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Indirect evidence for altered dopaminergic neurotransmission in very premature-born adults

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Abstract

While animal models indicate altered brain dopaminergic neurotransmission after premature birth, corresponding evidence in humans is scarce due to missing molecular imaging studies. To overcome this limitation, we studied dopaminergic neurotransmission changes in human prematurity *indirectly* by evaluating the spatial co-localization of regional alterations in blood oxygenation fluctuations with the distribution of adult dopaminergic neurotransmission. The study cohort comprised 99 very premature-born (<32 weeks of gestation and/or birth weight below 1500 g) and 107 full-term born young adults, being assessed by resting-state functional MRI (rs-fMRI) and IQ testing. Normative molecular imaging dopamine neurotransmission maps were derived from independent healthy control groups. We computed the co-localization of local (rs-fMRI) activity alterations in premature-born adults with respect to term-born individuals to different measures of dopaminergic neurotransmission. We performed selectivity analyses regarding other neuromodulatory systems

Abbreviations: ALFF, amplitude of low frequency blood fluctuations; BLS, Bavarian Longitudinal Study; BOLD, blood-oxygenation-level-dependent; BW, birth weight; D1, dopamine-1-receptor; D2, dopamine-2-receptor; D3, dopamine-3-receptor; DAT, dopamine transporter; fALFF, fractional amplitude of low frequency blood fluctuations; FDOPA, fluorodopa; FT, full-term; FWE, family wise error; GA, gestational age; IQ, intelligence quotient; rs, resting-state; spatial-RC, spatial regression coefficient; SPECT, single photon emission computed tomography; VLBW, very low birth weight; VP, very preterm.

and MRI measures. In addition, we tested if the strength of the co-localization is related to perinatal measures and IQ. We found selectively altered co-localization of rs-fMRI activity in the premature-born cohort with dopamine-2/3-receptor availability in premature-born adults. Alterations were specific for the dopaminergic system but not for the used MRI measure. The strength of the co-localization was negatively correlated with IQ. In line with animal studies, our findings support the notion of altered dopaminergic neurotransmission in prematurity which is associated with cognitive performance.

KEYWORDS
amplitude of low frequency fluctuations, Blood oxygenation fluctuations, dopamine PET, dopaminergic neurotransmission, premature birth, resting-state fMRI

1 | INTRODUCTION

Preterm birth (i.e., birth before 37 weeks of gestation) poses a major global health problem at an 11% prevalence worldwide (Chawanpaiboon et al., 2019; Howson et al., 2013; WHO, 1977). It is associated with a higher risk for adverse long-term effects, especially lasting neurocognitive deficits (Eves et al., 2021; Wolke et al., 2019). This risk increases with earlier gestational age (GA) or lower birth weight (BW) (D'Onofrio et al., 2013; Nosarti et al., 2012; Saigal & Doyle, 2008). Brains of preterm newborns are particularly vulnerable to preterm birth-related adverse events such as hypoxia-ischemia, neuroinflammation, brain hemorrhage, and/or perinatal stress, which might cause aberrant brain development. Such persistent aberrant brain development is, for example, demonstrated by findings of altered brain structure and function throughout infancy, childhood, adolescence, and early adulthood (Back et al., 2002; Hasler et al., 2019; Hedderich et al., 2019; Hedderich et al., 2020; McClendon et al., 2017; Menegaux et al., 2020; Meng et al., 2016; Pascoe et al., 2019; Schmitz-Koep et al., 2020; Skranes et al., 2013; Volpe, 2009).

At a microscopic level, aberrant brain development is mainly mediated by the aberrant development of pre-oligodendrocytes, GABAergic interneurons, and subplate neurons, which have a fundamental role in the early development of cortical microstructure and connectivity (Back et al., 2002; Ball et al., 2013; Buser et al., 2012; Deng, 2010; Kanold & Luhmann, 2010; Kinney et al., 2012; Kostović et al., 2014; McClendon et al., 2017; Salmaso et al., 2014). At a macroscopic level, brain changes include both white matter and grey matter: White matter alterations include reduced fiber density and volume throughout the entire forebrain (Ball et al., 2012; Ball et al., 2014; Eikenes et al., 2011; Meng et al., 2016; Skranes et al., 2007). Exemplary grey matter alterations include volume reduction in thalamus, striatum, claustrum, basal forebrain, and temporal cortices, as well as altered gyrification, especially in associative cortices (Grothe et al., 2017; Karolis et al., 2017; Meng et al., 2016; Nosarti et al., 2008; Pierson et al., 2007). In addition, evidence for functional changes, for example, altered patterns of blood oxygenation in task-based- and resting-state functional MRI (fMRI), overlap with structural changes for premature-born subjects (Bäuml et al., 2015; Daamen, Bäuml, Scheef, Meng, et al., 2015; Daamen, Bäuml, Scheef, Sorg, et al., 2015; Damaraju et al., 2010; Doria et al., 2010; Froudist-Walsh et al., 2015; Lubsen et al., 2011; Shang et al., 2018; Smyser et al., 2010; White et al., 2014). Both structural and functional changes have been associated with cognitive impairment not only in children but also in premature-born adults, indicating a persistent impact of premature birth on neurocognitive development and functioning (Ball et al., 2015; Farajdokht et al., 2017; Hedderich et al., 2019; Northam et al., 2011; Nosarti et al., 2014; Shang et al., 2018).

While these structural and functional brain alterations after premature birth have been widely described, knowledge about altered neurotransmission in prematurity is rather limited. Particularly, the development of neuromodulatory transmitter systems such as dopaminergic neurotransmission occurs during the 2nd and 3rd trimesters of gestation and may be disrupted due to preterm delivery (Boyson & Adams, 1997; de Graaf-Peters & Hadders-Algra, 2006; Verney et al., 1993). Previous results on the effects of preterm birth on the dopaminergic system mostly stem from animal experiments. For example, the dopaminergic system has been found to be specifically susceptible to adverse perinatal events in rodents e.g., stress or maternal separation, with lasting changes in dopamine function (Boksa & El-Khodor, 2003; Henry et al., 1995; Kehoe et al., 1998). Lipska et al. demonstrated delayed and persistent behavioral alterations with increased dopamine activity after damage to the ventral hippocampus in newborn rats (Lipska et al., 1993). Complementary, the only molecular imaging study of neurotransmission in human prematurity so far, an ^{18}F-DOPA-PET study in premature-born adults, found a reduction in striatal dopamine synthesis and storage associated with perinatal brain injury (Froudist-Walsh et al., 2017). These results suggest that dopaminergic neurotransmission might be altered in human prematurity. As the dopaminergic system is an important factor for individual cognitive functioning and performance, deviations from an optimum level can lead to cognitive deficits, prematurity-induced altered dopaminergic neurotransmission might be associated with neurocognitive impairments in premature-born individuals (Cools et al., 2008; Cools & D'Esposito, 2011).

The most direct way to test hypotheses about altered neuromodulatory transmission in prematurity is to use molecular imaging to map distinct aspects of neurotransmission in premature-born individuals (Froudist-Walsh et al., 2017). However, PET- or single-photon emission computed tomography (SPECT)-based investigations in premature-born children or adults are restricted due to radiation exposure and high costs, particularly for larger cohorts. An alternative strategy is to study potential changes through the *relationship* between neurotransmission and resulting functional brain activity, that is influenced by the respective neurotransmission (Dukart et al., 2018). For example, it is well-established that modulation of specific neurotransmitter systems such as dopamine or serotonin affects blood oxygenation fluctuations in the brain (Dukart et al., 2021; Li et al., 2020; Nugent et al., 2015). Such measures of regional blood oxygenation fluctuation, i.e. fractional (i.e., normalized) amplitude of low-frequency blood oxygenation fluctuations (fALFF), have been shown to be altered in premature-born individuals (Damaraju et al., 2010; Doria et al., 2010; Shang et al., 2018). By evaluating if these fALFF alterations co-localize with the non-pathological distribution of specific neurotransmission systems (as derived from independent adult cohorts), it is possible to estimate the potential contribution of the respective neurotransmission systems to the observed functional alterations (Dukart et al., 2021). Indeed, a novel analysis toolbox, developed by Dukart et al., implemented this idea of the indirect study of potential neurotransmission changes, providing an elegant analysis pipeline for calculating cross-sample spatial regression coefficients (spatial-RC) reflecting the relationship between brain metric individual difference maps and molecular imaging-derived normative neurotransmitter maps (Dukart et al., 2021). Previous studies using the toolbox provided reliable results and were able to validate the methodology (Chen et al., 2021; Dugré & Potvin, 2022; Han et al., 2022; Martins et al., 2022; Oldehinkel et al., 2022; Park et al., 2022; Sakreida et al., 2022; Tang et al., 2022; Xu et al., 2022; Zarkali et al., 2022). There are similar methodological approaches, for example, the Receptor-Enriched Analysis of functional Connectivity by Targets (REACT) toolbox (Dipasquale et al., 2019), whose analytic approach combines pharmacological rs-fMRI analyses and specific neurotransmitter receptor distributions by PET imaging in healthy brains, or, in general, toolboxes from the field of imaging transcriptomics that work in a similar way (e.g., Imaging Transcriptomics [Martins et al., 2021] or Gene Category Enrichment Analysis [Fulcher et al., 2021]). All of these approaches allow the identification of cross-sample spatial correlations between patterns of specific structural or functional brain properties as measured by MRI or fMRI, and a "microscopic" metric such as gene expression maps or PET map. However, in our study, primarily aimed at providing evidence of altered neurotransmission in premature-born adults compared with term-born adults, the JuSpace toolbox seemed to be most appropriate because it provides an integrated and more direct approach to potential group differences in PET-tracer-related fMRI changes by generating an explicit individual group contrast. More specifically, by subtracting the individual fALFF signal of a premature-born adult from the mean of term-born controls (the normative reference), a contrast can be generated that exclusively correlates fALFF alterations (i.e., premature vs. term-born) with the spatial distribution of neurotransmitters, thereby isolating changes specifically associated with the prematurity.

