Principle ERP reduction and analysis:

Estimating and using *principle ERP* waveforms underlying ERPs across tasks, subjects and electrodes

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In a nutshell

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4. Easy: `pERPred` package for `R`.

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- In a future experiment with different participants and a different task, amplitude around 300ms may not index the same thing. *Problematic to employ a P3-measure as an index of any process in any other experiment.*
- In general, changes in other, overlapping signals can cause the target signal to generate an ERP peak earlier, later, or not at all!
- We'll see an example where even a visual "N1" doesn't peak...but it's there.

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2. Estimate a suitable set of "principle-ERPs" from your multi-subject, multi-task, data via the **pERP-red** algorithm.

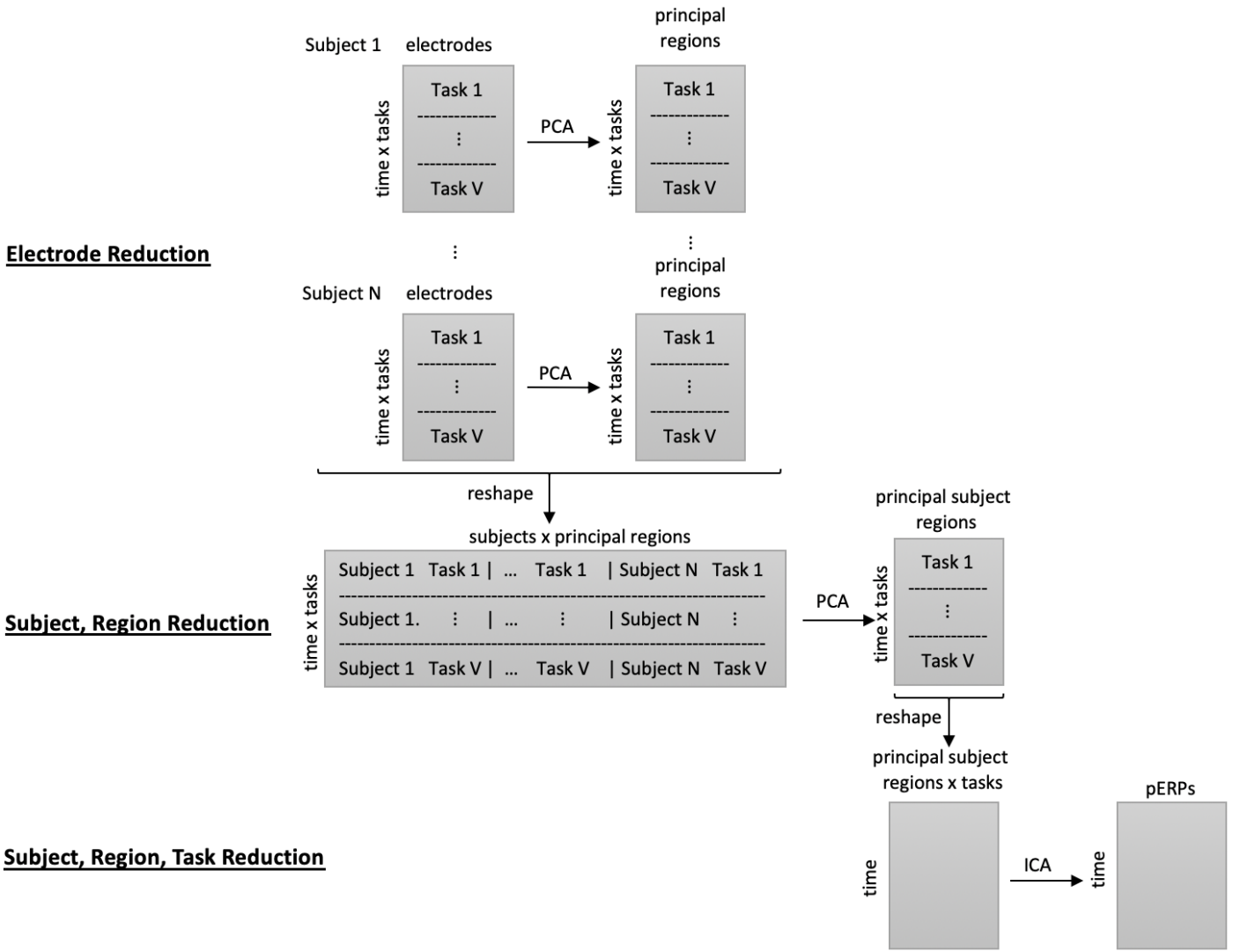
3. Analyze the observed ERPs by asking what pERPs contribute to them, how those contributions vary across individuals, groups, or conditions, **pERP-space analysis**.

The pERP-red procedure

1. *Data pre-processing.* Make your own ERP records. Split into a training set and test set. Normalize each of the resulting ERPs to have unit variance.
2. *Electrode reduction.* On training set, by subject, use PCA to go from all electrodes to a smaller set of "principle-electrodes" or "regions". Retain enough to explain (e.g.) 80-90% of variation.
3. *Subject-region reduction.* Take matrix with region-subject columns and rows given by trial-type and time. Use PCA to reduce this to N_R "principal subject-regions." Retain (e.g.) 80-90% of variation.
4. *Source separation.* Reshape into a matrix with all "principal subject-regions trial types" as the columns and time as the rows. Use ICA to produce C principle ERPs.
   - C chosen by regressing the true signal (in the test set) onto the components and obtaining an R^2 value.

The pERP-red procedure

Schematic of pERP-RED algorithm



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- That said, the bigger shift in what we propose is in the way these are then used, pERP-space analysis.

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where $Y_{i,v,e}(t)$ is the ERP signal observed for subject i (of 100) at task v (of 9) and electrode e (of 40).

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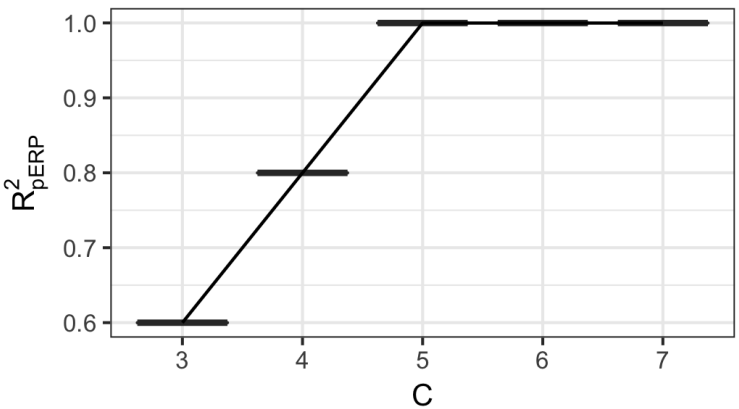
- $\zeta_{i,v,e}(t)$ is noise; we vary the total signal-to-noise ratio with a high noise setting (2/3 of the simulated ERP will be noise) and a low noise (1/3) setting.

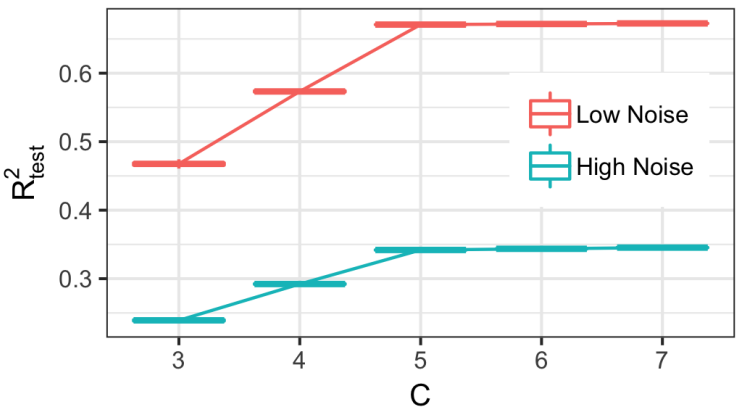
Simulation results

How accurately did we recover the true pERPs?

(a) pERP Regression



(b) Individual Record Regression



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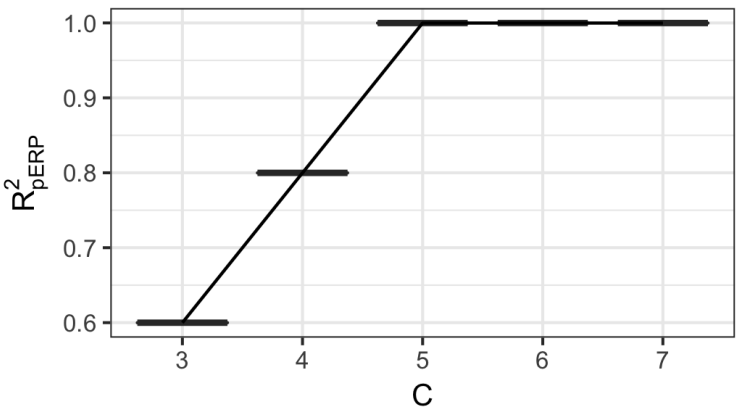

