Received: 20 December 2022 | Revised: 31 January 2024 | Accepted: 26 February 2024

DOI: 10.1002/dev.22484

RESEARCH ARTICLE

Developmental Psychobiology WILEY

The importance of decomposing periodic and aperiodic EEG signals for assessment of brain function in a global context

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Funding information
EU/EFPIA/SFARI/Autistica/AUTISM SPEAKS Innovative Medicines Initiative 2 Joint Undertaking (AIMS-2-TRIALS), Grant/Award Number: 777394; Innovative Medicines Initiative 1 Joint Undertaking (AIMS-2-TRIALS), Grant/Award Number: 115300; the Medical Research Council for the projects "The Development of Social Attention and Perception Abilities in Typical and At-risk Infants", Grant/Award Number: MR/K021389/1; "Human neurocognitive development: Early-stage processing, modifiers, and outcomes", Grant/Award Number: MR/T003057/1; Sir Henry Wellcome Postdoctoral Fellowship, Grant/Award Number: 213608/Z/18/Z; UK Research and Innovation, Grant/Award Number: MR/S036423/1

Abstract

Measures of early neuro-cognitive development that are suitable for use in low-resource settings are needed to enable studies of the effects of early adversity on the developing brain in a global context. These measures should have high acquisition rates and good face and construct validity. Here, we investigated the feasibility of a naturalistic electroencephalography (EEG) paradigm in a low-resource context during childhood. Additionally, we examined the sensitivity of periodic and aperiodic EEG metrics to social and non-social stimuli. We recorded simultaneous 20-channel EEG and eye-tracking in 72 children aged 4–12 years (45 females) while they watched videos of women singing nursery rhymes and moving toys, selected to represent familiar childhood experiences. These measures were part of a feasibility study that assessed the feasibility and acceptability of a follow-up data collection of the South African Safe Passage Study, which tracks environmental adversity and brain and cognitive development from before birth up until childhood. We examined whether data quantity and quality varied with child characteristics and the sensitivity of varying EEG metrics (canonical band power in the theta and alpha band and periodic and aperiodic features of the power spectra). We found that children who completed the EEG and eye-tracking assessment were, in general, representative of the full cohort. Data quantity was higher in children with greater visual attention to the stimuli. Out of the tested EEG metrics,

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periodic measures in the theta frequency range were most sensitive to condition differences, compared to alpha range measures and canonical and aperiodic EEG measures. Our results show that measuring EEG during ecologically valid social and non-social stimuli is feasible in low-resource settings, is feasible for most children, and produces robust indices of social brain function. This work provides preliminary support for testing longitudinal links between social brain function, environmental factors, and emerging behaviors.

KEYWORDS
development, EEG, eye-tracking, global health, longitudinal

1 | INTRODUCTION

Around ~80% of children are growing up in low- and middle-income countries (Bitta et al., 2018). In these settings, children more often experience adversities that impact their health and cognitive development, such as malnutrition, poverty, and limited stimulation in home environments. These early developmental factors may impact health, academic achievement, and income later in life (Grantham-McGregor et al., 2007). Evidence-based interventions focusing on improving health and cognitive development may help break generational cycles of inequality. To evaluate the impact of early environmental risk factors on the developing brain, and to track the efficacy of early intervention strategies, we need direct measures of child brain development (Troller-Renfree et al., 2022).

Whilst many studies have focused on anthropometric measures such as height and weight, recent advances in the portability and scalability of neurocognitive and brain imaging techniques have resulted in more direct measurements of neurocognitive function that are affordable and feasible (Lloyd-Fox et al., 2019). Standardized psychological assessments of cognitive functioning are frequently normed on samples from Western and high-income countries. Language, parenting techniques, and childhood experiences vary between cultures. Some assessment items of Western standardized assessments may not be culturally appropriate, feasible, or considered a developmental milestone in other cultures (Gladstone et al., 2010; McCray et al., 2023; Milosavljevic et al., 2019). Such cultural effects on such assessments can be a challenge in large-scale cross-cultural studies. Consequently, studies are focusing on the feasibility and use of *objective* measures of functional brain development to complement the (standardized) psychological assessments. Most previous work has focused on the infancy period (Gladstone et al., 2010; McCray et al., 2023; Milosavljevic et al., 2019), while less is known about suitable brain measures during childhood (Bhavnani et al., 2021).

Electroencephalography (EEG) is an objective and non-invasive technique that uses electrodes placed on the scalp to record differences in the electrical activity of the brain across different locations with high temporal sensitivity (Lopes da Silva, 2013). EEG directly measures the synchronization of populations of neurons, and the high temporal sensitivity allows for detecting the speed of neural processing. EEG is a particularly promising method for longitudinal research in low- and middle-income settings because it can be captured comparably across developmental stages and is low cost. However, despite its potential, there are very few studies demonstrating the successful use of specific paradigms to capture EEG in toddlerhood and childhood, where behavioral challenges are greater than in newborns or infants during data collections due to differences in attention spans, compliance, and mobility (Katus et al., 2019; Lockwood Estrin et al., 2023). Thus, exploring the utility and feasibility for the use of EEG in older children is important to determine its potential for scalable tracking of functional brain specialization.

The acceptability and flexibility of EEG recordings are major challenges to be considered in the design. Caregivers or families' understanding of research or resources, such as lack of time to participate or proximity of the EEG assessment location, may pose barriers for the acceptability of the EEG assessment (Lockwood Estrin et al., 2023). The willingness of the child participant to wear the EEG cap and maintain attention throughout the EEG assessment is also important to consider (Haartsen et al., 2021). Data loss due to children not completing the assessment is another challenge in the developmental research field. Developmental populations are often characterized by high drop-out rates. Included samples often consist of infants or children who were more attentive to the task and may therefore not be representative of the population. In addition to bias introduced by selective attrition, smaller samples will result in lower statistical power to detect a reliable experimental effect. It is thus important to examine the degree to which data loss is related to factors such as participants' age, EEG capping time, and children's level of interest in the stimuli presented.

Selecting appropriate paradigms with strong face and construct validity for the assessment of brain function is also important. One paradigm that has been widely used to assess brain development in infancy is dynamic naturalistic social and non-social videos (Haartsen et al., 2022; Jones et al., 2015; van der Velde et al., 2021), in which evoked brain responses to viewing singing people and moving toys are compared. Early social development is a particularly important domain to assess because it has cascading effects on learning and social interactions (Mundy et al., 2003). The development of the social brain network is characterized by experience-dependent specialization, suggesting increased experience with social stimuli results in brain regions showing specific responses to these stimuli (Mundy et al., 2003). Variability in cortical specialization to social stimuli may furthermore relate to variability in social cognition such as observed in autism (Jones et al., 2015). Recent studies in adults have suggested that measuring brain responses while watching dynamic videos provides stronger brain–behavior correlations than measuring brain responses while watching a fixation cross on a dark background (Finn & Bandettini, 2021). Furthermore, examining differences in brain responses to social and non-social stimuli may be more reproducible and provide larger effect sizes than examining baseline measures such as traditional eyes-open and eyes-closed paradigms (Gabard-Durnam et al., 2019; Huberty et al., 2021; Tierney et al., 2012). In addition, this passive viewing paradigm is suitable for comparisons across different age groups, neurodevelopmental backgrounds, and cultural backgrounds as no overt response is required (Haartsen et al., 2019; Jones et al., 2019; Loth et al., 2017; Webb et al., 2020). The dynamic videos in the paradigm also provide higher inclusion rates, compared to paradigms measuring event-related potentials in response to static images of faces (Webb et al., 2020), which are often used to measure social brain functioning during development. The social and non-social videos contain audio-visual synchrony that mimics everyday experiences more closely than resting-state or event-related paradigms.

Finally, construct validity requires the selection of appropriate EEG indices that are maximally sensitive to differences between selected conditions, in this case, between the social and non-social videos. Traditional EEG power analyses exploring resting-state or baseline EEG have focused on averaging spectral power across frequency bands while using a variety of metrics such as absolute, relative, and logarithmic power (e.g., 8–12 Hz for alpha band, see Figure 1). As age increases, there is a decrease in power for the lower frequency bands such as delta and theta bands, and an increase in power for the higher frequency bands such as alpha and beta bands (Eeg-Olofsson, 1971; Gasser et al., 1988; John et al., 1980; Marshall et al., 2002; Otero, 1994; Otero et al., 2003). The frequency of the alpha peak furthermore increases across age until late childhood (Eeg-Olofsson, 1971; Marshall et al., 2002; Stroganova et al., 1999). Individuals with a diagnosis or family history of neurodevelopmental conditions have also displayed differences in spectral power within frequency bands or ratios between bands (Begum-Ali et al., 2022; Dawson et al., 2012; Gabard-Durnam et al., 2019; Garcés et al., 2022; Huberty et al., 2021; Levin et al., 2017; Mathewson et al., 2012; Tierney et al., 2012). Previous studies using the social and non-social videos paradigm and exploring condition differences have used a similar analytic approach. Jones and colleagues showed 6- and 12-month-old infants the social and non-social videos (Jones et al., 2015). Theta log power (3–6 Hz) was increased during the social video watching, compared to the non-social videos at 12 months but did not differ between conditions at 6 months. Alpha log power (6–9 Hz) did not differ between videos at either age point but increased with age overall. Infants at 14 months of age also showed increased log theta (4–5 Hz) power while watching social video, compared to non-social video (Haartsen et al., 2022). This suggests theta band log power may be a sensitive EEG index of social brain development with high construct validity in infants, but the face and construct validity in mid-childhood remains to be tested.

The neural EEG power spectrum however is a combination of aperiodic activity with a 1/f shape as reflected by higher power for lower frequencies and lower power for higher frequencies and periodic activity reflected by peaks in the spectrum (Figure 1b). Differences observed in narrowband power analyses may arise from a range of factors, such as shifts in the aperiodic 1/f shape, which could include changes in the offset or slope, differences in the frequency of the periodic peaks, and true differences in amplitudes of the periodic peaks—see Figure 1c (Donoghue et al., 2020). Measures of aperiodic (offset and slope) and periodic activity (frequency and center frequency of peaks) can be extracted by applying the Fitting Oscillations and One Over F (FOOOF) algorithm (Figure 1d; Donoghue et al., 2020) to the power spectra. Parameterization of the EEG spectra into both periodic and aperiodic activity can reveal the underlying mechanisms of changes in patterns of neural oscillations observed in traditional frequency band analyses. Studies in developmental populations have revealed decreases in 1/f slope and offset and increases in the center frequency of the alpha peak with age (Carter Leno et al., 2021; Cellier et al., 2021; He et al., 2019; Hill et al., 2022; Schaworonkow & Voytek, 2021; Tröndle et al., 2023). Variability in 1/f slope and offset and in center frequency for the alpha peak have been associated with traits and diagnosis of neurodevelopmental disorders (Ahmad et al., 2022; Dickinson et al., 2018; Manyukhina et al., 2022). These measures may further show varying sensitivity to experimental conditions and are thus additional candidates for sensitive EEG indices of social brain development during the social and non-social videos.