In the current study, we investigated the cross-sample association of blood oxygenation-based fALFF with dopaminergic neurotransmission maps by regression analysis in a large sample of very preterm/very low birth weight (VP/VLBW) and term-born adults from the Bavarian Longitudinal Study. For dopaminergic neurotransmission, dopamine reuptake by dopamine transporter (DAT), and dopaminergic excitatory and inhibitory function by dopamine-2/3-(D2/3R) and dopamine-1-receptors (D1R). The analysis of aspects of dopaminergic neurotransmission was chosen to test the hypothesis of altered dopaminergic neurotransmission in prematurity. To prove this hypothesis, we primarily focused on individual differences in premature-born adults in a dopamine transmission-sensitive measure relative to a normative reference using the JuSpace toolbox, that computes an individual reference contrast by subtracting the individual fALFF signal of a premature-born adult from the mean of term-born controls. Furthermore, we expected potentially aberrant spatial-RCs for dopaminergic neurotransmission in premature-born adults to be associated with lower neurocognitive performance as indexed by IQ scores. The fALFF metric was derived from resting-state functional MRI, IQ scores by cognitive assessments.

2 | MATERIALS AND METHODS

2.1 | Participants

A detailed description of the evaluated prospective whole population-based Bavarian Longitudinal Study (BLS) cohort can be found in Lubsen et al. (2011); Sakreida et al., 2022; Zarkali et al. (2022). Briefly, in the BLS neonatal at-risk children and healthy controls from southern Bavaria were included between January 1985 and March 1986 (Wolke et al., 1994; Wolke & Meyer, 1999). 682 infants born VP/VLBW and 350 of 916 randomly selected full-term (FT) controls from the same obstetric hospitals were enrolled. FT controls were matched for sex and socioeconomic status. Participants were assessed longitudinally, from infancy to adulthood. At age of 26 years, 101 VP/VLBW and 111 FT controls underwent brain MRI. The MRI took place at the Department of Neuroradiology, Klinikum rechts der Isar, Technische Universität München ($n = 145$), and the Department of Diagnostic and Interventional Radiology, University Hospital Bonn, Germany ($n = 67$). Written informed consent was obtained from all participants. The study was performed in accordance with the Declaration of Helsinki and was approved by the local ethics committees of the Klinikum rechts der Isar and University Hospital Bonn.

2.2 | Birth variables

Gestational age (GA) was estimated from the maternal reports on the first day of the last menstrual period and serial ultrasounds during

pregnancy. In cases where discrepancies of more than 2 weeks occurred between the two methods, a clinical assessment using the Dubowitz method at birth was used (Dubowitz et al., 1970). Birth weight (BW) was obtained from obstetric records.

2.3 | Cognitive performance assessment

At the age of 26 years, cognitive performance was assessed by independent psychologists using the German version of the Wechsler Adult Intelligence Scale (WAIS III) (Molz et al., 2010), which was subsequently converted to age-normalized and full-scale IQ scores.

2.4 | Imaging data acquisition

The image data acquisition was previously described in Lubsen et al. (2011): MRI data was obtained in both centers using Philips Achieva 3 Tesla TX system and Philips Ingenia 3 Tesla system, respectively, with an 8-channel SENSE head coil, respectively. Subject and scanner distribution: Bonn Achieva 3T: 5 VP/VLBW, 12 FT, Bonn Ingenia 3T: 33 VP/VLBW, 17 FT, Munich Achieva 3T: 60 VP/VLBW, 65 FT, Munich Ingenia 3T: 3 VP/VLBW, 17 FT. We included scanner identities as covariates of no interest to prevent possible confounds. All scans were done with identical sequence parameters and scanners were checked regularly to provide optimal scanning conditions. MRI physicists at both sites ensured within-scanner stability by regularly scanning imaging phantoms. The signal-to-noise ratio was not significantly different between scanners (one-way ANOVA with factor ‚scanner-ID'[Bonn 1, Bonn 2, Munich 1, Munich 2]; $F(3, 182) = 1.84$, $p = .11$). High-resolution T1-weighted, 3D-MPRAGE sequence was performed with the following parameters: TI = 1300 ms, TR = 7.7 ms, TE = 3.9 ms, flip angle 15°; field of view: 256 mm × 256 mm, with a reconstructed isotropic voxel size of 1 mm^3. Resting-state fMRI data were collected for 10 min 52 s from a gradient-echo echo-planar sequence (TE = 35 ms, TR = 2608 ms, flip angle = 90°, FOV = 230 mm^2, matrix size = 64 × 63, 41 slices, thickness = 3.58 (no interslice gap), reconstructed voxel size = 3.59 × 3.59 × 3.59 mm^3), resulting in 250 volumes of BOLD fMRI data per subject. Immediately before the resting-state sequence, subjects were instructed to keep their eyes closed and to remain awake, which was verified by interrogating via intercom immediately after the scan. Two participants (1 VP/VLBW and 1 FT) received structural imaging only, resulting in rs-fMRI data from 210 participants.

2.5 | Data preprocessing and calculation of fALFF

Preprocessing and fALFF calculation were carried out using SPM12 (http://www.fil.ion.ucl.ac.uk/spm) and DPARSF (Chao-Gan & Yu-Feng, 2010; Yan, 2010). Before beginning with the canonical preprocessing steps, we applied two additional physiological and motion noise correction procedures to the raw fMRI data. First, removal of physiological noise through the Physiologic Estimation by Temporal Independent Component Analysis (PESTICA, http://www.nitrc.org/projects/pestica/), which uses slice-wise temporal independent component analysis (ICA) to detect noise caused by cardiac and respiratory fluctuation patterns (Beall & Lowe, 2007). The resulting PESTICA templates were then used for voxel-wise physiological noise correction (Glover et al., 2000). Second, retrospective application of Slice-Oriented Motion Correction (SLOMOCO, http://www.nitrc.org/projects/pestica), which consists of a rigid-body motion parameter estimation and subsequent voxel- and slice-specific second-order motion regression model (Beall & Lowe, 2014). To transform individual images into common MNI (Montreal Neurological Institute) space, spatial normalization and re-sampling to 3 mm isotropic voxels by DARTEL were applied (Ashburner, 2007). To estimate motion-induced artifacts, point-to-point head motion, and frame-wise displacement were assessed for each subject (Van Dijk et al., 2012). Data from 4 subjects (1 VP/VLBW subject and 3 FT subjects) were excluded from further analysis due to excessive head motion defined as a cumulative translation or rotation >3 mm or 3° (cumulative translation VP/VLBW 0.3 ± 0.22 mm, FT 0.32 ± 0.22 mm; cumulative rotation VP/VLBW 0.08 ± 0.06°, FT 0.10 ± 0.10°). Two-sample t-tests yielded no significant differences between groups regarding mean point-to-point translation or rotation of any direction ($p > .1$), and frame-wise displacement ($p > .1$). One should note that we did not apply additional "scrubbing" procedures to remove outliers in fMRI volumes (Power et al., 2012), as suggested by Babu and Stoica (2010), Yan et al. (2013). Removal of non-contiguous time points alters the underlying temporal structure of the data, precluding conventional frequency-based analyses of rs-fMRI data (in our case Fourier transformation-based fALFF, see next).

Next, nuisance covariates—including Friston-24 (Friston et al., 1996) head motion parameters (i.e., translational and rotational movement parameters and their derivatives), white matter, and cerebrospinal fluid signal intensities—were regressed out from preprocessed resting-state fMRI data. Subsequently, the data were smoothed using a Gaussian kernel with a full width at half-maximum of 6 mm. Then, after linear-trend removal, the time series were transformed to the frequency domain using fast Fourier transformation to obtain the power spectrum. To calculate fALFF, a ratio of the power of each frequency at the low-frequency range (0.01–0.08 Hz) to the full frequency range (0.01–0.25 Hz) was used (Zou et al., 2008). Finally, the fALFF data were then z-transformed, that is, subtracted by its mean and then divided by its standard deviation.

2.6 | Main outcome measure spatial-RC

To evaluate if fALFF alterations in VP/VLBW as compared with FT controls are spatially associated with specific aspects of dopaminergic neurotransmission, we calculated our main outcome measure of cross-sample spatial-RC, using the JuSpace toolbox version 1.4 available at: https://github.com/juryxy/JuSpace and the Statistical

