

## Background

- The pupillary light reflex (PLR) and resting state electroencephalography (rEEG) represent promising mechanistic markers for heterogeneity in autism (AT) because both demonstrate diagnosis-specific differences and correlate with behavioral characteristics of AT, such as dysregulated sensation and attention
- PLR indexes noradrenergic and cholinergic function and balance, neurotransmitters associated with sensation and arousal
- PLR latency (time from flash to pupillary constriction) is longer and associated with heightened sensory sensitivities in autistic (AT) participants compared to neurotypical (NT) participants
- Alpha spectral power (8-12hz) is associated with modulation of attention, and beta (13-30hz) is related to sensorimotor integration
- The process of collecting PLR and EEG data may lead to selective data loss in participants with increased sensory sensitivities
- Non-random data loss presents an empirical problem in neuroscience research that affects study outcomes and potentially biases samples to only include data from participants with fewer sensitivities or challenges with attention
- The present study sought to explore patterns in PLR latency and rEEG alpha and beta power, and how data loss across EEG and PLR is associated with sensory and attentional heterogeneity in AT

## Hypotheses

- Data Loss**
  - AT participants will lose more data than NT participants
  - This difference will be strongest for PLR data loss compared to non-PLR eye tracking measures (non-PLR ET) because AT participants are more likely to experience sensory sensitivities and the PLR flash is most likely to evoke these sensitivities
  - If data loss is non-random, PLR data loss will be correlated with rEEG data loss
- Sensory Sensitivities:** Participants with greater sensory sensitivities will...
  - Lose more PLR data than those with fewer sensitivities
  - Lose more rEEG data than those with fewer sensitivities
  - Lose more data overall
- Biomarker Variables**
  - Participants with more sensory sensitivities will have longer PLR latencies because PLR latency is mechanistically tied to sensory differences
  - Participants with more data loss will have longer PLR latencies because data loss may be another mechanistic proxy for sensory differences
  - Participants with more sensory sensitivities will have reduced alpha and beta spectral power in rEEG because these power bands are related to sensory processing
  - Participants with more data loss will have reduced alpha and beta spectral power in rEEG because these power bands are related to attentional differences

## Methods

### Participants

Data collected in the Autism Biomarkers Consortium for Clinical Trials (ABC-CT).

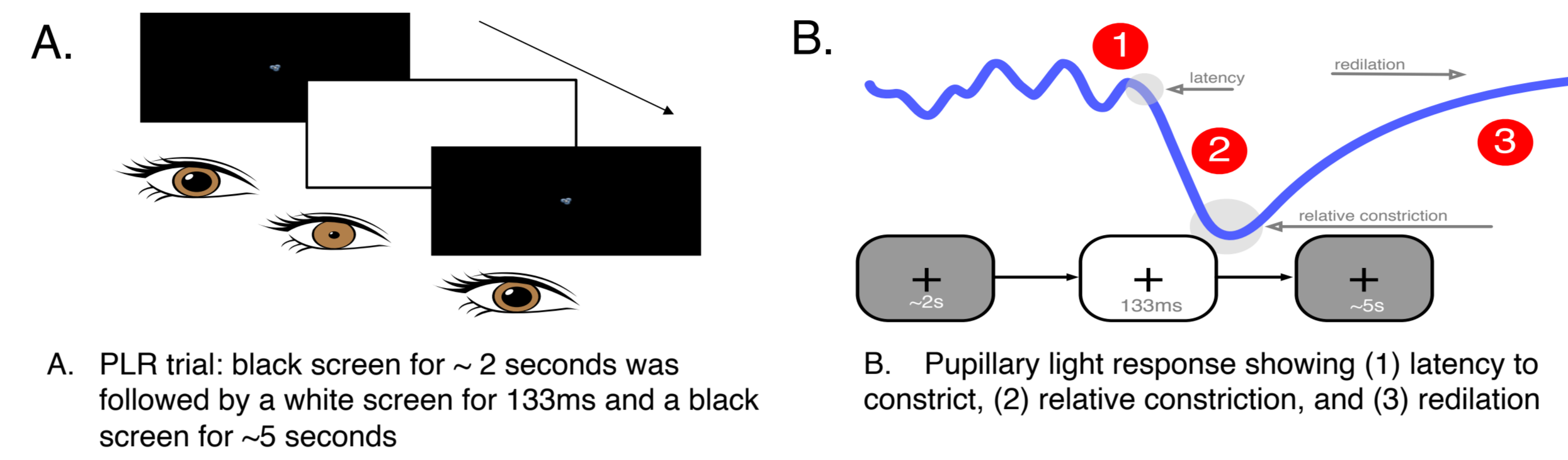
Group	n (n girls)	Mean Age (Y)	Age SD	FSIQ	FSIQ SD
ASD	280 (65)	8.55	1.65	96.58	18.11
TD	119 (36)	8.51	1.62	115.12	12.55