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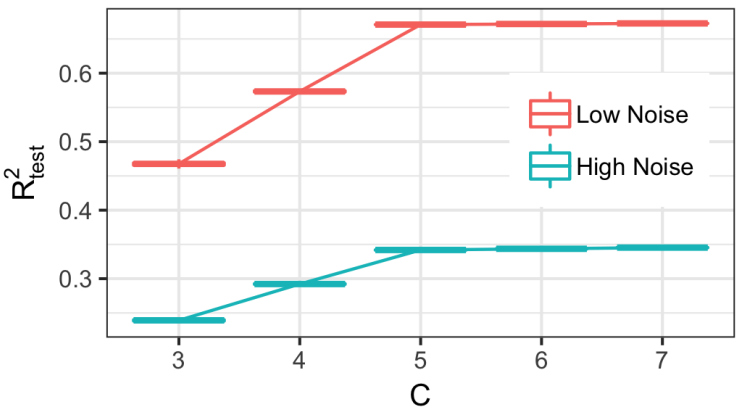

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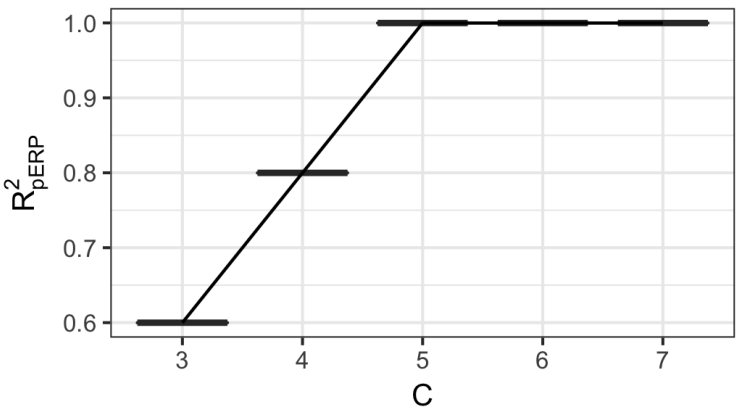

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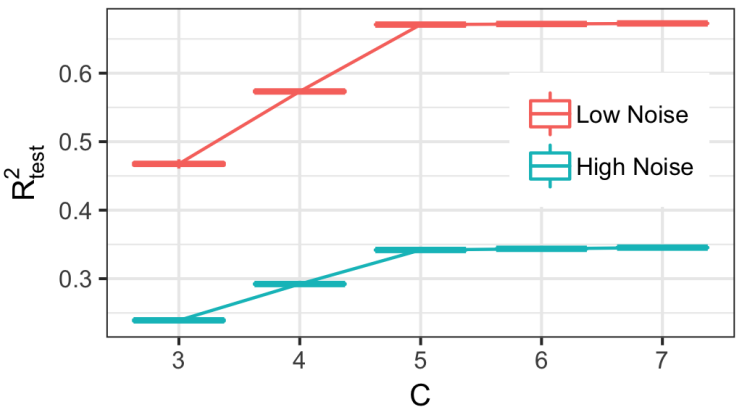
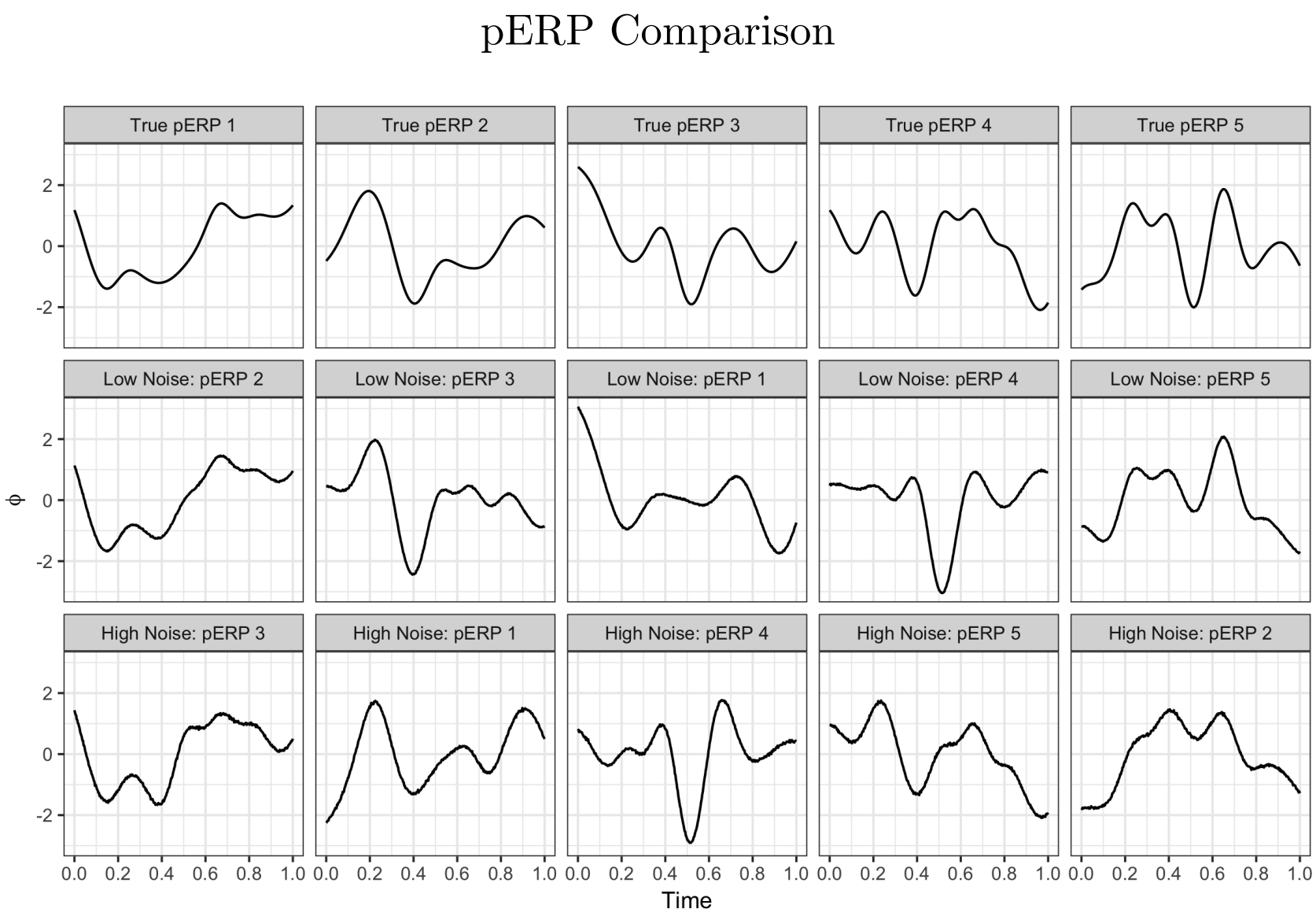


(a) R^2 from regressing the true pERPs on the estimated pERPs in 100 simulation runs.

(b) R^2 from regressing ERP records on the estimated pERPs, in the test data, for high and low noise simulations

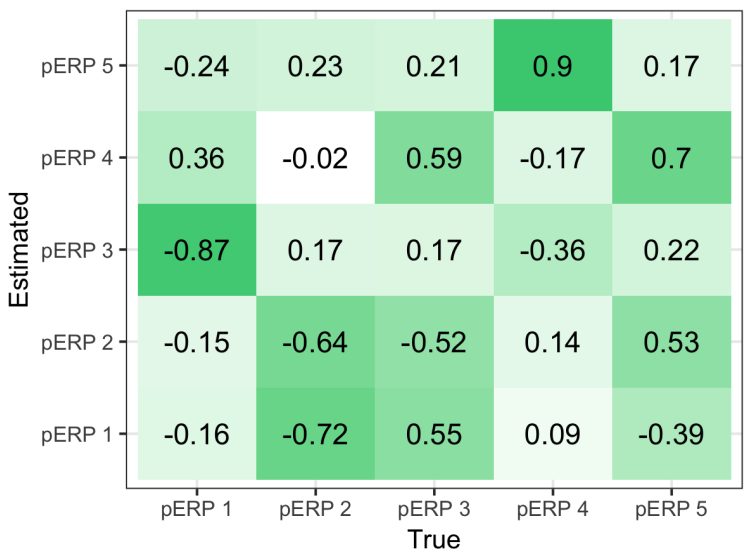
Simulation results 2



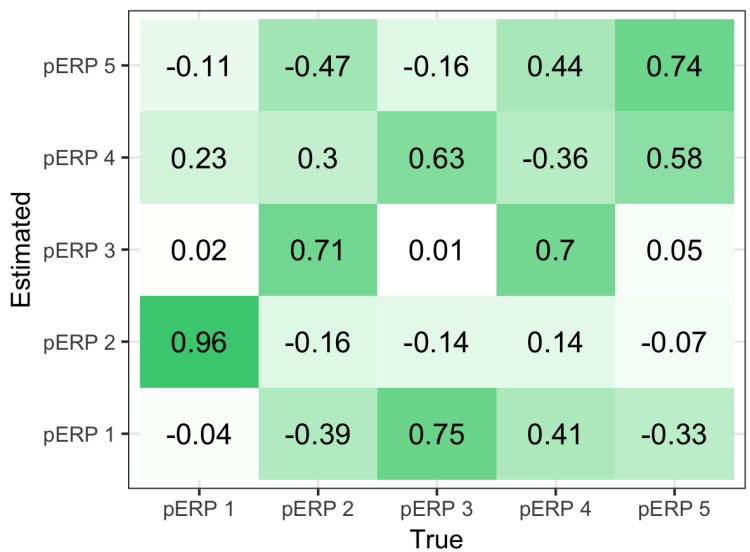
Simulation results 3

Regression coefficient heatmaps from regressing the true components on the pERPs

(a) High Noise



(b) Low Noise



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Main Idea

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Step 1: Individual scoring. For individual j and condition c, store the ERP in Y_{jc}. Regress Y_{jc} on the pERPs (columns of Φ),

$$\hat{\omega}_{jc} = (\Phi^{\mathrm{T}}\Phi)^{-1}\Phi^{\mathrm{T}}Y_{jc}. \tag{1}$$

- $\hat{\omega}_{jc}$ encodes the ERP Y_{jc} with a vector of coefficients (aka amplitudes, loadings, weights) describing each pERPs contribution.

