**Background**

- Disregulated attention and arousal are comorbid features of autism spectrum disorder (ASD). These symptoms are associated with differences in noradrenergic and cholinergic activity.
- Pupil diameter (PD) is a marker of noradrenergic and cholinergic (neuromodulatory) activity and indexes brain network dynamics.
- Prior work has established that individuals with ASD exhibit attenuated pupil response to light, suggesting altered neuromodulatory activity.
- However, there have been no studies in humans linking the dynamics of the pupillary light reflex (PLR) to EEG features.
- Understanding the relationship between PD and EEG may help to parse heterogeneity among individuals with ASD.

**Method**

**Sample**

<table>
<thead>
<tr>
<th>Group</th>
<th>n (n males)</th>
<th>Mean Age (Y)</th>
<th>Min. Age (Y)</th>
<th>Max. Age (Y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD</td>
<td>26 (20)</td>
<td>7.77</td>
<td>4.42</td>
<td>11.3</td>
</tr>
<tr>
<td>TD</td>
<td>26 (17)</td>
<td>6.59</td>
<td>4.01</td>
<td>11.4</td>
</tr>
</tbody>
</table>

**EEG Processing:**
- EEG was recorded at 1000 Hz with a 128-channel Hydrodesc Geodesic Sensor net.
- Resting data were collected while participants sat quietly watching an abstract video on a computer screen.
- Data were cleansed utilizing the HAPPE pipeline with noise removal, a high-pass filter, and rereferencing to an average reference.
- Data were filtered from 0.1-100 Hz.
- Participants were included in the EEG sample if they had at least 40 seconds of artifact-free resting data.
- Multitaper Fourier transforms were used to estimate band-specific power.
- EEG slope and peaks were measured using the FOOOF pipeline and customized MATLAB scripts.
- EEG power was averaged over 125 electrodes.

**Pupil Analysis:**
- Pupil dilation data were collected using an SR Eyelink-1000 binoocular remote camera system at 500 Hz.
- The PLR was calculated in response to a 133ms white flash followed by a black screen.
- PLR dynamics examined included relative constriction, latency of constriction, and redilation and constriction velocities.

**Behavioral Data:**
- Diagnosis was confirmed via the Autism Diagnostic Observation Schedule 2nd edition (ADOS), the Autism Diagnostic Interview (ADI), and clinician confirmation of meeting DSM-5 criteria for ASD.
- Social Responsiveness Scale 2nd edition (SRS).

**Method**

**Results**

**Neural Response, Pupillary Dilation, and Clinical Characterization**

**Correlations with PLR constriction and EEG power**

**Conclusions**

- These are the first data to examine relationships between EEG and PLR in individuals with ASD, revealing potential relationships between brainstem nuclei, cortical activity, and clinical symptomology.
- The relationship among the PLR and ASD symptomology suggests increased noradrenergic activity, indicated by increased PLR latency and attenuated constriction. These PLR features also predict atypical EEG profile and increased symptomology.
- The relationships between PLR and IAF suggest that, across groups, cortical network activity and neuromodulatory systems exhibit stable relationships.
- The strong relationship between PLR constriction and EEG in ASD suggest that variability in brain activity in ASD is more tightly tied to neuromodulatory function or increased variability in neuromodulatory function in ASD results in more variable EEG activity.
- These findings, showing linkages among brain markers and with clinical symptomology, show promise for these biomarkers as indicators of treatment response and as potential targets for treatment development.

**References**