- Diagnosis was confirmed via the Autism Diagnostic Observation Schedule 2<sup>nd</sup> Edition (ADOS), Autism Diagnostic Interview (ADI), and clinician confirmation of DSM-5 criteria
- Sensory sensitivities were measured with the Pervasive Developmental Disorders Behavior Inventory (PDDBI): Sensory Subscale

## Methods

### Pupil Data

- Pupil data were collected using an SR EyeLink 1000+ binocular remote camera system at 500 Hz
- PLR was calculated in response to a 133ms white flash followed by a black screen
- PLR latency was defined as the time from flash to pupillary constriction



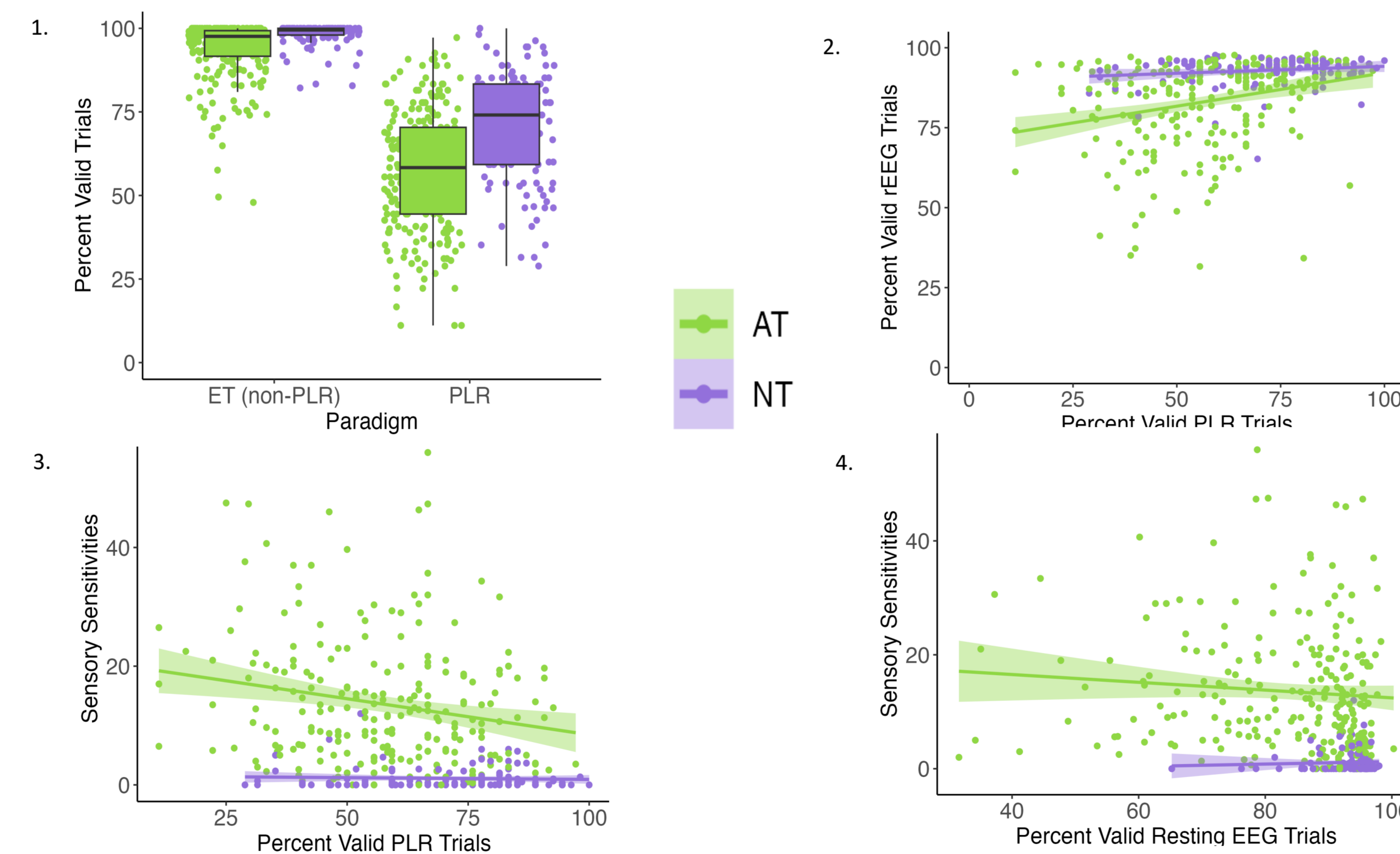
### rEEG Data

- rEEG data were recorded at 1000Hz with 128-channel EGI Hydrocel Geodesic sensor nets
- Alpha bands were measured at 8-13 Hz and Beta bands were measured at 13-30 Hz
