Mapping neural correlates of biological motion perception in autistic children using high-density diffuse optical tomography

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Abstract: We used high-density diffuse optical tomography (HD-DOT) to image brain function in 102 school-age children with and without autism while they performed a passive biological motion perception task. Our results show that both autistic and non-autistic school-age children tolerate HD-DOT, and HD-DOT is sensitive to autism-associated differences in brain function.

Introduction: Recent advances in functional brain imaging show promise to provide valuable biomarkers of autism spectrum disorder (ASD) diagnostic likelihood and behavioral trait severity. However, traditional neuroimaging modalities such as functional magnetic resonance imaging (fMRI) require participants to remain still in a loud, confined environment, posing difficulties for children, particularly those with ASD. Herein, we aimed to establish the feasibility of high-density diffuse optical tomography (HD-DOT) [1], a minimally constraining optical neuroimaging modality that can map brain function in an open and naturalistic environment, to assess brain function in ASD and non-autistic control (NAC) children using a biological motion perception paradigm [2].

Methods: We imaged 46 ASD children age 7-18 years, 49 NAC, and 17 proband siblings as they viewed coherent and scrambled movie clips of point-light biological motion. The HD-DOT instrument contained a dense array of 96 sources and 92 detectors that support >1,200 overlapping measurements within 4cm per wavelength and provide a smooth sensitivity profile on the cortical surface. Data processing and image reconstruction were performed using the NeuroDOT pipeline in MATLAB [1]. We assessed data quality using the pulse signal-to-noise ratio (SNR), good measurements (GM) percentage, and motion levels with the global variance in the temporal derivative (GVTD) [3]. We assessed group-level cortical brain function with statistical parametric mapping. Additionally, we tested for brain-behavior associations with dimensional metrics of autistic traits, as measured with the Social Responsiveness Scale-2 (SRS), with hierarchical regression models.

Results: Data quality assessments revealed no significant differences in data quality and motion between ASD and NAC. Additionally, confirming results in fMRI studies, we found that NAC participants presented stronger brain activity contrast (coherent > scrambled) than ASD children in six cortical regions related to visual, motor, and social processing. Moreover, regression models revealed multiple cortical regions in ASD participants where brain function is significantly associated with dimensional measures of autistic traits.

Conclusion: This study demonstrates that HD-DOT is sensitive to brain function that differentiates between NAC and ASD groups and correlates with dimensional measures of ASD traits. Overall, this study highlights the effectiveness of HD-DOT as a comparable tool to fMRI for studying brain function in autistic children throughout childhood development in a naturalistic setting.

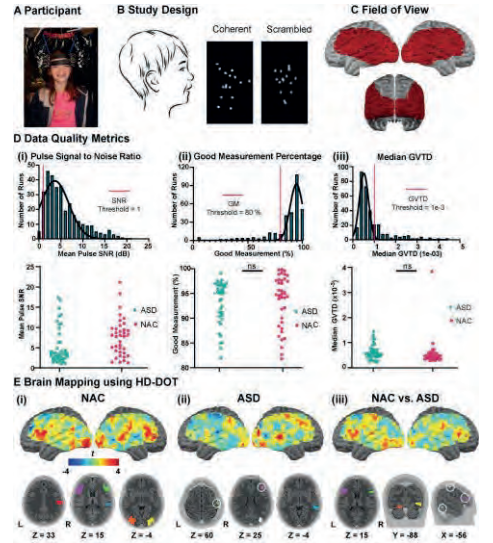

Figure 1 | Establishing feasibility for HD-DOT to measure brain function in autistic children. A HD-DOT array on a school age participant. **B** The study design. **C** The field of view of the HD-DOT system. **D** Data quality assessments**. E** Within- and between-group random effect unthresholded t-maps and cluster-corrected maps (voxel-wise $p < 0.0075$ and FDR-corrected at a cluster of $p < 0.00125$).

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Functional specialisation in the first years of life: longitudinal characterisation of social perception with fNIRS

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Abstract: By studying brain responses to social perception longitudinally in infants and children in The Gambia, we found that social vocal stimuli elicited a significantly slower and stronger response than auditory non-vocal stimuli across all 6 age points collected in the Brain Imaging for Global Health (BRIGHT) project from 5 months to 5 years old. We show the advantage of studying brain activation informed by the speed and magnitude of the response with functional near-infrared spectroscopy (fNIRS) to characterise the brain response more comprehensively.

Introduction: Infants and children in low- and middle-income countries have historically been under-represented in neurodevelopmental research, despite being often exposed to early adversity which can impact cognitive development. The Brain Imaging for Global Health (BRIGHT) project enabled the collection of a large dataset for studying cognitive development longitudinally from birth to 5 years old in The Gambia and UK[1]. While social processing has been studied often in infants younger than 1 year of age in high-income countries, we here present findings with functional near-infrared spectroscopy (fNIRS) on a social task in the Gambian cohort from 5 to 60 months.

Methods: Participants were presented with social videos accompanied by vocal and non-vocal sounds following a block design; a study paradigm common in previous literature and adapted to the local context[2]. Participants were tested at 5 months (*N*=127), 8 months (*N*=110), 12 months (*N*=116), 18 months (*N*=111), 24 months (*N*=112) and 60 months (*N*=124) with fNIRS from the temporal and inferior frontal brain regions. Channels with low scalp coupling were pruned and motion artefacts corrected using spline interpolation and wavelet filtering[3]. The data was converted into oxy- (HbO) and deoxy-haemoglobin (HbR), and blocks were averaged for each condition (vocal or non-vocal). We studied longitudinally the average time-to-peak (speed) and peak amplitude (magnitude) of the haemodynamic response function (HRF), for each condition, which informed the appropriate time window to selected for statistical analysis on HbO and HbR to investigate brain activation.

