Very preterm brain at rest: longitudinal social–cognitive network connectivity during childhood

Sarah I. Mossad, [ORCID][1] Julia M. Young,[1] Simeon M. Wong,[2,3] Benjamin T. Dunkley,[2,4,5] Benjamin A. E. Hunt,[6] Elizabeth W. Pang,[2,7] and Margot J. Taylor[2,8,4]

[1]Department of Psychology, Hospital for Sick Children, Toronto, ON M5G 1X8, Canada
[2]Neurosciences & Mental Health, SickKids Research Institute, Toronto, ON M5G 0A4, Canada
[3]Department of Psychology, University of Toronto, Toronto, ON M5S 1A1, Canada
[4]Department of Diagnostic Imaging, The Hospital for Sick Children, Toronto, ON M5G 1X8, Canada
[5]Department of Medical Imaging, University of Toronto, Toronto, ON M5S 1A1, Canada
[6]Division of Neurology, Hospital for Sick Children, Toronto, ON M5G 1X8, Canada
[7]Institute of biomaterials and biomedical engineering, University of Toronto, Toronto, ON M5S 1A1, Canada
[8]Sir Peter Mansfield Imaging Centre, School of Physics and Astronomy, University of Nottingham, Nottingham NG7 2RD, UK
Correspondence should be addressed to Sarah I. Mossad, Department of Psychology, Hospital for Sick Children, Peter Gilgan Centre for Research and Learning (PGCRL), 686 Bay Street, Toronto, ON M5G 1X8, Canada. E-mail: sarah.mossad@sickkids.ca.

Abstract

Very preterm (VPT: ≤32 weeks of gestational age) birth poses an increased risk for social and cognitive morbidities that persist throughout life. Resting-state functional network connectivity studies provide information about the intrinsic capacity for cognitive processing. We studied the following four social–cognitive resting-state networks: the default mode, salience, frontal-parietal and language networks. We examined functional connectivity using magnetoencephalography with individual head localization using each participant's MRI at 6 ($n = 40$) and 8 ($n = 40$) years of age compared to age- and sex-matched full-term (FT) born children ($n = 38$ at 6 years and $n = 43$ at 8 years). VPT children showed increased connectivity compared to FT children in the gamma band (30–80 Hz) at 6 years within the default mode network (DMN), and between the DMN and the salience, frontal-parietal and language networks, pointing to more diffuse, less segregated processing across networks at this age. At 8 years, VPT children had more social and academic difficulties. Increased DMN connectivity at 6 years was associated with social and working memory difficulties at 8 years. Therefore, we suggest that increased DMN connectivity contributes to the observed emerging social and cognitive morbidities in school age.

Key words: resting-state connectivity; preterm birth; magnetoencephalography (MEG); intrinsic networks; functional connectivity

Introduction

It is estimated that nearly 15 million babies are born prematurely, before 37 weeks of gestational age (GA) each year (Liu *et al.*, 2016), and there is a trend of increasing preterm birth rates globally from 2000 to 2014 (Chawanpaiboon *et al.*, 2019). Those born very preterm (VPT, ≤32 weeks of GA) demonstrate poorer average global functioning compared to their term born peers; up to 76% of VPT born children have some cognitive and/or social difficulties (e.g. Aarnoudse-Moens *et al.*, 2012; van Houdt *et al.*, 2020). Frequent academic difficulties emerge at school age and persist through adolescence (Allotey *et al.*, 2018). Despite the impact that VPT birth has on social and cognitive functioning, relatively few studies have focused on the functional brain correlates underlying these neurodevelopmental problems. A possible explanation for these sustained impairments across development is atypical structural and functional maturation of brain regions and brain networks underpinning these skills (Peterson *et al.*, 2000; Kesler *et al.*, 2008; Nosarti *et al.*, 2008; Ment *et al.*, 2009; Monson *et al.*, 2016; Vandewouw *et al.*, 2020).

Resting-state neuroimaging analyses have been used to study brain networks underlying a wide range of sensory and cognitive functions (Van Den Heuvel and Pol, 2011; Raichle, 2015) and can be based on correlations of the haemodynamic response in functional magnetic resonance imaging (fMRI, Fox and Raichle, 2007; Raichle, 2015) or on neurophysiological signals using magnetoencephalography and electroencephalography (MEG/EEG, Mantini *et al.*, 2007). These task-free scans are invaluable for assessing the intrinsic connectivity networks (ICNs) that are functionally specialized (Fox *et al.*, 2005) and thus provide insight into network connectivity related to sensory or cognitive processing. Resting-state functional connectivity (rs-FC) is based on the premise that regions in synchrony belong to the same network. Using resting-state fMRI, functional connectivity networks can be identified in infancy (Fransson *et al.*, 2007; Doria *et al.*, 2010) and continue to mature over childhood (Hoff *et al.*, 2013; Lee *et al.*, 2013). Although fMRI rs-FC is effective at capturing ICNs and their dynamics, the neurophysiological modalities, MEG/EEG, allow us to move beyond blood flow to quantify the synchrony

of firing among populations of neurons (Hari and Salmelin, 2012) and assess synchrony at neurophysiologically meaningful frequencies.

The high resolution of MEG/EEG in both the time and oscillatory domains has accelerated our understanding of connectivity underlying cognitive functions (Hari and Salmelin, 2012; O'Neill *et al.*, 2018). Task-based functional connectivity studies in MEG suggest that different frequency bands play specific roles in a range of cognitive abilities (Engel *et al.*, 2001; Androulidakis *et al.*, 2007; Jensen *et al.*, 2007; Knyazev, 2007; Palva and Palva, 2007, 2011; Fries, 2009). For example, theta is related to long-range communication underlying various aspects of cognition (Mellem *et al.*, 2013; Kaplan *et al.*, 2017), alpha with inhibition and mnemonic processing (Park *et al.*, 2014; Yuk *et al.*, 2020), beta is associated with motor processing (Gaetz *et al.*, 2010) and top-down control, while gamma is associated with local processing, binding and feedforward processes (Khan *et al.*, 2013; Levy *et al.*, 2017), thus offering another level of information on brain function. Although atypicalities in frequency bands related to cognitive function could elucidate the neurodevelopmental cognitive difficulties often experienced by VPT children, only a few studies have examined resting-state MEG in VPT children (Doesburg *et al.*, 2011; Ye *et al.*, 2015; Hunt *et al.*, 2019), and to our knowledge, none have examined the same cohort longitudinally.

Here, we investigated resting-state network connectivity at two timepoints using MEG in VPT children in the following four networks that underlie cognition and social–cognition: the default mode, the salience (SAL), the frontal-parietal (FP) and the language (LAN) networks (Brier *et al.*, 2012; de Pasquale *et al.*, 2012). The default mode network (DMN) is widely studied and includes the medial prefrontal cortex, posterior cingulate gyrus, bilateral angular and temporal gyri (Yeo *et al.*, 2011). The DMN is associated with self-reflection, autobiographical memory, as well as toggling between other networks (Schilbach *et al.*, 2008; de Pasquale *et al.*, 2012; Mars *et al.*, 2012; Li *et al.*, 2014; Spunt *et al.*, 2015). The SAL network includes the anterior cingulate and bilateral insular cortices and is involved in detecting relevant stimuli and subsequently coordinating neural resources to facilitate processing of salient stimuli (Uddin, 2015). Abnormal recruitment of the insular cortices in the SAL network has been reported as a feature of neuropsychiatric disorders. An fMRI study of resting-state networks in 19 late preterm (33–40 weeks of GA) children (ages 9–13 years) showed increased functional connectivity between the SAL and executive networks (Degnan *et al.*, 2015). The FP network, also known as the executive control network includes the bilateral middle frontal, inferior frontal cortices as well as the posterior parietal cortices. The FP is involved in initiating goal-directed responses, including regulating behaviour and emotions (Dosenbach *et al.*, 2008). The LAN network includes the left inferior frontal gyrus, bilateral anterior and posterior superior temporal gyri. Rowlands *et al.* (2016) studied VPT children at 8 and 16 years of age and found increased fMRI functional connectivity in the LAN network at 16 compared to 8 years of age, a trend not found in term-born children.