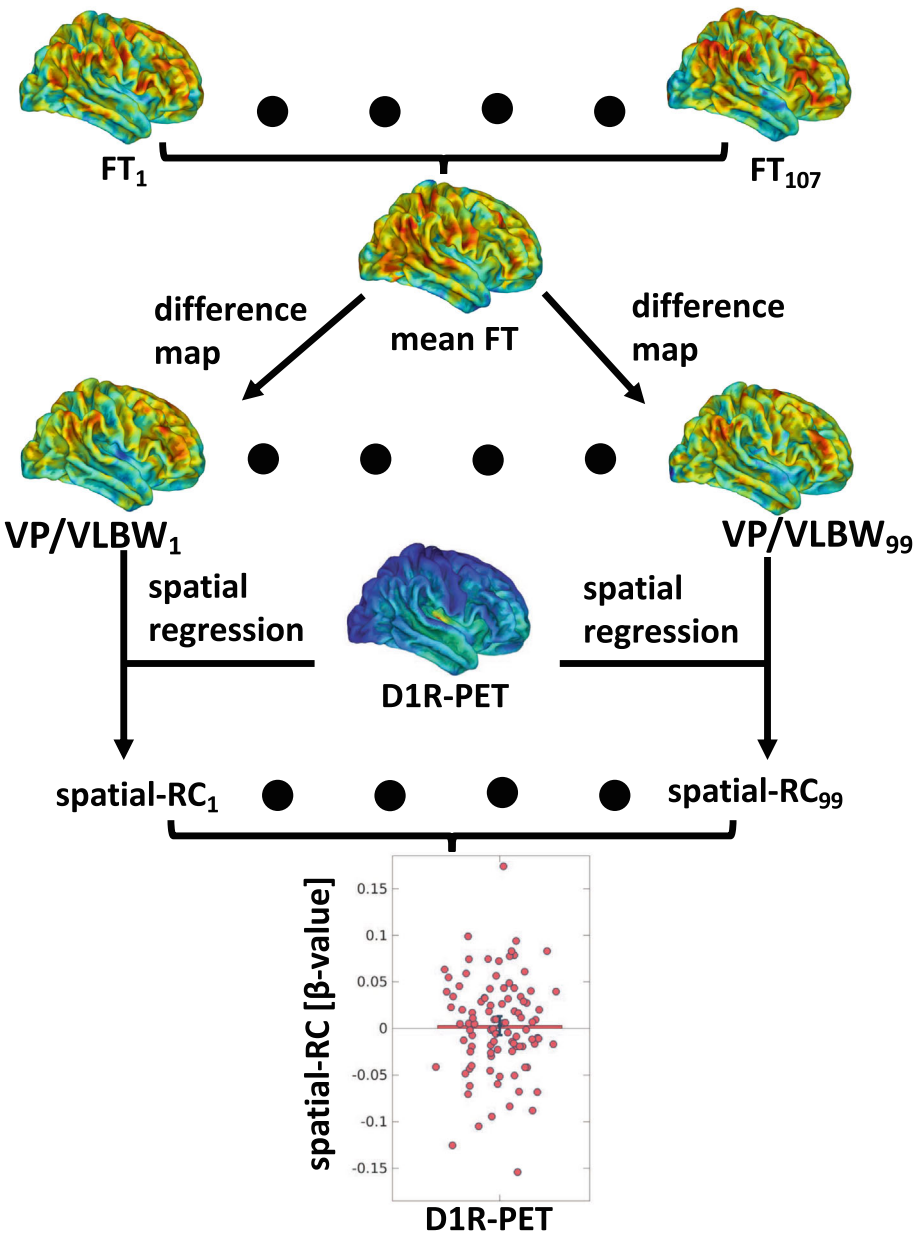

FIGURE 1 Work flow for cross-sample spatial-RC analysis. First, a mean fALFF map is generated from the individual fALFF maps of the full-term-born control. Second, individual fALFF reference-contrast maps are generated for each subject from the VP/VLBW group by subtracting individual fALFF maps from the mean fALFF map of the full-term-born controls. Third, the association between fALFF reference-contrast maps and normative dopamine transmission PET maps are tested by implementing a cross-sample spatial multiple linear regression model. This procedure yielded the outcome measure of individual spatial-RCs per VP/VLBW individual and PET map. Fourth, exact orthogonal permutation-based *p*-values (with 10,000 permutations) were computed. The threshold for statistical significance was set to $p < .05$. D1R, dopamine-1-receptor; fALFF, fractional amplitude of low frequency blood fluctuations; FT, full-term; spatial-RC, spatial regression coefficient; VP/VLBW, very preterm and/or very low birth weight.

Parametric Mapping Software (SPM12, https://www.fil.ion.ucl.ac.uk/spm/software/spm12/) for Matlab 2017a; see also Figure 1. First, we calculated an individual fALFF reference contrast for each premature-born adult by subtracting the individual fALFF signal from a premature-born adult from the mean fALFF map signal of FT controls. Second, normative dopaminergic neurotransmission PET maps are loaded into the atlas space as the mean value per file and region. The used atlas was the neuromorphometrics atlas from SPM12 excluding all white matter and cerebrospinal fluid regions (Friston et al., 1994). Then, the actual spatial regression analysis of neurotransmission PET maps and individual fALFF reference-contrast is computed by a single multiple spatial linear regression analysis that included the individual fALFF reference-contrast maps with respect to all dopaminergic neurotransmission PET maps as part of the regression function, with adjustment for spatial autocorrelation by local gray matter probabilities as estimated from the file *TPM.nii* as output by SPM12. *TPM.nii* defines the prior probability of finding a tissue type, for example, gray matter, at a particular location and was derived from the *ixi* dataset (http://brain-development.org/ixi-dataset/). The *ixi* dataset was derived from nearly 600 healthy subjects at three different hospitals in London. Neurotransmission PET maps were derived from the library of the JuSpace toolbox (see Table S1 for a complete list of PET maps). We did not include PET maps with insufficient whole-brain signal-to-noise reliability (Raclopride and F-DOPA-PET). In order to control for potential confounding effects due to distinct signal intensities (signal-to-noise ratios) across different dopaminergic neurotransmission maps, all PET maps were linearly rescaled to a minimum of 0 and a maximum of 100 (Dukart et al., 2021). To validate the linear rescaling, we calculated the total volume, mean intensity, standard deviation, and ratio of mean intensity to standard deviation of all used PET/SPECT templates in Data S1.

As a result of these procedures, we received our main outcome measures of cross-sample spatial-RCs for different dopaminergic neurotransmission PETs for each individual of very premature birth.

2.7 | Specificity analyses with respect to both different neuromodulatory systems and different MRI measures

To assure specificity to both, other neuromodulatory systems and other MRI measures, we computed—with respect to specificity for other neuromodulatory systems—the spatial-RCs—as described in the previous section—for serotonergic, noradrenergic, and cholinergic neurotransmission systems.

To assess whether significant spatial-RCs are specific to the fALFF measure, we performed the regression analysis—as described in the previous section—for structural MRI, i.e., voxel-based morphometry (VBM) and T1w/T2w-ratio images, with normative maps of dopaminergic neurotransmission.

To compute VBM, we followed our previous approach to VBM in the same dataset (Bäuml et al., 2015). T1w-images were preprocessed using the CAT12 toolbox (https://neuro-jena.github.io/cat/) within SPM12. T1w-images were normalized to a template space and segmented into gray matter (GM), white matter, and cerebrospinal fluid. Finally, images were smoothed with a Gaussian kernel of 6 mm (FWHM).

For the T1w/T2w-images, as described recently (Schmitz-Koep et al., 2023), we used SPM12 (SPM12, https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). The T2w-image was co-registered to the T1w-image through rigid body transformation, then the T1w- and T2w-images were bias-corrected, and intensity calibrated, and the ratio was calculated to generate the T1w/T2w-images. Finally, the previously segmented GM masks were used to calculate the T1w/T2w ratio within GM. GM T1w/T2w ratio maps were smoothed with a Gaussian kernel of 6 mm (FWHM).

To test whether the observed co-localizations of individual fALFF-difference maps of VP/VLBW with the target brain maps (dopaminergic neurotransmission maps) were significantly greater than randomly generated brain maps or spatially autocorrelated synthetic brain maps, we used a spatially constrained null model within the open-access BrainSMASH toolbox (github.com/murraylab/brainsmash) (Burt et al., 2020). We computed randomly shuffled ($n = 1000$) and spatial autocorrelation (SA) preserving surrogate brain maps ($n = 1000$) for the target brain map. Next, we performed Pearson's correlation to obtain null distributions of Pearson correlation coefficients between an average fALFF-difference map of VP/VLBW compared to FT controls and the SA-preserving and randomly shuffled surrogate brain maps derived from the target brain map. The results of this SA analysis can be found in Data S1.

2.8 | Statistical analysis

Statistical analyses concerning scalar variables were performed using IBM SPSS Version 27 (IBM Corp., Armonk, NY, USA): Differences of clinical variables between VP/VLBW and FT individuals were tested using Chi-squared test (sex) and two-sample *t*-tests (age, BW, GA, gray matter, and IQ). The threshold for statistical significance was set to $p < .05$.

fALFF. To investigate within-group fALFF patterns, voxel-wise one-sample *t*-tests as implemented in SPM12 correcting for the covariates "sex" and "scanner identity", were performed for the cohorts of VP/VLBW-born adults and FT controls respectively. To test for group differences (VP/VLBW vs. FT controls) in fALFF, voxel-wise fALFF maps per subject were entered into a general linear model as implemented in SPM12, with the between-subjects factor "group," and the covariates "sex" and "scanner identity". The threshold for statistical significance was set to $p < .05$ cluster FWE-corrected, with a voxel-wise threshold of $p < .001$.

Spatial multiple linear regression. To evaluate the significance of group changes in spatial-RCs between fALFF-, VBM-, and T1w/T2w-ratio-difference maps of VP/VLBW subjects and neurotransmission PET maps, we computed exact permutation-based p-values (with 10,000 permutations) for all analyses to test if the mean regression coefficients across the subjects were significantly different from the null distribution. The threshold for statistical significance was set to $p < .05$. The results of the main analysis of spatial multiple linear regression between fALFF-difference maps of VP/VLBW subjects and dopaminergic neurotransmission maps were Bonferroni-corrected for multiple testing.

Correlation analysis of spatial-RC, prematurity, and cognition. To analyze the associations between aberrant spatial-RCs and scores of prematurity and cognitive performance, respectively, spatial-RCs were extracted for all 99 VP/VLBW subjects and correlated with birth-related variables (BW and GA) and the cognitive performance variable (full-scale IQ), respectively. These correlations were investigated by two-tailed partial correlation analyses with "sex" and "age" as covariates-of-no interest. The threshold for statistical significance was set to $p < .05$.

3 | RESULTS

3.1 | Sample characteristics

Group demographic and clinical characteristics are presented in Table 1. There was no significant difference between the VP/VLBW and FT groups with respect to age at scanning ($p = .215$) and sex ($p = .745$). By design, the VP/VLBW cohort had significantly lower GA ($p < .001$) and lower BW ($p < .001$). Furthermore, VP/VLBW subjects had significantly lower full-scale IQ scores ($p < .001$) compared to FT controls.

3.2 | Aberrant fALFF in premature-born adults

Results of the voxel-wise fALFF comparison of VP/VLBW and FT controls showed significant fALFF increases in left insular cortex and fALFF decreases in right lateral temporal cortices (Figures S1 and S2).

TABLE 1 Demographical, clinical, and cognitive data.

	VP/VLBW ($n = 99$)			FT ($n = 107$)			
	Mean	SD	Range	Mean	SD	Range	*p* value
Sex (male/female)	57/42			64/43			.745
Age (years)	26.7	±0.6	25.7–28.3	26.8	±0.7	25.5–28.9	.215
GA (weeks)	30.6	±2.1	25–36	39.7	±1.1	37–42	**<.001**
BW (g)	1332	±311	630–2070	3384	±445	2120–4670	**<.001**
GM (mm^3)	684.4	±62.5	524.0–839.3	714.9	±57.5	555.1–861.2	**<.001**
Full-scale IQ[a]	94.4	±12.6	64–131	102.6	±12.0	77–130	**<.001**

Note: Statistical analysis: sex with χ^2 statistics; age, GA, BW, GM and full-scale IQ with two sample t-tests. Bold letters indicate statistical significance defined as $p < .05$.

