Microstate Analysis of Resting-State Electroencephalography in Autism Spectrum Disorder

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BACKGROUND

- Variability in the electroencephalogram (EEG) across the scalp can be parsed into a small set of canonical topographies (i.e., microstates) that shift every 80-120ms
- These topographies (labeled A, B, C, and D in Figure 1) are evident across studies and clinical populations and reflect activity in different brain networks
- Combined EEG and functional magnetic resonance (fMRI) studies indicate that: microstate A indexes activity in the auditory resting-state network; B in the visual network; C in the default mode network; and D in the dorsal attention network
- However, temporal parameters of microstates (e.g., duration, occurrence, and coverage) have not been well characterized in adults with autism spectrum disorder (ASD) and hold potential to provide useful information about activation of functional networks relevant to individual differences in behavior

OBJECTIVES:

1. Identify the four canonical microstates and compare their temporal parameters between groups of individuals with ASD and typical development (TD)
2. Given that specific microstates relate to specific resting-state networks, assess the relationship between microstate temporal parameters and clinical characteristics associated with these networks:
   - Microstate A temporal parameters and self-reported auditory sensitivity
   - Microstate B temporal parameters and self-reported visual sensitivity
   - Microstate C temporal parameters and clinician-rated ASD severity (given previously reported differences in default mode network activity in ASD)
   - Measures of attention were not collected in this study, so clinical relationships with Microstate D temporal parameters could not be examined

METHOD

- Participant information is presented in **Table 1**
- ASD diagnoses were confirmed via the Autism Diagnostic Observation Schedule (ADOS-2) and clinician endorsement of DSM-5 criteria for ASD
- Full Scale IQ (FSIQ): Wechsler Abbreviated Scale of Intelligence (WASI-2)
- Glasgow Sensory Questionnaire (GSQ): Auditory and visual hypersensitivity subscales

Table 1

	n	Age	FSIQ	ADOS CSS [a]	GSQ Auditory Hypersensitivity [a]	GSQ Visual Hypersensitivity [a]
TD	37 (57% male)	**27.22** (6.35); 18.57-39.65	**111.75** (15.24); 72-142 [b]	**1.47** (0.70); 1-3 [b]	**4.39** (1.70); 0-8 [b]	**2.00** (1.81); 0-7 [b]
ASD	22 (82% male)	**25.12** (5.72); 18.03-38.95	**103.95** (19.63); 70-142	**7.82** (1.76); 5-10	**6.81** (2.93); 2-12 [b]	**3.33** (2.39); 0-9 [b]

Presented as **Mean** (Standard Deviation); Range
CSS = Calibrated Severity Score
[a] Means significantly differ between groups, $p < .05$
[b] One participant missing score

EEG Acquisition:

- 160-seconds of eyes-closed resting-state EEG was recorded at 500 Hz with a 128-channel HydroCel Geodesic sensor net

EEG Preprocessing:

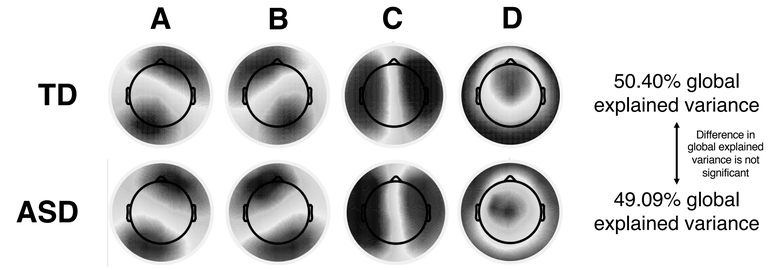
- EEG data were filtered to remove line frequencies at 60 Hz and 120 Hz and re-referenced to the average of all channels
- EEG data were then detrended and subject to a 1 Hz high pass filter
- For cleaning and artifact removal, EEG data were segmented into 2 second epochs and run through the Harvard Automated Processing Pipeline for EEG (HAPPE; Gabard-Durnam et al., 2018)
- Files that retained less than 70% original variance were rejected post-HAPPE

METHOD

Microstate Analysis:

- Microstate analysis was performed using the *Microstate EEGlab Toolbox* (Poulsen et al., 2018) to identify the four canonical microstates (**Figure 1**)
- Each microstate was characterized by three temporal parameters:
  1. Duration: The duration a given microstate remained stable before switching to a different microstate
  2. Occurrence: The frequency of occurrence of each microstate
  3. Coverage: The fraction of time for which a given microstate was dominant

Figure 1: Four Canonical Microstates Identified in Each Group



Statistical Analyses:

- Independent-samples *t*-tests were performed to compare the means of microstate parameters between groups
- In the ASD group only (due to a restriction-of-range in GSQ and ADOS scores in the TD group), linear regressions were performed to determine the relationship between:
  - Microstate A parameters and GSQ auditory hypersensitivity and hyposensitivity
  - Microstate B parameters and GSQ visual hypersensitivity and hyposensitivity
  - Microstate C parameters and ASD severity (ADOS CSS)

RESULTS

- All analyses with Microstate A and D as well as all analyses with GSQ visual hyposensitivity were not significant and are thus not reported

Tables 2 and 3: Independent-Samples *t*-Tests Comparing Means of Microstate Parameters between TD and ASD Groups

Table 2

Microstate B	TD ($n = 37$)	ASD ($n = 22$)	*p* value
Duration	74.19 (7.18)	78.41 (9.68)	.06
Occurrence	3.55 (0.44)	3.79 (0.32)	**.03 ***
Coverage	.27 (.06)	.30 (.06)	**.04 ***

Presented as **Mean** (Standard Deviation); Range
* Significant, $p < .05$

Table 3

Microstate C	TD ($n = 37$)	ASD ($n = 22$)	*p* value
Duration	64.51 (6.59)	61.31 (8.66)	.12
Occurrence	2.69 (0.48)	2.27 (0.74)	**.01 ***
Coverage	.18 (.05)	.15 (.07)	**.03 ***

Presented as **Mean** (Standard Deviation); Range
* Significant, $p < .05$

RESULTS

Figure 2: Relationship Between Microstate C Duration and ASD Severity

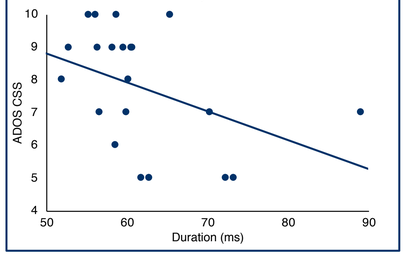


Figure 3: Relationship Between Microstate B Duration and Visual Hypersensitivity

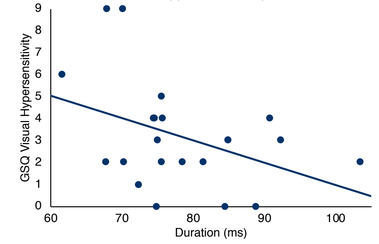


Figure 4: Relationship Between Microstate B Occurrence and Visual Hypersensitivity

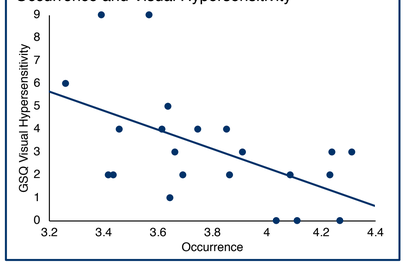
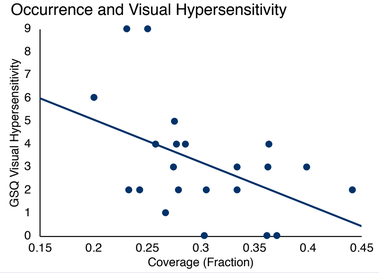


Figure 5: Relationship Between Microstate B Occurrence and Visual Hypersensitivity



Linear Regressions:

- Greater microstate C duration, but not occurrence or coverage, significantly predicted lower ASD severity, $R^2 = .188$, $p = .044$ (**Figure 2**)
- Greater microstate B duration significantly predicted lower visual hypersensitivity, $R^2 = .201$, $p = .042$ (**Figure 3**)
- Greater microstate B occurrence significantly predicted lower visual hypersensitivity, $R^2 = .279$, $p = .014$ (**Figure 4**)
- Greater microstate B coverage significantly predicted lower visual hypersensitivity, $R^2 = .235$, $p = .026$ (**Figure 5**)

DISCUSSION

- Differences in Microstate B and Microstate C parameters may reflect differences in visual processing and default mode network activity, respectively, between diagnostic groups
- Microstate B parameters predicted self-reported visual sensitivity in ASD, suggesting that these parameters may index individual differences in visual processing
- Lower Microstate C duration predicted greater ASD symptomatology in ASD, suggesting that Microstate C duration may index individual differences in default mode network activity in ASD
- Together, these results suggest that microstates may serve as markers for abnormal visual and default mode networks in ASD, and may help to quantify individual differences in behavior
- Future directions include using different EEG preprocessing strategies as well as different microstate clustering algorithms to further explore these relationships

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