The current study set out to explore the feasibility and sensitivity of the EEG social and non-social videos paradigm and the sensitivity of different extracted EEG parameters to key demographic variables during childhood. This study was conducted as part of a wider feasibility study that aimed to assess the feasibility and acceptability of a multi-disciplinary study protocol used to follow up 4500 children and young teenagers from the South African Safe Passage Study (Dukes et al., 2014). The original Safe Passage study included over 7000 pregnant women from two low-resource economical areas, Bishop Lavis and Belhar in Cape Town (South Africa) between 2007 and 2015, contributing to build a rich dataset of antenatal and postnatal factors (e.g., maternal physical and mental health, fetal, neonatal, and infant development). Resting state EEG was successfully collected during sleep at the neonatal time point (12–96 h after birth). EEG log power and aperiodic activity during sleep were associated with an increased likelihood of autism during toddlerhood (Brito et al., 2019; Shuffrey et al., 2022). This is consistent with findings from other studies showing associations between EEG metrics in infants with a family history of neurodevelopmental conditions and autistic behaviors during toddlerhood (Gabard-Durnam et al., 2019; Huberty et al., 2021; Karalunas et al., 2022; Tierney et al., 2012) and associations between EEG metrics measured at 6 and 36 months of age and environmental factors such as household wealth and maternal perceived stress (Jensen et al., 2021). Most of these paradigms however were recorded during an

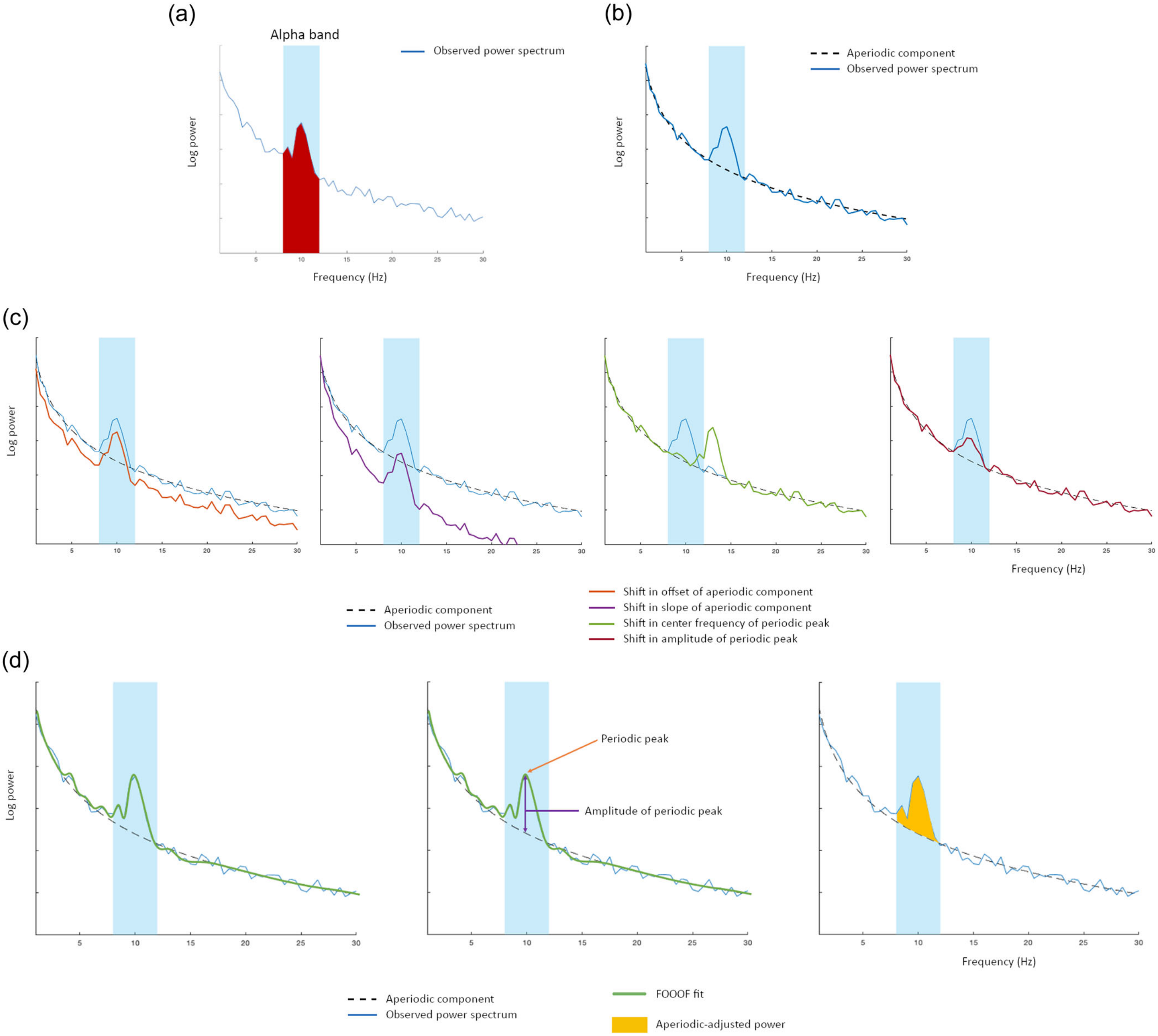

FIGURE 1 Analyzing spectral power. Traditional power analyses average the observed power across a narrow frequency band, such as alpha from 8 to 12 Hz (shown in red in (a)). These measures however are a combination of periodic peaks and aperiodic components (b). Reductions in observed power between condition may arise from a range of factors (b), such as a shift in the offset or slope of the aperiodic component (b, first and second columns), or shift in the center frequency or amplitude of the periodic peak (c, third and fourth columns). Fitting Oscillations and One Over F (FOOOF) applies a fit to the data and extracts the offset and slope of the aperiodic component (d, first column), identifies the center frequency and amplitude of the periodic peak (d, second column). Another possibility is to calculate the aperiodic-adjusted power as the difference between the observed power spectrum and the aperiodic component (d, third column).

infant baseline paradigm (sleep, across social and non-social videos or while looking at experimenters blowing bubbles or dynamic abstract shapes). In this study, our goal was to examine the sensitivity of brain responses to the social versus non-social videos as a measure of brain function during childhood in the feasibility phase.

The aim of the feasibility phase of the South Africa Safe Passage study was to test the feasibility of clinical, cognitive, and EEG assessments in children between 4 and 12 years to inform the final protocol and procedures of the planned follow-up study with 4500 children. For the feasibility phase, we collected a further EEG assessment in 100 children aged 4–12 years who had previously participated in the infant time points in the South Africa Safe Passage Study. Children watched the social and non-social videos while their EEG was measured. The feasibility of the EEG paradigm was investigated by examining potential variability in children's characteristics who were able to complete the task. In particular, we examined whether age, cognitive development (i.e., the Mullen Scales of Early Learning [MSEL]; Mullen, 1995; the Wechsler Intelligence Scale for Children (Wechsler, 2003), externalizing symptoms (i.e., the Strengths and Difficulties Questionnaire [SDQ]; Goodman, 1997), autistic traits (i.e., Childhood Autism Rating Scale [CARS]; Schopler et al., 1980), and socio-economic status (income) covaried with data loss (e.g., children with high externalizing symptoms may struggle to sit still enough to record high-quality EEG). For example, we hypothesized that data quantity and quality would be associated with attention to the screen, where children looking at the screen for longer would show increased data quantity and quality.

To determine the EEG indices with maximal construct validity, we tested the sensitivity to conditions in both canonical power and characteristics of the periodic and aperiodic neural activity within the theta (4 to 7 Hz) and alpha (8 to 12 Hz) frequency bands (Keller et al., 2017; Sato et al., 2021; Uhlhaas et al., 2009). We selected the theta and alpha frequency bands because they have shown modulation by social conditions in previous infant work with the same stimuli (Jones et al., 2015) and are less likely to be affected by muscle or electrical noise than higher frequencies (Goncharova et al., 2003). We expected to find overall higher sensitivity to conditions in the theta range measures than the alpha range measures, particularly for the canonical power measures. Despite this being one of the first examinations of condition sensitivity of aperiodic and periodic signals, we expected that condition effects could vary with cognitive and clinical scores (e.g., high externalizing symptoms may decrease condition effects by means of less engagement to the task).

2 | METHODS

2.1 | Participants

The feasibility study was advertised locally, and mothers who registered their interest to participate with their child were sampled based on age to obtain an age range of 4–12 years.

To evaluate the representativeness of the feasibility sample to the larger Safe Passage cohort, we compared the samples on demographics and key pre- and perinatal variables (including birth weight and alcohol exposure).

Descriptive statistics and analyses (*t*-test, Cohen's D) were conducted to determine similarities and differences between the feasibility sample and the original cohort. Furthermore, we report the number of children from the lower percentile (10th) of annual income who have clinically significant symptoms of autism on the CARS and who scored an IQ within the range labeled as "extremely low."

2.2 | Materials

2.2.1 | Stimuli

The stimuli were two videos of 1 min each: a video comprising five clips of two White women, appearing on screen individually, facing the camera and singing nursery rhymes whilst gesturing with their hands (social condition), and a video comprising six different toys (non-social condition). Both videos were displayed on full screen on the monitor. In the social condition, the two women wore gray t-shirts on a black background alternating telling 1–3 verses from five different nursery rhymes accompanied with gestures. The children participating in the feasibility study were brought up in an area of Cape Town that speaks Afrikaans and English in daily life and were therefore accustomed to and familiar with English nursery rhymes. In accordance with locally based co-authors, we therefore used the videos with English-spoken nursery rhymes (Hey Baby, The Wheels on the Bus, Itsy Bitsy Spider, Twinkle Twinkle Little Star, and Pat-a-cake: Figure 2a; Jones et al., 2015). In the non-social condition, five toys are shown in action, with accompanying audio, on a black background (Figure 2b; Jones et al., 2015). We chose these dynamic videos with varying social content as they are engaging and likely to yield high acquisition rates (Webb et al., 2020) and as they may be appropriate to examine social brain development (Jones et al., 2015). Furthermore, this choice is appropriate for studies in larger settings in which large effect sizes are more likely to yield usable markers for future work.