We examined VPT and FT born children at 6 and 8 years of age, a period of rapid social and cognitive development. Children also completed neuropsychological assessments at each timepoint. We used amplitude envelope correlation (AEC) to measure MEG network connectivity. AEC represents the correlation of neuronal activity over seconds and is the most similar conceptual analogue to connectivity computed in rs-fMRI (Brookes *et al.*, 2011; Hipp *et al.*, 2012), and thus our results can be more directly compared to and extend the fMRI literature.

Based on previous rs-fMRI connectivity studies, we hypothesized persistent altered functional connectivity in the SAL, FP and LAN networks at both 6 and 8 years. Additionally, the DMN has been linked to social cognition and introspection (Schilbach *et al.*, 2008), and altered oscillatory connectivity within this network could underlie the reported social cognitive difficulties. We also predicted that if VPT children were to catch up with their FT peers in behavioural measures at 8 years of age, effects would also be reflected in functional network connectivity.

Methods
Participants
Participants who were born ≤32 weeks of GA were recruited from the Neonatal Intensive Care Unit at the Hospital for Sick Children (SickKids), Toronto, Canada, between 2008 and 2010. Follow-up assessments were completed at 2, 4, 6 and 8 years of age. Forty children returned for testing at 6 years and then at 8 years. Clinical characteristics were measured at birth and are outlined in Supplementary Table S1 for the returning cohort at 8 years. The returning subset of participants at 6 and 8 years did not differ from the original cohort ($n = 105$) on GA, sex, birthweight or neonatal clinical characteristics.

A full-term (FT) group (GA ≥37 weeks) was recruited as controls for the VPT born group and matched on sex and age. Thirty-eight FT children participated in the study at 6 years, while 43 FT participants took part in the study at 8 years (see Table 1).

Exclusion criteria included standard MEG/MRI contraindications, language impairments, uncorrected vision problems or Intelligence quotient (IQ) ≤ 70. Two VPT participants were excluded from the analyses due to persistent alterations in anatomy (enlarged ventricles) on MRI (see Young *et al.*, 2020). All procedures performed in this study were approved by the SickKids research ethics board and are in accordance with the Helsinki Declaration. Written informed consent was obtained from parents and verbal assent from children.

Neuropsychological assessments
Full-scale IQ was estimated using the vocabulary and matrix reasoning subtests of the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999). Children and parents completed standardized assessments and questionnaires from the following domains: social functioning, executive functioning and attention at both timepoints.

An academic screener of basic reading skills was measured on the Wechsler Individual Achievement Test–Third Edition (WIAT-III, Psychological Corporation, 2002) at the 8-year timepoint. Children completed the affect recognition subtest from the Developmental NEuroPSYchological Assessment (NEPSY-II, Korkman *et al.*, 2007) and the block recall, forward and backward digit recall subtests from the Working Memory Test Battery for Children (WMTB-C, Pickering *et al.*, 2001). Parents rated their children's social functioning on the Social Responsiveness Scale-2 (SRS-2, Constantino and Gruber, 2014) and the strengths and difficulties questionnaire, which measures social-emotional functioning including emotional, conduct, hyperactivity/inattention, peer and prosocial problems (Goodman, 1997). Parents also rated their child's executive functioning skills on the Behavior Rating Inventory of Executive Function (BRIEF, Gioia *et al.*, 2000). Parents provided the mother's highest level of education, as a proxy for socio-economic status (Harding *et al.*, 2015). Group differences were assessed at each timepoint using two-tailed independent samples *t*-test for normally distributed outcomes

Table 1. Characteristics of VPT and FT children

	6 years old			
	VPT ($n = 40$)	**FT ($n = 38$)**	**t(df)/χ^2**	**P**
Sex (M:F)	25:15	16:22	$\chi^2(1) = 2.4$	0.11
Age (years)	6.6 ± 0.3	6.5 ± 0.5	$t(60) = 1.1$	0.24
Birth weight (g)	1200 ± 240	3500 ± 590	$t(29) = 19$	<0.001
GA (weeks)	29 ± 1.6	39 ± 1.6	$t(64) = 26$	<0.001
Mother's education	Grade school ($n = 1$)	Some post-secondary ($n = 5$)	$\chi^2(4) = 4$	0.3
	High school ($n = 1$)	University/college ($n = 22$)		
	Some post-secondary ($n = 12$)	Post-graduate training ($n = 9$)		
	University/college ($n = 19$)			
	Post-graduate training ($n = 7$)			
	8 years old			
	VPT ($n = 40$)	**FT ($n = 43$)**	**t(df)/χ^2**	**P**
Sex (M:F)	24:16	22:21	$\chi^2(1) = 0.5$	0.47
Age (years)	8.7 ± 0.5	8.6 ± 0.5	$t(78) = 1$	0.27
Birth weight (g)	1200 ± 220	3500 ± 600	$t(54) = 24$	<0.001
GA (weeks)	29 ± 1.41	39 ± 1.35	$t(67) = 27$	<0.001
Mother's education	Grade school ($n = 1$)	High school ($n = 1$)	$\chi^2(5) = 6.7$	0.53
	High school ($n = 5$)	Some post-secondary ($n = 7$)		
	Some post-secondary ($n = 6$)	University/college ($n = 19$)		
	University/college ($n = 20$)	Post-graduate training ($n = 16$)		
	Post-graduate training ($n = 8$)			

and Mann–Whitney–Wilcoxon test for non-normal outcomes in R. *P*-values were adjusted for multiple comparisons within each domain using false discovery rate (FDR, Benjamini and Hochberg, 1995) correction.

MEG and MRI data acquisition

Children's MEG scans were obtained at the MEG lab at Sick-Kids in a magnetically shielded room on a 151-channel MEG (CTF Omega, CTF MEG International LP, Coquitlam, Canada). Three fiducial coils were placed at the left and right pre-auricular points and the nasion to measure head position continuously during recording. Five minutes of resting-state MEG data (600 Hz sampling rate, 250 Hz low pass filter, third-order spatial gradient noise cancellation) were acquired with the children in the supine position with eyes open. Participants were instructed to try to minimize eye movements and to maintain fixation on a '+' within a circle, centred on a monitor at a viewing distance of 80 cm.

Children completed an MRI scan following the MEG. The fiducial coils were replaced with MRI contrast markers to co-register the MEG data with each subject's MRI. At 6 years (for both VPT and FT children), T1-weighted structural MRIs were obtained using three-dimensional magnetization prepared rapid gradient echo sequences on a 3T Siemens MAGNETOM Trio scanner with a 12-channel head coil (TR/TE/TI: 2300/2.96/900 ms; FA: 9°; FOV: 240 × 256 mm; 192 slices; resolution: 1.0 mm isotropic) with (Repetition time (TR)/Echo time (TE)/Inversion Time (TI): 2300/2.96/900ms; flip angle (FA): 9°; Field of View (FOV): 240 × 256 mm; 192 slices; resolution: 1.0 mm isotropic).