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- Treat these as data.

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- **SD**: Variation across participants on pERP c, the across-person-standard-deviation (APSD),

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- **SE**: Statistical uncertainty around the mean

$$SE_{g,c} = \sqrt{\frac{\sum_{j \in G_g} \frac{(\omega_{jc} - \overline{\omega}_c)^2}{||N_g|| - 1}}{N_g}}$$

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1. For a given group/condition, test each pERP's average magnitude, $\overline{\omega}_c(g)$ against null hypothesis of zero. i.e.

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8. Outlier detection: individuals with unusual ω_{jc}.

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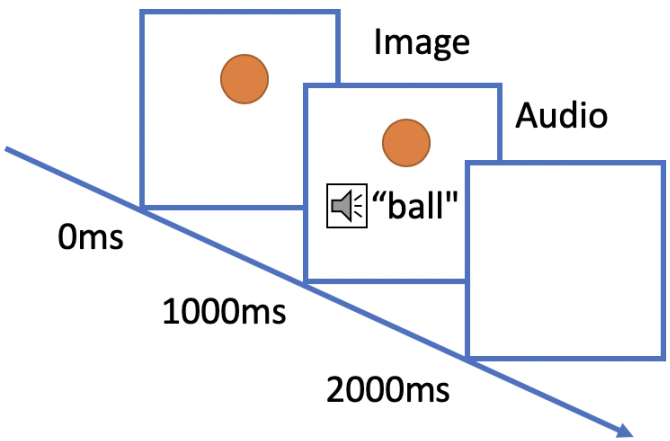

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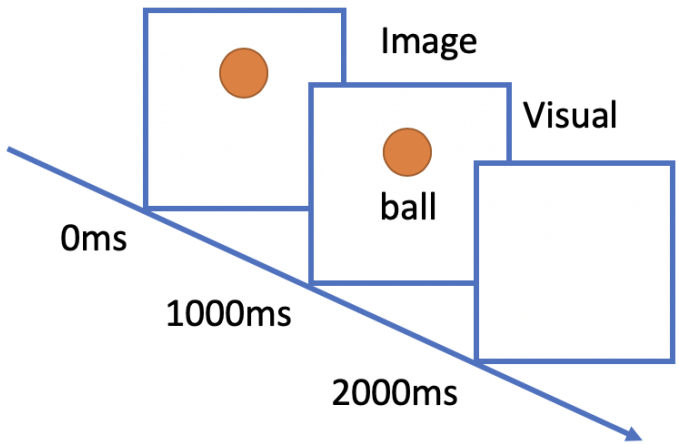

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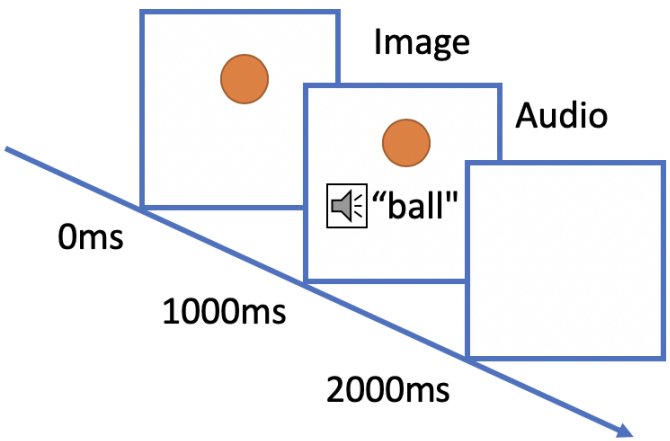

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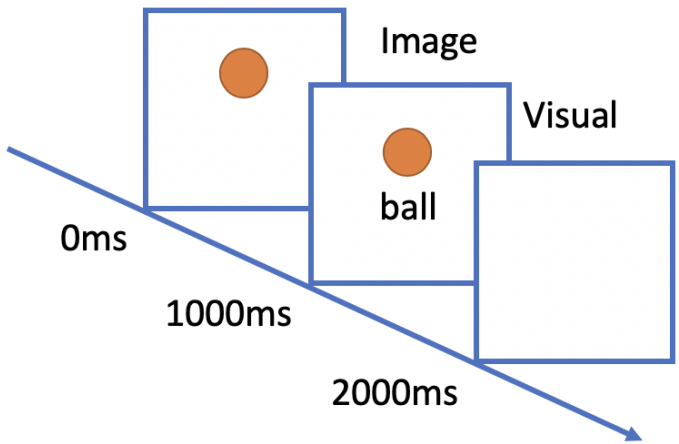
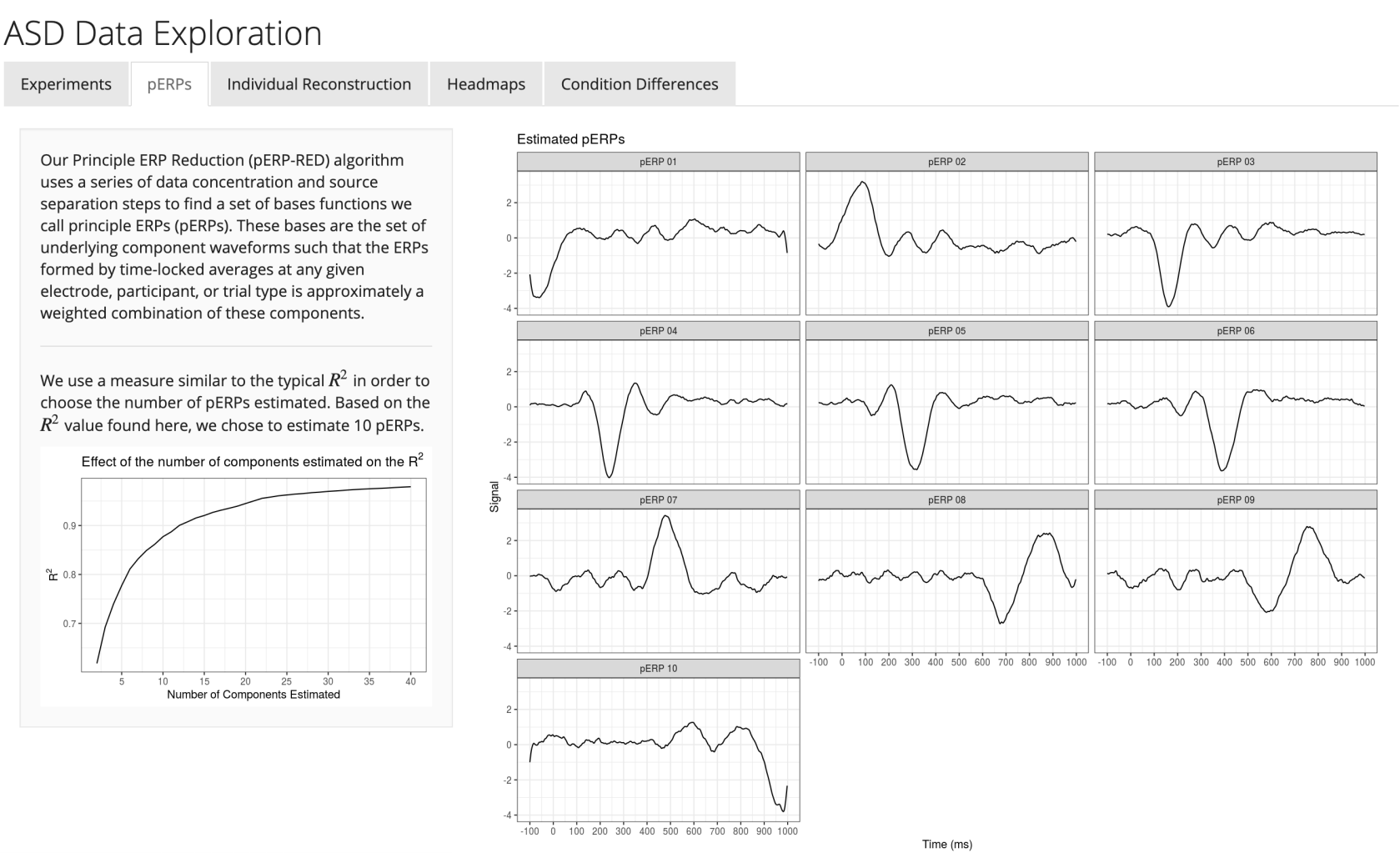


- ERPs time-locked to: Image, Audio-Match, Audio-Mismatch, Visual-Match, Visual-Mismatch
- pERP-red: 10 components capture 89% of variation

ASD Study: See the pERPs

Explore: `https://perpred.shinyapps.io/asd_exploration/`



ASD Study: ERP reconstruction example

ASD Data Exploration

Experiments | pERPs | Individual Reconstruction | Headmaps | Condition Differences

Each of the observed ERPs can be reconstructed using the pERPs. The observed ERP is regressed on the pERPs to obtain a set of scores and using those scores, the pERPs are projected onto the observed ERP. This typically results in a smoother ERP.