2.2.2 | EEG system

We used an Enobio EEG system composed of a flexible neoprene cap, assembled with 20 electrodes according to the standard 10-10 map (Oostenveld & Praamstra, 2001), and the Neuroelectrics Control Box (Necbox), that connects wirelessly with the operating laptop via WiFi connection. The resolution of the Enobio system reaches 24 bits/0.05 μV and a sampling rate of 500 Hz. EEG was recorded at the following locations: Fpz, AF7, AF8, F3, Fz, F4, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, PO7, Oz, and PO8 (see layout in Supporting Information S1).

Two shapes of electrode holders were used: geltrodes (with a small aperture, holding a smaller quantity of gel) and NG geltrodes (screwable top with direct access to the scalp, holding larger amounts of gel; see Figure 2d). The choice for the electrode shape was made at the start of each session and was based on the hair of the participant (see Procedure). An earclip applied to the earlobe was used as a reference, except for 12 children who found this intolerable and thus had two sticktrodes applied over the mastoid process. The protocol did not allow changes between references in session.

2.2.3 | Eye tracker

We used a Tobii Pro X2 eye tracker (Tobii, Stockholm; 50 × 36 cm headbox at 70 cm), with a sampling rate of 30 Hz, mounted in the middle of the bottom frame of the 1920 × 1080monitor used for stimulus presentation.

2.2.4 | Software

Stimuli were presented on an Apple Macbook Pro laptop (Apple Inc.), using the custom-written stimulus presentation framework *Task Engine*, running in Matlab v2018b using Psychtoolbox 3 (Brainard, 1997) and GStreamer (gstreamer.freedesktop.org).

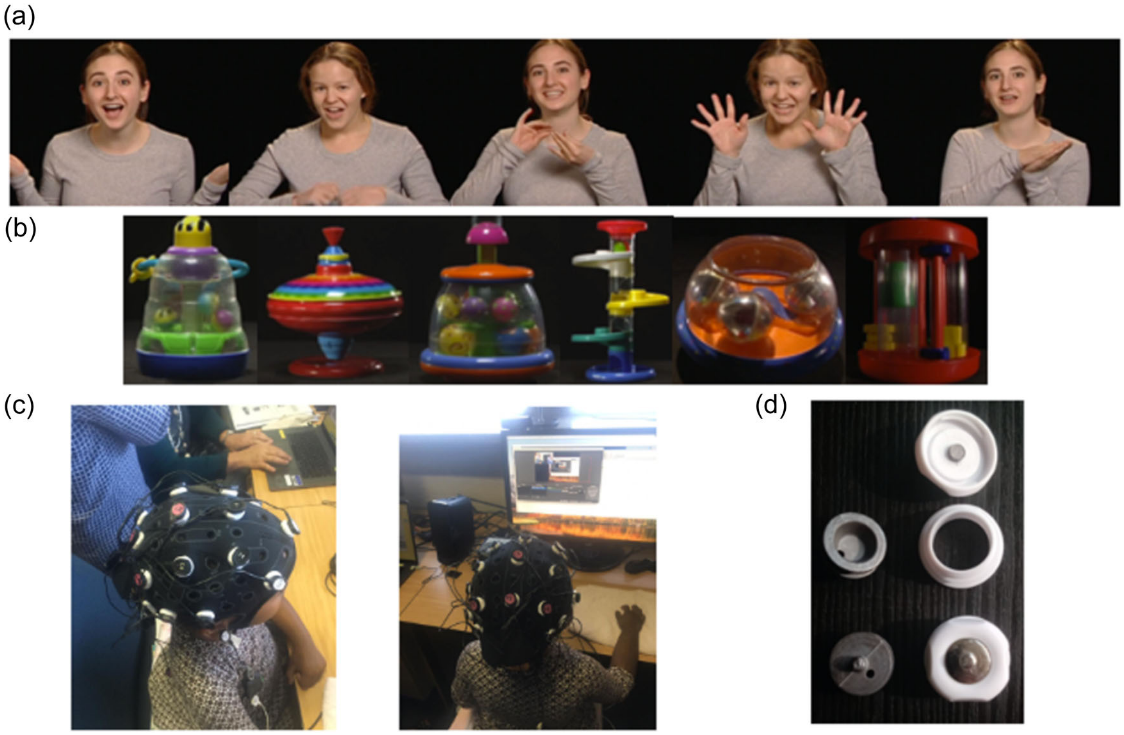

FIGURE 2 (a) Screenshots of the five scenes of the social condition video, (b) screenshots of the six top toys of the non-social condition, (c) one participant wearing the electroencephalography (EEG) cap in front of the monitor, and (d) geltrodes (left) and NG geltrodes (right).

The recording of raw gaze data was performed with Tobii Pro SDK version 3.0. The recording of raw EEG data was performed with NIC2 version 2.0.10.3 (Neuroelectrics).

2.2.5 | Session sheet

The researchers recorded the start and end of the capping procedure and other information about the experimental EEG session (reference used, type of electrodes, head circumference), age at the time of the session, and sex on a session sheet.

2.2.6 | Participants' characteristics

We assessed age (years), sex (male/female), and ethnicity with a demographic questionnaire. Household income (South African rand [ZAR] per month) was collected from the mother antenatally.

Developmental level/cognitive ability was measured using two different assessments depending on the age of the participants, a practice employed in studies with wide age range, geographical locations, and levels of ability (Baker et al., 2019; Bishop et al., 2011; Courchesne et al., 2019). Participants 6 years of age or younger completed the full MSEL (Mullen, 1995), while participants above the age of 6 completed the Wechsler Abbreviated Scales of Intelligence—second edition (WASI-2; Wechsler, 2003). For analysis, we calculated full-scale IQ (FSIQ), the Verbal Comprehension Index (VCI), and the Perceptual Reasoning Index (PRI) from the MSEL (4–6-year-olds) and the WASI-2 (>6-year-olds). The FSIQ was either calculated as a standardized aggregate from the WASI-2, scored conventionally with Western norms, or as a standardized Early Learning Composite of summed Visual Reception, Receptive Language and Expressive Language scores of the MSEL. Standardization referred to the sample's mean and standard deviation. The VCI was derived from the normalized T-scores in the Receptive and Expressive Language scales in the MSEL and from the scores on the Similarities, Vocabulary, and Comprehension subtests in the WASI-2. The PRI was calculated from the normalized T-scores in the Visual Reception scale in the MSEL and from the scores on the Block Design, Picture Concepts, and Matrix Reasoning in the WASI-2.

The CARS-2 (Schopler et al., 1980)—a clinician-report behavior rating scale—was used to screen autistic traits. All 15 categories available in the CARS-2 were used for allocated scores.

The SDQ—a 25-item parent-report screening—was used to investigate conduct problems, hyperactivity, emotional symptoms, peer problems, and pro-social behavior (Goodman, 1997). Different versions of the SDQ are available for different age groups: the version for 2- to 4-year-olds was used for 13 participants, while the version for 4- to 17-year-olds was used for 87 children.

2.3 | Procedure

The session took place in a dedicated room inside the Department of Obstetrics and Gynaecology, at Tygerberg Academic Hospital in Cape Town. After reviewing and accepting the informed consent, cognitive assessments and CARS were assessed with the participants (by MP, CdP). Caregivers were answering the questionnaires (SDQ, income) in the meantime.

Next, the EEG session was conducted according to our in-house Standard Operating Procedures (available at https://osf.io/7j4f9/?view_only =1b91755f4a54474c87e0128c855f0833) by two researchers (MP, WM, PS, CdP) trained by TDB in Cape Town during a 1-week, intensive, in-person training with the Enobio System including preparation, recording, and monitoring. This training included collecting 12 pilot participants aged 4–12 under the supervision of TDB.

The participant sat approximately 70 cm from the monitor; the parent could sit next to the child if they requested so or could go to another room to complete the study questionnaires. The tester fitted an appropriately sized neoprene cap on the participant's head, parted the hair inside the cap's apertures containing the electrode holders, exposing the scalp, and inserted conductive gel into the electrode holders with a syringe with a disposable plastic tip. The tester used NG electrodes with participants with thick hair, cornrows, or braids. In case of very thick hair, the tester partially filled the electrode holder with gel before putting the cap on and then filled up each electrode holder again with more gel. Alternatively, the tester used a hair grip to part the hair through an adjacent aperture in the cap while inserting the gel and/or added a headband on top of the EEG cap. To distract the child during this phase, the children were offered coloring books, puzzles, or toys; alternatively, they watched a video clip on the monitor or actively helped the tester by handing the electrodes (Figure 2c). Electrodes were adjusted or gel was added where necessary until all electrodes obtained a green color code in NIC2, indicating a low Neuroelectrics Quality Index calculated from line noise (power in 49–51 Hz range), main noise (power in the 1–40 Hz frequency range), and the offset of the signal every 2 s, and good data (Haartsen et al., 2021). Finally, the tester performed the eye-tracker calibration sequence until obtaining accuracy and precision >2.5° for at least one eye on all five calibration points (corners and center of the monitor).

The duration of the full EEG battery was approximately 25 min. Each 60 s video (social/non-social) was presented twice for a total of four repetitions, in predefined alternating order starting with a social video, each interspersed among other tasks (not reported here). Each presentation was preceded by a gaze-contingent fixation stimulus (a small schematic icon) at the center of the screen, ensuring that the task would only start when the participant was attending. Experimenters had the option to skip tasks if the child was not attending the screen or refused to continue.

Throughout the study, TDB and RH performed interim quality checks on recently acquired datasets, selecting them randomly for evaluation (total = 25). The checks primarily focused on identifying and addressing visual artifacts, 50 Hz noise, electrode variance, and correlation of individual recordings. Regular monthly calls were conducted with the researchers at the testing site to communicate the outcome of these checks to identify potential issues and provide feedback and suggestions to maintain and improve data quality to the site researchers.