MEG preprocessing

MEG data were bandpass filtered offline from 1 to 150 Hz with a 60 Hz notch filter and analysed in Fieldtrip (Oostenveld *et al.*, 2011). Independent component analysis (ICA) was used to remove artefacts related to cardiac activity, eye blinks and eye movements using the 'fastica' function in Fieldtrip. Components were visually inspected and rejected if representing artefacts by SIM.

Epochs of 2 s of resting-state data were selected from the 5 min recording such that (i) the head position during each epoch deviated less than 8 mm from the recording median, (ii) portions of data that contained MEG sensor resets or exceeded a threshold of ±2 pT after ICA component rejection was excluded and (iii) at least 2.8 min of resting-state data survived artefact rejection. In the 6-year-old group, 10 VPT and 6 FT data sets were excluded based on these criteria. After removal of these data, there were no group differences in the numbers of clean data segments, and an average of 4.38 ± 0.67 min of useable data was acquired. There were also no group differences in head motion (mean head motion in VPT = 5.56 ± 2.58 mm, mean head motion in FT = 5.58 ± 2.29 mm, $P = 0.98$). In the 8-year-old group, eight VPT and three FT data sets were excluded due to excess motion. After excluding these data sets, there were no group differences in the number of clean data segments, and an average of 4.39 ± 0.50 min of useable data was acquired. There were also no differences in head motion between groups (mean head motion in VPT = 5.82 ± 2.49, mean head motion in FT = 5.87 ± 2.46, $P = 0.94$).

Subject-specific single shell head models were created from each subject's T1-weighted MRI. The centroids of previously reported ICN nodes (Brier *et al.*, 2012; de Pasquale *et al.*, 2012) were warped using a non-linear transformation from template Montreal Neurological Institute (MNI) coordinates into subject-specific MEG coordinates (Supplementary Table S2).

The Fieldtrip implementation of the linearly constrained minimum variance vector beamformer (Van Veen *et al.*, 1997) was used to reconstruct the neural activity index (NAI, also called pseudo-Z) time series at all resting-state functional network node locations (ICN; de Pasquale *et al.*, 2012) with 5% regularization. Lead fields were computed from the single-shell subject head model for a unit current dipole in three dimensions at each node. The beamformer weights for the three-dimensional activity at each node were computed by projecting the sensor weights along the axis with the highest singular value decomposition variance resulting in a one-dimensional activity time series for each node. The NAI time series for each node were then filtered into theta

(4–7 Hz), alpha (8–14 Hz), beta (15–29 Hz), gamma 1 (30–55 Hz) and gamma 2 (65–80 Hz). A symmetric orthogonalization procedure (Colclough *et al.*, 2015) was applied to the filtered NAI time series to remove the effects of signal leakage. Amplitude envelopes were computed using the absolute value of the Hilbert transform and then downsampled to 1 Hz by averaging the amplitude over 1 s intervals (Brookes *et al.*, 2011; Hipp *et al.*, 2012). To obtain the AECs, the Pearson correlation coefficient was computed for down-sampled amplitude envelopes from each pair of nodes. AEC was chosen over other measures of synchrony (for example, phase lag index or phase locking value) as it has been shown to be the most reliable measure of connectivity across sessions, pointing to the greatest reliability as well as the lowest susceptibility to co-registration-related errors (Liuzzi *et al.*, 2017).

Connections between nodes belonging to the same network were averaged to provide the magnitude of the intra-network connectivity. Similarly, connections between nodes from different networks were averaged to calculate inter-network connectivity. These matrices were contrasted between groups and significant differences identified using non-parametric permutation testing with 10 000 permutations, correcting for multiple comparisons between networks using family-wise error (FWE) correction. Both corrected (P_{FWE}) and uncorrected *P*-values are reported.

Brain–behaviour associations

An exploratory analysis of the association between scores on neuropsychological measures and DMN connectivity was completed to determine the role of this network in orchestrating social and cognitive functions. The Spearman correlation coefficient was computed between the DMN connectivity values and scores on the social–cognitive domain, the executive functioning domain and basic reading, and results were corrected for multiple comparisons across tasks within each of these neuropsychological domains.

Results
Assessments
VPT children performed more poorly than the FT children at 6 and 8 years on full-scale IQ. Other differences in the neuropsychological measures between the FT and VPT groups were not seen at 6 years of age. However, at 8 years, a number of difficulties manifested in the VPT group, as significantly lower scores on social responsiveness, visual working memory (block recall), single-word reading and phonetic decoding (Table 2).

MEG results
We found increased global network connectivity with age in FT children in the gamma band. There were no significant group differences seen in theta, alpha or beta bands; thus, subsequent analyses were completed on the two gamma bands [gamma 1 (30–55 Hz) and gamma 2 (65–80 Hz)]. Linear mixed effects models were used to measure the effect of group and age on global connectivity. Global connectivity was defined as mean connectivity across all regions of the default mode, LAN, SAL and FP networks from 6 to 8 years, across frequencies and was measured by taking the mean of the correlation coefficients. Group by time effects were significant in gamma 1 ($P = 0.01$) and gamma 2 ($P = 0.02$). Post-hoc analyses using Tukey's range test revealed group differences at the 6-year timepoint, where VPT children showed increased connectivity compared to FT children in gamma 1

Table 2. Neuropsychological outcome of VPT and FT children at 6 and 8 years

	6 years				
	VPT ($n = 40$)	FT ($n = 38$)	t(df)/U	P	P_{FDR}
1. Intelligence					
Full scale 2-subtest IQ (WASI)	103.5 ± 13.4	110.0 ± 13.0	t(75) = 2.1	0.03*	
2. Social–cognition					
Affect recognition (NEPSY-II)	9.4 ± 2.9	10.8 ± 3.9	U = 857.5	0.23	0.4
Social responsiveness total score (SRS-2)	53.9 ± 30.6	48.5 ± 26.4	U = 481	0.41	0.4
3. Executive functioning					
Global Executive Composite Score (BRIEF)	48.6 ± 8.9	50.3 ± 8.5	t(75) = 0.8	0.4	0.4
Digit Recall (WMTB-C)	105.85 ± 19	112.9 ± 13.9	t(68) = 1.79	0.07	0.14
	8 years				
	VPT ($n = 40$)	FT ($n = 43$)	t(df)/U	P	P_{FDR}
1. Intelligence					
Full scale 2-subtest IQ (WASI)	105.6 ± 14.5	119.7 ± 11	t(72) = 5	<0.001*	
2. Social–cognition					
Affect recognition (NEPSY-II)	12.2 ± 10.7	11.1 ± 2.3	U = 863.5	0.4	0.4
Social responsiveness scale total score (SRS-2)	57.2 ± 27.9	43.1 ± 30.2	U = 604	0.02*	0.04*
Total difficulties (SDQ)	57.16	43.11	t(79) = 2.18	0.03*	0.04*
3. Executive functioning					
Global Executive Composite Score (BRIEF)	48.4 ± 9.4	46.9 ± 8.4	t(77.8) = −0.76	0.4	0.4
Backward Digit Recall (WMTB-C)	91.8 ± 19.8	98.3 ± 15.8	t(74) = 1.6	0.106	0.2
Block Recall (WMTB-C)	90.4 ± 20	99.76	t(66.9) = −2.4	0.016*	0.01*
Digit Recall (WMTB-C)	102.2 ± 17	104.7 ± 16.5	t(79) = 0.6	0.5	0.8
4. Language					
Word reading (WIAT-III)	100.6 ± 17	107.9 ± 15	t(73.9) = 2.0	0.04*	0.04*
Pseudoword decoding (WIAT-III)	95.3 ± 18.3	104.4 ± 12.9	t(65.9) = 2.5	0.01*	0.02*