Abbreviations: BW, birth weight; FT, full-term; GA, gestational age; GM, grey matter; IQ, intelligence quotient; SD, standard deviation; VP/VLBW, very preterm and/or very low birth weight.

[a]Data are based on 95 VP/VLBW and 104 FT-born individuals.

3.3 | Altered spatial-RCs in premature-born adults for dopaminergic neurotransmission

Using cross-sample spatial multiple linear regression analysis, we observed that individual fALFF differences of VP/VLBW adults from average fALFF maps of FT adults were significantly spatially associated with normative PET maps for D2/3R-availability ([^{18}F]Fallypride) (mean β-coefficient = −.014; $p = .012$; Cohen's $d = -.37$). In contrast, for other normative PET maps, spatial-RCs of VP/VLBW adults were not significantly different from zero, namely D1R-availability ([^{11}C]SCH23390) (mean β-coefficient = .006; $p = .295$; Cohen's $d = .13$) and dopamine reuptake ([^{123}I]FP-CIT) (β-coefficient = .008; $p = .295$; Cohen's $d = .16$) (Figure 2a; Table 2).

To provide further evidence that significant spatial-RCs for D2/3R availability were associated with premature birth, we correlated spatial-RCs with birth-related variables (i.e., GA and BW) within the VP/VLBW group. We found no significant correlation of BW or GA with spatial-RCs for D2/3R-availability ($p = .37$ and $p = .426$, respectively; Table 3).

3.4 | Association of altered spatial-RCs for dopaminergic neurotransmission with IQ in premature-born adults

To test whether significant spatial-RCs in the VP/VLBW subjects were associated with cognitive deficits, we performed partial correlation analyses for spatial-RCs for D2/3-receptor availability and IQ scores. The full-scale age-normed IQ showed a significant negative correlation with spatial-RCs for D2/3R-availability ($r = -.230$; $p = .031$; $R^2 = .053$; Table 3, Figure 2b).

3.5 | Results of specificity analyses

To control for specificity of our finding with respect to other neuromodulatory systems beyond the dopaminergic ones, we performed a cross-sample spatial multiple linear regression analysis, including serotonergic, cholinergic, and noradrenergic neurotransmitter PET maps. Spatial-RCs of VP/VLBW adults were not significantly different from zero for other neurotransmitter systems, i.e., cholinergic, noradrenergic, and serotonergic (Table S3). Identical to the analysis for the dopaminergic neurotransmitter system, spatial-RCs of the VP/VLBW cohort remained significantly deviated from the null distribution for D2/3R-availability ([^{18}F]Fallypride) (mean β-coefficient = −.019, $p = .046$; Cohen's $d = -.30$), but was also significant for D1R-availability ([^{11}C]SCH23390) (mean β-coefficient = .021, $p = .045$; Cohen's $d = .26$).

To control for specificity of our finding with respect to other MRI-derived measures beyond fALFF, we tested whether spatial associations of dopaminergic neurotransmission maps were associated with not only functional but structural MRI-derived measures. We performed cross-sample spatial multiple linear regression analysis for individual differences in voxel-based GM-masks of VP/VLBW adults from average GM-masks of FT adults and dopaminergic neurotransmission maps. Spatial-RCs were significantly different from zero for D1R- (mean β-coefficient = −.010, $p = .018$; Cohen's $d = .38$) and D2/3R-availability (mean β-coefficient = −.012, $p = .001$; Cohen's $d = -.55$) (Table S4).

Similarly, we performed spatial multiple linear regression analysis for individual T1w/T2w ratio differences of VP/VLBW adults from average T1w/T2w ratios of FT adults and dopaminergic neurotransmission maps. Spatial-RCs were significantly different from zero for D2/3R-availability (mean β-coefficient = −.006, $p = .007$; Cohen's $d = -.39$) and dopamine reuptake (mean β-coefficient = .005, $p = .026$; Cohen's $d = .34$) (Table S5).

4 | DISCUSSION

Using cross-sample spatial regression between individual fALFF reference-contrast maps from premature-born adults with respect to term-born ones and dopaminergic neurotransmission maps derived from normative molecular imaging data, we found selectively significant spatial regression coefficients for D2/3R-availability for very premature-born adults. Although these alterations were small, they

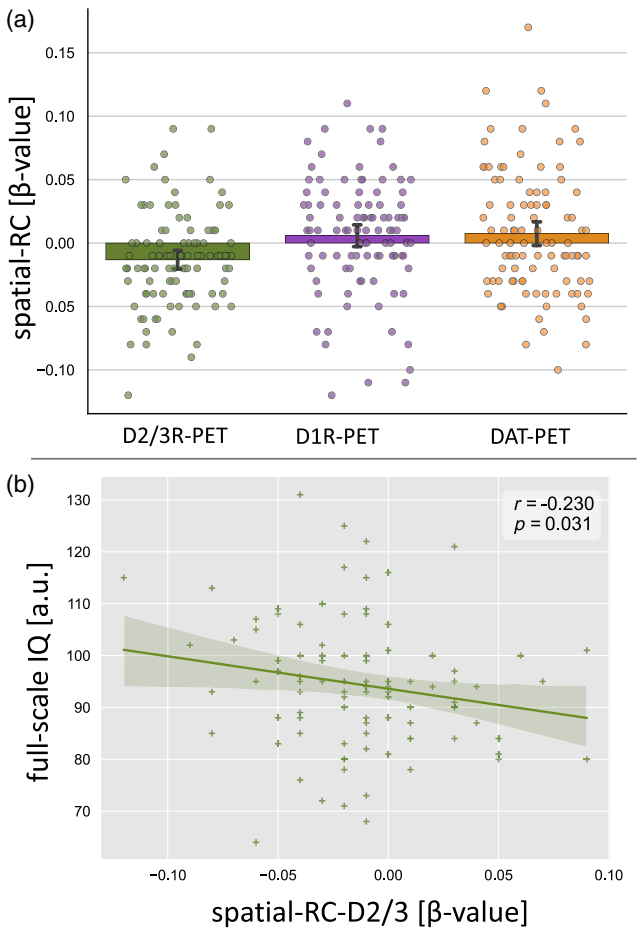

FIGURE 2 Significant spatial-RCs in premature-born adults and their relationship to birth weight. (a) Each dot represents an individual spatial-RC value of the VP/VLBW group based on cross-sample spatial regression analysis between fALFF reference-contrast maps of a premature-born adult and a given normative dopaminergic neurotransmission PET map. Error bars represent the parametric 95% confidence interval of the mean spatial RC. (b) Associations between spatial-RCs and IQ-values are shown as scatter plots. IQ is plotted on the y-axes and spatial-RCs on the x-axes. Linear regression lines, 90% confidence interval bands, correlation coefficients *r* and *p*-values were added. D1R, dopamine-1-receptor; D2/3R, dopamine-2/3-receptor; DAT, Dopamine transporter; fALFF, fractional amplitude of low-frequency fluctuations; FT, full-term; IQ, intelligence quotient; VP/VLBW, very preterm and/or very low birth weight.

were related to cognitive performance, emphasizing their functional relevance. Specificity analyses proved that the measured spatial neuromodulatory alterations were specific toward the dopaminergic neurotransmission but not for the used MRI measure (i.e., structural or functional MRI). Results indicate—to the best of our knowledge for the first time—a relationship between aberrant blood oxygenation fluctuations and dopaminergic neurotransmission in very premature-born adults. Data suggest impaired dopaminergic neurotransmission in adult prematurity, potentially due to altered development of the dopaminergic system after very premature birth.

4.1 | Indirect evidence for selectively altered D2/3R-availability in very premature-born adults

The main finding of our study was the selectively altered spatial-RCs for individual blood oxygenation fluctuation differences with respect to D2/3R-availability in premature-born adults (Figure 2).

We interpret this finding as indirect evidence for selectively altered dopaminergic neurotransmission in very premature-born adults (Boksa & El-Khodor, 2003; Froudist-Walsh et al., 2017; Henry et al., 1995; Kehoe et al., 1998; Lipska et al., 1993). First, significant spatial RCs reflect that for premature-born adults, individual difference maps of blood oxygenation fluctuations (more precisely of fractional amplitudes of such fluctuations) are associated with (i.e., do spatially correlate with) normative dopaminergic neurotransmission maps (namely D2/3R-availability). This suggests that blood oxygenation differences link to aspects of dopaminergic neurotransmission; this link is not general as it holds not for all tested aspects of dopaminergic neurotransmission but was specifically observed for D2/3R availability but not for D1R-availability and dopamine reuptake. As very premature-born adults indeed have significant changes in blood oxygenation fluctuations (Figure S2), one can infer that D2/3R availability might be relevant for these changes. Second, dopamine synthesis and storage have been demonstrated to be aberrant in human prematurity. More concretely, Froudist-Walsh et al. compared a small cohort of 16 very premature-born adults with perinatal damage to 13 very premature-born adults without perinatal damage and 14 control subjects using dopamine synthesis and storage PET (Froudist-Walsh et al., 2017). Only for very-premature-born adults

TABLE 2 Results of the spatial regression analysis for fALFF-differences between VP/VLBW and FT controls and dopaminergic neurotransmission maps.

Neurotransmission Maps	Tracer	Mean β coefficient	*p* value	Source
D1-receptor availability	(^{11}C)SCH23390	.006	.295	Kaller et al. (2017)
D2/3-receptor availability	(^{18}F)Fallypride	−.014	**.004**	Jaworska et al. (2020)
Dopamine reuptake	(^{123}I)FP-CIT	.008	.261	Dukart et al. (2018)

Note: Multiple spatial regression analysis for the co-localization of fALFF-differences between VP/VLBW and FT controls and the non-pathological distribution of specific dopaminergic neurotransmission systems (as derived from independent adult cohorts). Exact permutation-based *p* values (with 10,000 permutations) were computed. The threshold for statistical significance was set to $p < .05$.
Abbreviations: D1R, Dopamine receptor 1; D2/3R, Dopamine receptor 2 and 3; fALFF, fractional amplitude of low-frequency fluctuations; FT, full-term; VP/VLBW, very preterm and/or very low birthweight.