2.4 | Pre-processing and data extraction

2.4.1 | EEG during the social and non-social videos

Preprocessing

EEG data were processed in Matlab (version 2018b, Mathworks) using the Fieldtrip toolbox (Oostenveld et al., 2010) and in-house fully automated processing scripts. Data for the social and non-social conditions were first segmented from the whole EEG session. Video EEG recordings were considered valid if (a) the duration was between 10 and 70 s and (b) the percentage of looking time (as calculated by the eye tracker) at the video was at least 20% (no less than the 2.3 percentile of normally distributed data, corresponding to a two standard deviations limit). Valid EEG video segments were then further epoched into 2-s epochs with 50% overlap. We chose a duration of 2 s to provide a higher frequency resolution for later modeling of the power spectra (Donoghue et al., 2020). We furthermore opted for a 50% overlap to retain data while using a taper during the frequency analyses.

Epoched data were filtered using a bandpass filter from 0.1 to 48 Hz and a Discrete Fourier Transform (DFT) filter to remove 50 Hz line noise and then de-trended to remove DC drift. We also added 3 s of mirror padding to avoid filter effects. Further analyses were performed on channels Fpz, AF7, AF8, F3, Fz, F4, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, PO7, Oz, and PO8 (see Figure S1 in Supporting Information S1).

The next step in our preprocessing was artifact identification. First, we identified blink artifacts. Data for the channels AF7/8 and FPz (where blink artifacts are maximal) were bandpass filtered (3–10 Hz, with 3-s mirror padding) to isolate frequencies representing blinks. Each sample of EEG data was z-scored relative to the distribution of voltages across all epochs. Epochs were considered as containing an ocular artifact if they contained a period where z-scores exceeded a value of 2.5 for longer than 50 ms for any of the three frontal channels.

Next, we identified eye movement drift artifacts on AF7/8 and FPz as trials where a quadratic fit of voltage on time exceeded $R^2 = 0.65$ (Mason et al., 2022). Trials containing blink artifacts and drift artifacts were removed from further analyses.

In our second round of artifact identification, we identified channels with a flat signal (abstract values of the signal do not exceed 0.0001 μV), exceeding thresholds (below $-150\,\mu$V or above $150\,\mu$V), and showing jumps (peak-to-peak amplitudes exceed 200 μV (Shephard et al., 2020), or signal exceeds 100 μV within 4 ms (Orekhova et al., 2014) for each epoch. Channels were marked as bad in all epochs if 80% or more of the epochs contained these artifacts. Next, we interpolated the data on an epoch-by-channel basis using spline interpolation. Neighbors were defined using the distance method and a value of 0.25 as a distance. Channels were interpolated per epoch if there were three or more artifact-free neighbors.

We performed a final round of artifact identification to detect any remaining artifacts after interpolation. Note that interpolation may have been unsuccessful if there were insufficient numbers of artifact-free neighbors available. For each epoch, channels were marked as bad if they were flat, exceeded a threshold, or displayed jumps (parameters identical to the previous). We marked channels as bad in all epochs if they contained artifacts in 80% or more epochs or if they were artifact-free in 20 or fewer epochs. We marked the epoch bad in all channels if 15 or more channels contained artifacts.

Finally, we re-referenced the data to average reference on an epoch-by-epoch basis to avoid the topographies of the signal being biased toward the right (where the reference was recorded and to account for the differences in reference location (earlobe or mastoid). For each epoch, data were re-referenced to the average across all channels that were not marked as bad. Any bad channels, epochs, or segments (i.e., channel bad within an epoch only) were excluded from further analyses. Values in bad channels for epochs and bad epochs were set to 0/0 (i.e., Not a Number, NaN), and subsequent averaging was done while including the NaN values to account for situations where not the whole epoch or whole channel was bad.

Spectral power was calculated for each epoch for each good channel before extracting EEG characteristics for outcome variables using the Fieldtrip function *ft_freqanalysis* with the following settings: *cfg.output* = 'pow', *cfg.method* = 'mtmfft', *cfg.taper* = 'hanning', *cfg.foi* = 1:.5:48, and *cfg.keeptrials* = 'yes'. This resulted in power for each of the epochs for each good channel for 1 to 48 Hz in steps of 0.5 Hz.

To assess the qualitative performance of this preprocessing pipeline, we report R^2 and error fits of the power spectra and across various peak parameters (see Supporting Information Figures S2–S7) and individual power metrics and interpolated segments (Supporting Information Figures S9–S11).

EEG metrics

The EEG metrics of interest here were data quantity, to examine the feasibility of the paradigm, and neural power metrics, to examine the sensitivity of the social brain responses. We extracted the number of good epochs and canonical power for the traditional frequency bands in our frequency ranges of interest. Next, we used the FOOOF approach to examine aperiodic features, namely, 1/f offset and slope, and periodic features, namely, the frequency and amplitude of peaks within the theta and alpha frequency bands. We also extracted differences between the aperiodic power and the observed spectrum. Each EEG metric was extracted for each condition (social and non-social condition) and each region of interest (frontal, central, parietal, and occipital).

More details on the extraction of EEG metrics follow below.

Number of good epochs: We counted the number of good epochs (80% or more artifact-free channels per epoch) for the social and non-social conditions.

Canonical power: We calculated power within traditional frequency bands (as in Figure 1a). Spectral power was first averaged across epochs for the social and non-social conditions, separately. Log power values were calculated with the natural logarithm. Power was averaged across channels within each region of interest: the frontal (channels F3, Fz, and F4), central (channels C3, Cz, and C4), parietal (P3, Pz, and P4), and occipital (PO7, Oz, and PO8) regions (also see Figure S1 in Supporting Information S1 for regions of interest). Finally, power for the regions was averaged from 4 to 7 Hz for the theta power and 8 to 12 Hz for alpha power.

Aperiodic and periodic components: We used the FOOOF algorithm in Python (https://fooof-tools.github.io/fooof/; Donoghue et al., 2020) to extract periodic and aperiodic components of the power spectrum. FOOOF analyses were performed on the untransformed power spectra for the separate two conditions and four regions, for a total of eight power spectra per participant. FOOOF creates a model of the power spectrum consisting of the aperiodic component, also known as the 1/f shape, and the periodic components, also known as peaks. The algorithm fits an aperiodic shape to the power spectrum after which this shape is subtracted from the power spectrum resulting in a flattened spectrum. Next, the algorithm identifies peaks in the spectrum based on the parameters used, and a periodic fit is applied to the spectrum. This fit including periodic peaks is then removed from the spectrum. Another aperiodic fit is fitted to the spectrum to find a better estimate of the aperiodic fit. Finally, a complete model of the spectrum is created, and the R^2 and error of the model are calculated to test how well the model fits the observed data. The output of the FOOOF algorithm includes: (1) 1/f offset of the aperiodic component, (2) 1/f slope of the aperiodic component, (3) the center frequency and amplitude of identified periodic peaks within the 1–30 Hz power spectrum (Figure 1d), and (4) the R^2 and error of the model as a measure of model fit.

In the current study, we ran FOOOF across our power spectra covering 1–30 Hz. Periodic peaks were identified if they had a width between 1 and 8 Hz (FOOOF parameter: peak_width_limits = [1,8]), and exceeded a threshold of 0.1 (FOOOF parameter: peak_threshold = 0.1). The maximum number of peaks allowed to be identified in the 1–30 Hz power spectrum was 4 (FOOOF parameter: max_n_peaks = 4). The other parameters were set to default. The values for these parameters were based on visual inspection of the fits for different values on a subsample of the current dataset. On 20% of the total amount of power spectra in the dataset, we explored the effects on R^2 and error of the FOOOF model for three different frequency ranges, five different peak thresholds, and three different peak width ranges. We visually compared the different effects of the different parameter settings on the FOOOF model fit and aperiodic components and decided the values described above resulted in the highest R^2 and lowest error of the FOOOF model fit (see Supporting Information S3 for further details and graphs). For further analyses, we only included data from model fits with $R^2 > 0.95$ (Schaworonkow & Voytek, 2021). Two peaks or more were identified for all children in each region and each condition for those with more than 20 epochs per condition and an $R^2 > 0.95$ (see Supporting Information S4).

Aperiodic 1/f offset and slope: We extracted the 1/f offset and slope from the FOOOF output for further analyses.

Periodic peaks: Canonical power analyses assume periodic peaks occur within a pre-defined narrow frequency band, typically one large peak in the alpha range and one smaller one in the theta range. However, power spectra do not always show clear periodic peaks in the expected frequency band. We therefore examined whether the peaks in the 1–30 Hz power spectra identified by FOOOF occurred in the theta and alpha frequency range. We also tested how this would affect inclusion rates if the researcher would use FOOOF identified peaks as the measure. We focused on the three largest peaks identified by the algorithm. An alpha peak was defined as a peak with a center frequency within the alpha band (8–12 Hz). A theta peak was defined as a peak with a center frequency within the theta band (4–7 Hz). We extracted center frequencies and amplitudes of the theta and alpha peaks for the statistical analyses. If none of center frequencies for the three peaks fell within the alpha band, the value for center frequency and amplitude for the alpha peak was set to NaN (see section “Statistical Analysis” for further details on handling of missing data). If multiple peaks had a center frequency within the alpha band, the peak with the highest amplitude was defined as the alpha peak. The same method was followed for defining theta peaks in the theta frequency range.

Aperiodic-adjusted power: Finally, we wanted to accommodate cases where peaks are not identified. Researchers might have to exclude participants for peak analyses if peaks were not identified with the FOOOF algorithm. This can be problematic as it decreases the sample size and statistical power to detect a significant effect. In addition, the sample would be biased toward individuals who do show a clear peak. We therefore calculated another metric of power while correcting for the aperiodic component: aperiodic-adjusted power (Tröndle et al., 2023). The aperiodic-adjusted power is the remaining power after the aperiodic power has been subtracted (also termed the flattened spectrum as derived from the FOOOF model). We calculated the aperiodic-adjusted power as the difference between the mean aperiodic power and the mean observed power within the frequency bands of interest (Figure 1d). The predicted aperiodic power was calculated as

$$L(F) = b - \log 10(k + F\hat{\ }x), \tag{1}$$

where b is the 1/f offset, k is the knee (here 0), and x is the 1/f slope (FOOOF uses a logarithm with a base of 10). F is the array for frequency values (here we used 1:.5:30 Hz). Next, we extracted the mean of this aperiodic component and the mean of the observed power spectrum within our frequency range of interest. We finally subtracted the mean aperiodic power from the mean observed power. Aperiodic-adjusted power was calculated across the theta and alpha bands and for each condition and region of interest.

