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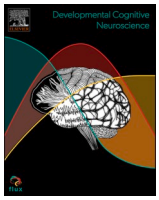

Next-gen tools

Multi-site EEG studies in early infancy: Methods to enhance data quality

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ABSTRACT

Brain differences linked to autism spectrum disorder (ASD) can manifest before observable symptoms. Studying these early neural precursors in larger and more diverse cohorts is crucial for advancing our understanding of developmental pathways and potentially facilitating earlier identification. EEG is an ideal tool for investigating early neural differences in ASD, given its scalability and high tolerability in infant populations. In this context, we integrated EEG into an existing multi-site MRI study of infants with a higher familial likelihood of developing ASD. This paper describes the comprehensive protocol established to collect longitudinal, high-density EEG data from infants across five sites as part of the Infant Brain Imaging Study (IBIS) Network and reports interim feasibility and data quality results. We evaluated feasibility by measuring the percentage of infants from whom we successfully collected each EEG paradigm. The quality of task-free data was assessed based on the duration of EEG recordings remaining after artifact removal. Preliminary analyses revealed low data loss, with average in-session loss rates at 4.16 % and quality control loss rates at 11.66 %. Overall, the task-free data retention rate, accounting for both in-session issues and quality control, was 84.16 %, with high consistency across sites. The insights gained from this preliminary analysis highlight key sources of data attrition and provide practical considerations to guide similar research endeavors.

1. Introduction

Autism spectrum disorder (ASD) is a complex neurodevelopmental condition characterized by social and behavioral impairments that typically emerge in the latter part of the first and second year of life (American Psychiatric Association., 2013; Estes et al., 2015; Zwaigenbaum and Penner, 2018). Identifying early brain differences associated with ASD holds significant promise for detecting at-risk infants (Girault and Piven, 2020; Hazlett et al., 2017; Jeste et al., 2015; McPartland et al., 2020), elucidating early neurobiological pathways (Jeste and Nelson, 2009; Modi and Sahin, 2017), and paving the way for timely interventions that leverage the brain's heightened plasticity early in life.

EEG is a scalable and non-invasive tool for investigating early brain

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development in infants with a higher likelihood (HL) of developing ASD (~20 %) (Ozonoff et al., 2011) compared to the general population (~2 %) (Maenner et al., 2023). EEG studies describe differences in spectral power and connectivity during the first year of life that precede ASD diagnosis or its associated behavioral symptoms (Dickinson et al., 2020; Gabard-Durnam et al., 2019; Haartsen et al., 2019; Jones et al., 2016; Orekhova et al., 2014; Peck et al., 2021; Righi et al., 2014). However, given that only a subset of HL infants will progress to an ASD diagnosis, large-scale, multisite studies are necessary to improve our understanding of these early neural differences and advance their potential in clinical settings. By pooling resources, expertise, and participants across various geographical locations, multi-site studies can ultimately reach larger and more representative participant groups, maximizing the clinical utility of identified neural markers. One such initiative is the Infant Brain Imaging Study (IBIS) Network. Spanning five US data collection sites, IBIS combines behavioral assessments, magnetic resonance imaging (MRI), and EEG in HL infants at 6, 12, and 24 months to examine brain and behavioral predictors and trajectories linked to subsequent ASD diagnosis at 24 months.

Previously, IBIS has used MRI to examine early brain development, identifying functional and structural brain differences that precede ASD diagnosis (Emerson et al., 2017 Hazlett et al., 2017; Shen et al., 2013; Shen et al., 2017; Wolff et al., 2012). While MRI provides intricate structural images and information about brain function using the blood oxygen level-dependent (BOLD) signal as a proxy for brain activity, EEG directly measures the electrical activity of neuronal ensembles, capturing rapid and dynamic temporal shifts in neural patterns. As such, EEG allows us to examine functional patterns and neural correlates of sensory processing while infants are awake, offering insights that complement those obtained from infant MRI, typically conducted during sleep. For instance, EEG may be beneficial in capturing measures of active visual processing that can complement recent MRI findings implicating visual system differences in ASD (Girault et al., 2022). EEG is also cost-effective and adaptable to various environments, making it highly suitable for extensive longitudinal studies and the development of scalable ASD screening markers.

Combining EEG and MRI in large-scale, multi-site studies is essential for a comprehensive understanding of early neural development in ASD. However, integrating EEG into multisite studies such as IBIS presents significant challenges. Reliable EEG data collection requires rigorous protocols and strict standardization across sites (McPartland et al., 2020; Webb et al., 2023). Furthermore, infants are generally more sensitive to unfamiliar lab settings, and this can affect various types of data collection, including behavioral assessments, MRI, and EEG. For instance, infants may struggle to complete EEG recording sessions and frequently exhibit physiological or movement artifacts that compromise data usability (Hervé et al., 2022; Van Diessen et al., 2015). Incomplete sessions, shorter recording durations, and artifacts lead to EEG data loss rates as high as 50 % (Cuevas et al., 2014; Stets et al., 2012), limiting generalizability. Given that IBIS was originally established based on MRI expertise, the potential for data loss was further exacerbated by varying levels of EEG experience across the participating sites.

This paper describes our standardized approach to address these challenges and incorporate EEG into the IBIS network. We combined our team's in-house expertise with established guidance from the literature, specifically focusing on recommended procedures for infant EEG acquisition (Cuevas et al., 2014; Hervé et al., 2022; Van Der Velde and Junge, 2020; Webb et al., 2015; Van Noordt et al., 2020) and best practices for multi-site data collection (Abraham et al., 2017; Jones et al., 2019; Volkow et al., 2021; Webb et al., 2020). This paper has two primary goals: (1) to describe the comprehensive protocol designed for the collection, harmonization, and quality control of multi-site infant EEG data within the IBIS network (see Fig. 1), and (2) to examine EEG data quality using this standardized approach. Our assessments provide insight into the protocol's feasibility, evaluated through protocol completion rates, and data quality, measured by the amount of usable data remaining after artifact removal.

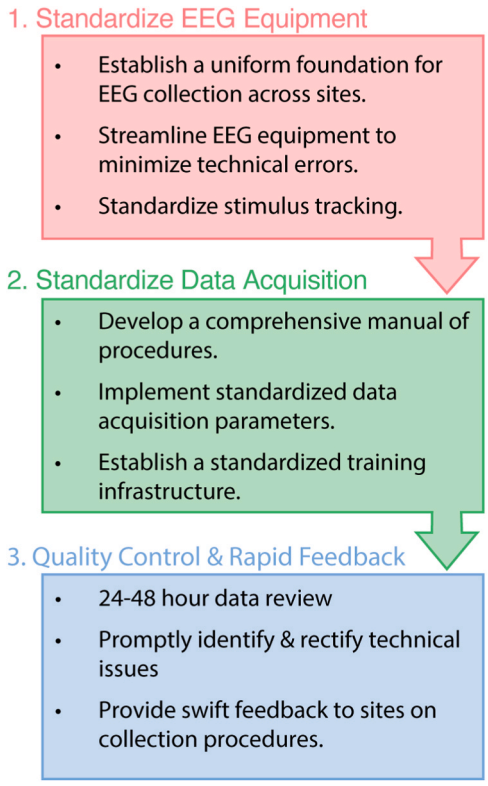

Fig. 1. Schematic diagram illustrating the structured three-phased approach used to integrate EEG data collection into IBIS.