TABLE 3 Relationship between spatial multiple linear regression coefficients and birth-related variables and IQ, respectively.

Spatial-RC	Full-scale IQ	Gestational age	Birth weight
D2/3R-availability	−0.230 (***p* = .031**)	−0.086 ($p = .426$)	0.096 ($p = .371$)

Note: Two-tailed partial correlation analysis for the VP/VLBW group between beta coefficients—of spatial multiple linear regression analysis for VP/VLBW and FT controls—and full-scale IQ, gestational age, and birth weight, respectively. "Sex" and "age at scan" were included as covariates of no-interest. Bold letters indicate statistical significance defined as $p < .05$.

Abbreviations: D2/3R, Dopamine receptor 2 and 3; FT, full-term; IQ, intelligence quotient; RC, regression coefficient; VP/VLBW, very preterm and/or very low birthweight.

with perinatal brain damage, a reduction in striatal dopamine synthesis capacity and storage was demonstrated, suggesting impaired dopamine synthesis in at least subgroups of premature-born individuals. However, while this supports the notion of altered dopaminergic neurotransmission in premature-born adults, we did not include dopamine synthesis and storage PET in our indirect analyses because of insufficient cortical signal reliability of F-DOPA-PET which would have been necessary for our analyses. Third, dopaminergic neurotransmission influences blood oxygenation fluctuations (Dukart et al., 2018). For example, blood oxygenation fluctuations-derived measures are modulated by externally administered dopamine levels (Shafiei et al., 2019); stimulation of the dopaminergic ventral tegmental area in swine induces dopamine release that correlates with fMRI-based blood oxygenation-based amplitude changes (Settell et al., 2017). Fourth, critical phases of development of dopaminergic neurotransmission overlap with times of preterm birth and are highly vulnerable to hypoxic–ischemic events, which typically occur perinatally in prematurity. More concretely, prenatal development of dopaminergic neurotransmission occurs in distinct phases, beginning as early as the 6th–8th week of gestation with the emergence of first dopaminergic neurons (de Graaf-Peters & Hadders-Algra, 2006; Sundström et al., 1993). Especially in the last trimester, the period overlapping with premature birth, there are substantial developmental changes in the dopaminergic neurotransmission system. For example, there is a dramatic increase in the availability of both D1R and D2R across the forebrain, which leads to transient receptor densities 10–15-times larger than those in adulthood (Boyson & Adams, 1997). Furthermore, these developmental changes are highly vulnerable to hypoxic–ischemic events (Pagida et al., 2013), which co-occurring with premature birth.

Taking all these points together, our finding of significant spatial-RCs for individual blood oxygenation fluctuation differences with respect to D2/3R-availability is consistent with the notion of selectively aberrant dopaminergic neurotransmission in premature-born adults. It is clear that our indirect and correlative approach does not provide definitive evidence; further molecular imaging studies of dopaminergic neurotransmission, including the use of pharmacological aided examination, specifically focused on D2/3R-availability, validate our findings.

4.2 | Association of spatial-RCs and cognitive performance

The second main finding of our study was the association between significant spatial-RCs for D2/3R-availability with cognitive performance in very premature-born adults. Following the above-outlined interpretation of significant spatial-RCs, this result suggests that aberrant D2/3R-availability is relevant for cognitive performance in premature-born adults. In general, dopaminergic neurotransmission is critically involved in many aspects of cognitive functioning (Cools & D'Esposito, 2011; Klein et al., 2019; Sawaguchi & Goldman-Rakic, 1991; Williams & Goldman-Rakic, 1995). While there is consistent evidence for cognitive performance with respect to D1R-availability following an inverted U-shaped model (Cools et al., 2008; Gjedde et al., 2010; Weber et al., 2022), the functioning of D2-like receptors is more complex and much less understood, with some authors reporting a link between D2R-availability with cognitive performance while others demonstrated no association (Kellendonk et al., 2006; Klein et al., 2019; Lee et al., 2021; Vyas et al., 2018).

Indeed, very premature-born adults show on average lower general cognitive performance (on average about 12 points in IQ (Basten et al., 2015; Eves et al., 2021; Kroll et al., 2017; Volpe, 2009; Wolke et al., 2019)), aberrant dopaminergic neurotransmission might contribute to this deficit. However, beyond the definitive link between significant spatial-RC for D2/3R availability and cognitive performance, the current study can only indirectly support the relationship between aberrant D2/3R availability and IQ due to the indirect nature of spatial-RCs. Further molecular imaging studies in prematurity are required to test this link more directly.

4.3 | Strengths and Limitations

Some points should be carefully considered when interpreting the indirect approach of spatial co-localization of regional blood oxygenation fluctuations with normative PET maps of dopaminergic neurotransmission. First, while the large sample size (99 VP/VLBW and 107 FT adults) enhances the generalizability of our findings, the current sample is biased to VP/VLBW adults with less severe neonatal complications, as individuals with stronger birth complications and/or severe lasting impairments in the initial BLS sample were more likely to be excluded in the initial screening for MRI or to reject MRI scanning or even continuation in the study. Therefore, the indirectly measured altered dopaminergic neurotransmission in VP/VLBW adults is a conservative estimate of true difference, which might partly explain the small effect sizes for the altered spatial-RC and non-significant associations with BW and GA. Additionally, the used preprocessing protocol including PESTICA/SLOMOCO to account for both different slice acquisition time- and physiology-induced artifacts is rather strict.

Second, cross-sample spatial regression coefficients derived from fMRI and their relationship with variables of premature birth as well as cognitive performance is influenced by multiple other individual, social, and environmental factors. The rationale for using the approach to correlate fMRI-based signal and PET-derived measures is based on both high test–retest reliability shown in previous studies (e.g., rs-fMRI changes associated with D2 and 5-HT1b receptors in patients with Parkinson's disease by Dukart et al. (Dukart et al., 2021) and on a clear hypothesis for aberrant dopaminergic neurotransmission in premature-born adults by previous animal and human studies. Nevertheless, the results, in this case, should be interpreted with caution because of the general 'indirectness' of the approach. Fourth, as fMRI and therefore its derived metric fALFF has no intrinsic selectivity for specific aspects of neurotransmission, e.g., dopaminergic neurotransmission, our indirect approach of cross-sample regression analyses does not provide definitive evidence and must be interpreted carefully. Rather, it facilitates further molecular imaging studies in VP/VLBW adults, specifically focused on dopaminergic neurotransmission.

5 | CONCLUSION

In conclusion, our approach to study dopaminergic neurotransmission in prematurity via cross-sample spatial regression analysis of blood oxygenation fluctuation changes provides indirect evidence for altered dopaminergic neurotransmission in very premature-born adults. Results suggest specific studies about potentially aberrant dopamine-2/3-receptor availability in prematurity.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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REFERENCES

Ashburner, J. (2007). A fast diffeomorphic image registration algorithm. *NeuroImage*, *38*, 95–113.

Babu, P., & Stoica, P. (2010). Spectral analysis of nonuniformly sampled data—a review. *Digital Signal Processing*, *20*, 359–378.

Back, S. A., Han, B. H., Luo, N. L., Chricton, C. A., Xanthoudakis, S., Tam, J., Arvin, K. L., & Holtzman, D. M. (2002). Selective vulnerability of late oligodendrocyte progenitors to hypoxia–ischemia. *The Journal of Neuroscience*, *22*, 455–463.

Ball, G., Aljabar, P., Zebari, S., Tusor, N., Arichi, T., Merchant, N., Robinson, E. C., Ogundipe, E., Rueckert, D., Edwards, A. D., & Counsell, S. J. (2014). Rich-club organization of the newborn human brain. *Proceedings of the National Academy of Sciences of the United States of America*, *111*, 7456–7461.

Ball, G., Boardman, J. P., Rueckert, D., Aljabar, P., Arichi, T., Merchant, N., Gousias, I. S., Edwards, A. D., & Counsell, S. J. (2012). The effect of preterm birth on thalamic and cortical development. *Cerebral Cortex*, *22*, 1016–1024.

Ball, G., Pazderova, L., Chew, A., Tusor, N., Merchant, N., Arichi, T., Allsop, J. M., Cowan, F. M., Edwards, A. D., & Counsell, S. J. (2015). Thalamocortical connectivity predicts cognition in children born preterm. *Cerebral Cortex*, *25*, 4310–4318.

Ball, G., Srinivasan, L., Aljabar, P., Counsell, S. J., Durighel, G., Hajnal, J. V., Rutherford, M. A., & Edwards, A. D. (2013). Development of cortical microstructure in the preterm human brain. *Proceedings of the National Academy of Sciences of the United States of America*, *110*, 9541–9546.

Basten, M., Jaekel, J., Johnson, S., Gilmore, C., & Wolke, D. (2015). Preterm birth and adult wealth: Mathematics skills count. *Psychological Science*, *26*, 1608–1619.

Bäuml, J. G., Daamen, M., Meng, C., Neitzel, J., Scheef, L., Jaekel, J., Busch, B., Baumann, N., Bartmann, P., Wolke, D., Boecker, H., Wohlschläger, A. M., & Sorg, C. (2015). Correspondence between aberrant intrinsic network connectivity and gray-matter volume in the ventral brain of preterm born adults. *Cerebral Cortex*, *25*, 4135–4145.

Beall, E. B., & Lowe, M. J. (2007). Isolating physiologic noise sources with independently determined spatial measures. *NeuroImage*, *37*, 1286–1300.

Beall, E. B., & Lowe, M. J. (2014). SimPACE: generating simulated motion corrupted BOLD data with synthetic-navigated acquisition for the development and evaluation of SLOMOCO: a new, highly effective slicewise motion correction. *NeuroImage*, *101*, 21–34.

Boksa, P., & El-Khodor, B. F. (2003). Birth insult interacts with stress at adulthood to alter dopaminergic function in animal models: Possible implications for schizophrenia and other disorders. *Neuroscience & Biobehavioral Reviews*, *27*, 91–101.