Subject:

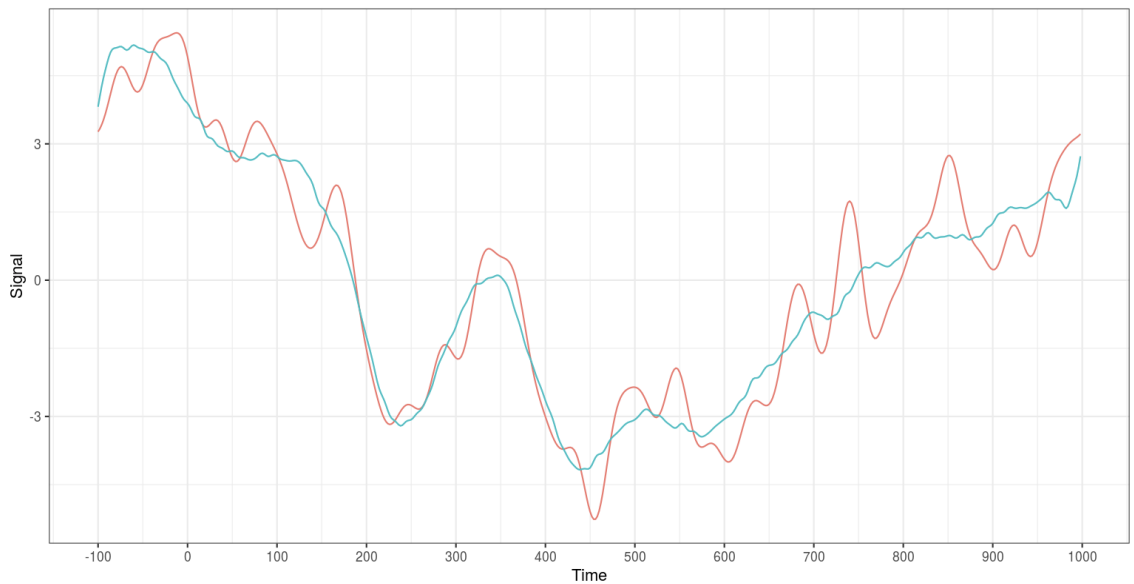
Subject0001 mvASD

Task:

Image

Electrode:

C3



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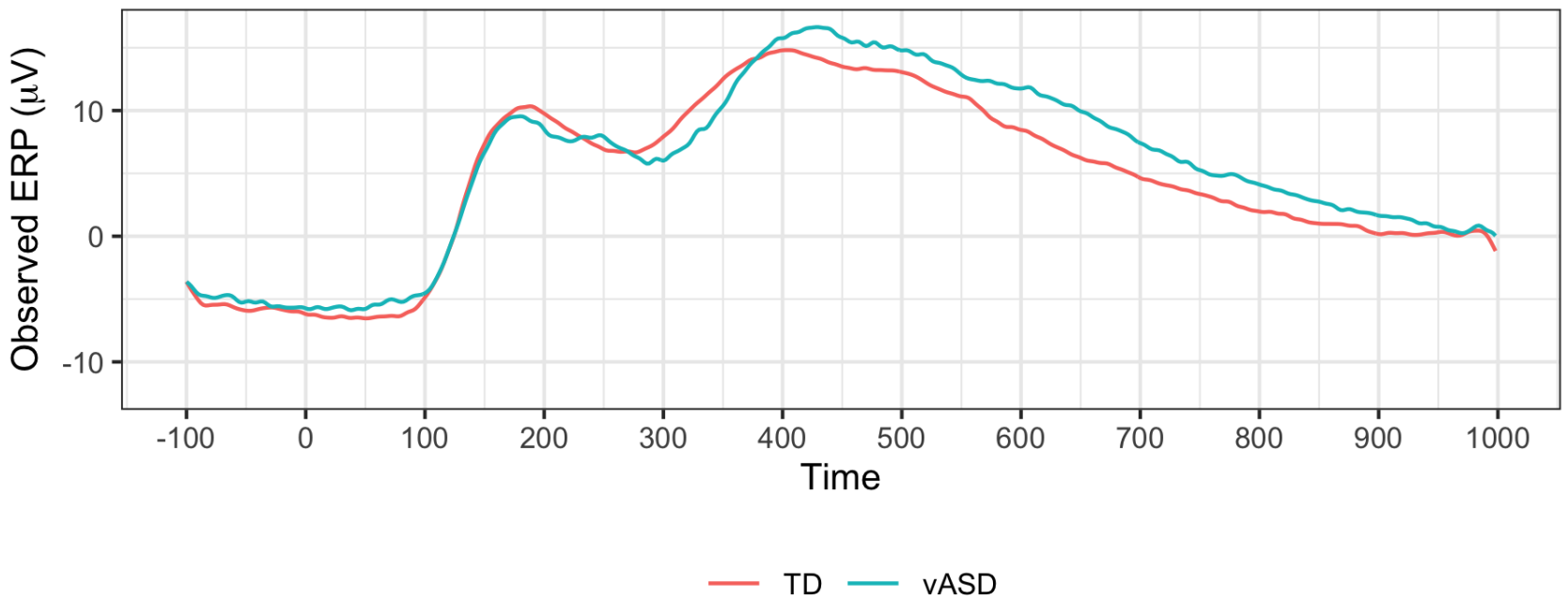

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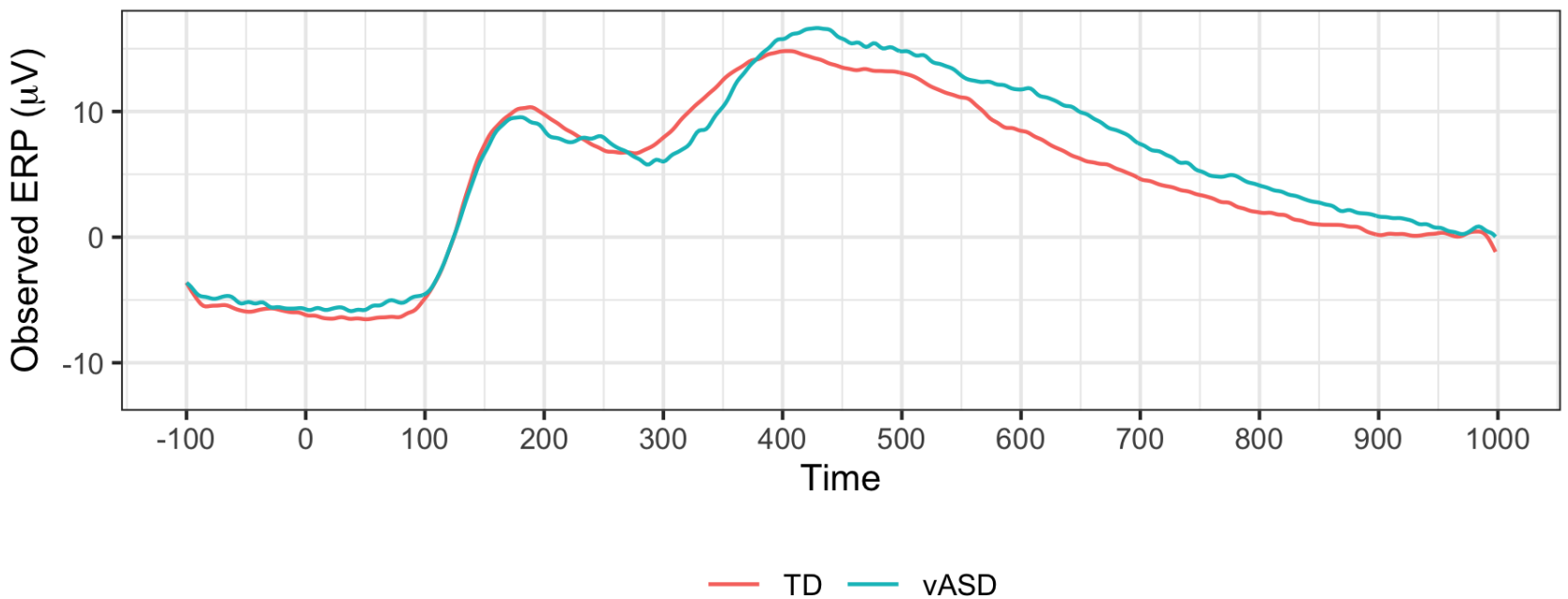
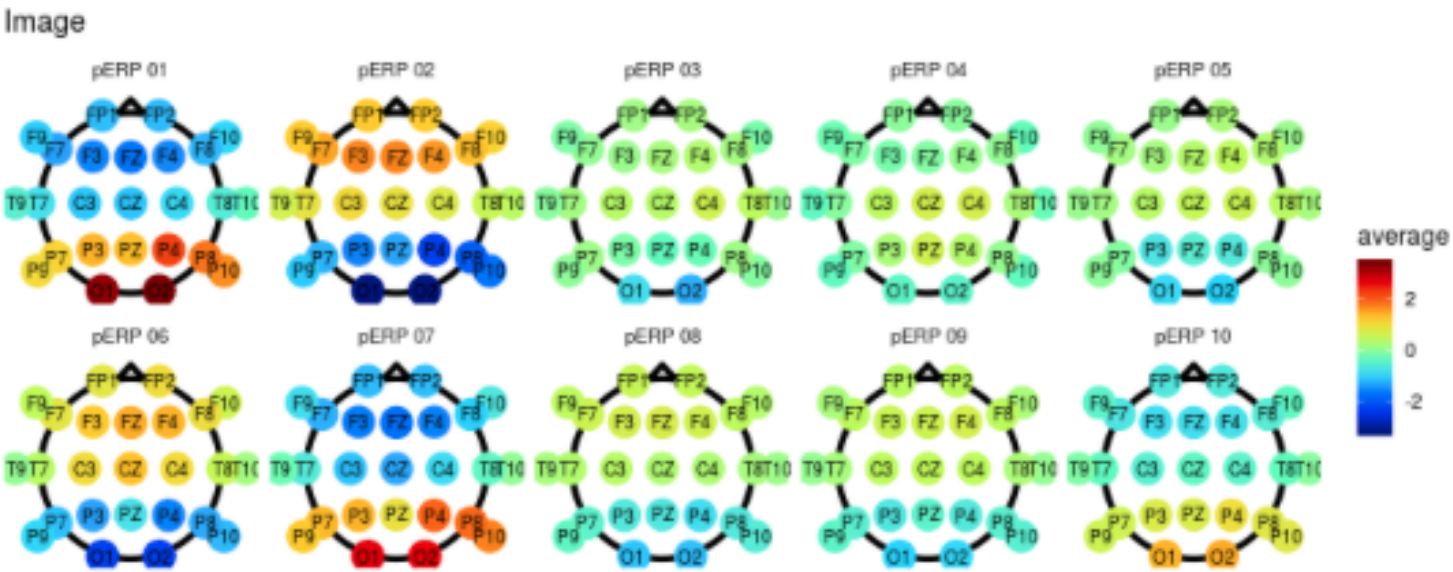