- Data was collected while participants watched 174 0.7s abstract screensaver videos (2min)
- Data was processed and analyzed using BEAPP and HAPPE pipelines

### Lost Data

- Defined as % of valid trials out of total trials for a given experiment
- Overall lost data calculated by taking the mean of non-PLR ET valid data (x/33), PLR valid data (x/18), and rEEG valid data (x/174) for each participant
- PLR trials were valid when a latency could be hand coded (no blinks close to flash)
- Valid rEEG data were trials with sufficient artifact free data to derive DVs
- ET trials were valid if overall %looking to the screen >50% and minimum calibration error <2.5degrees for each trial

## Results



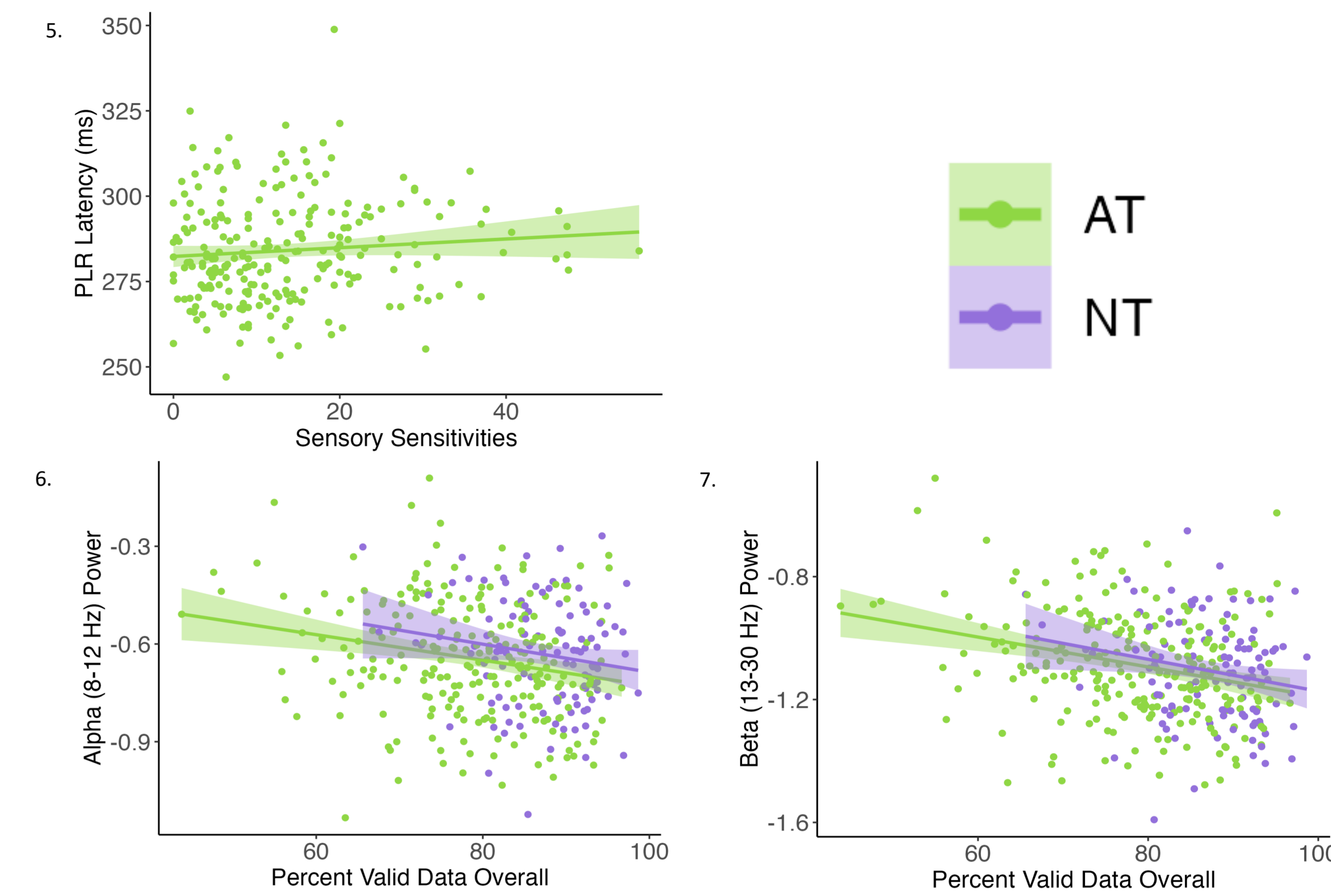
### Data loss (Hypothesis 1; Figures 1, 2)