*Asterisks represent a significant difference at $P < 0.05$.
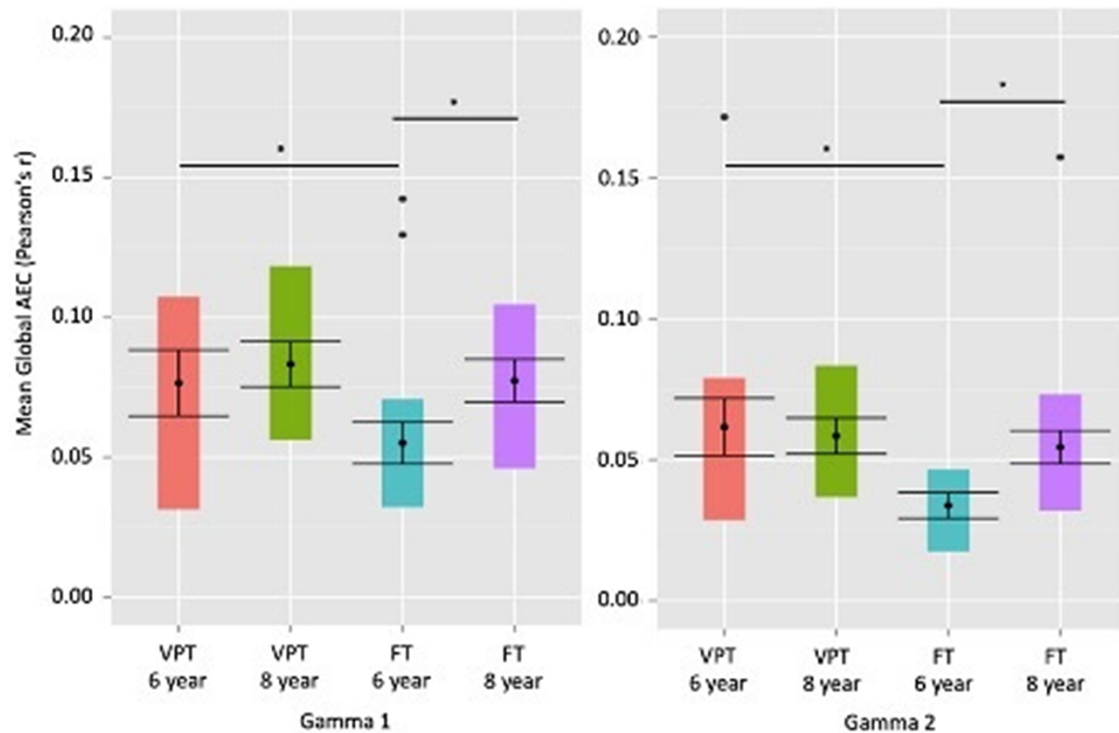
Fig. 1. Mean global connectivity measured by mean amplitude envelope correlations of all nodes in the networks of interest (Y-axis) in gamma band across the different groups at each timepoint (X-axis). The figure shows group differences at the 6-year timepoint and increased connectivity over the 2-year time period between 6 and 8 years only in the FT group. Coloured bars represent the spread of data points, with the mean represented as a circle between the standard error bars. Circles outside the coloured bars are outliers. Asterisks represent a significant difference at $P < 0.05$.

($t(106) = 3.2$, $P = 0.001$) and gamma 2 ($t(106) = 2.38$, $P = 0.019$). Increases in mean global connectivity in the FT group were found between 6 and 8 years in the gamma band (30–80 Hz) but not the VPT group, in gamma 1 ($t(66.3) = 2.93$, $P = 0.004$) and gamma 2 ($t(64) = 2.5$, $P = 0.01$) (Figure 1).

We then analysed network connectivity within and between the networks at 6 years. Figure 2 shows the resting-state functional connectivity results for the frequency bands where we found significant results. Between groups, significantly higher AEC intra-network connectivity was observed in the VPT group in the gamma band (30–80 Hz) at 6 years and in the theta (4–7 Hz) band at 8 years. At 6 years, increased connectivity in the VPT children was found within the DMN in gamma 1 (30–55 Hz, $P_{FWE} = 0.02$) and gamma 2 (55–80 Hz, $P = 0.02$), as well as increased connectivity between the DMN and the other three networks: LAN (30–55 Hz, $P = 0.02$), SAL (30–55 Hz, $P = 0.01$) and FP (30–80 Hz, $P_{FWE} = 0.008$). We also found increased connectivity between the FP and all other networks (30–80 Hz, $P_{FWE} = 0.03$). At 8 years, we found increased connectivity in the VPT compared to the FT group between the DMN and LAN networks ($P = 0.03$) in theta only, although this did not pass correction for multiple comparisons. There were no instances where connectivity in the FT group was greater than in the VPT group.

Brain–behaviour associations

Exploratory analysis of the relationship between DMN connectivity and neuropsychological functions showed that increased functional connectivity in the DMN at 6 years in gamma 1 (30–55 Hz) was correlated with more difficulties in social functioning ($rho = 0.33$, $P = 0.04$) and lower working memory scores on both a backward digit recall task ($rho = -0.32$, $P_{FDR} < 0.05$)

and block recall task ($rho = -0.41$, $P_{FDR} < 0.05$) (see Supplementary Figure S1) at 8 years. Increased connectivity in the DMN in gamma 2 (65–80 Hz) at 6 years was related to worse performance on working memory tasks at 8 years, but correlations were marginally significant for backward digit recall ($rho = -0.31$, $P = 0.05$) and block recall ($rho = -0.27$, $P = 0.08$).