2. Methods

2.1. Participants

Participants were enrolled in the Infant Brain Imaging Study-Early Prediction (IBIS-EP) project, a prospective cohort study across five sites: Washington University in St. Louis, University of Washington in Seattle, Children's Hospital of Philadelphia, University of Minnesota, and the University of North Carolina at Chapel Hill. Infants were required to have a full older sibling diagnosed with ASD. Sibling diagnoses were validated using medical records, the Social Communication Questionnaire (SCQ) (Rutter, Bailey, et al., 2003), and the Autism Diagnostic Interview-Revised (ADI-R) (Rutter, Le Couteur, et al., 2003). Additional eligibility criteria included: 1) Gestational age > 36 weeks; 2) Absence of medical or neurological conditions influencing growth, development, cognition (e.g., seizure disorders), or significant sensory impairments (e.g., vision or hearing loss); 3) No known genetic syndromes associated with ASD; 4) No immediate family history of psychosis, schizophrenia, or bipolar disorder (Family Interview for Genetic Studies; (Maxwell, 1992)); 5) No MRI contraindications, and 6) English as primary home language. These criteria were ascertained during a family history interview and aligned with those used in previous IBIS studies (Emerson et al., 2017; Hazlett et al., 2017).

The target recruitment for IBIS-EP is 250 infants, with 50 infants at each of the five participating sites. The protocol includes EEG and MRI recordings (non-simultaneous) at 6, 12, and 24 (MRI only) months of age and behavioral testing at 6, 12, and 24 months (See Fig. 2A). Infants were enrolled at 6 months of age. Research visits were scheduled over two days to avoid overwhelming families and participants. MRI and behavioral assessment data were collected on the first day, followed by EEG and the remaining behavioral assessments on the second day. Visits at 6 and 12 months were scheduled within a testing window of −1 week/

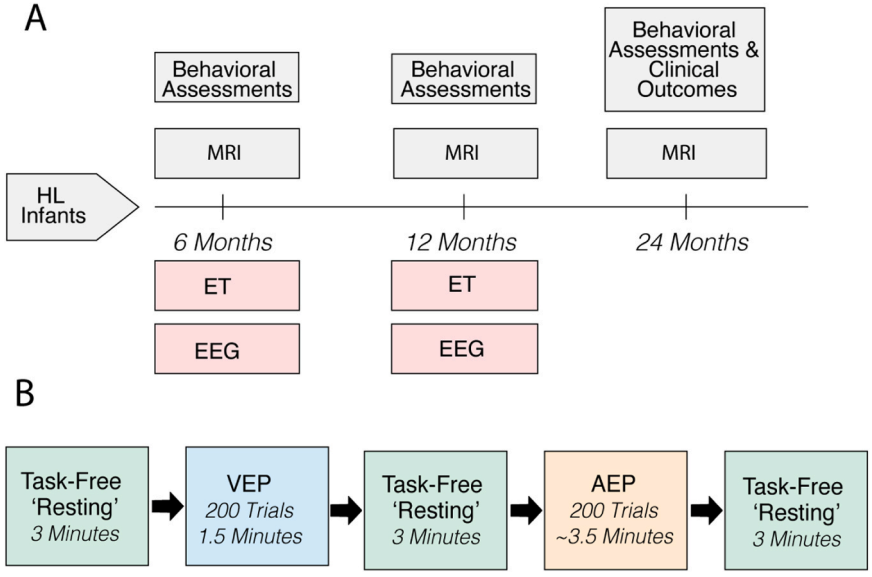

Fig. 2. Schematics figures detailing A) The IBIS-EP protocol, with new additions (EEG and eye tracking) in red, and B) the paradigm-specific protocol for EEG recordings.

+3 weeks from the preferred date based on the infant's birth date. Prior to data collection, all study protocols were reviewed and approved by a centralized IRB at Washington University in St. Louis. A parent or guardian provided written informed consent for each participating infant, in compliance with the Declaration of Helsinki. The data described in this paper include all 6-month (n = 73) and 12-month (n = 47) EEG recordings conducted before the preliminary data review cutoff date of January 1st, 2023. Demographic information for this preliminary sample is detailed in Table 1.

Table 1
Demographic characteristics of the interim sample, collapsed across sites.

	6 Months *N = 73*		12 Months *N = 47*	
	n	**Percent**	**n**	**Percent**
Sex				
Female	28	38.36 %	18	38.30 %
Male	45	61.64 %	29	61.70 %
Ethnicity				
Hispanic	22	30.14 %	14	29.79 %
Non-Hispanic	51	69.86 %	33	70.21 %
Race				
Asian	3	4.11 %	3	6.38 %
Black	3	4.11 %	3	6.38 %
White	51	69.86 %	31	65.96 %
More than one race	4	5.48 %	3	6.38 %
Unknown or not reported	12	16.44 %	7	14.89 %
Family Income				
<25 K	5	6.85 %	2	4.26 %
25–35 K	5	6.85 %	3	6.38 %
35–50 K	5	6.85 %	4	8.51 %
50–75 K	13	17.81 %	7	14.89 %
75–100 K	7	9.59 %	7	14.89 %
100–150 K	10	13.70 %	4	8.51 %
150–200 K	10	13.70 %	10	21.28 %
>200 K	9	12.33 %	5	10.64 %
Unknown or not reported	9	12.33 %	5	10.64 %

Note. While there is partial overlap between the 6- and 12-month samples, it is not complete. As of January 1st, 2023, 39 infants had participated in both their 6- and 12-month EEG sessions. Additionally, 8 infants were enrolled at 12 months, having been unable to participate earlier due to the COVID-19 pandemic. The remaining infants in the sample either had not reached the age of 12 months (n = 15) or missed their 12-month EEG for various reasons (n = 19).

A dedicated team, independent from the five data collection sites, coordinated EEG efforts, including training, troubleshooting, and data quality reviews. Clinical outcomes and EEG-derived variables pertinent to our research objectives are outside the scope of this paper since data collection is still in progress. However, we present feasibility and quality metrics related to our initial efforts in EEG data acquisition.

2.2. EEG paradigms

EEG data were collected during three distinct paradigms, organized into five testing blocks (Fig. 2B). We selected these paradigms based on their suitability for infant populations and their capacity to provide insights into different aspects of brain function, including resting-state functional architecture and low-level visual and auditory processing. These paradigms also align with established IBIS-EP goals, providing opportunities for integrated analyses.