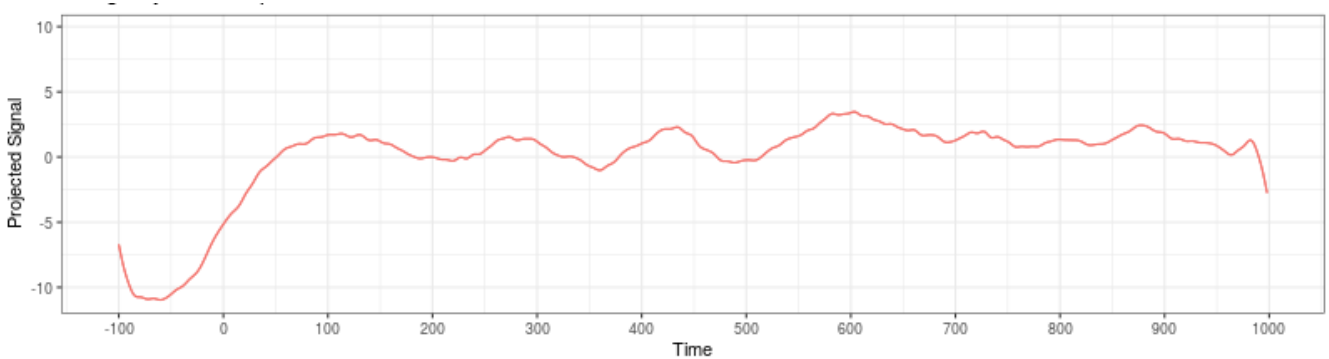
Surprising shape, particularly flat line where N1 might be expected – let's see what is happening early on.

Early activity despite flat line



pERP1 and pERP2 at O1

pERP1 contribution (mean=3.23, se=0.28, t=11.6):



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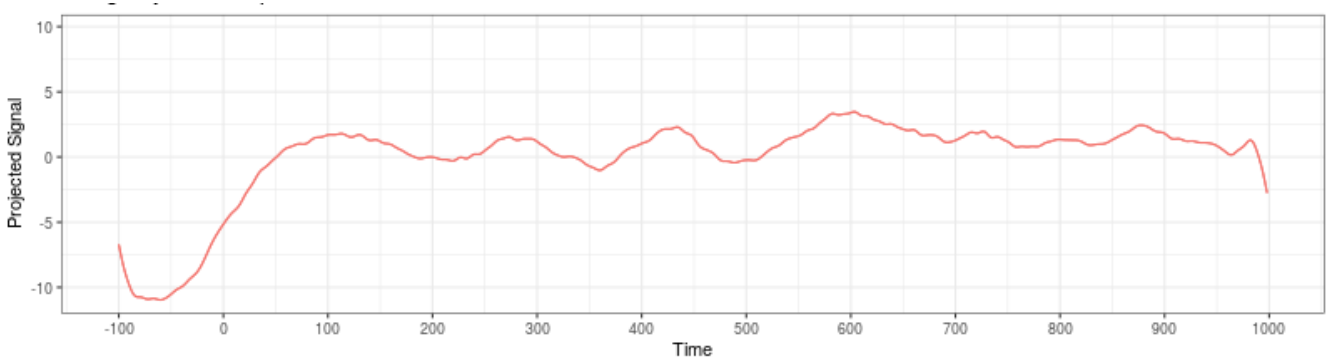
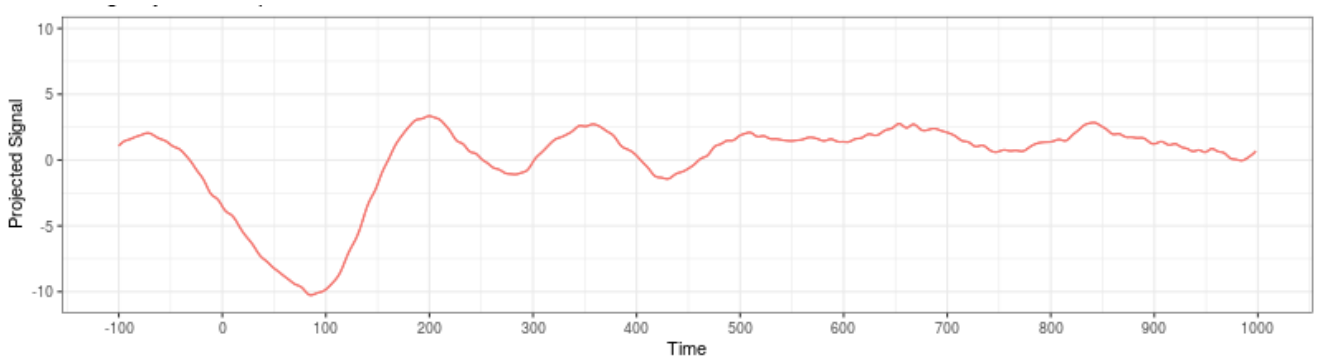


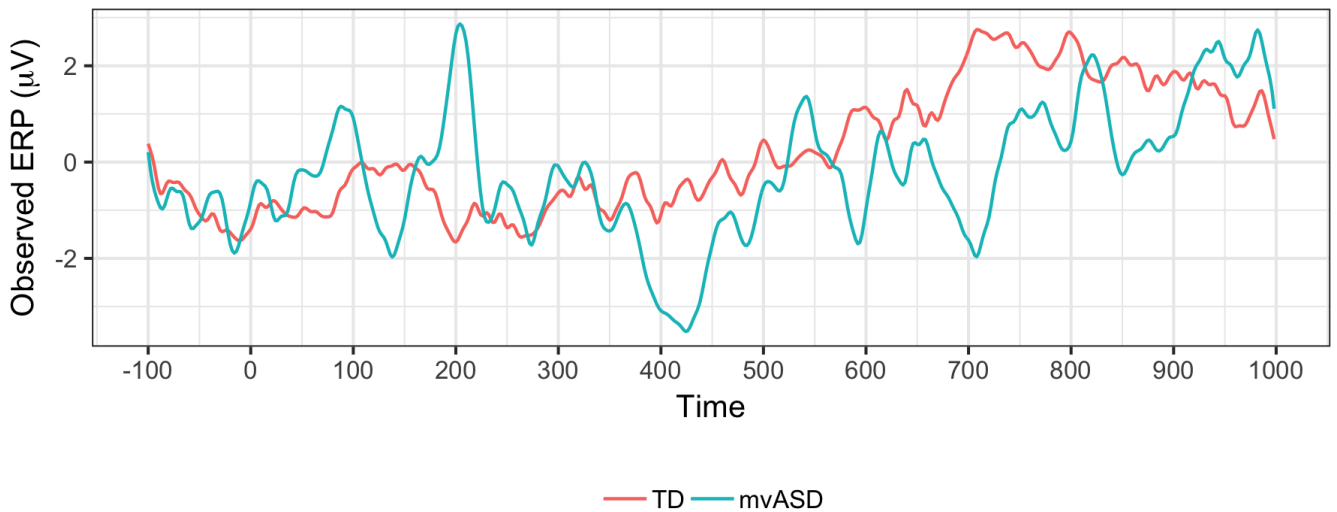
pERP2 contribution (mean=3.21, se=0.32, t=10.1)



It appears an N1-like component was there but overlap from prior trials made it not peak in the ERP.