2.4.2 | Session characteristics

Visual attention

For each participant, the eye-tracking data were segmented based on the onset and offset of the video in the social/non-social condition for each repetition. We extracted the time each stimulus was on the screen (video duration; max 60 s), the time the gaze was on the screen (eye-tracking looking time), and calculated the proportion of gaze on the screen by dividing the eye-tracking looking time by the video duration (eye-tracking looking proportion; see average in Table 2), to use as a general index of visual attention.

2.4.3 | Statistical analysis

First, we set out to evaluate whether participants who provided valid EEG data were representative of the recruited sample (N = 100). We calculated Cohen’s D for each clinical/demographic characteristic between the recruited sample and the included sample used for the final analysis (where Cohen’s D values <0.20 were interpreted as a small difference and >0.80 as a large difference).

Second, we tested whether the data quantity was significantly affected by age or session characteristics using linear mixed models (LMMs). The mixed model assumed condition, participant’s age, and session characteristics (capping time and eye-tracking looking proportion) and as fixed effects, the number of artifact-free epochs as a dependent variable, with varying intercepts and slopes to account for variability between participants and regions (i.e., the random effect). Linear regression models were run for the number of artifact-free epochs in the social condition and the non-social condition. All models included the interaction between the fixed effects and the social and non-social conditions. We report the estimated coefficients (a measure of the unstandardized effect size) and their standard error and the p-values for each fixed effect. Note that we included all participants with valid EEG data and used no cut-off to examine the data quantity.

Finally, to investigate which brain measure was sensitive to the condition effects across children with different characteristics, we performed separate models for each of the EEG metrics. Each model assumed the participant’s age, sex, cognitive ability, internalizing/externalizing, autistic traits, and household income as fixed effects, with varying intercepts and slopes to account for variability between participants and regions (i.e., the random effect). Correlations between the variables entered as fixed effects are reported in the Supporting Information Table S5. All models included the interaction between the independent variables and the social and non-social conditions. The separate models were performed with the following dependent variables: (1) canonical theta power, (2) canonical alpha power, (3) aperiodic 1/f offset, (4) aperiodic 1/f slope, (5) frequency, and (6) amplitude of the periodic peak within the theta band, (7) frequency and (8) amplitude of the periodic peak within the alpha band, (9) aperiodic-adjusted power within the theta band, and (10) aperiodic-adjusted power within the alpha band. For each separate model, we report the intercept (the estimated baseline of the model when all independent variables are set to constant), the estimated coefficients (a measure of the unstandardized effect size of each independent variable), their standard error, and the p-values for each fixed effect. On a technical note, the LMM excludes missing data (NaN) automatically and allows for analyses with unequal numbers of observations per level. In contrast, analysis of variance does not allow for unequal numbers of observations leading to the exclusion of the participant in the analyses and lower sample sizes. Note, here we included participants with valid EEG data, more than 20 artifact-free epochs per condition, and with an $R^2 > 0.95$ for the FOOOF model fit to ensure reliable estimates of spectral power for our social and non-social conditions (Carter Leno et al., 2022; Schaworonkow & Voytek, 2021).

As an additional sanity check of our findings, the models were replicated with relative power as the dependent variable (see Supporting Information Table S6) and assuming the proportion of interpolated channels as a covariate (Supporting Information Table S7).

3 | RESULTS

3.1 | Participant sample

3.1.1 | Generalizability

The feasibility sample included participants within an age range of 4.14 to 11.79 years, which closely aligns with the pre-registered age range of 4–12 years for the childhood follow-up. In terms of demographics, the feasibility sample consisted of 45% females, which aligns with the female proportions observed at perinatal timepoints, for example, neonatal EEG (49.3% females) and fetal heart rate monitoring (49% females). Regarding income, the feasibility sample's average income (M = 719.89 ZAR, SD = 428.08) was compared to the annual income reported separately for three enrolment waves perinatally (see Supporting Information S2, Table S1). The analysis revealed no significant differences in income between the feasibility and the enrollment waves (see Supporting Information S2, Table S1). Additionally, the feasibility phase included participants from a mixed ethnic background only, which corresponds to the population of interest in the protocol and has been the focus of the perinatal analysis. Regarding key variables, the protocol pre-registered an aim of 2% participants on the lowest z-score of birth weight among the 4500 prospective participants and 4% with the highest antenatal exposure to alcohol. Frequencies in the feasibility sample did not differ significantly from those, with 4% of participants falling into the lowest birth weight percentile (third percentile, ≤1490 g), and 3% with the highest antenatal alcohol exposure (97th percentile, ≥25 drinks per day).

None of the children obtained a CARS-2 above the threshold suggestive of mild/moderate (>= 30) or severe autism (>= 37). Five children were from families whose annual income was below the 10th percentile of the sample average income (<250 ZAR). 33 children >6 years of age assessed with the WASI-2 and 3 children <6 years of age assessed with the MSEL scored below the threshold of 69 (labeled "extremely low").

3.1.2 | EEG data availability

Participants of the recruited and final sample of the feasibility phase all had a mixed ethnic background. Data for the EEG task was missing for eight participants (reasons not recorded), and different parts of the data were missing for a further 17 participants (EEG equipment was out for repair for $N = 13$ and technical errors for $N = 4$). A further three participants were excluded due to bad data quality (not looking at the screen for $N = 1$, bad EEG signal for $N = 1$, and insufficient number of artifact-free epochs for $N = 1$; see Figure 3). Of the remaining 72 participants, all participants also had records of both clinical and demographic information. This resulted in a final included sample of 72 participants with both sufficient EEG data and clinical and demographic data. See Table 1 for comparisons in characteristics between the recruited sample and the included sample. The highest Cohen's D obtained for VCI was small (<0.20), indicating that there are no significant differences in characteristics between the recruited feasibility sample and the included sample.

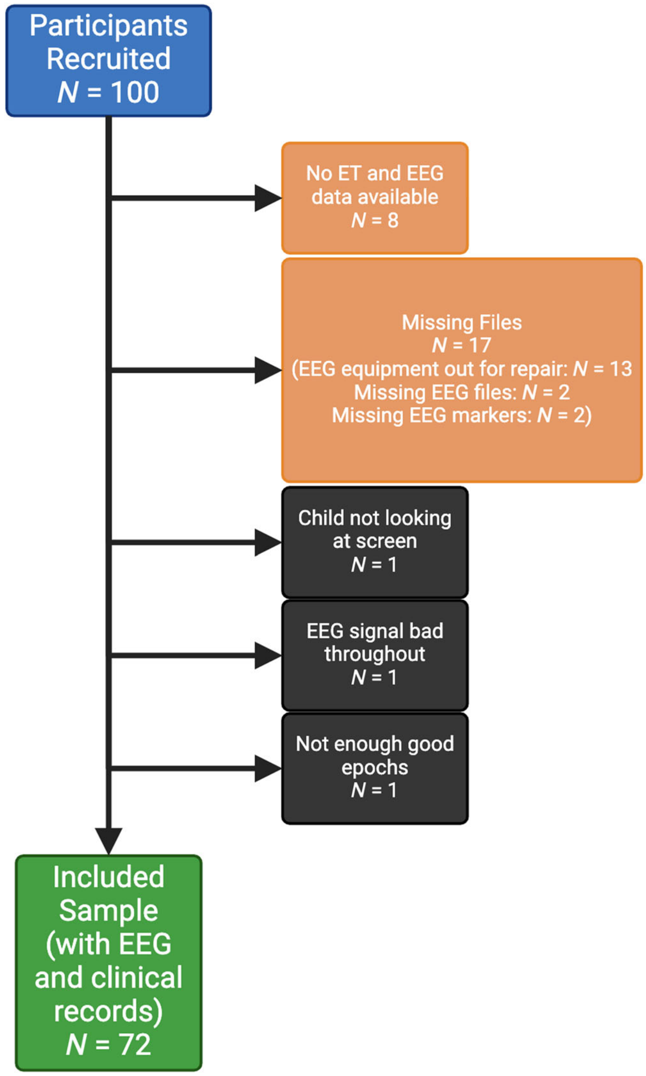

FIGURE 3 Flowchart of the number of participants.

The average to cap the children with the EEG was 18.18 min (SD = 5.83, range = 10–39 min). On the total number of sessions that reported the type of electrode used (79% of all sessions), geltrodes were used 56% of the times; NG electrodes—indicated for thicker hair—were used 24% of the times. The minimum number of clean epochs per condition provided was 23 (also, 40% as the minimum percentage of clean epochs per condition), while the minimum eye-tracking looking proportion was 32%. Further, participants were looking at the screen overall for 86% of the task (SD = 13, range = 45%–98%): where proportional looking time was 85% during the social videos (SD = 16%, range = 32%–99%) and 87% during the non-social videos (SD = 12%, range = 40%–99%).

TABLE 1 Descriptive statistics of the recruited sample and the included sample of the feasibility phase.

	Recruited sample	Included sample	Cohen's D/McNemar test (included, compared to recruited sample)
N	100	72	
N females	45	30	OR = 1.31, *p*-value = 0.29
Variable (mean, SD or range)	Mean (SD, minimum–maximum)		
Age	7.92 (2.32, 4.14–11.79)	8.21 (2.25, 4.14–11.79)	0.12
VCI	84.19 (16.52, 47–133.57)	81.53 (15.09, 55–116.4)	0.14
PRI	88.47 (14.32, 46–135.67)	87.36 (14.2, 60–135.67)	0.07
MSEL Full Composite Standard Score (100, 15)	106.2 (12.41, 68.29–121.49)	107.81 (8.81, 96.79–120.54)	0.14
WASI-2 full scale (100, 15)	76.54 (9.92, 42–107)	77.13 (9.59, 59–101)	0.04
CARS-2 (15–60)	16.18 (2.31, 15–30)	16.27 (2.15, 15–30)	0.01
SDQ (0–50)	14.03 (5.64, 3–26)	13.73 (5.54, 3–26)	0.02
Household income, ZAR/month[a]	717.51 (428.08, 83.33–2000)[a]	701.97 (390.04, 83.33–2000)	0.04

Abbreviations: CARS-2, Childhood Autism Rating Scale-2; MSEL, Mullen Scales of Early Learning; PRI, Perceptual Reasoning Index; SDQ, Strengths and Difficulties Questionnaire; SD, standard deviation; VCI, Verbal Comprehension Index; WASI-2, Wechsler Abbreviated Scales of Intelligence–second edition; ZAR, South African rand.