2.2.1. Task-free

We recorded continuous EEG data under task-free conditions for a total of 9 minutes, divided into three 3-minute blocks. Floating bubbles were presented on a laptop screen, consistent with the procedures used to obtain task-free recordings from infant populations (Levin et al., 2017).

2.2.2. Visual evoked potentials (VEP)

A conventional VEP paradigm displayed a black-and-white square checkerboard pattern on the IBIS laptop screen, set against a mean luminance background with a small red fixation cross in the center. The contrast of the checkerboard was reversed every 500 ms for 160 trials.

2.2.3. Auditory evoked potentials (AEP)

A sound bar (ELEGIANT SR200) presented a pure tone, calibrated to 80 dB SPL. The auditory stimulus was a 500 Hz pure tone with a duration of 300 ms, including a 10 ms onset and offset ramp. The tone was presented 140 times, with a randomized inter-stimulus interval varying between 800 and 1200 ms. A video of floating bubbles (identical to the task-free paradigm) was displayed to keep infants engaged This paradigm lasted approximately 3.5 minutes.

2.3. Standardized EEG acquisition setup

EEG acquisition relies on multiple components functioning together, with millisecond precision communication, including a data-acquisition computer (DAC) and an experiment control computer (ECC) that typically has two screens that allow for experimental control and stimulus display to the participant. Despite these standard components, equipment, and setup can vary significantly across EEG labs due to unique study requirements and shared equipment use. Such variations can affect data consistency and quality and impede data processing and troubleshooting, particularly in remote multi-site studies. Standardizing and streamlining equipment ensures consistent data collection across sites and reduces technical disruptions and variations that may emerge over time.

2.3.1. Streamlining EEG equipment

Due to budgetary considerations, we optimized the use of existing EEG equipment at each site. All sites had consistent foundational components, such as the EGI NetAmps amplifier and associated Hydrocel Geodesic Sensor Nets (see Fig. 3A for relevant site-specific differences). To enhance consistency, each site received an IBIS-specific laptop which dually functioned as an ECC and a participant display monitor (see Fig. 3B). This streamlined hardware setup minimized disruptions to and from other ongoing studies at each site. Despite DAC variations across sites, stringent control over recording parameters was achieved using EGI NetStation software with a standardized acquisition template. Consistent peripheral hardware was also used across sites, including devices for stimulus presentation (ELEGIANT SR200 Soundbar), controlling and timing stimuli (wireless keyboard; AV device), and video recording (Cimkiz A860 USB 2.0 HD Webcam) as described below.

2.3.2. Synchronizing stimulus-specific timing

Precisely aligning timing markers with the causal stimuli is crucial during AEP and VEP paradigms, which are designed to capture stimulus-elicited responses on a millisecond level. Although the ECC transmits stimulus presentation markers to the DAC, hardware communication latencies can compromise the temporal accuracy of these markers. We used the Audio/Visual (AV) Device provided with the EGI system to test stimulus timing, as a stimulus tracking device. We repurposed the Audio/Visual (AV) Device from the EGI system, originally meant for testing stimulus timing, as a stimulus tracking device. Specifically, by directly recording sound output from the laptop (AEP) and detecting luminance changes using a photodiode sensor affixed to the laptop screen (VEP), the AV device ensured the precise stimulus-EEG data alignment, which is critical for ERP analysis.

2.4. Standardized training and data collection protocols

2.4.1. Data collection standardization

The core EEG team visited each data collection site to implement equipment and provide hands-on training, which included an introduction to EEG, nuances of infant EEG data collection, and guidelines for interacting with participants/families and ensuring their comfort. A comprehensive Manual of Procedures (MOP) was developed and maintained to detail standardized protocols for EEG data acquisition, including electrode placement, calibration procedures, and procedural checklists to ensure that each session adhered to a systematic and consistent approach. The MOP also detailed equipment specifications, the functionality of each component, and how they communicated. This ensured that research assistants at each site were proficient in the equipment set-up and could identify and address challenges.

We implemented a specific EEG acquisition template within NetStation's Workbench to ensure session uniformity of pre-set filters, visualization layouts, sampling rates, and synchronized audio-video participant recordings. Identical E-Prime (Psychology Software Tools) scripts implemented through the IBIS-specific laptop were used to control experimental stimuli, timing, and data collection across sites. Each site also received a 'calibration file' to run before every EEG session. The calibration file allowed the experimenter to identify any issues before starting the session. This included checks for accurate stimulus presentation, successful transmission of stimulus markers to the DAC, and calibration of the external speakers' volume to 75 dB SPL using a sound level meter.

2.4.2. Training

We developed a comprehensive training program tailored to meet the needs of all team members and address the specialized requirements of infant populations. This program included online workshops, hands-on sessions, and continuous support for troubleshooting. Training was ongoing and systematically structured to ensure consistency and standardization in data acquisition methodologies, particularly in the context of staff turnover inherent to longitudinal, multi-site studies. The training sessions were specifically designed to optimize data quality by balancing infant comfort with required adaptations while maintaining consistent site procedures and practices. We scheduled regular calls bi-weekly for EEG coordinators and monthly for broader EEG teams, and tracked and updated all issues in the MOP with resolutions. The MOP served as a dynamic reference for current research assistants and a vital tool for training new staff, ensuring continuity in the context of staff turnover. Examples of training materials are available on our OSF page (https://osf.io/73wbs/?view_only=823d2a95dec74fa8a975330c4b0805dd).

2.5. Quality control checks

We established a rapid feedback and quality control framework to maintain consistent EEG data quality across sites. After each session, sites uploaded EEG data to LORIS (Longitudinal Online Research and Imaging System), a secure central database managed by McGill University. LORIS is a web-based, open-source platform originally designed

A

Site	Amplifier (Net Amps)	Sampling Rate (Hz)	Cap Montage
A	400 series	1000	129
B	400 series	1000	129
C	400 series	1000	129
D	400 series	1000	65
E	300 series	500	129

B

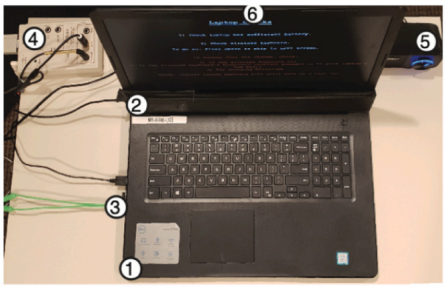

Fig. 3. A) Site-specific EEG system details B) Standardized laptop implemented across sites (1) Standardized IBIS Laptop; 2) Integrated photocell for monitoring visual stimuli; 3) Auxiliary connection transmits auditory timing from laptop to AV device; 4) AV Device relays stimulus timing to DAC; 5) Soundbar for auditory stimuli; 6) Guidelines for pre-session laptop checks).

for large neuroimaging datasets (Das et al., 2012). The core EEG team evaluated data files and corresponding in-session video recordings, providing in-depth feedback (described in more detail below) within 24–48 hours.