Sound, match-vs-mismatch condition

Hard to see much in actual ERPs (F4):



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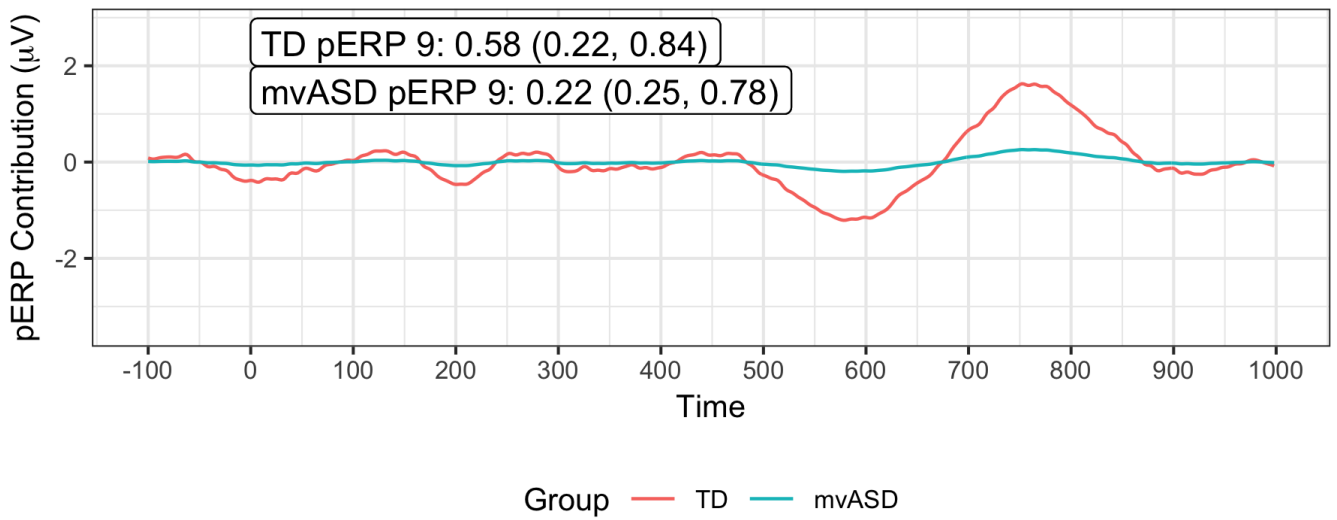
Focusing on pERP loadings with significant group differences:



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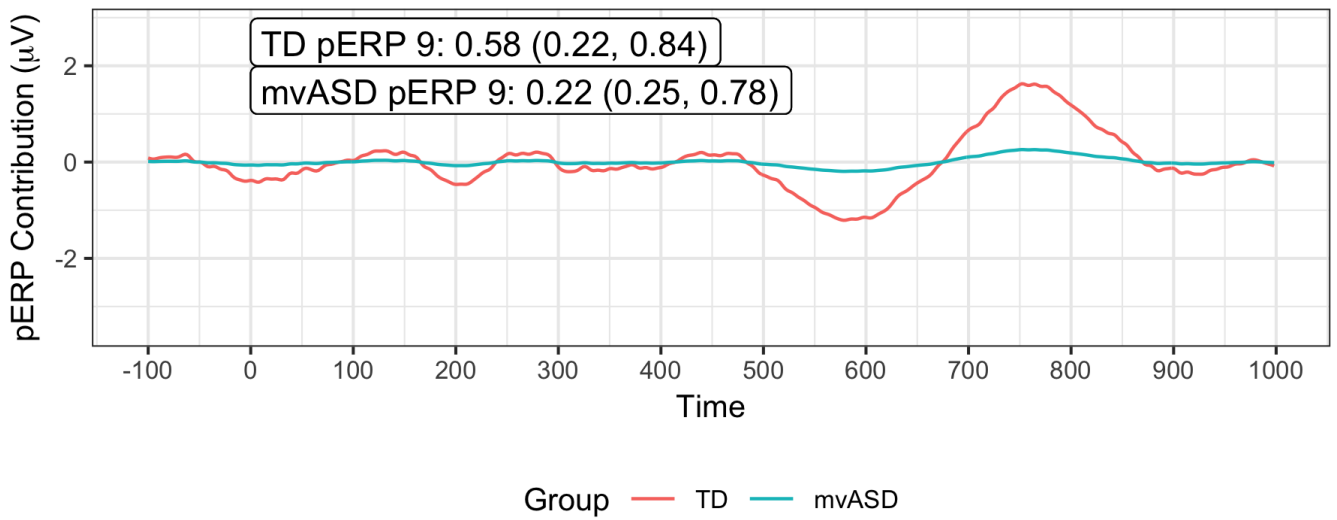

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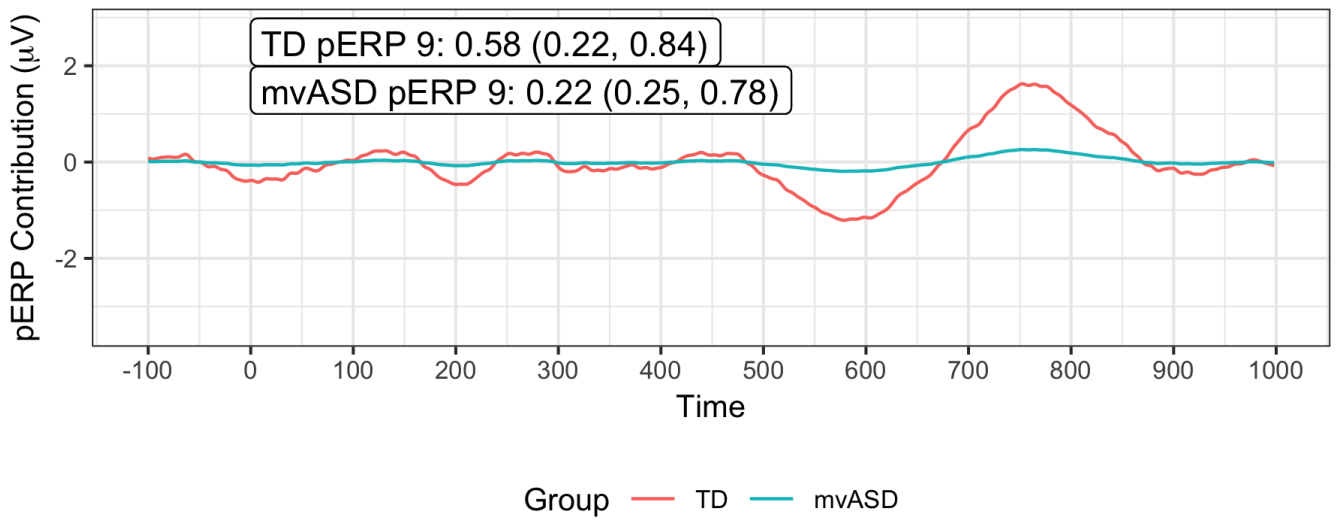

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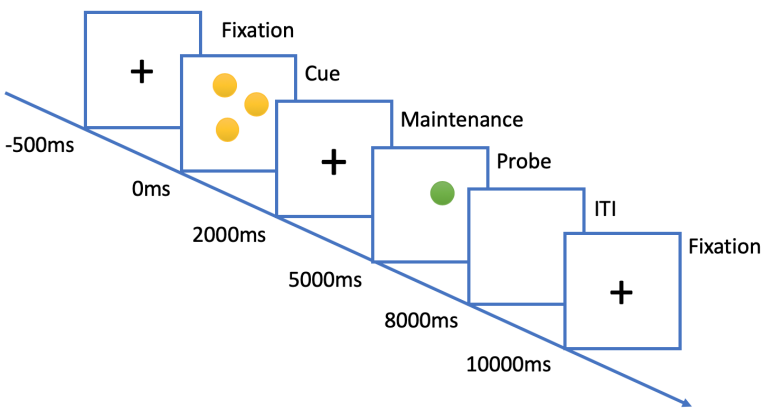
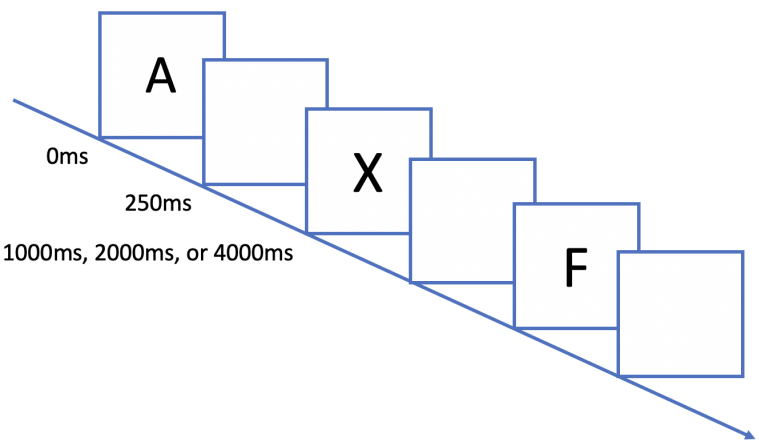


(b) ADHD CPT



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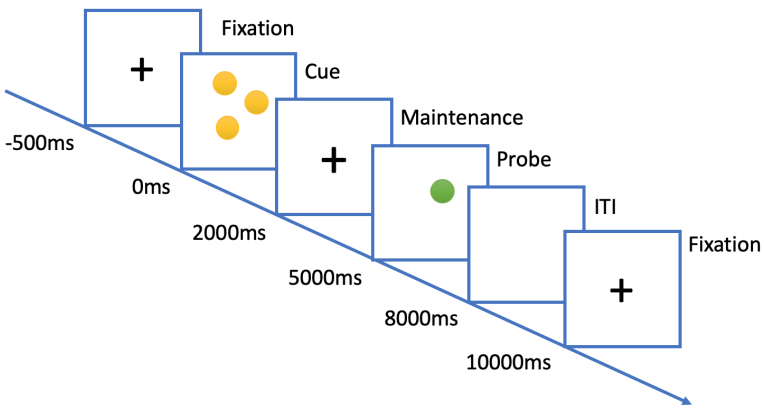