[a]The average monthly household income of Wave 1 at the antenatal time point was 648 ZAR (SD = 500; Odendaal et al., 2020).

3.1.3 | Data quantity and quality

To further explore the feasibility of EEG, we examined the number of good epochs as a measure of data quantity, and the R^2 of the FOOOF fit as a measure of data quality in our included sample ($N = 72$, see Table 2). A higher number of good epochs during the session was associated with greater proportional looking time (*estimate* = 90.66, $p < 0.00001$), suggesting the number of good epochs increased with increased looking at the screen. The number of good epochs was similar across conditions ($p = 0.94$) and there was no interaction between condition and age ($p = 0.46$) confirming the stimuli were equally suitable for attracting attention across the broad age range. There was a negative effect of capping time just above the significance level (estimate = –0.89, $p = 0.055$), and no significant effects for sex, household income, or the clinical measures (SDQ or CARS-2).

The model for the R^2 of FOOOF revealed that age had a significant effect on the fit of the model (*estimate* = –0.001, $p = 0.001$). This suggests that the algorithm was better able to fit a 1/f function across the power spectrum (indicating better data quality) in younger children. None of the other predictors showed a significant estimate on the R^2 of FOOOF. Condition, looking, capping time, sex, household income and clinical traits were thus unlikely to influence the FOOOF model fit.

3.1.4 | EEG metrics

We first took the traditional approach and examined canonical power modulations in the included sample (see Table 3). Canonical power in the theta range was higher in the social condition compared to the non-social (*estimate* = 0.24, $p < 0.0001$) and negatively associated with age (*estimate* = –0.09, $p < 0.001$) such that power was decreased with increasing age. The significant interaction between condition and age was negative (*estimate* = –0.02, $p = 0.003$), meaning that condition differences decreased with age. Canonical power in the theta range was also negatively associated with the number of good epochs (*estimate* = –0.001, $p = 0.006$) with lower power values for higher numbers of epochs. Canonical power in the alpha range displayed the same but less reliable negative association with age as was found for the theta power just below the significance level (*estimate* = –0.07, $p = 0.04$), but no other associations reached significance.

Next, we extracted the aperiodic components: the 1/f offset and slope (see Table 4). Age had a negative effect on the 1/f offset (*estimate* = –0.01, $p = 0.003$) where the 1/f offset was decreased with increasing age. The number of good epochs had a negative effect on both components displaying a lower 1/f offset (*estimate* = –0.001, $p = 0.0001$) and lower/flatter 1/f slope (*estimate* = –0.0009, $p = 0.0014$) with higher numbers of epochs. The aperiodic components did not further vary with condition or other demographic or clinical variables.

Not all participants had identified periodic peaks within the theta and alpha range, within each region, in separate or both conditions. Percentages for children with peaks identified varied between 15% (children with peaks identified in both conditions, both frequency ranges, and all four regions) and 94% (children with peaks identified during the non-social condition within the alpha frequency range in the central region, see more details in Table S3 in Supporting Information S4). Overall, periodic peaks were more often identified in central regions than other regions and more often in the alpha than theta frequency band. This demonstrates that sample sizes would be small if researchers would only include participants with peaks identified

TABLE 2 Results for the linear mixed models (LMMs) with data quantity (number of artifact-free epochs) and quality (R^2 of Fitting Oscillations and One Over F [FOOOF]).

Term	Number of good epochs		R^2 of FOOOF	
	Estimate (se), *p*-value	95% confidence intervals	Estimate (se), *p*-value	95% Confidence Intervals
Intercept	50.28 (50.71), .32	-46.25~150.01	**1.00 (0.01), <0.0001*****	0.97~1.04
Condition (social)	-0.97 (13.54), 0.94	-27.59~26.71	-0.002 (0.002), 0.27	-0.007~0.002
Age (years)	-2.51 (1.48), .097	-5.64~0.56	**-0.001 (0.0004), 0.007****	-0.002~-0.0004
Condition × Age	1.13 (1.54), 0.468	-1.92~4.15	0.0004 (0.0005), 0.183	-0.0002~0.001
Sex (male)	-0.16 (5.20), 0.974	-10.09~10.20	< 0.0001 (0.001), 0.984	-0.0034~0.0033
MSEL/WASI-2	0.15 (0.17), 0.40	-0.18~0.50	< 0.001, (0.0001), 0.96	-0.00011~0.00012
Capping time	-0.89 (0.45), 0.055	-1.79~-0.05	-0.0001, (0.0001), 0.678	-0.0004~0.0002
Looking proportion	**90.66 (18.95), <0.0001*****	54.23~130.18	< 0.0001 (0.004), 0.996	-0.0085~0.0087
SDQ	0.61 (0.41), 0.153	-0.25~1.53	0.0001 (0.0001), 0.366	-0.0002~0.0004
CARS-2	−2.03 (2.14), 0.349	-6.53~1.98	-0.0001 (0.0007), 0.923	-0.0015~0.0013
Household income	2.25 (1.54), 0.396	-3.08~7.85	0.0004 (0.0009), 0.641	-0.001~0.002

Note: Effects reaching significance are highlighted in blue and printed in bold.
Abbreviations: CARS-2, Childhood Autism Rating Scale-2; SDQ, Strengths and Difficulties Questionnaire; se, standard error of the estimate.
*$p < 0.050$; ** $p < 0.010$; *** $p < 0.0001$.

by FOOOF in every combination of conditions, frequency range, and region ($N = 11$). We therefore analyzed both features of these periodic peaks identified by FOOOF and the aperiodic-adjusted power (the mean of the aperiodic signal subtracted from the mean of the observed signal in the frequency range, which does not require an identified peak) in separate LMMs for the two frequency ranges.

Results for the LMMs with the periodic components are displayed in Table 5. First, we focus on the results for condition, age, and the condition-by-age interaction. Theta peak frequency was higher in the social versus non-social conditions (*estimate* = 0.82, $p = 0.011$), and this difference between conditions became smaller with increasing age (*estimate* = –0.11, $p < 0.004$). Theta peak amplitude was higher during the social versus non-social conditions (*estimate* = 0.20, $p = < 0.0001$) and overall decreased with increasing age (*estimate* = –0.01, $p = 0.0004$). Theta aperiodic-adjusted power was higher during the social versus non-social conditions (*estimate* = 0.11, $p = < 0.0001$) and overall decreased with increasing age (*estimate* = –0.008, $p = 0.0014$). The interaction between age and condition was negative (*estimate* = –0.02, $p = 0.016$) suggesting the difference between conditions decreased with increasing age. The alpha peak frequency was higher in the social versus non-social condition (*estimate* = 0.56, $p = 0.004$), and this difference decreased with increasing age (*estimate* = –0.05, $p = 0.021$). The alpha peak frequency furthermore increased with age (*estimate* = 0.11, $p = 0.020$). The amplitude of the alpha peak decreased with age (*estimate* = –0.02, $p = 0.039$). We did not observe any further condition differences in alpha aperiodic-adjusted power.

Next, we examined the effects of data quantity and clinical and demographic variables on the periodic and aperiodic-adjusted components. We observed a few associations of small to medium size between the periodic components and other measures (frequency of peak theta: FSIQ estimate = –0.02, $p = 0.006$, CARS-2 estimate = –0.19, $p = 0.01$; frequency of peak alpha: SDQ estimate = 0.03, $p = 0.05$; amplitude of alpha peak: household income estimate = –0.07, $p = 0.01$; theta periodic power: household income estimate = –0.03, $p = 0.05$; alpha periodic power: household income estimate = –0.04, $p = 0.02$). The associations for condition, age, and interaction between condition and age were clearer than the ones with data quantity and environmental variables.

4 | DISCUSSION

Incorporating measures of brain development in studies of global health requires a demonstration of the feasibility and robustness of assessment protocols. In this study, we examined the data from an EEG paradigm in the feasibility phase of the childhood follow-up in the Safe Passage study and focused on the interaction between neu-

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TABLE 3 Results for the LMMs with canonical power.

Frequency band	Theta		Alpha	
Term	Estimate (se), *p*-value	95% confidence intervals	Estimate (se), *p*-value	95% confidence intervals
Intercept	2.1 (1.29), 0.113	-0.51~4.54	0.98 (1.35), 0.474	-1.67~3.52
Condition (social)	**0.24 (0.04), <0.0001*** **	0.15~0.33	-0.02 (0.04), 0.584	-0.001~0.001
Age (years)	**-0.09 (0.03), 0.008** **	-0.15~-0.02	**-0.07 (0.03), 0.042* **	-0.13~0.0008
Condition × Age	**-0.02 (0.005), 0.003** **	-0.02~-0.005	0.002 (0.004), 0.722	-0.007~0.01
Number of good epochs	**-0.001 (0.0006), 0.006** **	-0.002~-0.0005	0.0003 (0.0005), 0.621	-0.001~0.001
Sex (male)	0.09 (0.11), 0.416	-0.14~0.31	0.09 (0.11), 0.420	-0.15~0.33
Full scale IQ	0.002 (0.005), 0.620	-0.006~0.012	0.004 (0.005), 0.426	-0.005~0.01
SDQ	0.004 (0.01), 0.718	-0.02~0.02	0.006 (0.01), .589	-0.02~0.03
CARS-2	-0.03 (0.06), 0.612	-0.14~0.09	-0.05 (0.06), 0.415	-0.16~0.07
Household income	-0.03 (0.06), 0.680	-0.15~0.09	-0.09 (0.06), 0.185	-0.21~0.03

Note: Effects reaching significance are highlighted in blue and printed in bold.
Abbreviations: CARS-2, Childhood Autism Rating Scale-2; SDQ, Strengths and Difficulties Questionnaire; se, standard error of the estimate.
$^*p < 0.050$; ** $p < 0.010$; *** $p < 0.0001$.

TABLE 4 Results for the LMMs with aperiodic components.