2.5.1. Identifying technical issues

Various technical issues can arise during EEG recordings, potentially compromising data integrity if left undetected. To mitigate this, the central EEG team carefully reviewed each recording for protocol adherence, correct stimulus tagging, and technical irregularities. This thorough review process allowed for the prompt detection of issues such as inconsistent stimulus markers or elevated levels of environmental noise. Upon identifying any issues, we addressed them using troubleshooting guides and virtual real-time support when necessary. These proactive measures ensured problems were resolved before impacting future recordings.

2.5.2. Tailored feedback

Beyond technical oversight, the core EEG team reviewed each recording to assess data quality. We evaluated the recorded data and associated video files to provide specific feedback on protocol adherence and collection procedures. This process included verifying proper electrode net positioning and reviewing behavioral management methods. Common feedback suggestions included incorporating breaks to alleviate infant fatigue, minimally distracting toys, and avoiding specific soothing techniques that introduced additional movement-based artifacts (e.g., rocking the infant or providing a pacifier). These suggestions were informed by our team's collective experience with developmental populations and established guidance available in the literature (Abraham et al., 2017; Volkow et al., 2021; Webb et al., 2020). Feedback after each session ensured consistent, high-quality data across sites and served as an effective training tool to refine data collection practices. The prompt response time allowed for rapid issue detection, which was crucial given the narrow age window for infant data collection in this study. Additionally, the quick turnaround in feedback helped all team members maintain uniform standards for protocols and data quality.

2.6. Analysis

2.6.1. Feasibility

We assessed protocol feasibility by measuring completion rates and analyzing variations by paradigm, site, and timepoint.: We evaluated overall protocol completion rates at 6 and 12 months by categorizing the extent of the EEG protocol completed into three categories: full protocol, partial protocol, or no data. Paradigm-Specific Completion Rates: We further assessed completion rates for each of the three paradigms separately (task-free, AEP, and VEP) by determining whether at least one full paradigm block was completed. This metric allowed us to investigate if data losses disproportionately affected a particular paradigm and to identify any paradigm-specific issues across different sites or timepoints. We used Fisher's exact and chi-square tests to inspect site- or timepoint-specific variations in protocol completion rates, paradigm-specific completion rates, and sources of data loss. To examine site-specific variations, we compared each site's feasibility metrics to the combined average of the others using Fisher's exact test (Table 2).

Table 2
Outcome metrics for assessing feasibility and data quality.

	Outcome Metrics		
	Quantitative		Qualitative
Feasibility	Overall Protocol Completion Rates.	Paradigm-Specific Completion Rates.	
Data Quality	Seconds of task-free EEG data retained after artifact removal.	Number of channels retained in task-free EEG data after artifact removal.	Inspect signal characteristics (using PSDs).

2.6.2. Data quality

To assess data quality, we quantified the amount of task-free data remaining after artifact removal. Artifact removal procedures prioritized an unbiased quality assessment over specific data analysis needs. Offline data processing was performed using EEGLAB (Delorme and Makeig, 2004) and custom MATLAB scripts. Specifically, we used a general amplitude-based detection algorithm to remove artifacts consistently, rather than using more sophisticated measures that vary in their aggressiveness based on the quality of the data collected for each infant (e.g., artifact subscale reconstruction, Chang et al., 2018). While artifact removal can vary depending on the specific metric under study (power, coherence, connectivity, etc.), we used an objective amplitude-based approach to provide a more transparent benchmark of EEG data quality. Data were imported into EEGLAB and filtered (1–50 Hz). Continuous data were examined for artifacts using the erplab toolbox function *pop_continuousartdet*, implemented in eeglab (Delorme and Makeig, 2004; Lopez-Calderon and Luck, 2014). To mitigate the impact of artifact rejection being unduly influenced by the sequence of data removal (channels or segments), we implemented a two-stage cleaning process. First, we targeted channels and segments impacted by large amplitude artifacts, using a threshold of $\pm 600\ \mu V$. Specifically, any channels that deviated beyond this threshold for more than 25 % of an infant's total resting recording, followed by segments where more than 5 % of channels exceeded this limit, were removed. After removing channels and data segments contaminated by large artifacts, continuous EEG data then underwent a second stage of cleaning to remove channels that deviated $\pm 200\ \mu V$ for more than 5 % of an infant's total resting recording, and then data segments where >5 % of channels deviated $\pm$ $200\ \mu V$. This stepwise approach allowed us to effectively remove both prominent and subtle artifacts while balancing the preservation of channels and data segments.

Data quality was defined as the duration (seconds) of task-free EEG retained after artifact removal. As a secondary assessment of data quality, we also examined channel retention rates. We used separate generalized linear mixed models (GLMMs) to model data quality metrics (seconds retained; proportion of channels retained) and examine if they varied across sites and timepoints. When modelling longitudinal data, GLMMs allow for both fixed and time-varying covariates, and automatically handle the random missing data due to incomplete EEG visits. GLMMs incorporated main effects for site, timepoint, and their interactions, with a subject-level random intercept. Site D was excluded from channel retention analyses as its electrode montage comprised 64 electrodes instead of the 128 electrodes used at other sites. While evaluating the proportion of channels retained might seem less biased, montages with fewer electrodes might inherently retain a larger proportion of channels as researchers can dedicate more time to reducing impedances when there are fewer electrodes.

2.6.3. Signal characteristics

In addition to data quality metrics, we present power spectral density (PSD) plots of the artifact-free spontaneous EEG data. Examining PSDs helps to confirm the consistency of the signals captured across sites, identify any atypical patterns, and examine if we see expected age-related shifts. As such, although a formal analysis of spectral power is not within the scope of the current paper, providing the PSDs for qualitative examination serves to provide a more transparent understanding of the data collected so far and signal characteristics across various sites.

Before extracting power measures, we applied Independent Component Analysis (ICA) and removed any components where *iclabel* determined the primary source to be non-neural. To ensure uniformity across all sites, we interpolated the data to a consistent 64-channel montage and reduced its sampling rate to 500 Hz. Power was computed using the *pwelch* function implemented in MATLAB, with two-second windows and a 50 % overlap. Recognizing varied data duration

among participants, we employed a permutation-based approach to calculate power. Specifically, we derived power from a random 60-second segment of the EEG, repeating this 500 times for each participant, with the average of all permutations representing the final power for each individual. This approach helps to ensure that differences in the amount of available data do not impact power estimates (Xie et al., 2022). Plotted PSDs represent average power across all channels.

3. Results

3.1. Feasibility

3.1.1. Overall completion rates

Of the 73 infants who attended an EEG session at 6 months, 100 % (n = 73) were netted and EEG recording was successfully initiated. Only two sessions (2.74 %) were terminated before the completion of any paradigms, 1 due to infant fussiness and 1 due to a technical error. EEG data were successfully collected from 71 infants at 6 months, with 52 participants (71.23 %) completing the full protocol and an additional 19 (26.03 %) completing at least one paradigm (task-free, AEP, or VEP; See Table 3). Of the 47 infants who attended an EEG session at 12 months, 100 % (n = 47) were netted and EEG recording was successfully initiated. One session was terminated before the completion of any paradigms due to infant fussiness that could not be alleviated. Additionally, technical issues interrupted two recordings before any paradigms were finished, resulting in three 12-month files with no completion (6.38 %). As such, data was successfully collected from 44 infants at 12 months, with 35 participants (74.47 %) completing the full protocol and an additional 9 (19.14 %) participants completing at least one paradigm (See Table 3).