Discussion

This is the first study to reveal intrinsic rs-FC differences in children born VPT across age using MEG. The high-frequency resolution of MEG allowed us to disentangle group differences in resting-state brain networks that may impact social and cognitive outcomes in children born VPT. We found increased connectivity in VPT compared to FT children in gamma (30–80 Hz) at 6 years within the DMN and between the DMN and the three cognitive networks: SAL, LAN and FP. At 8 years, increased connectivity in the VPT group was found only between the DMN and LAN network, but these did not pass correction for multiple comparisons. VPT children were rated as having more social and academic difficulties at 8 years than at 6 years, consistent with reports of emerging difficulties over the early school years. Increased DMN connectivity in the gamma band at 6 years was associated with parent ratings of social difficulties and worse performance on working memory tasks at 8 years of age. MEG differences at the 6-year timepoint, an age marked by rapid social and cognitive changes as children enter school, point to atypical maturation of these networks early in childhood. Since VPT children continue to experience difficulties throughout the school years in the social as well as academic domains (such as basic reading), continued follow-up of VPT children into adolescence will be important to determine downstream effects of resting-state hyperconnectivity at 6 years.
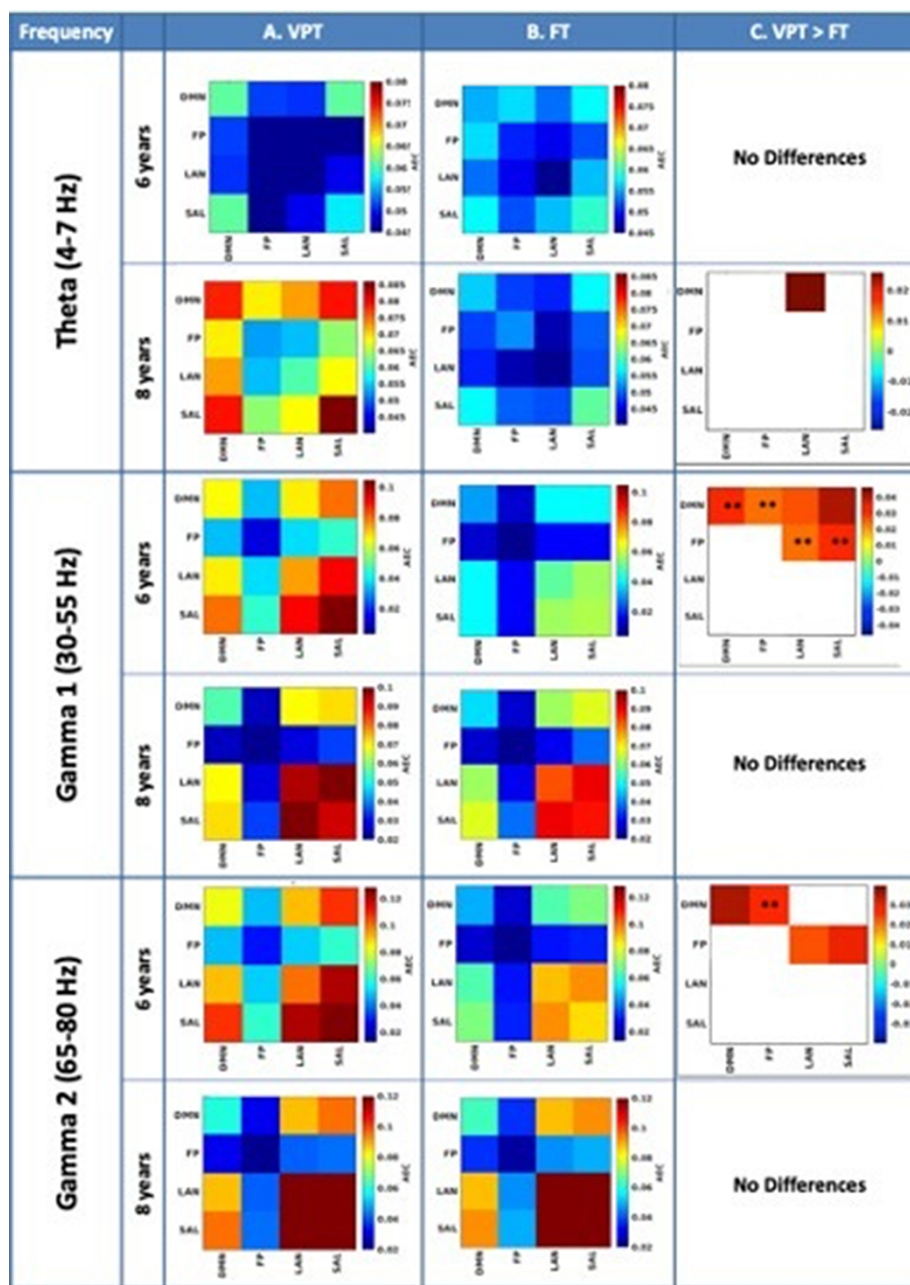
Fig. 2. (A, B) Within-group amplitude envelope correlation (AEC) of intra (diagonal) and inter (off-diagonal) network connectivity at 4–7, 30–55 and 65–80 Hz for the VPT (column A) and FT (column B) cohorts. C) Between-group differences in network connectivity in the VPT compared to the FT group. We found significantly stronger AECs in VPT compared to FT children. Differences in column C are reported at $P < 0.05$ and ** indicates P_{FWE} <0.05 (corrected for multiple comparisons).

Increased global connectivity in VPT children

We found increased connectivity overall in the four resting-state networks of interest in VPT compared to FT children at 6 years of age in the gamma band. At this age, important cognitive processes associated with these networks such as mentalizing (Theory of Mind), language and executive functioning are emerging and improving with age (Garon *et al.*, 2008; Shahaeian *et al.*, 2011), and global hyperconnectivity across the brain in resting-state networks may indicate immature neural processing. Two hypotheses for increased connectivity in VPT children have been presented in the literature. The first is that preterm birth disrupts typical synaptic pruning early in development and that hyperconnectivity may be related to this disruption, as

Degnan *et al.* (2015) suggested with their finding of hyperconnectivity within the posterior DMN in preterm born children aged 9–13 years. An alternative explanation was that preterm born children have immature resting-state network connectivity, where networks are more diffusely connected to other regions throughout the brain (Degnan *et al.*, 2015); increased connections among key regions in resting-state networks and diffuse connections between key network players and the rest of the cortex are characteristic of very young children.

Although sensory-motor resting-state networks can be detected in VPT children in the neonatal period (Fransson *et al.*, 2007) and components of the DMN are qualitatively similar by 4 years (Lee *et al.*, 2013) using fMRI, clear differences in

connectivity in resting-state networks underlying cognitive skills such as language have been reported and persist into adulthood (Kwon *et al.*, 2016). In a longitudinal resting-state fMRI study, Rowlands *et al.* (2016) found that although functional connectivity differences in a LAN network were not found in preterm born children at 8 years of age, they had greater connectivity at 16 years of age in many regions. Johns *et al.* (2019) found increased amygdala–DMN rs-FC in young adults born preterm compared to term born controls using fMRI. Increased amygdala–DMN connectivity was related to worse social competence in late adolescence, suggesting that social difficulties observed in our study persist through adolescence and highlight the importance of studying the relations between the DMN and regions involved in emotion processing. With the greater sensitivity of MEG, we were able to determine connectivity differences related to specific frequency bands, bringing us closer to understanding the physiological underpinnings of these effects; importantly, we found significant differences only in the gamma band (30–80 Hz). Gamma oscillations are generated by an interplay between excitatory pyramidal cells and inhibitory interneurons (Traub *et al.*, 1996; Markram *et al.*, 2004; Buzsaki and Wang, 2012). These develop from differentiation of the cortical layers from the cortical plate during the third trimester, and as VPT birth occurs during this important period of brain development, it can cause disruptions of typical cytoarchitectural development and synaptogenesis (Kostović and Judas, 2002). Our findings that group differences in gamma band were present at 6 years of age support this model. The fact that differences were not present at 8 years of age may suggest catch-up by 8 years of age; however, problems in the social and academic domains were present at 8 years. It is interesting to note that gamma band atypicality particularly increases in gamma are noted in those with neurodevelopmental disorders such as children with autism spectrum disorder (ASD) (Wright *et al.*, 2012), and since VPT children are at much higher risk of ASD than their FT peers, they may share some underlying neuroanatomical abnormalities that can be detected with neurophysiological measures.