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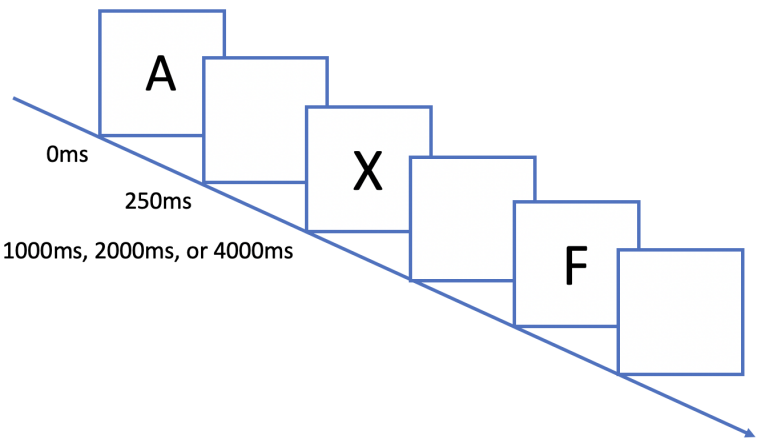

Use ERPs time-locked to: SDRT CUE, SDRT Probe, SDRT Response, SDRT Maintenance, CPT-X Correct, CPT-X Incorrect, CPT Not-X Correct, CPT Not-X Incorrect.

Cross-task expectations: N1/P2-like contributions

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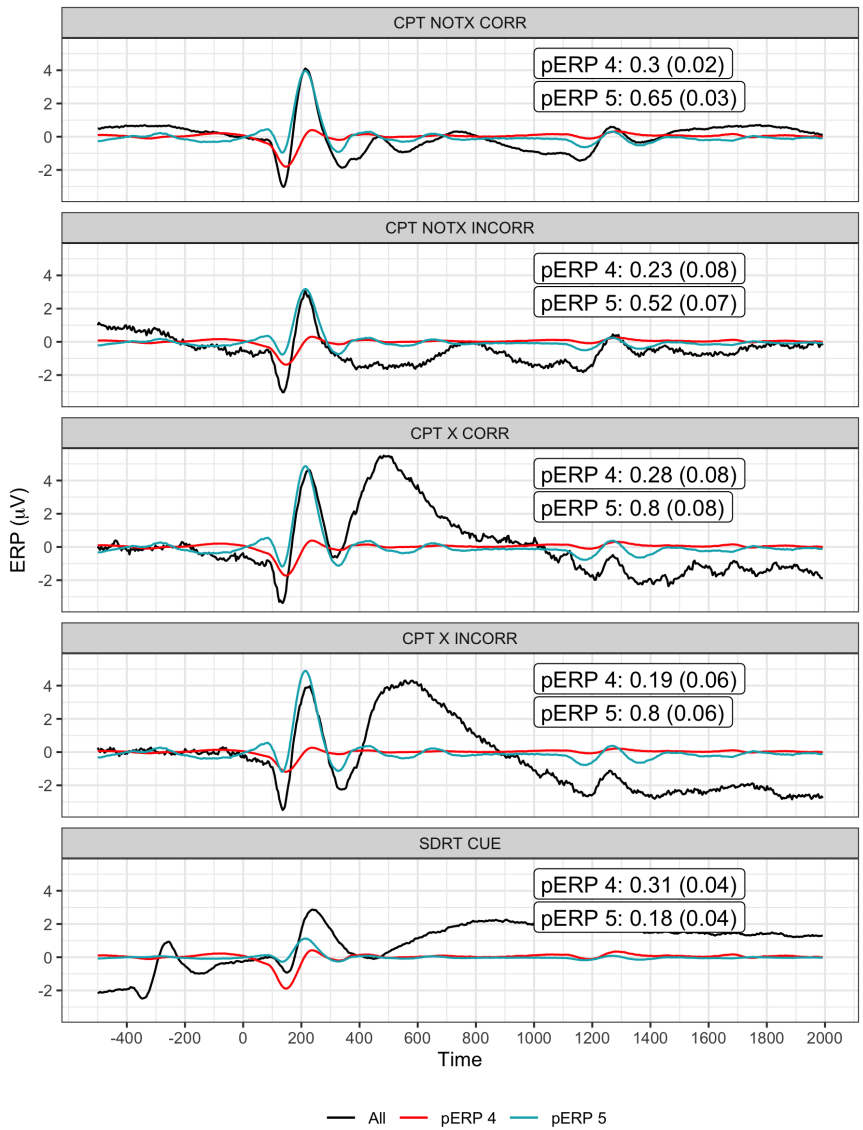
  - For other trial types (response-locked, probe-locked, maintenance) we don't see this.

N1/P2-like contributions where expected

Five trial types time-locked to visual stimuli, Cz:



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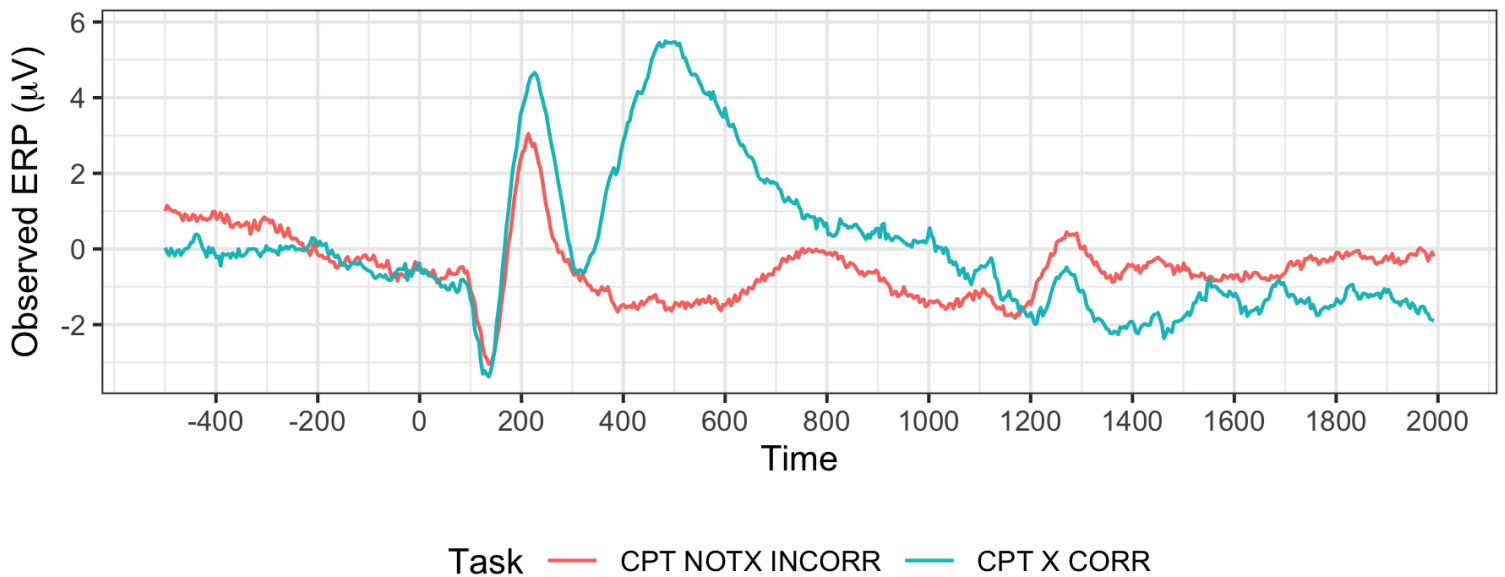

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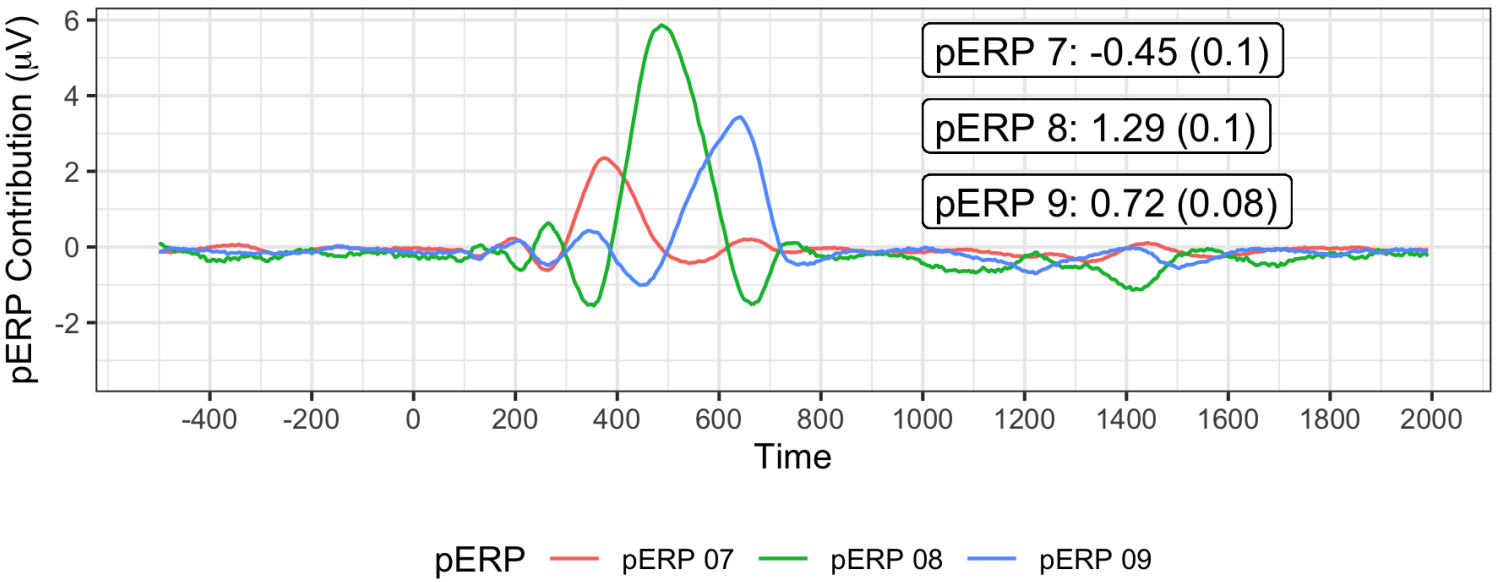