We categorized participants based on full completion, partial completion, and no completion of the protocol (See Fig. 4). Given the low numbers of infants in the no-completion group, our analysis centered on comparing full and partial completion rates. A Fisher's exact test indicated no significant difference in the distribution of full versus partial completions across the two timepoints ($p = 0.82$). Chi square tests found no significant differences in full vs partial completion between sites at 6 (x^2 (df) = 3.739 (4), $p = 0.44$), or 12 months (x^2 (df) = 7.421 (4), $p = 0.12$). In terms of data collection, there were only two failed sessions at 6 months and three at 12 months (i.e., no data were collected for at least one paradigm). We examined in-session success by comparing each sites collection rate in relation to the combined average of the others, finding no site-specific differences for in-session success at 6 ($p > 0.43$) or 12 months ($p > 0.16$).

Table 3
Completion rates for the full EEG protocol, as well as paradigm-specific completion rates, at each timepoint. 'Full Protocol' describes participants who completed all 5 EEG blocks. Task-Free, AEP and VEP numbers reflect participants who engaged in a minimum of one block for the respective paradigms.

6 Months						
		Total Sample	Full Protocol	Task-Free	VEP	AEP
Site A	n	12	7	12	11	8
	%		58.33 %	100 %	91.67 %	66.67 %
Site B	n	14	11	14	12	14
	%		78.57 %	100 %	85.71 %	100 %
Site C	n	18	12	17	14	13
	%		66.66 %	94.44 %	82.35 %	76.47 %
Site D	n	7	6	7	7	6
	%		85.71 %	100 %	100 %	85.71 %
Site E	n	22	16	21	19	21
	%		72.73 %	95.45 %	90.48 %	100 %
Total	n	73	52	71	63	62
	%		71.23 %	97.260 %	88.73 %	87.32 %
12 Months						
		Total Sample	Full Protocol	Task-Free	VEP	AEP
Site A	n	9	6	8	8	7
	%		66.67 %	88.89 %	88.89 %	77.78 %
Site B	n	6	2	6	2	6
	%		33.33 %	100 %	33.33 %	100 %
Site C	n	12	10	11	11	12
	%		83.33 %	91.67 %	91.67 %	100 %
Site D	n	9	8	8	8	8
	%		88.89 %	88.89 %	88.89 %	88.89 %
Site E	n	11	9	11	11	11
	%		81.82 %	100 %	100 %	100 %
Total	n	47	35	44	40	44
	%		74.47 %	93.62 %	85.11 %	93.62 %

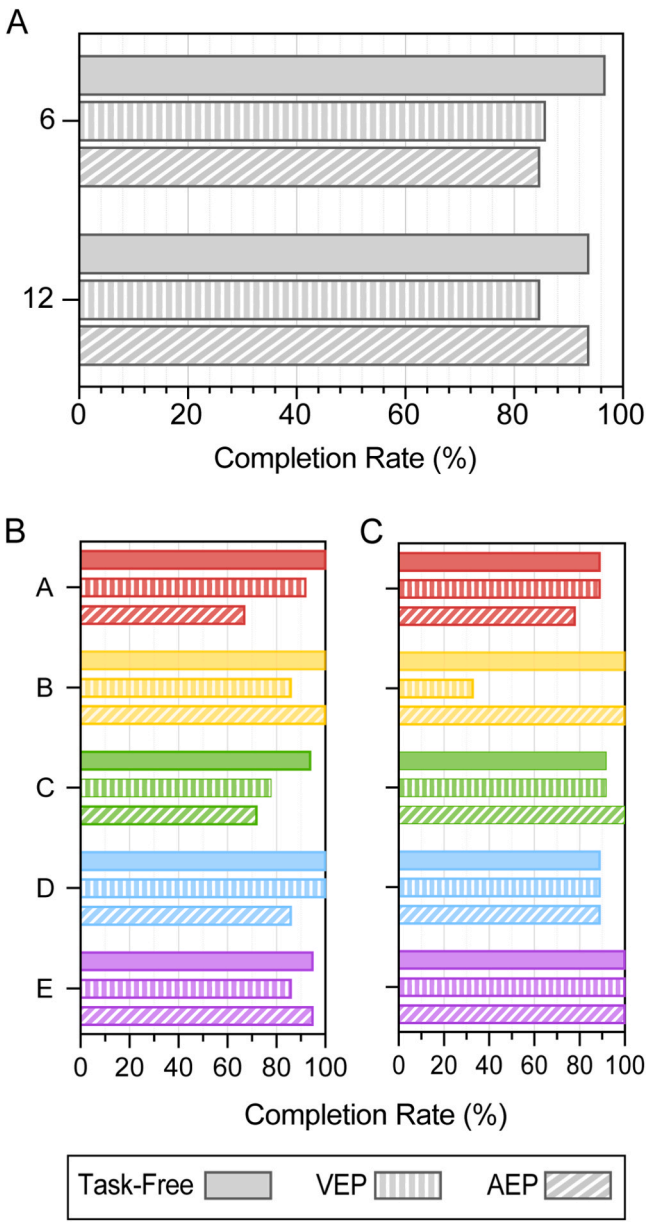

Fig. 4. Paradigm-Specific EEG Completion Rates Across Sites and Time Points. (A) Completion rates for Task-Free, AEP, and VEP paradigms aggregated across all five sites at 6 and 12 months. (B-C) Detailed completion rates for each paradigm, broken down by individual site at the B) 6-month, and (C) 12-month timepoint.

3.1.2. Paradigm-specific completion rates

The EEG protocol included 3 blocks of task-free EEG, one block of AEP, and one block of VEP. However, the number of completed paradigms for each infant varied (see Fig. 4). Chi square test revealed no significant differences in paradigm completion rates and timepoint (x^2

(*df*) = 0.272 (2), $p = 0.87$). Separate chi square tests at 6 and 12 months also indicated no differences in paradigm completion rates across sites (6 months: x^2 (*df*) = 1.143 (8), $p = 0.997$; 12 months: x^2 (*df*) = 2.249 (8), $p = 0.972$ (Figs. 5 and 6).

3.2. Data quality

3.2.1. Data quality attrition

Files contaminated with line noise exceeding our amplitude-based cleaning threshold were deemed unusable. This affected 13.7 % (n = 10) of recordings at 6 months, and 8.5 % (n = 4) at 12 months (see Table 4). Detailed metrics on the number of seconds and channels retained for the remaining participants (6 months n = 61; 12 months n = 40) are provided in Table 5, offering more nuanced insights into the overall data quality achieved across our sample.

