education	-0.15	-0.34	0.235	-0.893	0.219
Maternal Ethnicity	0.08	0.30	0.554	-0.691	1.289
Gender	0.13	0.42	0.318	-0.404	1.243
Average Age	0.00	0.00	0.999	-0.596	0.595
Date of Third Assessment	-0.08	-0.02	0.402	-0.077	0.031
Anxiety (13 yrs)	0.06	0.01	0.670	-0.029	0.045
Flanker Task Accuracy	0.07	0.11	0.772	-0.654	0.881
ERN	**0.56**	**0.35**	**0.009**	**0.086**	**0.611**
CRN	-0.38	-0.29	0.053	-0.588	0.004
AX-CPT d'	-0.07	-0.12	0.682	-0.691	0.452
ERN x AX-CPT d'	-0.41	-0.24	0.106	-0.534	0.051
CRN x AX-CPT d'	0.30	0.24	0.239	-0.158	0.633

Note: ERN = Error-related Negativity; Gender is coded as 0 = Females and 1 = Males; Maternal Ethnicity is coded as Non-Hispanic Caucasian = 1 and Other = 0. This model fit the data well, $\chi^2(16) = 21.07$, $p = .18$, RMSEA = .03, SRMR = .02, CFI = .98).

Reliability analysis of ERPs

We examined the internal consistency reliability of the ERN, CRN, and the delta-ERN in our sample in increasing numbers of trials from 4 to 40 trials using a Spearman-Brown split-half correlation procedure with multiple iterations (N = 3000) (Leach et al., 2020; Morales et al., 2021).This procedure helped us determine the minimum number of trials needed to obtain an ERN estimate with average acceptable reliability (.6). As shown in Figure S5, results suggested that participants needed at least 10 trials for a reliable ERN and at least 15 trials for a reliable delta-ERN. As such, in the main manuscript, we only include participants with at least 15 trials per condition. Importantly, the overall reliability of the delta-ERN was good (Spearman-Brown r=.84). Moreover, the results are very similar when using an a priori minimum trial cutoff of six trials (Pontifex et al., 2010; Steele et al., 2016), which provides three more participants with ERN data. Namely, the delta-ERN predicted the anxiety trajectories; the delta-ERN predicted the intercept, b= -1.89, p = .005, and the slope, b= 0.76, p = .004. Moreover, the delta-ERN interaction with cognitive control strategy (d') also predicted the anxiety trajectories, such that adolescents with an enhanced delta-ERN an increased reliance on more reactive control (as opposed to planful/proactive control) displayed a larger intercept (greater anxiety in Month 1; b= 2.34, p = .006), but a more negative slope (i.e., greater decreases in anxiety across time; b= -0.81, p = .034). This suggests that this methodological decision does not have a significant impact in the results.

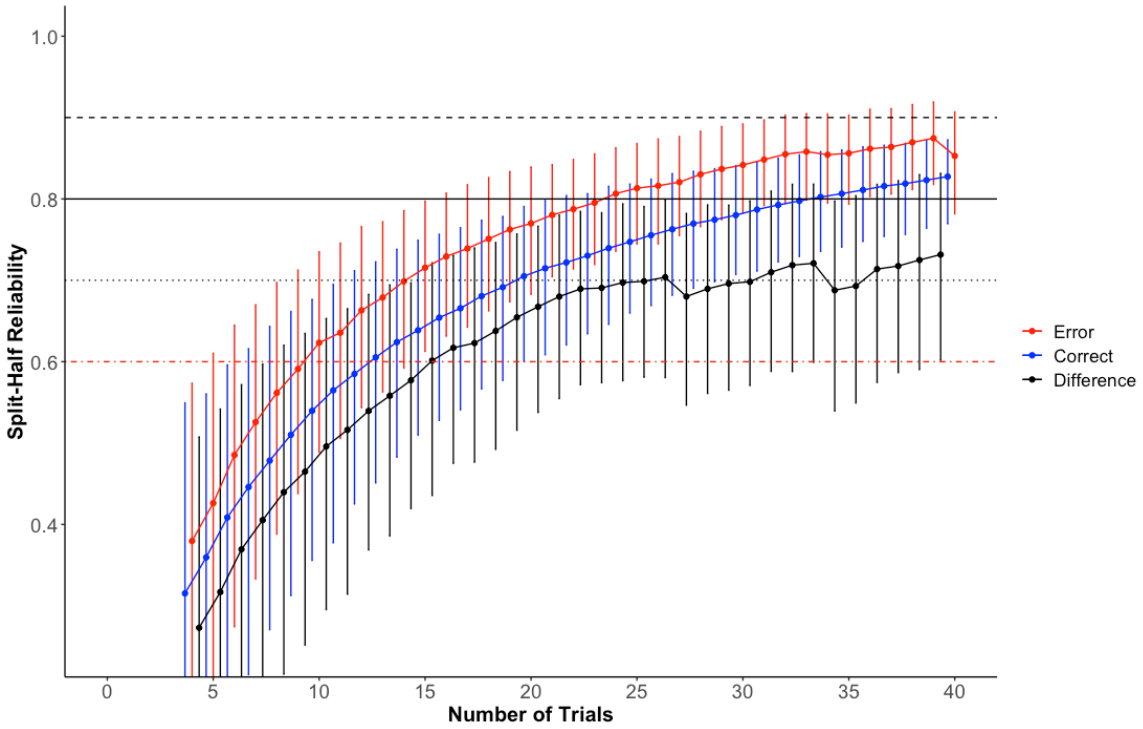

Figure S5. ERP reliability. The plot shows the split-half reliability for the ERN, CRN, and their difference score (delta-ERN) in increasing numbers of trials. Error bars indicate the 95% CI of the resampling distributions (N=3000).

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