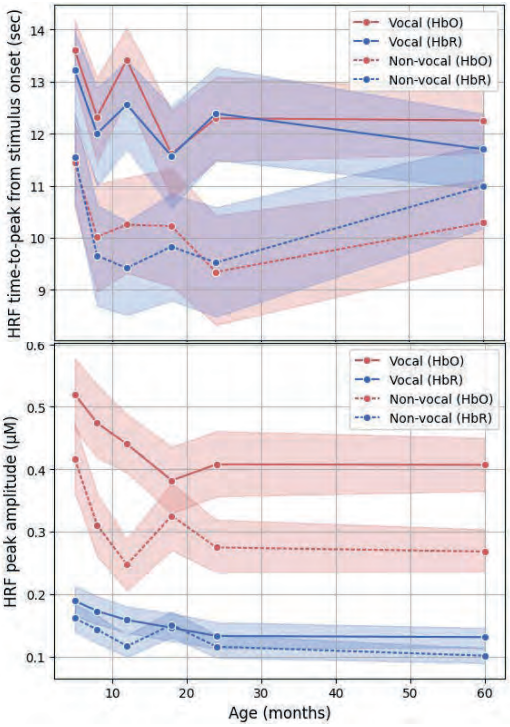

Fig. 1: Characteristics of the HRF across ages

Results: We found a significantly greater activation in response to vocal compared to non-vocal stimuli across all ages, located bilaterally in temporal regions but also in the inferior frontal gyri. This becomes more widespread with age, with activation on 8 out of 34 channels at 5 months compared to 21 out of 34 at 60 months on this vocal minus non-vocal contrast. Furthermore, HbO and HbR reached their peak amplitude significantly slower in response to social vocal compared to non-vocal stimuli (*Fig. 1*) consistently from 5 to 60 months (all p-values < 0.05 except HbR at 60 months where p-value < 0.1), with the absolute amplitude of the peak also appearing to decrease with age up to 24 months.

Conclusion: Studying the speed and magnitude of the response with fNIRS enabled to have more details about the brain responses to social perception in infants and children longitudinally, but also to inform the time window on which to focus statistical analysis. Ongoing work is now investigating whether amplitude and time-to-peak change as a function of the cortical location to gain further insight into the dynamics of the response across ages.

1. S Lloyd-Fox et al., 2023 - 2. S Lloyd-Fox et al., 2014 - 3. C Bulgarelli et al., 2020

Developmental changes in neurocognitive function in a large low-to-middle-income cohort.

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Abstract: The nature of early developmental changes in neurocognitive function in children in low-to-middle-income countries (LMIC) are under-explored. To address this, we examined longitudinal changes in visual neurocognition from infancy to toddlerhood in 6- and 9-month-old children from low and middle/high socioeconomic status (SES) backgrounds in a large LMIC cohort. We found that there were developmental changes in both behavioural performance and associated left-lateralized parietal activation from infancy to toddlerhood, with more robust changes in children from the high SES 9-month-old cohort. Our findings contribute to the growing literature on neurocognition in children from LMIC countries.

Introduction: Each year, 250 million children in LMIC fail to reach their developmental potential. Despite this, the nature of developmental changes in neurocognitive function in the first 1000 days of life remains under-explored, especially using longitudinal methods. In the current study, we first examined developmental changes in visual neurocognition from infancy to toddlerhood in children in rural India. Second, we inquired whether these changes varied as a function of age and SES.

Methods: High and low SES families with 6-month-old and 9-month-old infants from in and around Shivgarh, rural Uttar Pradesh, India took part in the study (N=223 infants). Data were collected from these families at two time-points. At the first time-point during infancy, children were 6 or 9 months of age, and at the second time-point during toddlerhood, they were 18 or 21 months of age, respectively. Visual cognition was assessed at both time-points using a preferential looking task. In this task, two side-by-side blinking displays of colored squares were presented, with one side showing a change in colors, while the colors on the other side stayed constant. Load was varied between 1 and 3 items during infancy and between 2 and 6 items during toddlerhood. Portable eye-tracking and video recordings were used to extract looking behaviour, and functional near-infrared spectroscopy was used to collect brain function while children engaged with the task. Two key measures of visual cognition were extracted – total looking time (TLT) was calculated by summing the total time spent looking at both sides and, a change preference (CP) score was calculated by dividing the total time spent looking at the changing side divided by TLT. Image reconstruction techniques were used to transform channel-based neuroimaging data into voxel space using segmented head volumes obtained from MRI scans. Linear mixed effects modelling was used to examine developmental changes and associations with age and SES.

Results. Our behavioural results revealed two key interactions involving age and SES. First, there was a positive association between CP scores during infancy and CP scores during toddlerhood; however, this association was stronger for high SES children compared to low SES children. Second, we found that the positive association between CP scores in infancy and toddlerhood was generally stronger for the 9-month-old cohort compared to 6-month-old cohort, except for the low SES 9-month-old cohort with longer TLT. Our brain results revealed engagement across canonical regions of the frontoparietal visual cognition network. There were developmental and SES-related effects in left-lateralized anterior intraparietal sulcus (laIPS), a region in the dorsal attention network associated with maintaining working memory representations and impacted by stunting status as demonstrated by our previous work. Specifically, the 9-month-old cohort showed greater laIPS activation from infancy to toddlerhood, compared to the 6-month-old cohort. Activation in this region was also associated with behavioural measures: children with better CP scores showed an increase in laIPS activation from infancy to toddlerhood compared to children with lower CP scores.

Conclusions. Our findings show that developmental changes in neurocognitive function in the first 1000 days of life are affected by SES and cohort effects, thus, uniquely contributing to the growing literature on neurocognition in children from LMIC countries.