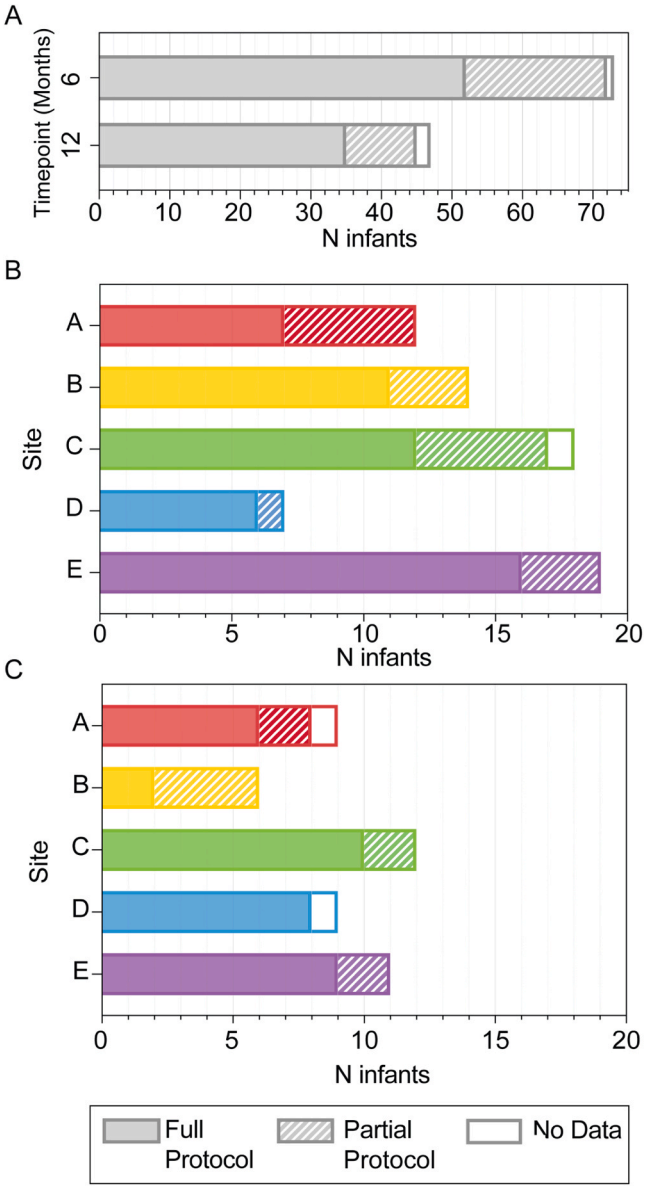

Fig. 5. EEG Protocol Completion Rates Across Sites and Time Points. (A) Total protocol completion rates aggregated across all five sites at 6 and 12 months. (B) Protocol completion rates broken down by site for the 6-month time point. (C) Protocol completion rates broken down by site for the 12-month time point.

3.2.2. Data duration

The average duration of artifact-free data was 463.07 seconds (SD = 126.34) at 6 months, and 496.93 seconds (SD = 89.40) at 12 months (See Table 4 and Fig. 4). Statistical analysis (GLMM) found no significant effect of age (t (90) = 0.426, $p = 0.671$), suggesting that the data duration retained did not differ significantly between time points. Furthermore, non-significant p-values for all interaction terms (all $p >$ 0.27) indicated no interactions between time and site. However, a marginal main effect of site was observed, with Site D showing higher data lengths compared to the reference site (Site A) (t (90) = 1.949, $p =$ 0.054).

3.2.3. Channel retention

In a secondary assessment of data quality, we also examined the proportion of channels retained. On average, 71.10 % (SD = 10.83) of channels were retained at month 6, and 73.98 % (SD = 11.82) at month 12. Statistical analysis (GLMM) found no significant effect of age (t (77) = 0.592, $p = 0.555$), site, ($p > 0.09$) or interactions between site and age ($p > 0.20$) on the proportion of channels retained.

3.2.4. Signal characteristics

Qualitative inspection of power spectral density (PSD) plots (see Fig. 7) revealed typical characteristics of infant brain activity, including consistent power distribution across sites and expected developmental shifts with age. Furthermore, the power distribution indicates no significant contamination from higher-frequency noise sources. This initial examination of signal properties, alongside quantitative feasibility and quality metrics, confirms the reliability and suitability of the data for future analysis.

4. Discussion

EEG and MRI studies have revealed early indicators of brain differences in ASD before behavioral symptoms emerge. By capturing data across distinct task-free, auditory, and visual paradigms, we can examine the overall functional architecture of the brain as well as specific circuit mechanisms involved in sensory processing. This multifaceted approach provides opportunities to detect early indicators of atypical neural development and better understand infant circuit development in ASD. Here, we describe a framework for integrating EEG into a multi-site MRI study of early ASD infant brain development. We provide a transparent reference to guide future endeavors and discuss the implications of these methods for our ongoing data collection strategies and multi-site infant EEG research more broadly.

4.1. Protocol feasibility

Interim analysis revealed consistently high completion rates across sites, timepoints, and paradigms (AEP, VEP, and task-free). An average of 72.5 % of infants successfully completed the entire protocol over both timepoints, and 95.8 % completed at least one paradigm. These data suggest that the protocol duration is appropriately calibrated for infant participants, neither underutilizing nor exceeding their engagement capacity. Striking this balance is crucial for maximizing data collection while ensuring a comfortable participant experience. For task-free data specifically, attrition rates due to in-session issues (including technical errors and infant fussiness) were 2.74 % at 6 months and 6.38 % at 12 months. These rates are consistent with the in-session data attrition rates for task-free EEG data described in a large study (n >1000) of similarly aged infants collected at one site (5 months: 3.2 %; 10 months: 4.4 %; Van der Velde and Junge, 2020).

Furthermore, despite strict stimulus timing controls that can increase the likelihood of equipment-related data loss, we observed similarly high completion rates in both AEP and VEP paradigms. The implementation of real-time stimulus presentation recording minimized timing disruptions that could affect VEP and AEP data integrity, and