The default mode system is a network of brain regions with higher intrinsic activity during periods of 'rest' than during tasks requiring the involvement of other brain regions, giving it its name 'the default network'. However, the term 'rest' is a misnomer. Bar (2007) proposed that during task-free wakefulness, the human brain is constantly and actively generating predictions about the future based on information stored in memory. While the DMN has been widely accepted to be involved during task-free scans, the cognitive role of the DMN is less well established. For example, some have implicated the DMN in navigating social situations (Mars *et al.*, 2012; Moran *et al.*, 2013; Li *et al.*, 2014; Spunt *et al.*, 2015), while others have linked the DMN to retrieval of information. Schilbach *et al.* (2008) associated the DMN with social cognition by noting the striking overlap between regions of the DMN and regions of the social–cognitive network. They further proposed that the DMN provides a social context or narrative in which stimulus-driven events become meaningful based on retrieving information about oneself and others. Our results corroborate these previous findings and suggest that increased DMN connectivity at 6 years of age is related to worse performance on both everyday social functioning and working memory skills at 8 years of age. However, further studies are required to investigate the mechanism by which DMN supports these skills. We suggest that increased connectivity within the DMN in the early school years of VPT children could negatively impact how information is processed, retrieved and then used to navigate social situations, which may underlie some of the reported social difficulties at 8 years of age.

Increased inter-network connectivity in VPT children

We also found that VPT children showed increased connectivity between the DMN and the three cognitive networks compared to FT children at 6 years of age. The DMN is important in toggling between other networks, being reported as a hub of neurophysiological interactions (de Pasquale *et al.*, 2012). Increased inter-network interactions could negatively impact the function in the individual task networks; it could be interpreted as an excess of cross-talk between networks. Our finding that children born VPT have significantly increased inter-network connectivity between the LAN network and DMN supports previous fMRI reports of an alternate circuitry in language processing in VPT children, including both increased (Degnan *et al.*, 2015) and decreased connectivity (Wilke *et al.*, 2014; Choi *et al.*, 2018) in VPT compared with age-matched controls.

Using rs-fMRI to examine connectivity between specific regions and networks, Uddin (2015) suggested that signals from the SAL network influence the DMN and the FP network. The DMN generally underlies internally directed cognitive processes, and the FP network (also known as the central executive network) is responsible for goal-directed processing, while the SAL network plays a key role in switching between the networks, to respond appropriately to salient stimuli. In this study, there was increased connectivity between the SAL and DMN and between the SAL and FP networks in the VPT group at 6 years of age. We suggest that the attentional and control networks have increased cross-talk in the VPT children and hence less efficient network performance, impacting both self-directed and goal-directed systems that are mediated by the SAL network. These differences may contribute to the social, behavioural and cognitive differences between VPT and FT children and to the persistence of these problems at 8 years of age. It is important to note that at 8 years, connectivity differences between the two groups diminished due to FT children showing a significant increase in connectivity between 6 and 8 years of age. While this suggests that typical development involves a trajectory of increased connectivity (Schäfer *et al.*, 2014), increased global connectivity earlier in development across resting-state networks that support important cognitive processes may underlie negative outcomes, as problems actually emerge rather than diminish in the VPT group. Future studies should combine resting-state paradigms with task-based MEG studies in VPT cohorts to provide further evidence for the relations between canonical resting-state networks and cognition in VPT children.

Conclusion

This study demonstrated that VPT birth impacts aspects of functional brain connectivity during childhood. Using MEG, we found that gamma oscillatory connectivity was significantly increased in intrinsic networks including the default mode, FP, LAN and SAL networks. Our findings of increased connectivity across these cognitive networks support hypotheses of more diffuse processing in the VPT born group. Differences in gamma band in VPT children can be attributed to VPT birth occurring during a critical period of brain development and synaptogenesis, which may alter gamma oscillations that arise through coordinated interactions between excitatory and inhibitory neurons. Although these brain differences diminished by 8 years of age, poorer outcomes

were still observed at this timepoint, suggesting that early differences impact later outcomes. A major strength of this study is the use of a high-resolution neurophysiological measure as well as a longitudinal design, which is crucial to determine whether differences persist throughout childhood. Another strength is that we used a battery of standardized neuropsychological measures of social and cognitive functioning. Consistent with the practical challenges of using MEG in paediatric clinical populations (Pang, 2011), this longitudinal data set is relatively small and further analysis of the data including the subcategorization of the VPT group based on the severity of prematurity (for example, fewer than 28 weeks' GA) may have yielded important findings with a larger sample size. Future studies in this area should continue to use neuroimaging modalities that employ precise metrics, validated and standardized neuropsychological assessments, and follow a large cohort of VPT children over several stages of development.

Funding

Conflict of interest

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

Supplementary data

Supplementary data are available at *SCAN* online.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author contributions

S.I.M. collected and analysed the data and wrote the manuscript. J.M.Y. contributed to data collection and manuscript development. S.M.W., B.T.D. and B.A.E.H. contributed to data analysis and manuscript development. E.W.P. and M.J.T. contributed to the design of the study and manuscript development. All authors reviewed the manuscript.

References

Aarnoudse-Moens, C.S.H., Duivenvoorden, H.J., Weisglas-Kuperus, N., Van Goudoever, J.B., Oosterlaan, J. (2012). The profile of executive function in very preterm children at 4 to 12 years. *Developmental Medicine and Child Neurology*, **54**(3), 247–53.

Allotey, J., Zamora, J., Cheong-See, F., *et al.* (2018). Cognitive, motor, behavioural and academic performances of children born preterm: a meta-analysis and systematic review involving 64 061 children. *BJOG: An International Journal of Obstetrics and Gynaecology*, **125**(1), 16–25.

Androulidakis, A.G., Doyle, L.M.F., Yarrow, K., Litvak, V., Gilbertson, T.P., Brown, P. (2007). Anticipatory changes in beta synchrony in the human corticospinal system and associated improvements in task performance. *European Journal of Neuroscience*, **25**(12), 3758–65.

Bar, M. (2007). The proactive brain: using analogies and associations to generate predictions. *Trends in Cognitive Sciences*, **11**, 280–9.

Benjamini, Y., Hochberg, Y. (1995). Controlling the FDR: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society. Series B*, **57**(1), 289–300.

Brier, M.R., Thomas, J.B., Snyder, A.Z., *et al.* (2012). Loss of intranetwork and internetwork resting state functional connections with Alzheimer's disease progression. *Journal of Neuroscience*, **32**(26), 8890–9.

Brookes, M.J., Hale, J.R., Zumer, J.M., *et al.* (2011). Measuring functional connectivity using MEG: methodology and comparison with fcMRI. *NeuroImage*, **56**(3), 1082–104.

Buzsaki, G., Wang, X.-J. (2012). Mechanisms of gamma oscillations. *Annual Review of Neuroscience*, **35**, 203–25.

Chawanpaiboon, S., Vogel, J.P., Moller, A.B., *et al.* (2019). Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *The Lancet Global Health*, **7**(1), e37–46.

Choi, E.J., Vandewouw, M.M., Young, J.M., Taylor, M.J. (2018). Language network function in young children born very preterm. *Frontiers in Human Neuroscience*, **12**, 512.

Colclough, G.L., Brookes, M.J., Smith, S.M., Woolrich, M.W. (2015). A symmetric multivariate leakage correction for MEG connectomes. *NeuroImage*, **117**, 439–48.