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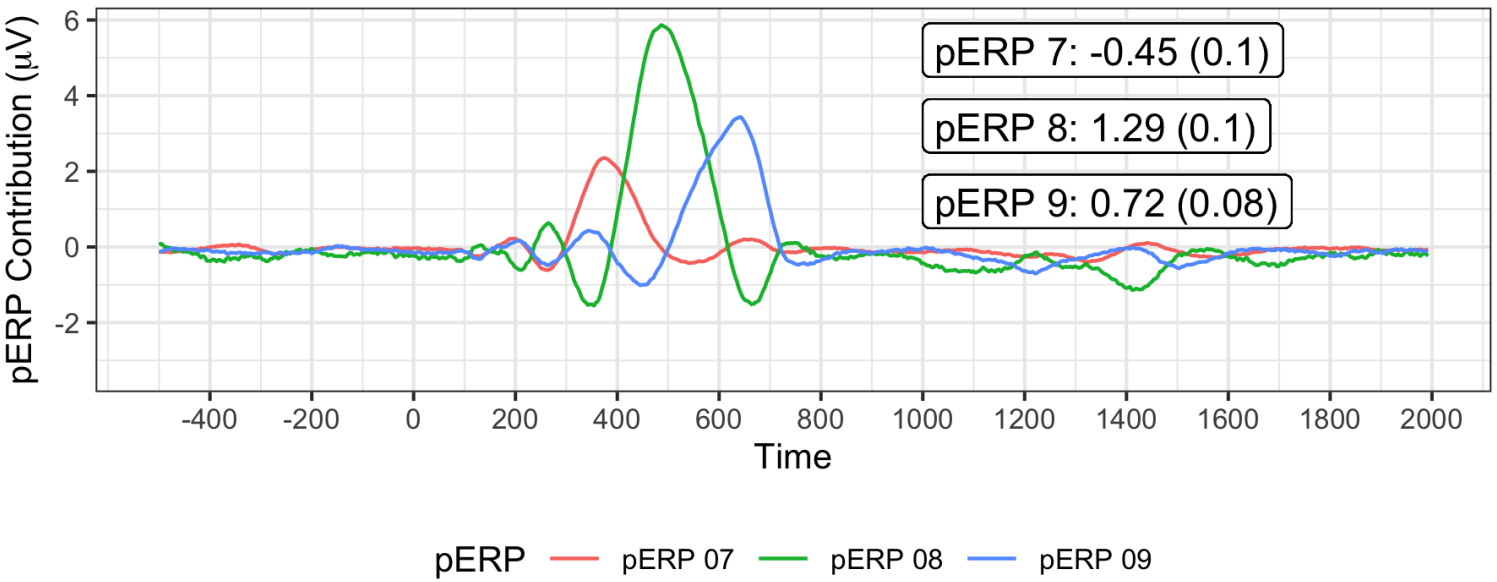

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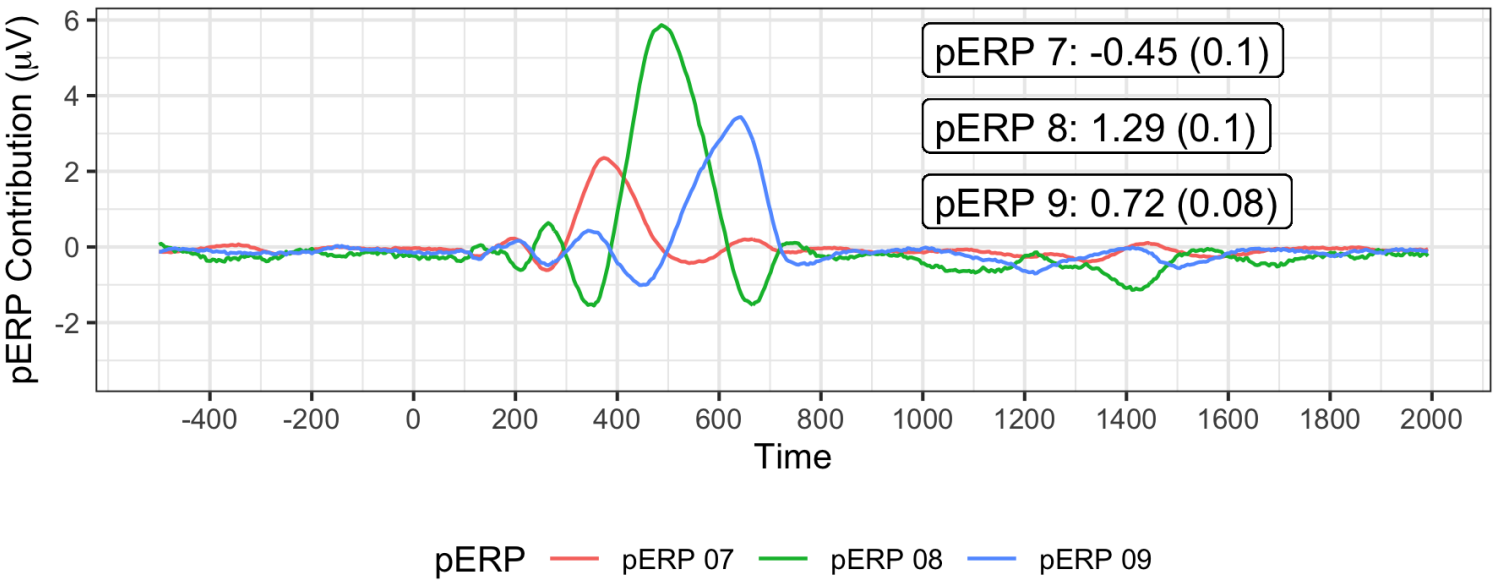

- Potential use: might such decompositions provide more stable indices than individual-level windowed amplitudes or latencies?
- Here, the three pERPs' contrasts (go vs. no-go) are remarkably similar across ADHD and non-ADHD groups, and by age.

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Example: Maintenance period in the SDRT

- ADHD has implications for the ability to maintain attention and working memory resources on task so we may expect differences here.

ADHD and TD Groups: Maintenance Condition (Cz)

	Hyperactive (or both)		Inattention		TD	
pERP	Mean (SE)	APSD	Mean (SE)	APSD	Mean(SE)	APSD
pERP 01	-0.11 (0.27)	2.94	**0.32 (0.14)**	1.50	**0.41 (0.15)**	1.44
pERP 02	0.18 (0.28)	3.01	-0.29 (0.15)	1.68	**-0.41 (0.18)**	1.69
pERP 03	0.10 (0.18)	1.91	-0.11 (0.13)	1.41	**-0.32 (0.15)**	1.44
pERP 04	0.02 (0.10)	1.07	0.09 (0.09)	0.94	**0.22 (0.10)**	0.90
pERP 05	0.21 (0.11)	1.15	0.10 (0.08)	0.90	-0.02 (0.09)	0.87
pERP 06	0.13 (0.11)	1.17	0.07 (0.09)	0.94	0.08 (0.10)	0.90
pERP 07	**0.28 (0.12)**	1.29	**0.35 (0.09)**	1.02	**0.45 (0.09)**	0.86
pERP 08	-0.13 (0.12)	1.34	-0.14 (0.09)	0.94	**-0.31 (0.10)**	0.93
pERP 09	0.07 (0.15)	1.56	-0.01 (0.07)	0.79	-0.07 (0.09)	0.80
pERP 10	-0.17 (0.17)	1.83	0.04 (0.08)	0.88	-0.03 (0.08)	0.74
pERP 11	-0.01 (0.11)	1.18	-0.04 (0.06)	0.70	-0.06 (0.07)	0.68
pERP 12	0.09 (0.14)	1.55	-0.08 (0.06)	0.65	-0.04 (0.06)	0.56
pERP 13	-0.08 (0.18)	1.97	0.09 (0.08)	0.91	0.13 (0.11)	1.07
pERP 14	-0.07 (0.15)	1.56	0.1 (0.11)	1.25	0.11 (0.11)	1.01
pERP 15	-0.26 (0.19)	2.01	0.16 (0.13)	1.42	0.14 (0.15)	1.38

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- Easy. Get your own ERPs, then use our `R` package:
  `install.packages("pERPred")`
  `github.com/emjcampos/pERPred`

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- test usefulness for discovering and extracting biomarkers that prove clinically or behaviorally predictive