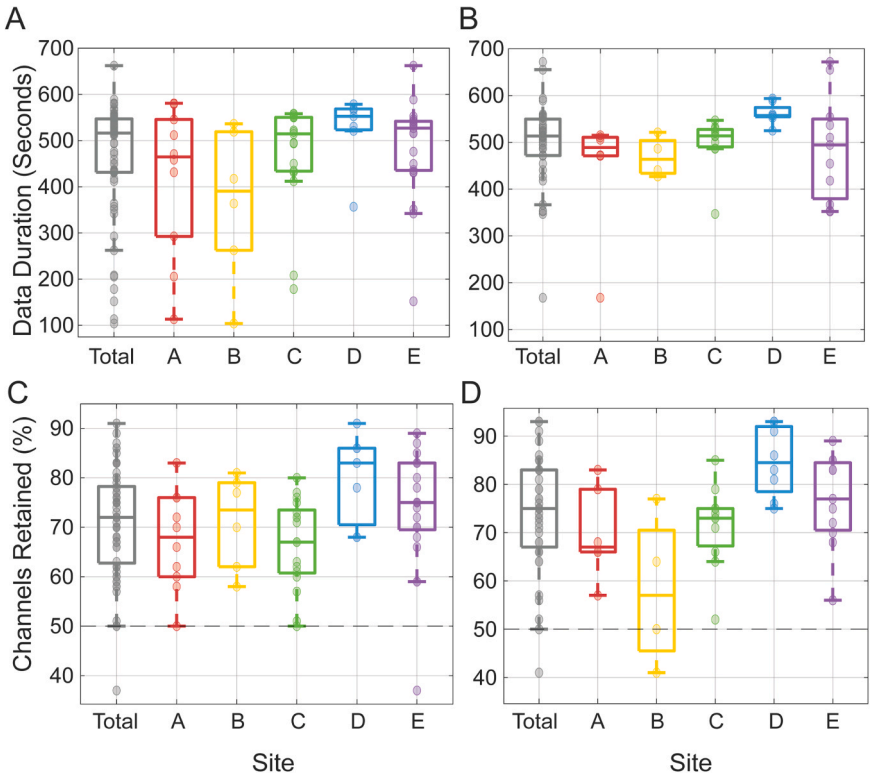

Fig. 6. A-B) Box plots showing the retained data duration (in seconds) at each site, with a total average plotted in gray for A) 6 and B) 12 months. C-D) Box plots showing the proportion of channels retained at each site, with a total average plotted in gray for C) 6 and D) 12 months.

Table 4
Data Attrition Rates. This table presents the percentage of data loss at each site (and the overall total), categorized by the source of attrition. Sources include in-session issues (infant fussiness or technical errors) and data loss due to low-quality data. Note that in the present study, all files rejected for low-quality data were due to the presence of pervasive line noise.

	Month 6			Month 12		
	In Session	Quality Control	Total Data Loss	In Session	Quality Control	Total Data Loss
Site A	0/12 0 %	2/12 16.67 %	2/12 16.67 %	1/9 11.11 %	2/9 22.22 %	3/9 33.33 %
Site B	0/14 0 %	8/14 57.14 %	8/14 57.14 %	0/6 0 %	2/6 33.33 %	2/6 33.33 %
Site C	1/18 5.56 %	0/18 0 %	1/18 5.56 %	1/12 8.33 %	0/12 0 %	1/12 8.33 %
Site D	0/7 0 %	0/7 0 %	0/7 0 %	1/9 11.11 %	0/9 0 %	1/9 11.11 %
Site E	1/22 4.55 %	0/22 0 %	1/22 4.55 %	0/11 0 %	0/11 0 %	0/11 0 %
Total	2/73 2.74 %	10/73 13.70 %	12/73 16.44 %	3/47 6.38 %	4/47 8.51 %	7/47 14.89 %

rapid feedback identified and addressed any issues that emerged.

4.2. Data quality

We assessed data retention rates after artifact removal as a marker of data quality and usability. A subset of participants failed the data cleaning algorithm, as pervasive line noise above specified amplitude thresholds led to all channels being removed. This resulted in the exclusion of 13.7 % of recordings at 6 months and 8.5 % at 12 months. Despite this issue, our attrition rates compare favorably with those in similar age-group EEG studies. For example, Van der Velde & Junge (2020) reported attrition rates of 23.4 % at 5 months and 18.5 % at 10 months for continuous task-free data (< 90 seconds of data).

Table 5
Quality metrics for task-free data. This table presents the metrics used to assess data quality, the absolute data duration (in seconds), and the percentage of channels retained post-cleaning. Values are described individually for each site, with the average across sites presented as 'Total.'.

Site	Month 6		Month 12	
	Duration Retained (Seconds)	Channels Retained (%)	Duration Retained (Seconds)	Channels Retained (%)
	Mean (SD) [Range]	Mean (SD) [Range]	Mean (SD) [Range]	Mean (SD) [Range]
Site A	418.95 (161.85) [113.32–580.63]	67.3 (9.98) [50–83]	440.45 (134.89) [167.90–515.10]	69.83 (9.54) [57–83]
Site B	367.17 (163.94) [104.04–536.26]	71.17 (9.50) [58–81]	468.91 (43.29) [426.93–521.37]	58 (15.81) [41–77]
Site C	469.34 (114.55) [178.63–558.32]	66.71 (8.96) [50–80]	499.94 (54.01) [347.03–546.84]	71.55 (8.61) [52–85]
Site D	524.93 (77.11) [356.67–578.56]	80 (9.07) [68–91]	561.44 (21.62) [525.02–593.59]	84.75 (7.23) [75–93]
Site E	485.78 (107.02) [152.05–662.18]	73.48 (11.75) [37–89]	487.98 (112.29) [352.32–671.80]	76.64 (9.71) [56–89]
Total	463.07 (126.34) [104.04–662.18]	71.10 (10.83) [37–91]	496.93 (89.40) [167.90–671.80]	73.98 (11.82) [41–93]

The remaining participants contributed at least five minutes of artifact-free data (6 months: 419 seconds; 12 months: 440 seconds). This duration is suitable for many metrics of interest, including spectral power, connectivity, entropy, and complexity (Gudmundsson et al., 2007; Haartsen et al., 2020; Miljevic et al., 2022). For instance, ~20–40 seconds of data is adequate for stable calculation of many