- AT participants lost more ET data than NT ( $\beta=4.81, p<.01$ )
- All participants lost more data on PLR trials compared to non-PLR ET trials ( $\beta=-35.25, p<.0001$ )
  - Linear mixed effects model demonstrated a diagnosis by trial type interaction; the difference between PLR and ET data loss is stronger for AT than NT ( $\beta=7.63, p<.0001$ )
- PLR data loss correlated with rEEG data loss for AT participants in a pearson correlation ( $r(348)=.33, p<.0001$ )

### Sensory Sensitivities Across Groups (Hypothesis 2; Figures 3, 4)

- Higher sensitivities correlated with greater PLR data loss( $r(348)=-.31, p<.0001$ )
- Higher sensitivities correlated with greater rEEG data loss( $r(348)=-.26, p<.0001$ )
- Increased lost data correlated with higher sensory sensitivities  $r(348)=-.36, p<.0001$

## Results



### Biomarker Variables (Hypothesis 3)

- Figure 5.
- Higher sensory sensitivities correlated with longer PLR latency in AT participants ( $r(348)=.12, p<.05$ ; Pearson correlation)
- Figures 6,7.
- Increased overall data loss correlated with decreased alpha ( $r(348)=-.17, p=.01$ ) and beta across groups ( $r(348)=-.25, p<.0001$ ; Pearson correlation)

## Conclusions

- AT participants demonstrated longer PLR latencies, more lost data, and greater sensory sensitivities than NT children indicating that lost data is non-random
- AT participants lost more data on PLR trials than other ET measures, suggesting that the PLR paradigm is specifically vulnerable to data loss in AT participants
- Participants with more sensory sensitivities had fewer valid PLR, ET, and rEEG trials indicating that sensory sensitivities may contribute to non-random data loss
- Participants with greater data loss had decreased alpha and beta frequency band activity, suggesting that non-random data loss may differentially affect biomarker variables in AT research
- Although there were no correlations between sensory sensitivities and alpha and beta power bands, the correlation with lost data may indicate a relationship with sensation or attention not captured by the PDDBI: Sensory Subscale
- Consistent with previous research, these findings suggest that data loss may represent an important aspect of biomarker data collection and that data loss metrics could add an additional dimension by which to assess heterogeneity

## References

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