Boyson, S. J., & Adams, C. E. (1997). D1 and D2Dopamine receptors in perinatal and adult basal ganglia. *Pediatric Research*, *41*, 822–831.

Burt, J. B., Helmer, M., Shinn, M., Anticevic, A., & Murray, J. D. (2020). Generative modeling of brain maps with spatial autocorrelation. *NeuroImage*, *220*, 117038.

Buser, J. R., Maire, J., Riddle, A., Gong, X., Nguyen, T., Nelson, K., Luo, N. L., Ren, J., Struve, J., Sherman, L. S., Miller, S. P., Chau, V., Hendson, G., Ballabh, P., Grafe, M. R., & Back, S. A. (2012). Arrested preoligodendrocyte maturation contributes to myelination failure in premature infants. *Annals of Neurology*, *71*, 93–109.

Chao-Gan, Y., & Yu-Feng, Z. (2010). DPARSF: A MATLAB toolbox for "Pipeline" data analysis of resting-state fMRI. *Frontiers in Systems Neuroscience*, *4*, 13.

Chawanpaiboon, S., Vogel, J. P., Moller, A.-B., Lumbiganon, P., Petzold, M., Hogan, D., Landoulsi, S., Jampathong, N., Kongwattanakul, K., Laopaiboon, M., Lewis, C., Rattanakanokchai, S., Teng, D. N., Thinkhamrop, J., Watananirun, K., Zhang, J., Zhou, W., & Gülmezoglu, A. M. (2019). Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *The Lancet Global Health*, *7*, e37–e46.

Chen, J., Müller, V. I., Dukart, J., Hoffstaedter, F., Baker, J. T., Holmes, A. J., Vatansever, D., Nickl-Jockschat, T., Liu, X., Derntl, B., Kogler, L., Jardri, R., Gruber, O., Aleman, A., Sommer, I. E., Eickhoff, S. B., & Patil, K. R. (2021). Intrinsic connectivity patterns of task-defined brain networks allow individual prediction of cognitive symptom dimension of schizophrenia and are linked to molecular architecture. *Biological Psychiatry*, *89*, 308–319.

Cools, R., & D'Esposito, M. (2011). Inverted-U–shaped dopamine actions on human working memory and cognitive control. *Biological Psychiatry*, *69*, e113–e125.

Cools, R., Gibbs, S. E., Miyakawa, A., Jagust, W., & D'Esposito, M. (2008). Working memory capacity predicts dopamine synthesis capacity in the human striatum. *Journal of Neuroscience*, *28*, 1208–1212.

Daamen, M., Bäuml, J. G., Scheef, L., Meng, C., Jurcoane, A., Jaekel, J., Sorg, C., Busch, B., Baumann, N., Bartmann, P., Wolke, D., Wohlschläger, A., & Boecker, H. (2015). Neural correlates of executive attention in adults born very preterm. *NeuroImage: Clinical*, *9*, 581–591.

Daamen, M., Bäuml, J. G., Scheef, L., Sorg, C., Busch, B., Baumann, N., Bartmann, P., Wolke, D., Wohlschläger, A., & Boecker, H. (2015). Working memory in preterm-born adults: load-dependent compensatory activity of the posterior default mode network. *Human Brain Mapping*, *36*, 1121–1137.

Damaraju, E., Phillips, J. R., Lowe, J. R., Ohls, R., Calhoun, V. D., & Caprihan, A. (2010). Resting-state functional connectivity differences in premature children. *Frontiers in Systems Neuroscience*, *4*, 23.

de Graaf-Peters, V. B., & Hadders-Algra, M. (2006). Ontogeny of the human central nervous system: What is happening when? *Early Human Development*, *82*, 257–266.

Deng, W. (2010). Neurobiology of injury to the developing brain. *Nature Reviews. Neurology*, *6*, 328–336.

Dipasquale, O., Selvaggi, P., Veronese, M., Gabay, A. S., Turkheimer, F., & Mehta, M. A. (2019). Receptor-Enriched Analysis of functional connectivity by targets (REACT): A novel, multimodal analytical approach informed by PET to study the pharmacodynamic response of the brain under MDMA. *NeuroImage*, *195*, 252–260.

D'Onofrio, B. M., Class, Q. A., Rickert, M. E., Larsson, H., Långström, N., & Lichtenstein, P. (2013). Preterm birth and mortality and morbidity: A population-based quasi-experimental study. *JAMA Psychiatry*, *70*, 1231–1240.

Doria, V., Beckmann, C. F., Arichi, T., Merchant, N., Groppo, M., Turkheimer, F. E., Counsell, S. J., Murgasova, M., Aljabar, P., Nunes, R. G., Larkman, D. J., Rees, G., & Edwards, A. D. (2010). Emergence of resting state networks in the preterm human brain. *Proceedings of the National Academy of Sciences of the United States of America*, *107*, 20015–20020.

Dubowitz, L. M. S., Dubowitz, V., & Goldberg, C. (1970). Clinical assessment of gestational age in the newborn infant. *The Journal of Pediatrics*, *77*, 1–10.

Dugré, J. R., & Potvin, S. (2022). The origins of evil: From lesions to the functional architecture of the antisocial brain. *Frontiers in Psychiatry*, *13*, 969206.

Dukart, J., Holiga, Š., Chatham, C., Hawkins, P., Forsyth, A., McMillan, R., Myers, J., Lingford-Hughes, A. R., Nutt, D. J., Merlo-Pich, E., Risterucci, C., Boak, L., Umbricht, D., Schobel, S., Liu, T., Mehta, M. A., Zelaya, F. O., Williams, S. C., Brown, G., … Sambataro, F. (2018). Cerebral blood flow predicts differential neurotransmitter activity. *Scientific Reports*, *8*, 4074.

Dukart, J., Holiga, S., Rullmann, M., Lanzenberger, R., Hawkins, P. C. T., Mehta, M. A., Hesse, S., Barthel, H., Sabri, O., Jech, R., & Eickhoff, S. B. (2021). JuSpace: A tool for spatial correlation analyses of magnetic resonance imaging data with nuclear imaging derived neurotransmitter maps. *Human Brain Mapping*, *42*, 555–566.

Eikenes, L., Løhaugen, G. C., Brubakk, A.-M., Skranes, J., & Håberg, A. K. (2011). Young adults born preterm with very low birth weight demonstrate widespread white matter alterations on brain DTI. *NeuroImage*, *54*, 1774–1785.

Eves, R., Mendonça, M., Baumann, N., Ni, Y., Darlow, B. A., Horwood, J., Woodward, L. J., Doyle, L. W., Cheong, J., Anderson, P. J., Bartmann, P., Marlow, N., Johnson, S., Kajantie, E., Hovi, P., Nosarti, C., Indredavik, M. S., Evensen, K. A. I., Räikkönen, K., … Wolke, D. (2021). Association of very preterm birth or very low birth weight with intelligence in adulthood: An individual participant data meta-analysis. *JAMA Pediatrics*, *175*, e211058.

Farajdokht, F., Sadigh-Eteghad, S., Dehghani, R., Mohaddes, G., Abedi, L., Bughchechi, R., Majdi, A., & Mahmoudi, J. (2017). Very low birth weight is associated with brain structure abnormalities and cognitive function impairments: A systematic review. *Brain and Cognition*, *118*, 80–89.

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J., Frith, C. D., & Frackowiak, R. S. (1994). Statistical parametric maps in functional imaging: a general linear approach. *Human Brain Mapping*, *2*, 189–210.

Friston, K. J., Williams, S., Howard, R., Frackowiak, R. S. J., & Turner, R. (1996). Movement-related effects in fMRI time-series: Movement artifacts in fMRI. *Magnetic Resonance in Medicine*, *35*, 346–355.

Froudist-Walsh, S., Bloomfield, M. A., Veronese, M., Kroll, J., Karolis, V. R., Jauhar, S., Bonoldi, I., McGuire, P. K., Kapur, S., Murray, R. M., & Nosarti, C. (2017). The effect of perinatal brain injury on dopaminergic function and hippocampal volume in adult life. *eLife*, *6*, e29088.

Froudist-Walsh, S., Karolis, V., Caldinelli, C., Brittain, P. J., Kroll, J., Rodríguez-Toscano, E., Tesse, M., Colquhoun, M., Howes, O., Dell'Acqua, F., Thiebaut de Schotten, M., Murray, R. M., Williams, S. C. R., & Nosarti, C. (2015). Very early brain damage leads to remodeling of the working memory system in adulthood: A combined fMRI/tractography study. *The Journal of Neuroscience*, *35*, 15787–15799.

Fulcher, B. D., Arnatkeviciute, A., & Fornito, A. (2021). Overcoming false-positive gene-category enrichment in the analysis of spatially resolved transcriptomic brain atlas data. *Nature Communications*, *12*, 2669.

Gjedde, A., Kumakura, Y., Cumming, P., Linnet, J., & Møller, A. (2010). Inverted-U-shaped correlation between dopamine receptor availability in striatum and sensation seeking. *Proceedings of the National Academy of Sciences of the United States of America*, *107*, 3870–3875.

Glover, G. H., Li, T. Q., & Ress, D. (2000). Image-based method for retrospective correction of physiological motion effects in fMRI: RETROICOR. *Magnetic Resonance in Medicine*, *44*, 162–167.

Grothe, M. J., Scheef, L., Bäuml, J., Meng, C., Daamen, M., Baumann, N., Zimmer, C., Teipel, S., Bartmann, P., Boecker, H., Wolke, D., Wohlschläger, A., & Sorg, C. (2017). Reduced cholinergic basal forebrain integrity links neonatal complications and adult cognitive deficits after premature birth. *Biological Psychiatry*, *82*, 119–126.

Han, S., Zheng, R., Li, S., Zhou, B., Jiang, Y., Wang, C., Wei, Y., Pang, J., Li, H., Zhang, Y., Chen, Y., & Cheng, J. (2022). Integrative functional, molecular, and transcriptomic analyses of altered intrinsic timescale gradient in depression. *Frontiers in Neuroscience*, *16*, 826609.

Hasler, H. M., Brown, T. T., & Akshoomoff, N. (2019). Variations in brain morphometry among healthy preschoolers born preterm. *Early Human Development*, *140*, 104929.