	FOOOF 1/f offset		FOOOF 1/f slope	
Term	Estimate (se), *p*-value	95% confidence intervals	Estimate (se), *p*-value	95% confidence intervals
Intercept	**1.7 (0.41), <0.0001*** **	1.17~2.82	**1.50 (0.31), <0.0001*** **	0.89~2.13
Condition (social)	-0.02 (0.03), 0.446	-0.08~0.03	-0.02 (0.02), 0.304	-0.07~0.02
Age (years)	**-0.03 (0.01), 0.003** **	-0.05~-0.01	-0.01 (0.007), 0.149	-0.02~0.004
Condition × Age	0.001 (0.003), 0.730	-0.005~0.008	0.0007 (0.003), 0.807	-0.004~0.006
Number of good epochs	**-0.001 (0.0004), 0.0001*** **	-0.002~-0.0007	**-0.0009 (0.0003), 0.001**	-0.001~-0.0003
Sex (male)	0.04 (0.03), 0.234	-0.03~0.11	0.05 (0.03), 0.067	-0.003~0.104
Full scale IQ	0.001 (0.001), 0.392	-0.001~0.004	0.002 (0.001), 0.071	-0.0002~0.004
SDQ	0.002 (0.003), 0.611	-0.005~0.008	0.0008 (0.002), 0.761	-0.005~0.006
CARS-2	-0.01 (0.02), 0.421	-0.05~0.02	0.02 (0.01), 0.205	-0.01~0.04
Household income	-0.001 (0.02), 0.946	-0.04~0.03	-0.001 (0.01), 0.941	-0.03~0.02

Note: Effects reaching significance are highlighted in blue and printed in bold.
Abbreviations: CARS-2, Childhood Autism Rating Scale-2; SDQ, Strengths and Difficulties Questionnaire; se, standard error of the estimate.
* $p < 0.050$; ** $p < 0.010$; *** $p < 0.0001$.

ral measures and social and non-social stimuli that elicited condition differences in other contexts (Jones et al., 2015), to verify which metrics had the best sensitivity to different brain responses to conditions. The team were able to collect good-quality EEG data from a representative sample of children across a range of demographic variables that included socio-economic status, IQ, and autistic and behavioral traits. Data quantity was influenced by visual attention to the paradigm, while data quality was influenced by age. Canonical theta power was affected by condition and age, while canonical alpha power was affected by age only. Aperiodic components were mostly affected by age and data quantity, whereas aperiodic-adjusted power was affected by condition, age, and the interaction between condition and age, especially measures in the theta band. Thus, the isolation of periodic theta and alpha rhythms and aperiodic-adjusted power may provide the most sensitive measures of different brain responses to social and non-social stimuli for studies of individual differences in child development.

4.1 | Representativeness of the included sample

The feasibility sample demonstrates certain generalizability to the perinatal and follow-up studies populations. The demographics and key variable patterns align to a significant extent with previously reported values from the same pool of data and the pre-registered aims of the

TABLE 5 Results for the LMMs with periodic components.

Frequency band	Frequency of peak				Amplitude of peak				Aperiodic-adjusted power			
	Theta		Alpha		Theta		Alpha		Theta		Alpha	
Term	Estimate (se), *p*-value	95% confidence intervals	Estimate (se), *p*-value	95% confidence intervals	Estimate (se), *p*-value	95% confidence intervals	Estimate (se), *p*-value	95% confidence intervals	Estimate (se), *p*-value	95% confidence intervals	Estimate (se), *p*-value	95% confidence intervals
Intercept	**9.87 (1.70), <0.0001*****	**6.30~12.98**	**8.67 (1.88), <0.0001*****	4.878 12.384	**1.45 (0.59), 0.017***	0.322 2.599	0.44, (0.62), 0.480	-0.79~1.70	0.56 (0.36), 0.131	-0.19~1.26	0.59 (0.42), 0.169	-0.29~1.42
Condition (social)	**0.82 (0.32), 0.011***	**0.15~1.43**	**0.56 (0.19), 0.004***	0.194 0.945	**0.20 (0.04), <0.0001*****	0.122 0.292	-0.02 (0.04), 0.562	-0.1~0.05	**0.11 (0.02), <0.0001 *****	0.07~0.15	-0.01 (0.01), 0.546	-0.04~0.02
Age (years)	0.04 (0.04), 0.326	**-0.04~0.13**	**0.11 (0.04), 0.020***	**0.02~0.20**	-0.02 (0.01), 0.050	-0.05~0.001	**-0.02 (0.01), 0.039***	-0.06~0.00	**-0.02 (0.009), 0.016***	-0.04~-0.004	-0.01 (0.01), 0.107	-0.03~0.004
Condition × Age	**-0.11 (0.03), 0.004***	**-0.18~-0.03**	**-0.05 (0.02), 0.021***	-0.09~-0.009	**-0.01 (0.005), 0.0004****	-0.03~-0.009	-0.0007 (0.005), 0.892	-0.01~0.01	**-0.008 (0.002), 0.001****	-0.01~-0.003	0.0002 (0.002), 0.921	-0.004~0.004
Number of good epochs	0.003 (0.003), 0.318	-0.003~0.01	-0.0004 (0.002), 0.850	-0.005~0.004	0.0002 (0.0005), 0.744	-0.001~0.001	0.0006 (0.0005), 0.223	-0.0004~0.001	0.0002 (0.0003), 0.525	-0.0004~0.001	**0.0007 (0.0002), 0.002**	0.0003~0.001
Sex (male)	0.01 (0.13), 0.914	-0.28~0.29	-0.10 (0.15), 0.500	-0.41~0.21	-0.03 (0.04), 0.491	-0.12~0.05	-0.030 (0.04), 0.507	-0.13~0.07	-0.01 (0.03), 0.639	-0.08~0.05	-0.004 (0.03), 0.891	-0.08~0.07
MSEL/WASI-2	**-0.02 (0.006), 0.006***	-0.03~-0.005	-0.001 (0.006), 0.828	-0.01~0.01	-0.001 (0.002), 0.411	-0.006~0.002	0.001 (0.002), 0.596	-0.003~0.01	0.0008 (0.001), 0.543	-0.002 ~0.004	0.001 (0.001), 0.352	-0.001~0.004
SDQ	-0.01 (0.01), 0.467	-0.04~0.02	0.030 (0.01), 0.057	0.0003~0.06	-0.007 (0.004), 0.102	-0.01~0.001	-0.004 (0.004), .390	-0.01~0.01	-0.001 (0.003), 0.670	-0.008~0.005	-0.0009 (0.003), 0.792	-0.009~0.006
CARS-2	**-0.19 (0.07), 0.013***	-0.34~-0.04	-0.005 (0.08), 0.945	-0.17~0.16	-0.04 (0.026), 0.106	-0.09~0.005	0.005 (0.02), 0.841	-0.05~0.07	-0.01 (0.01), 0.410	-0.04~0.02	-0.02 (0.01), 0.191	-0.06~0.01
Household income	0.15 (0.08), 0.065	-0.01~0.32	0.08 (0.08), 0.351	-0.09~0.25	-0.03 (0.02), 0.190	-0.08~0.02	**-0.07 (0.02), 0.010***	-0.12~-0.02	**-0.03 (0.01), 0.052***	-0.07~-0.0003	**-0.04 (0.02), 0.026***	-0.0~-0.0094

Note: Effects reaching significance are highlighted in blue and printed in bold.

Abbreviations: CARS-2, Childhood Autism Rating Scale-2; SDQ, Strengths and Difficulties Questionnaire; se, standard error of the estimate.

* $p < 0.050$; ** $p < 0.010$; *** $p < 0.0001$.

protocol. In terms of data availability, the majority of missingness was explained by technical issues or the equipment being out for repair that had little to do with the data acquisition protocol. We are unfortunately unable to report on the reason of missingness for eight out of our 100 recruited participants as those reasons were not recorded. Possibly, there were technical issues, such as issues with the EEG equipment or recording software. Alternatively, the researchers attempted the EEG session, but the child refused to wear the EEG cap. Typically, 1%–10% of young participants refuse to wear the EEG in developmental studies (Brooker et al., 2019). If the loss of data occurs at random and is unrelated to child characteristics, one would expect the included sample to be representative of the recruited sample in terms of child characteristics. If the data loss occurs due to characteristics of the child, child characteristics may differ between samples, and the included sample with EEG data may not be representative.

Participants contributing to the EEG analysis however did not significantly differ from the feasibility phase recruited sample on age, verbal IQ, performance IQ, FSIQ, autistic traits, behavioral traits, or socio-economic status measured by household income. This is expected since most of our data was excluded due to technical reasons rather than child characteristics (not looking at the screen or refusing the EEG cap). These findings further suggest that the EEG protocol did not introduce exclusion bias across a range of relevant traits and that EEG can be captured from a representative sample of young children in low-resource settings. This is important in demonstrating that EEG can result in unbiased samples that can be used to study brain development and developmental outcomes.

4.2 | Data quantity and quality

We did not find that data quantity or quality related to condition or age by condition, suggesting the quantity and quality of the data recorded during the social and non-social videos were similar and remained similar across ages. This indicates that any variation between the videos found for the EEG metrics is unlikely to be confounded by data quantity or quality. Data quantity and quality were not affected by sex, autistic or behavioral traits, or socio-economic status. This again indicates that relations between EEG features and developmental measures are unlikely to be confounded by data quality and that the results of the studies would have higher generalizability to the developmental population.

We found only two associations between data quantity and quality and covariates of this analysis. Data quantity was influenced by looking proportion: children who looked more at the screen during the task were likely more attentive and sitting relatively still, leading to fewer artifacts in the EEG signal and larger quantities of good data. Despite the fact that we did not find any relation between age and data quantity, there was a correlation of small size between age and looking times (rho = 0.21); therefore, alternative types of relations between data quantity, age, and looking time—such as mediation and non-linear association—should be explored in the larger sample of follow-up. Data quality as operationalized by the fit of the FOOOF algorithm was only associated with age: the fit decreased with increasing age. Another possibility is that the parameters most suitable for the FOOOF algorithm are dependent on age group. Previous studies using the FOOOF algorithm have used similar parameter settings across datasets spanning wide age ranges and similar age groups, for example, 4–11 year-olds (Levin et al., 2020), 3–6 and 8–24 year-olds (Cellier et al., 2021), and 5–21 year-olds (Tröndle et al., 2023)—also see Table S2 in Supporting Information S3, but these mainly focused on variations of age with aperiodic and periodic components instead of the FOOOF model fit. We opted for one set of parameter values for the whole cohort following these previous approaches and guidelines of the FOOOF developers (Donoghue et al., 2020). Future studies are needed to validate this novel finding of an association between age and FOOOF model fit. A systematic comparison between different parameters settings across different age ranges and how these parameter settings affect findings is an important question but is outside the scope of the current study (see Supporting Information S5).