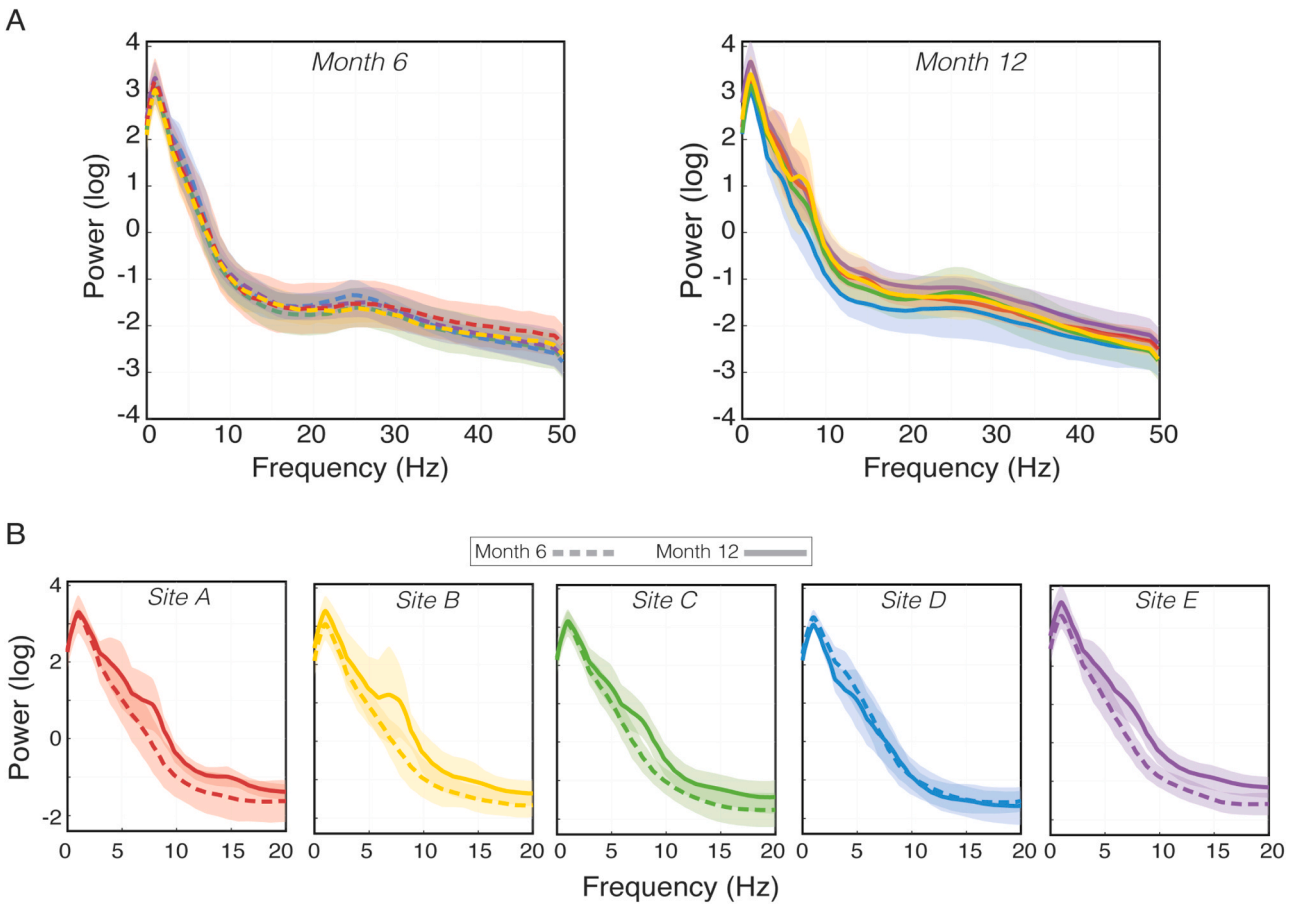

Fig. 7. Power Spectral Densities (PSDs) for 6-month and 12-month EEG data, averaged across all scalp channels. Shaded regions represent 95 % confidence intervals. A) Overlaying PSDs from each site reveals high consistency in signal characteristics at both 6- and 12-month timepoints. B) PSDs show consistent age-related changes in signal characteristics between 6 and 12 months at each site, aligning with anticipated developmental trends.

spectral characteristics, including power (Gudmundsson et al., 2007). Furthermore, 40 seconds of data has been used as a benchmark in many studies of developmental populations (Dickinson et al., 2017), including infants (Gabard-Durnam et al., 2019). Data quality metrics also showed low variation across sites, indicating consistent retention of task-free data. Analysis of PSDs further confirmed this consistency, revealing expected infant power distributions. Combined with feasibility metrics, these data quality assessments indicate that thorough training and standardized protocols can support consistently high-quality data, regardless of prior experience levels.

Our preliminary analysis highlights external environmental noise interference as the main source of data loss. Specifically, despite successful initial data capture, several files were identified as unusable due to disruptions affecting the integrity of the recorded data, providing insight into potential systematic problems. The sources of post-session data loss can generally be categorized into internal issues (file corrupted, recording error) or external sources (large mains line noise). Overall, we saw higher rates of external issues (compared to internal). Recognizing this, we will take future efforts to preemptively detect and address noise issues, integrating quantitative metrics of 60 Hz noise levels during file reviews. While not all sources of noise are easily addressable, such as construction-related 60 Hz interference (Site B), continuous monitoring of these rates will facilitate early detection of emerging noise concerns, enabling us to proactively mitigate potential data losses.

4.3. Limitations & next steps

This study employed an amplitude-based artifact detection method to objectively measure the seconds of data retained post-cleaning, providing a clear, tangible view of signal integrity. This initial assessment offered a valuable "snapshot" of data quality, but it was not tailored to extract specific metrics of interest. Although this objective method shows consistent cleaning rates across timepoints, more advanced techniques, such as artifact subspace reconstruction (ASR) (Chang et al., 2018), which flexibly accommodate each infant's unique data characteristics, may be better suited for specific future analyses. Furthermore, these estimates will not necessarily translate to other paradigms (AEP and VEP). While we saw high completion of AEP and VEP paradigms, task-specific considerations, such as visual inattention, impacted data retention. For instance, the first stage of VEP data processing will involve removing periods of inattention to the screen, identified through a review of synchronized video footage. Finally, it remains a challenge to establish a standard benchmark for data retention rates, especially in infant studies. Nonetheless, these initial evaluations suggest that we will retain a significant amount of high-quality data, versatile enough to support a broad range of metrics and analyses, as described above.

There are multiple approaches to establishing research collaborations across multiple sites, each with unique advantages and challenges. For example, retrospective pooling of data from independent studies offers flexibility and logistical simplicity, potentially yielding larger datasets. Conversely, stringent cross-site standardization, while ensuring uniform data collection and reducing variability, may restrict the number of participating sites. This study adopted a standardized approach to maximize consistency across sites, a decision partly driven by the substantial heterogeneity inherent in ASD and typical infant development, in order to reduce additional variability in data collection

that could otherwise obscure or misrepresent crucial neural differences.

Less tightly controlled multi-site approaches will also play a vital role in autism biomarker discovery. To have a meaningful impact, biomarkers must be consistently and reliably measurable across different systems and conditions, extending beyond the specific methodologies of any single study or research group. In practice, clinics and research institutions may operate with varying levels of resources, employ diverse procedures, and utilize different EEG systems. Therefore, future endeavors, adopting more flexible multi-site approaches and varied procedures and systems will help us to establish biomarkers that are consistently detectable across diverse real-world settings. Ultimately the goal is to identify biomarkers that are both scientifically robust and broadly applicable in diverse clinical and research environments.

4.4. Conclusions

Despite the inherent unpredictability of infant data collection, it is feasible to obtain consistent EEG signals across sites with varying acquisition parameters and levels of expertise. Our approach offers a practical and realistic framework for future research, aiming to achieve high-quality data collection while maintaining the integrity and goals of the broader study. The balance between standardization and adaptability in our methodology is key for advancing multi-site, multimodal neuroscience research. This strategy establishes a solid foundation for identifying biomarkers, which can be further explored in multi-site initiatives, ensuring both precision and versatility in their application.

Ethical statement

The research was conducted in accordance with the principles embodied in the Declaration of Helsinki and local statutory requirements. Human subjects oversight was provided by the Washington University in St. Louis institutional review board and Human Research Protection Office.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data for the present study will be accessible via NIMH NDA (#3358).

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