Constantino, J.N., Gruber, C.P. (2012). *Social Responsiveness Scale, Second Edition (SRS-2)*. Torrance, CA: Western Psychological Services.

de Pasquale, F., Della Penna, S., Snyder, A.Z., *et al.* (2012). A cortical core for dynamic integration of functional networks in the resting human brain. *Neuron*, **74**(4), 753–64.

Degnan, A.J., Wisnowski, J.L., Choi, S., *et al.* (2015). Altered structural and functional connectivity in late preterm preadolescence: an anatomic seed-based study of resting state networks related to the posteromedial and lateral parietal cortex. *PLoS One*, **10**(6), e0130686.

Doesburg, S.M., Ribary, U., Herdman, A.T., *et al.* (2011). Magnetoencephalography reveals slowing of resting peak oscillatory frequency in children born very preterm. *Pediatric Research*, **70**(2), 171–5.

Doria, V., Beckmann, C.F., Arichi, T., *et al.* (2010). Emergence of resting state networks in the preterm human brain. *Proceedings of the National Academy of Sciences*, **107**(46), 20015–20.

Dosenbach, N.U.F., Fair, D.A., Cohen, A.L., Schlaggar, B.L., Petersen, S.E. (2008). A dual-networks architecture of top-down control. *Trends in Cognitive Sciences*, **12**(3), 99–105.

Engel, A.K., Fries, P., Singer, W. (2001). Dynamic predictions: oscillations and synchrony in top–down processing. *Nature Reviews Neuroscience*, **2**(10), 704–16.

Fox, M.D., Snyder, A.Z., Vincent, J.L., Corbetta, M., Van Essen, D.C., Raichle, M.E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences of the United States of America*, **102**(27), 9673–8.

Fox, M.D., Raichle, M.E. (2007). Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nature Reviews Neuroscience*, **8**(9), 700–11.

Fransson, P., Skiöld, B., Horsch, S., *et al.* (2007). Resting-state networks in the infant brain. *Proceedings of the National Academy of Sciences*, **104**(39), 15531–6.

Fries, P. (2009). Neuronal gamma-band synchronization as a fundamental process in cortical computation. *Annual Review of Neuroscience*, **32**, 209–24.

Gaetz, W., MacDonald, M., Cheyne, D., Snead, O.C. (2010). Neuromagnetic imaging of movement-related cortical oscillations in

children and adults: age predicts post-movement beta rebound. *NeuroImage*, **51**(2), 792–807.

Garon, N., Bryson, S.E., Smith, I.M. (2008). Executive function in preschoolers: a review using an integrative framework. *Psychological Bulletin*, **134**(1), 31–60.

Gioia, G.A., Isquith, P.K., Guy, S.C., Kenworthy, L., Baron, I.S. (2000). Behavior rating inventory of executive function. *Child Neuropsychology*, **6**(3), 235–8.

Goodman, R. (1997). The strengths and difficulties questionnaire: a research note. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, **38**(5), 581–6.

Harding, J.F., Morris, P.A., Hughes, D. (2015). The relationship between maternal education and children's academic outcomes: a theoretical framework. *Journal of Marriage and Family*, **77**(1), 60–76.

Hari, R., Salmelin, R. (2012). Magnetoencephalography: from SQUIDs to neuroscience. Neuroimage 20th anniversary special edition. *NeuroImage*, **61**(2), 386–96.

Hipp, J.F., Hawellek, D.J., Corbetta, M., Siegel, M., Engel, A.K. (2012). Large-scale cortical correlation structure of spontaneous oscillatory activity. *Nature Neuroscience*, **15**(6), 884–90.

Hoff, G.E.A.-J., Van den Heuvel, M.P., Benders, M.J.N.L., Kersbergen, K.J., De Vries, L.S. (2013). On development of functional brain connectivity in the young brain. *Frontiers in Human Neuroscience*, **7**(650), 1–7.

Hunt, B.A.E., Scratch, S.E., Mossad, S.I., Emami, Z., Taylor, M.J., Dunkley, B.T. (2019). Disrupted visual cortex neurophysiology following very preterm birth. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, **5**(10), 951–60.

Jensen, O., Kaiser, J., Lachaux, J.P. (2007). Human gamma-frequency oscillations associated with attention and memory. *Trends in Neurosciences*, **30**(7), 317–24.

Johns, C.B., Lacadie, C., Vohr, B., Ment, L.R., Scheinost, D. (2019). Amygdala functional connectivity is associated with social impairments in preterm born young adults. *NeuroImage: Clinical*, **21**, 101626.

Kaplan, R., Bush, D., Bisby, J.A., Horner, A.J., Meyer, S.S., Burgess, N. (2017). Medial prefrontal–medial temporal theta phase coupling in dynamic spatial imagery. *Journal of Cognitive Neuroscience*, **29**(3), 507–19.

Kesler, S.R., Reiss, A.L., Vohr, B., *et al.* (2008). Brain volume reductions within multiple cognitive systems in male preterm children at age twelve. *Journal of Pediatrics*, **152**(4), 513–20.

Khan, S., Gramfort, A., Shetty, N.R., *et al.* (2013). Local and long-range functional connectivity is reduced in concert in autism spectrum disorders. *Proceedings of the National Academy of Sciences of the United States of America*, **110**(8), 3107–12.

Knyazev, G.G. (2007). Motivation, emotion, and their inhibitory control mirrored in brain oscillations. *Neuroscience and Biobehavioral Reviews*, **31**(3), 377–95.

Korkman, M., Kirk, U., Kemp, S. (2007). *NEPSY—Second Edition (NEPSY-II)*. San Antonio, TX: Harcourt Assessment.

Kostović, I., Judas, M. (2002). Correlation between the sequential ingrowth of afferents and transient patterns of cortical lamination in preterm infants. *The Anatomical Record*, **267**(1), 1–6.

Kwon, S.H., Scheinost, D., Vohr, B., *et al.* (2016). Functional magnetic resonance connectivity studies in infants born preterm: suggestions of proximate and long-lasting changes in language organization. *Developmental Medicine and Child Neurology*, **58**, 28–34.

Lee, W., Morgan, B.R., Shroff, M.M., Sled, J.G., Taylor, M.J. (2013). The development of regional functional connectivity in preterm infants into early childhood. *Neuroradiology*, **55**(Suppl 2), S105–11.

Levy, J., Goldstein, A., Feldman, R. (2017). Perception of social synchrony induces mother-child gamma coupling in the social brain. *Social Cognitive and Affective Neuroscience*, **12**(7), 1036–46.

Li, W., Mai, X., Liu, C. (2014). The default mode network and social understanding of others: what do brain connectivity studies tell us. *Frontiers in Human Neuroscience*, **8**, 74.

Liu, L., Oza, S., Hogan, D., *et al.* (2016). Global, regional, and national causes of under-5 mortality in 2000-15 SUPPPEMENTAL. *Lancet (London, England)*, **388**(10063), 3027–35.

Liuzzi, L., Gascoyne, L.E., Tewarie, P.K., Barratt, E.L., Boto, E., Brookes, M.J. (2017). Optimising experimental design for MEG resting state functional connectivity measurement. *NeuroImage*, **155**, 565–76.

Mantini, D., Perrucci, M.G., Del Gratta, C., Romani, G.L., Corbetta, M. (2007). Electrophysiological signatures of resting state networks in the human brain. *Proceedings of the National Academy of Sciences of the United States of America*, **104**(32), 13170–5.