The lack of confound between data quantity/quality and EEG features suggests that using a low-channel EEG system is feasible for use in the clinic. Previous lab studies have used high-density EEG systems to collect EEG in large samples (Levin et al., 2020). High-density EEG systems however often come with other equipment such as amplifiers and are therefore not mobile and not suitable for use in the field. Due to technological advances, mobile and low-density EEG systems are gaining in popularity (Lau-Zhu et al., 2019). Recent findings have shown that low-density EEG systems also provide robust data with high test–retest reliability in developmental research with event-related potentials (Haartsen et al., 2021). The noise levels across sessions are lower, compared to other studies, as shown in Figure S8 of Supporting Information *S6* (Lockwood Estrin et al., 2023). The current study demonstrates the potential of low-density EEG in non-lab settings.

4.3 | Selecting sensitive indices of brain function

The current findings suggest periodic components and aperiodic-adjusted power may be more sensitive to condition differences than other power metrics in this study. Selecting the appropriate EEG metrics, pre-processing steps, and paradigm that is sensitive to brain responses is crucial when setting up large-scale studies, and analytic flexibility available during pre-processing and statistical analysis, and different labs using different approaches has substantially hindered agreement and replication of sensitive measures (Desjardins et al., 2021; Meyer et al., 2021; Pernet et al., 2020; Robbins et al., 2020). Furthermore, research on the sensitivity of EEG measures to condition differences in developmental populations, analyses, and findings beyond the pre-registration of methods are still lacking, preventing researchers to make informed decisions on their planned analyses. Assessing which EEG measures are sensitive to condition differences in a feasibility sample as done here will help inform future research.

In our approach, we have separated aperiodic and aperiodic-adjusted components whose isolated or combined variation can lead to differences in canonical power (Donoghue et al., 2020). Canonical spectral power has often been used as a measure of interest and a potential metric showing condition differences or associations with developmental outcomes. Findings however have been mixed (Carter Leno et al., 2018; Dawson et al., 2012; Gabard-Durnam et al., 2019; Garcés et al., 2022; Huberty et al., 2021; Mathewson et al., 2012; Tierney et al., 2012). One possible explanation is variation in the shape of the power spectrum and features of peaks between individual participants. Traditional canonical EEG power analyses focused on power within a certain frequency range. It is therefore important to differentiate between the aperiodic and periodic components to examine how these vary with experimental conditions or characteristics. By splitting the aperiodic and aperiodic-adjusted components, we can more precisely quantify individual variability in power spectra and peaks. It is common that not all participants in the sample show a peak that can be clearly identified (visually or by FOOOF). Moreover, not all participants show peaks within the frequency range of interest. If researchers would focus on peaks, this would result in substantial missing data and a reduced sample size. One way to handle missing data is the use of LMMs that allow the inclusion of participants if data are present for some variables but not others. Missing data that do not fully occur at random and the lack of variables that predict missingness can pose real problems for data analyses and interpretation. The use of statistical approaches able to handle missing data is not a perfect substitute for real data. Another strategy to deal with the challenge of absent peaks is to calculate periodic power as the average observed power within a frequency range minus the average power from the aperiodic component. We explored how both approaches varied with condition and found fairly consistent results indicating peaks and aperiodic-adjusted power in the theta range were affected by condition, age, and the interaction between condition and age. Overall, this suggests that examining aperiodic-adjusted components of power may be more fruitful to examine differences between conditions in the naturalistic videos than canonical power or aperiodic components. This will inform the design and pre-registration for future studies such as the childhood follow-up in the Safe Passage study and other studies in larger samples for a global context. Indeed, we found that not canonical power or aperiodic components but aperiodic-adjusted components in the power spectrum varied with conditions showing the best sensitivity to this paradigm.

While the discussion of mechanisms underlying these findings is beyond the scope of the feasibility analysis, we found some notable associations that can inform the hypothesis making of the childhood follow-up. First, age was associated with canonical power, aperiodic and aperiodic-adjusted components. Decreases in canonical power with increasing age have previously been explained by changes in the offset and slope of the aperiodic signal (He et al., 2019; McSweeney et al., 2021; Tröndle et al., 2023). We also observed the decrease in 1/f offset in the current study, which is consistent with previous findings (Schaworonkow & Voytek, 2021). This pattern may result from changes in noise in the brain affecting the 1/f shape of the power spectrum. Other studies also suggest that peak frequency increases with increasing age (Cellier et al., 2021). Together, these findings replicate previous age-related changes in canonical power and suggest these may arise from changes in both aperiodic and aperiodic-adjusted components. Further research in samples with larger age ranges is needed to further examine how the power spectrum changes with age. For example, how peak frequencies in the alpha range change with age. Further research could also examine how periodic peak detection methods such as automatic extraction by FOOOF and visual inspection compare in their results.

Second, these results suggest that the individual variation in periodic and aperiodic-adjusted components may relate to individual differences in participant characteristics rather than canonical power or aperiodic components. Specifically, we observed the theta peak frequency decreasing with increased IQ and CARS and decreasing alpha peak amplitude and aperiodic-adjusted power with higher household income. Despite being preliminary, these associations may indicate that theta oscillations may play a role in cognitive processes related to early learning, while also being potential markers of neural differences related to autistic traits, similar to what has been reported within groups of autistic children (Dickinson et al., 2018; Gabard-Durnam et al., 2019). Further, children from more affluent families may experience different cognitive demands and attentional load, reflected in differences in alpha power (D'angiulli et al., 2012), which is consistent with our findings. The childhood follow-up, with 10 times the sample of the feasibility sample, will offer the occasion to deeply investigate these patterns, especially by comparing children who receive or do not a diagnosis of neurodevelopmental conditions, and integrating into the analysis additional environmental factors (e.g., up to date living conditions, family dynamics) that may explain the influence of income.

4.4 | Limitations

In terms of cognitive development, scores were obtained from two different scales for younger and older participants, cautioning the interpretation of the proportion of children with and without developmental delay (Baker et al., 2019). Further, FSIQ scores in South African children have consistently been reported significantly below Western IQ distributions (Cluver et al., 2019; Sherr et al., 2017; Warne, 2023), calling into question the cultural validity of these instruments that may not fully reflect adaptive behavior of South African children. One limitation of the study is that by using dynamic videos with combined auditory and visual information, we limit the interpretation of the underlying mechanisms of condition differences between the videos. The current paradigm consists of naturalistic dynamic videos that are more interesting for the participants than static images as often used in developmental research. In addition, traditional resting-state paradigms (eyes open/closed) used in older participants are not suitable for younger participants. The social and non-social videos differ in both visual and auditory information and a range of social factors (eye gaze, gestures, human vocal sounds). Conclusions about what factors lead to differences in the EEG metrics should therefore be taken with caution. In addition, one might argue that the stimuli were not developed locally and may be less consistent with the children's daily experiences. Future studies could examine responses to more locally adapted stimuli or explore responses to a range of stimuli (faces, toys, houses, etc.) using neuroadaptive Bayesian Optimization methods (Gui et al., 2022; Wass & Jones, 2023).

The approach to interpolation of channels with artifacts can also introduce additional noise. Rather than remove any trial that had a single artifact on any channel, to increase data retention, we interpolated channels with artifact on a trial-by-trial basis if there were three or more neighboring artifact-free channels. Epochs with fewer than 15 artifact-free channels at the end of the cleaning process were removed from analysis; and channels with artifacts on >80% of channels were interpolated throughout. This allows us to retain more data but also results in some trial-by-trial variability in the resulting average reference montage. However, no channels were consistently bad across all participants, meaning that the topography of the average reference was not systematically biased (see Supporting Information S7.1) and the proportion of interpolated data was very small (0%–5.67%). Second, we repeated the analyses for canonical log power using canonical relative power (which corrects for the possibility that a slightly different average reference montage influences overall amplitude) and observed a similar pattern of results as for canonical relative power (with the exception of a significant age effect for relative alpha power, see Supporting Information S7.2). Third, we calculated the proportion of interpolated channels across all trials per participant and included this metric as a covariate in the models to explore how this affected the findings for the FOOOF fit and canonical log and relative power in the theta and alpha band (see Supporting Information S7.3). Results revealed no significant effects of the interpolation covariate nor did the inclusion of the covariate change the direction or the strengths of the condition effects. Also note, region (frontal, central, parietal, occipital) was included into all LMMs as a random effect to account for any individual variability between regions. Thus, our interpolation and re-referencing approaches would unlikely have influenced our pattern of findings.

5 | CONCLUSION

In this feasibility study, EEG data of good quality were collected, with 72% of participants contributing sufficient data for analysis; these participants were representative of the recruited cohort in developmental and behavioral profiles as expected due to the random technical issues as the main reason for the data loss. Data quality and quantity were related to attention to the task but not condition, indicating that both videos capture similar levels of attention and interest. Canonical power and aperiodic components also varied with age but were not sensitive to social vs non-social context. Isolation of periodic components, particularly in the theta frequency band, was sensitive to both condition and age effects. Taken together, these findings suggest that measurement of EEG during naturalistic videos can capture sensitive metrics of brain activity during early childhood for use in low- and middle-income settings.

ACKNOWLEDGMENTS

We thank the participants and their families for their participation. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results. Any views expressed are those of the authors and not necessarily those of the funders.

CONFLICT OF INTEREST STATEMENT

Mark H. Johnson received book royalties from Wiley-Blackwell, OUP, and MIT Press. The other authors have no disclosures to declare.

DATA AVAILABILITY STATEMENT

The consent forms used in this feasibility study do not allow us to share the data with the wider scientific community. At the start of the feasibility study, consent forms only included consent to sharing data between the data collection and data analysis sites involved in the study (Stellenbosch University and Birkbeck University of London, respectively). Data for the main South Africa Safe Passage Study will be made available when data collection has been completed. MATLAB scripts used for the pre-processing of the EEG data and R scripts used for the statistical analysis are available on Github: https://github.com/RianneHaartsen/FeasibilityStudy_SafePassage.

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How to cite this article: Del Bianco, T., Haartsen, R., Mason, L., Leno, V. C., Springer, C., Potter, M., Mackay, W., Smit, P., Plessis, C. D., Brink, L., Johnson, M. H., Murphy, D., Loth, E., Odendaal, H., & Jones, E. J. H. (2024). The importance of decomposing periodic and aperiodic EEG signals for assessment of brain function in a global context. *Developmental Psychobiology*, *66*, e22484. https://doi.org/10.1002/dev.22484