Hedderich, D. M., Bäuml, J. G., Berndt, M. T., Menegaux, A., Scheef, L., Daamen, M., Zimmer, C., Bartmann, P., Boecker, H., Wolke, D., Gaser, C., & Sorg, C. (2019). Aberrant gyrification contributes to the link between gestational age and adult IQ after premature birth. *Brain*, *142*, 1255–1269.

Hedderich, D. M., Bäuml, J. G., Menegaux, A., Avram, M., Daamen, M., Zimmer, C., Bartmann, P., Scheef, L., Boecker, H., Wolke, D., Gaser, C., & Sorg, C. (2020). An analysis of MRI derived cortical complexity in premature-born adults: Regional patterns, risk factors, and potential significance. *NeuroImage*, *208*, 116438.

Henry, C., Guegant, G., Cador, M., Arnauld, E., Arsaut, J., Moal, M. L., & Demotes-Mainard, J. (1995). Prenatal stress in rats facilitates amphetamine-induced sensitization and induces long-lasting changes in dopamine receptors in the nucleus accumbens. *Brain Research*, *685*, 179–186.

Howson, C. P., Kinney, M. V., McDougall, L., Lawn, J. E., & Born Too Soon Preterm Birth Action Group. (2013). Born too soon: preterm birth matters. *Reproductive Health*, *10*(Suppl 1), S1.

Jaworska, N., Cox, S. M. L., Tippler, M., Castellanos-Ryan, N., Benkelfat, C., Parent, S., Dagher, A., Vitaro, F., Boivin, M., Pihl, R. O., Côté, S. M., Tremblay, R. E., Séguin, J. R., & Leyton, M. (2020). Extra-striatal D2/3 receptor availability in youth at risk for addiction. *Neuropsychopharmacology*, *45*, 1498–1505.

Kaller, S., Rullmann, M., Patt, M., Becker, G.-A., Luthardt, J., Girbardt, J., Meyer, P. M., Werner, P., Barthel, H., Bresch, A., Fritz, T. H., Hesse, S., & Sabri, O. (2017). Test–retest measurements of dopamine D1-type receptors using simultaneous PET/MRI imaging. *European Journal of Nuclear Medicine and Molecular Imaging*, *44*, 1025–1032.

Kanold, P. O., & Luhmann, H. J. (2010). The subplate and early cortical circuits. *Annual Review of Neuroscience*, *33*, 23–48.

Karolis, V. R., Froudist-Walsh, S., Kroll, J., Brittain, P. J., Tseng, C.-E. J., Nam, K.-W., Reinders, A. A. T. S., Murray, R. M., Williams, S. C. R., Thompson, P. M., & Nosarti, C. (2017). Volumetric grey matter alterations in adolescents and adults born very preterm suggest accelerated brain maturation. *NeuroImage*, *163*, 379–389.

Kehoe, P., Shoemaker, W. J., Arons, C., Triano, L., & Suresh, G. (1998). Repeated isolation stress in the neonatal rat: Relation to brain dopamine systems in the 10-day-old rat. *Behavioral Neuroscience*, *112*, 1466–1474.

Kellendonk, C., Simpson, E. H., Polan, H. J., Malleret, G., Vronskaya, S., Winiger, V., Moore, H., & Kandel, E. R. (2006). Transient and selective overexpression of dopamine D2 receptors in the striatum causes persistent abnormalities in prefrontal cortex functioning. *Neuron*, *49*, 603–615.

Kinney, H. C., Haynes, R. L., Xu, G., Andiman, S. E., Folkerth, R. D., Sleeper, L. A., & Volpe, J. J. (2012). Neuron deficit in the white matter and subplate in periventricular leukomalacia. *Annals of Neurology*, *71*, 397–406.

Klein, M. O., Battagello, D. S., Cardoso, A. R., Hauser, D. N., Bittencourt, J. C., & Correa, R. G. (2019). Dopamine: Functions, signaling, and association with neurological diseases. *Cellular and Molecular Neurobiology*, *39*, 31–59.

Kostović, I., Jovanov-Milošević, N., Radoš, M., Sedmak, G., Benjak, V., Kostović-Srzentić, M., Vasung, L., Čuljat, M., Radoš, M., Hüppi, P., & Judaš, M. (2014). Perinatal and early postnatal reorganization of the subplate and related cellular compartments in the human cerebral wall as revealed by histological and MRI approaches. *Brain Structure & Function*, *219*, 231–253.

Kroll, J., Karolis, V., Brittain, P. J., Tseng, C.-E. J., Froudist-Walsh, S., Murray, R. M., & Nosarti, C. (2017). Real-life impact of executive function impairments in adults who were born very preterm. *Journal of the International Neuropsychological Society*, *23*, 381–389.

Lee, M., Fatouros-Bergman, H., Plavén-Sigray, P., Ikonen Victorsson, P., Sellgren, C. M., Erhardt, S., Flyckt, L., Farde, L., & Cervenka, S. (2021). No association between cortical dopamine D2 receptor availability and cognition in antipsychotic-naive first-episode psychosis. *NPJ Schizophrenia*, *7*, 46.

Li, G., Chen, Z., Zhou, L., Yao, M., Luo, N., Kang, W., Chen, S., & Liu, J. (2020). Abnormal intrinsic brain activity of the putamen is correlated with dopamine deficiency in idiopathic rapid eye movement sleep behavior disorder. *Sleep Medicine*, *75*, 73–80.

Lipska, B. K., Jaskiw, G. E., & Weinberger, D. R. (1993). Postpubertal emergence of hyperresponsiveness to stress and to amphetamine after neonatal excitotoxic hippocampal damage: A potential animal model of schizophrenia. *Neuropsychopharmacology*, *9*, 67–75.

Lubsen, J., Vohr, B., Myers, E., Hampson, M., Lacadie, C., Schneider, K. C., Katz, K. H., Constable, R. T., & Ment, L. R. (2011). Microstructural and functional connectivity in the developing preterm brain. *Seminars in Perinatology*, *35*, 34–43.

Martins, D., Giacomel, A., Williams, S. C. R., Turkheimer, F., Dipasquale, O., Veronese, M., & PET Templates Working Group. (2021). Imaging transcriptomics: Convergent cellular, transcriptomic, and molecular neuroimaging signatures in the healthy adult human brain. *Cell Reports*, *37*, 110173.

Martins, D., Veronese, M., Turkheimer, F. E., Howard, M. A., Williams, S. C. R., & Dipasquale, O. (2022). A candidate neuroimaging biomarker for detection of neurotransmission-related functional alterations and prediction of pharmacological analgesic response in chronic pain. *Brain Communications*, *4*, fcab302.

McClendon, E., Shaver, D. C., Degener-O'Brien, K., Gong, X., Nguyen, T., Hoerder-Suabedissen, A., Molnár, Z., Mohr, C., Richardson, B. D., Rossi, D. J., & Back, S. A. (2017). Transient hypoxemia chronically disrupts maturation of preterm fetal ovine subplate neuron arborization and activity. *The Journal of Neuroscience*, *37*, 11912–11929.

Menegaux, A., Hedderich, D. M., Bäuml, J. G., Manoliu, A., Daamen, M., Berg, R. C., Preibisch, C., Zimmer, C., Boecker, H., Bartmann, P., Wolke, D., Sorg, C., & Stämpfli, P. (2020). Reduced apparent fiber density in the white matter of premature-born adults. *Scientific Reports*, *10*, 17214.

Meng, C., Bäuml, J. G., Daamen, M., Jaekel, J., Neitzel, J., Scheef, L., Busch, B., Baumann, N., Boecker, H., Zimmer, C., Bartmann, P., Wolke, D., Wohlschläger, A. M., & Sorg, C. (2016). Extensive and interrelated subcortical white and gray matter alterations in preterm-born adults. *Brain Structure & Function*, *221*, 2109–2121.

Molz, C., Schulze, R., Schroeders, U., & Wilhelm, O. (2010). Wechsler Intelligenztest für Erwachsene WIE. Deutschsprachige Bearbeitung und Adaptation des WAIS-III von David Wechsler. *Psychologische Rundschau*, *61*, 229–230.

Northam, G. B., Liégeois, F., Chong, W. K., Wyatt, J. S., & Baldeweg, T. (2011). Total brain white matter is a major determinant of IQ in adolescents born preterm. *Annals of Neurology*, *69*, 702–711.

Nosarti, C., Giouroukou, E., Healy, E., Rifkin, L., Walshe, M., Reichenberg, A., Chitnis, X., Williams, S. C. R., & Murray, R. M. (2008). Grey and white matter distribution in very preterm adolescents mediates neurodevelopmental outcome. *Brain*, *131*, 205–217.

Nosarti, C., Nam, K. W., Walshe, M., Murray, R. M., Cuddy, M., Rifkin, L., & Allin, M. P. G. (2014). Preterm birth and structural brain alterations in early adulthood. *NeuroImage: Clinical*, *6*, 180–191.

Nosarti, C., Reichenberg, A., Murray, R. M., Cnattingius, S., Lambe, M. P., Yin, L., MacCabe, J., Rifkin, L., & Hultman, C. M. (2012). Preterm birth and psychiatric disorders in young adult life. *Archives of General Psychiatry*, *69*, E1–E8. https://doi.org/10.1001/archgenpsychiatry.2011.1374

Nugent, A. C., Martinez, A., D'Alfonso, A., Zarate, C. A., & Theodore, W. H. (2015). The relationship between glucose metabolism, resting-state fMRI BOLD signal, and GABA $_A$-binding potential: A preliminary study in healthy subjects and those with temporal lobe epilepsy. *Journal of Cerebral Blood Flow and Metabolism*, *35*, 583–591.

Oldehinkel, M., Llera, A., Faber, M., Huertas, I., Buitelaar, J. K., Bloem, B. R., Marquand, A. F., Helmich, R. C., Haak, K. V., & Beckmann, C. F. (2022). Mapping dopaminergic projections in the human brain with resting-state fMRI. *eLife*, *11*, e71846.