Markram, H., Toledo-Rodriguez, M., Wang, Y., Gupta, A., Silberberg, G., Wu, C. (2004). Interneurons of the neocortical inhibitory system. *Nature Reviews Neuroscience*, **5**(10), 793–807.

Mars, R.B., Neubert, F.-X., Noonan, M.P., Sallet, J., Toni, I., Rushworth, M.F.S. (2012). On the relationship between the 'default mode network' and the 'social brain'. *Frontiers in Human Neuroscience*, **6**, 189.

Mellem, M.S., Friedman, R.B., Medvedev, A.V. (2013). Gamma- and theta-band synchronization during semantic priming reflect local and long-range lexical-semantic networks. *Brain and Language*, **127**(3), 440–51.

Ment, L.R., Hirtz, D., Hüppi, P.S. (2009). Imaging biomarkers of outcome in the developing preterm brain. *The Lancet Neurology*, **8**(11), 1042–55.

Monson, B.B., Anderson, P.J., Matthews, L.G., *et al.* (2016). Examination of the pattern of growth of cerebral tissue volumes from hospital discharge to early childhood in very preterm infants. *JAMA Pediatrics*, **170**(8), 772–9.

Moran, J.M., Kelley, W.M., Heatherton, T.F. (2013). What can the organization of the brain's default mode network tell us about self-knowledge? *Frontiers in Human Neuroscience*, **7**, 391.

Nosarti, C., Giouroukou, E., Healy, E., *et al.* (2008). Grey and white matter distribution in very preterm adolescents mediates neurodevelopmental outcome. *Brain*, **131**(1), 205–17.

O'Neill, G.C., Tewarie, P., Vidaurre, D., Liuzzi, L., Woolrich, M.W., Brookes, M.J. (2018). Dynamics of large-scale electrophysiological networks: a technical review. *NeuroImage*, **180**(Pt B), 559–76.

Oostenveld, R., Fries, P., Maris, E., Schoffelen, J.M. (2011). FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Computational Intelligence and Neuroscience*, **2011**, 156869.

Palva, S., Palva, J.M. (2007). New vistas for α-frequency band oscillations. *Trends in Neurosciences*, **30**(4), 150–8.

Palva, S., Palva, J.M. (2011). Functional roles of alpha-band phase synchronization in local and large-scale cortical networks. *Frontiers in Psychology*, **2**(SEP), 204.

Pang, E.W. (2011). Practical aspects of running developmental studies in the MEG. *Brain Topography*, **24**(3–4), 253–60.

Park, H., Lee, D.S., Kang, E., *et al.* (2014). Blocking of irrelevant memories by posterior alpha activity boosts memory encoding. *Human Brain Mapping*, **35**, 3972–87.

Peterson, B.S., Vohr, B., Staib, L.H., *et al.* (2000). Regional brain volume abnormalities and long-term cognitive outcome in preterm infants. *Journal of the American Medical Association*, **284**(15), 1939–47.

Pickering, S.J., Gathercole, S.E. (2001). *Working Memory Test Battery for Children (WMTB-C)*. London: The Psychological Corporation.

Psychological Corporation. (2009). *WIAT III: Wechsler Individual Achievement Test*. San Antonio, TX: Psychological Corporation.

Raichle, M.E. (2015). The restless brain: how intrinsic activity organizes brain function. *Philosophical Transactions of the Royal Society B: Biological Sciences*, **370**(1668), 20140172.

Rowlands, M.A., Scheinost, D., Lacadie, C., *et al.* (2016). Language at rest: a longitudinal study of intrinsic functional connectivity in preterm children. *NeuroImage: Clinical*, **11**, 149–57.

Schäfer, C.B., Morgan, B.R., Ye, A.X., Taylor, M.J., Doesburg, S.M. (2014). Oscillations, networks, and their development: MEG connectivity changes with age. *Human Brain Mapping*, **35**(10), 5249–61.

Schilbach, L., Eickhoff, S.B., Rotarska-Jagiela, A., Fink, G.R., Vogeley, K. (2008). Minds at rest? Social cognition as the default mode of cognizing and its putative relationship to the default system' of the brain. *Consciousness and Cognition*, **17**(2), 457–67.

Scott, A., Winchester, S.B., Sullivan, M.C. (2017). Trajectories of problem behaviors from 4 to 23 years in former preterm infants. *International Journal of Behavioral Development*, **42**(2), 237–47.

Shahaeian, A., Peterson, C.C., Slaughter, V., Wellman, H.M. (2011). Culture and the sequence of steps in theory of mind development. *Developmental Psychology*, **47**(5), 1239–47.

Spunt, R.P., Meyer, M.L., Lieberman, M.D. (2015). The default mode of human brain function primes the intentional stance. *Journal of Cognitive Neuroscience*, **27**(6), 1116–24.

Traub, R.D., Whittington, M.A., Stanford, I.M., Jefferys, J.G.R. (1996). A mechanism for generation of long-range synchronous fast oscillations in the cortex. *Nature*, **383**(6601), 621–4.

Uddin, L.Q. (2015). Salience processing and insular cortical function and dysfunction. *Nature Reviews Neuroscience*, **16**(1), 55–61.

Van Den Heuvel, M.P., Pol, H.E.H. (2011). Exploring the brain network: a review on resting-state fMRI functional connectivity. *Psiquiatria Biologica*, **18**(1), 28–41.

van Houdt, C.A., Oosterlaan, J., Aarnoudse-Moens, C.S.H., van Kaam, A.H., van Wassenaer-leemhuis, A.G. (2020). Subtypes of behavioral functioning in 8–12 year old very preterm children. *Early Human Development*, **30**(5), 785–97.

Van Veen, B.D., Van Drongelen, W., Yuchtman, M., Suzuki, A. (1997). Localization of brain electrical activity via linearly constrained minimum variance spatial filtering. *IEEE Transactions on Biomedical Engineering*, **44**(9), 867–80.

Vandewouw, M.M., Young, J.M., Mossad, S.I., *et al.* (2020). Mapping the neuroanatomical impact of very preterm birth across childhood. *Human Brain Mapping*, **41**(4), 892–905.

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence*. New York, NY: The Psychological Corporation: Harcourt Brace and Company.

Wilke, M., Hauser, T.K., Krägeloh-Mann, I., Lidzba, K. (2014). Specific impairment of functional connectivity between language regions in former early preterms. *Human Brain Mapping*, **35**(7), 3372–84.

Wright, B., Alderson-Day, B., Prendergast, G., *et al.* (2012). Gamma activation in young people with autism spectrum disorders and typically-developing controls when viewing emotions on faces. *PLoS One*, **7**(7), e41326.

Ye, A.X., Aucoin-Power, M., Taylor, M.J., Doesburg, S.M. (2015). Disconnected neuromagnetic networks in children born very preterm: disconnected MEG networks in preterm children. *NeuroImage: Clinical*, **9**, 376–84.

Yeo, B.T.T., Krienen, F.M., Sepulcre, J., Sabuncu, M.R. Others. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, **106**(3), 1125–65.

Young, J.M., Vandewouw, M.M., Whyte, H.E.A., Leijser, L.M., Taylor, M.J. (2020). Resilience and vulnerability: neurodevelopment of very preterm children at four years of age. *Frontiers in Human Neuroscience*, **14**, 219.

Yuk, V., Dunkley, B.T., Anagnostou, E., Taylor, M.J. (2020). Alpha connectivity and inhibitory control in adults with autism spectrum disorder. *Molecular Autism*, **11**(1), 95.