Pagida, M. A., Konstantinidou, A. E., Tsekoura, E., Mangoura, D., Patsouris, E., & Panayotacopoulou, M. T. (2013). Vulnerability of the mesencephalic dopaminergic neurons of the human neonate to prolonged perinatal hypoxia: an immunohistochemical study of tyrosine hydroxylase expression in autopsy material. *Journal of Neuropathology and Experimental Neurology*, *72*, 337–350.

Park, B., Kebets, V., Larivière, S., Hettwer, M. D., Paquola, C., van Rooij, D., Buitelaar, J., Franke, B., Hoogman, M., Schmaal, L., Veltman, D. J., van den Heuvel, O. A., Stein, D. J., Andreassen, O. A., Ching, C. R. K., Turner, J. A., van Erp, T. G. M., Evans, A. C., Dagher, A., … Bernhardt, B. C. (2022). Multiscale neural gradients reflect transdiagnostic effects of major psychiatric conditions on cortical morphology. *Communications Biology*, *5*, 1024.

Pascoe, M. J., Melzer, T. R., Horwood, L. J., Woodward, L. J., & Darlow, B. A. (2019). Altered grey matter volume, perfusion and white matter integrity in very low birthweight adults. *NeuroImage: Clinical*, *22*, 101780.

Pierson, C. R., Folkerth, R. D., Billiards, S. S., Trachtenberg, F. L., Drinkwater, M. E., Volpe, J. J., & Kinney, H. C. (2007). Gray matter injury associated with periventricular leukomalacia in the premature infant. *Acta Neuropathologica*, *114*, 619–631.

Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage*, *59*, 2142–2154.

Saigal, S., & Doyle, L. W. (2008). An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet*, *371*, 261–269.

Sakreida, K., Chiu, W.-H., Dukart, J., Eickhoff, S. B., Frodl, T., Gaser, C., Landgrebe, M., Langguth, B., Mirlach, D., Rautu, I. S., Wittmann, M., & Poeppl, T. B. (2022). Disentangling dyskinesia from parkinsonism in motor structures of patients with schizophrenia. *Brain Communications*, *4*, fcac190.

Salmaso, N., Jablonska, B., Scafidi, J., Vaccarino, F. M., & Gallo, V. (2014). Neurobiology of premature brain injury. *Nature Neuroscience*, *17*, 341–346.

Sawaguchi, T., & Goldman-Rakic, P. S. (1991). D1 dopamine receptors in prefrontal cortex: Involvement in working memory. *Science*, *251*, 947–950.

Schmitz-Koep, B., Bäuml, J. G., Menegaux, A., Nuttall, R., Zimmermann, J., Schneider, S. C., Daamen, M., Scheef, L., Boecker, H., Zimmer, C., Gaser, C., Wolke, D., Bartmann, P., Sorg, C., & Hedderich, D. M. (2020). Decreased cortical thickness mediates the relationship between premature birth and cognitive performance in adulthood. *Human Brain Mapping*, *41*, 4952–4963.

Schmitz-Koep, B., Menegaux, A., Gaser, C., Brandes, E., Schinz, D., Thalhammer, M., Daamen, M., Boecker, H., Zimmer, C., Priller, J., Wolke, D., Bartmann, P., Sorg, C., & Hedderich, D. M. (2023). Altered gray matter cortical and subcortical T1-weighted/T2-weighted ratio in premature-born adults. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *8*, 495–504.

Settell, M. L., Testini, P., Cho, S., Lee, J. H., Blaha, C. D., Jo, H. J., Lee, K. H., & Min, H. K. (2017). Functional circuitry effect of ventral tegmental area deep brain stimulation: imaging and neurochemical evidence of mesocortical and mesolimbic pathway modulation. *Frontiers in Neuroscience*, *11*, 104. https://doi.org/10.3389/fnins.2017.00104

Shafiei, G., Zeighami, Y., Clark, C. A., Coull, J. T., Nagano-Saito, A., Leyton, M., Dagher, A., & Mišic, B. (2019). Dopamine signaling modulates the stability and integration of intrinsic brain networks. *Cerebral Cortex*, *29*, 397–409. https://doi.org/10.1101/252528

Shang, J., Bäuml, J. G., Koutsouleris, N., Daamen, M., Baumann, N., Zimmer, C., Bartmann, P., Boecker, H., Wolke, D., & Sorg, C. (2018). Decreased BOLD fluctuations in lateral temporal cortices of premature born adults. *Human Brain Mapping*, *39*, 4903–4912.

Skranes, J., Løhaugen, G. C. C., Martinussen, M., Håberg, A., Brubakk, A.-M., & Dale, A. M. (2013). Cortical surface area and IQ in very-low-birth-weight (VLBW) young adults. *Cortex*, *49*, 2264–2271.

Skranes, J., Vangberg, T. R., Kulseng, S., Indredavik, M. S., Evensen, K. I., Martinussen, M., Dale, A. M., Haraldseth, O., & Brubakk, A. M. (2007). Clinical findings and white matter abnormalities seen on diffusion tensor imaging in adolescents with very low birth weight. *Brain*, *130*, 654–666.

Smyser, C. D., Inder, T. E., Shimony, J. S., Hill, J. E., Degnan, A. J., Snyder, A. Z., & Neil, J. J. (2010). Longitudinal analysis of neural network development in preterm infants. *Cerebral Cortex*, *20*, 2852–2862.

Sundström, E., Kölare, S., Souverbic, F., Samuelsson, E.-B., Pschera, H., Lunell, N.-O., & Seiger, Å. (1993). Neurochemical differentiation of human bulbospinal monoaminergic neurons during the first trimester. *Developmental Brain Research*, *75*, 1–12.

Tang, C., Ren, P., Ma, K., Li, S., Wang, X., Guan, Y., Zhou, J., Li, T., Liang, X., & Luan, G. (2022). The correspondence between morphometric MRI and metabolic profile in Rasmussen's encephalitis. *NeuroImage: Clinical*, *33*, 102918.

Van Dijk, K. R. A., Sabuncu, M. R., & Buckner, R. L. (2012). The influence of head motion on intrinsic functional connectivity MRI. *NeuroImage*, *59*, 431–438.

Verney, C., Milosevic, A., Alvarez, C., & Berger, B. (1993). Immunocytochemical evidence of well-developed dopaminergic and noradrenergic innervations in the frontal cerebral cortex of human fetuses at midgestation. *The Journal of Comparative Neurology*, *336*, 331–344.

Volpe, J. J. (2009). Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. *Lancet Neurology*, *8*, 110–124.

Vyas, N. S., Buchsbaum, M. S., Lehrer, D. S., Merrill, B. M., DeCastro, A., Doninger, N. A., Christian, B. T., & Mukherjee, J. (2018). D2/D3 dopamine receptor binding with [F-18]fallypride correlates of executive function in medication-naïve patients with schizophrenia. *Schizophrenia Research*, *192*, 442–456.

Weber, M. A., Conlon, M. M., Stutt, H. R., Wendt, L., Ten Eyck, P., & Narayanan, N. S. (2022). Quantifying the inverted U: A meta-analysis of prefrontal dopamine, D1 receptors, and working memory. *Behavioral Neuroscience*, *136*, 207–218.

White, T. P., Symington, I., Castellanos, N. P., Brittain, P. J., Froudist Walsh, S., Nam, K.-W., Sato, J. R., Allin, M. P. G., Shergill, S. S., Murray, R. M., Williams, S. C. R., & Nosarti, C. (2014). Dysconnectivity of neurocognitive networks at rest in very-preterm born adults. *NeuroImage: Clinical*, *4*, 352–365.

WHO. (1977). WHO: Recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976. *Acta Obstetricia et Gynecologica Scandinavica*, *56*, 247–253.

Williams, G. V., & Goldman-Rakic, P. S. (1995). Modulation of memory fields by dopamine Dl receptors in prefrontal cortex. *Nature*, *376*, 572–575.

Wolke, D., Johnson, S., & Mendonça, M. (2019). The life course consequences of very preterm birth. *Annual Review of Developmental Psychology*, *1*, 69–92.

Wolke, D., & Meyer, R. (1999). Cognitive status, language attainment, and prereading skills of 6-year-old very preterm children and their peers: the Bavarian longitudinal study. *Developmental Medicine and Child Neurology*, *41*, 94–109.

Wolke, D., Ratschinski, G., Ohrt, B., & Riegel, K. (1994). The cognitive outcome of very preterm infants may be poorer than often reported: An empirical investigation of how methodological issues make a big difference. *European Journal of Pediatrics*, *153*, 906–915.

Xu, Z., Xia, M., Wang, X., Liao, X., Zhao, T., & He, Y. (2022). Meta-connectomic analysis maps consistent, reproducible, and transcriptionally relevant functional connectome hubs in the human brain. *Communications Biology*, *5*, 1056.

Yan, C-G., Cheung, B., Kelly, C., Colcombe, S., Craddock, R. C., Di Martino, A., Li, Q., Zuo, X-N., Castellanos, F. X., & Milham, M. P. (2010). DPARSF: a MATLAB toolbox for "pipeline" data analysis of resting-state fMRI. *Frontiers in Systems Neuroscience*, *4*, 13. https://doi.org/10.3389/fnsys.2010.00013

Yan, C.-G., Cheung, B., Kelly, C., Colcombe, S., Craddock, R. C., Di Martino, A., Li, Q., Zuo, X.-N., Castellanos, F. X., & Milham, M. P. (2013). A comprehensive assessment of regional variation in the impact of head micromovements on functional connectomics. *NeuroImage*, *76*, 183–201.

Zarkali, A., Luppi, A. I., Stamatakis, E. A., Reeves, S., McColgan, P., Leyland, L.-A., Lees, A. J., & Weil, R. S. (2022). Changes in dynamic transitions between integrated and segregated states underlie visual hallucinations in Parkinson's disease. *Communications Biology*, *5*, 928.

Zou, Q.-H., Zhu, C.-Z., Yang, Y., Zuo, X.-N., Long, X.-Y., Cao, Q.-J., Wang, Y. F., & Zang, Y. F. (2008). An improved approach to detection of amplitude of low-frequency fluctuation (ALFF) for resting-state fMRI: Fractional ALFF. *Journal of Neuroscience Methods*, *172*, 137–141.

SUPPORTING INFORMATION

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