# The developing Human Connectome Project automated functional processing framework for neonates

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Abstract Submission

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**Introduction:**

The developing Human Connectome Project (dHCP) is a large-scale imaging project that aims to create a detailed 4-dimensional connectome of the developmental period spanning 20 to 44 weeks post-menstrual age (PMA), recording structural, diffusion and functional MRI measures in over 1000 in- and ex-utero subjects. Neonates present significant challenges to data processing due to low and variable contrast and high levels of head motion. This abstract presents the latest features to be incorporated into the fMRI processing framework for neonates. Specifically, dynamic distortion correction, multimodal registration to standard space, neonatal HRF prior for estimating RSNs, improved FIX training, and a new automated QC framework.

**Methods:**

Imaging was acquired at St. Thomas Hospital, London, on a Philips 3T scanner. High temporal resolution fMRI optimized for neonates [Price et al., 2015] used MB9 accelerated echo-planar imaging and was collected for 15 minutes, TE/TR=38/392ms, 2300 volumes, with an acquired resolution of 2.15mm isotropic.

Distortion and motion correction now incorporates slice-to-volume (S2V; Fig. 1a) correction to mitigate intra-volume movement (EDDY [Andersson et al., 2016]) and dynamic distortion correction (DDC) to correct time-varying susceptibility-induced distortions due to subject movement [Andersson et al., 2001].

The standard space is defined as the 40-week template from the Gousias atlas [Gousias et al., 2012], which contains T1/T2 volumetric templates per week from 28-44 weeks PMA. We have augmented it with week-to-week nonlinear transforms estimated using a diffeomorphic multi-modal (T1/T2) registration (ANTs SyN [Avants et al., 2008]).

Functional-to-structural registration is performed in 2-stages: (1) linear registration (6-dof) of the multiband EPI to a single-band EPI (SBref), and (2) boundary-based registration of the SBref to the T2 structural.

Standard-to-structural registration is performed with a multimodal non-linear registration (ANTs SyN) of the age-appropriate T1/T2 template to the subjects T1/T2 structural, which is then combined with the appropriate atlas week-to-week warps to yield a (40wk) standard-to-structural warp.

ICA denoising is performed using FIX [Salimi-Khorshidi et al., 2014], pre-trained on manually-labelled data from 25 subjects, to identify artefactual ICs (median TPR=100%, median TNR=95.4%).

Group-average RSNs are identified with PROFUMO[Harrison et al., 2015], a Bayesian framework that identifies probabilistic functional modes using constraints associated with the neonatal hemodynamic response function [Arichi et al., 2012] and inter-subject variability.

The pipeline incorporates a new automated QC which compares numerous individual subject quality metrics reflecting different stages of the pipeline against the population distribution and flags outliers for manual inspection (Fig. 1b).

**Results:**

We assessed the pipeline on a subset of 40 subjects. S2V correction significantly ($p<0.001$) improves SNR compared to traditional rigid-body motion correction (Fig. 1c), and DDC further improves SNR in anterior and posterior areas where susceptibility distortions are expected. There was significant additional improvement ($p<0.001$) in SNR after ICA denoising (Fig. 1d).

PROFUMO was performed on 267 subjects (aged 37-44 weeks PMA), and 13 RSNs that correspond qualitatively to known adult [Smith et al., 2009] and neonate [Doria et al., 2010] RSNs (Fig. 2) were resolved with fine spatial detail. Previous revisions of the framework could only resolve 9 reliable RSNs.

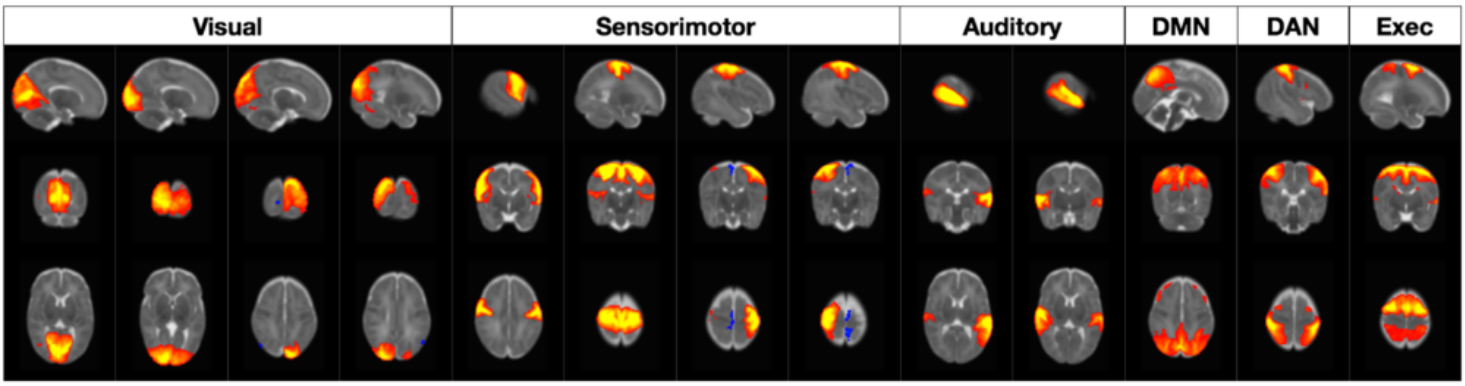


**Figure 2.** PROFUMO modes assessed as corresponding to adult visual, sensorimotor, auditory, default mode network (DMN), executive control (EC), and dorsal attentional network (DAN) resting-state networks

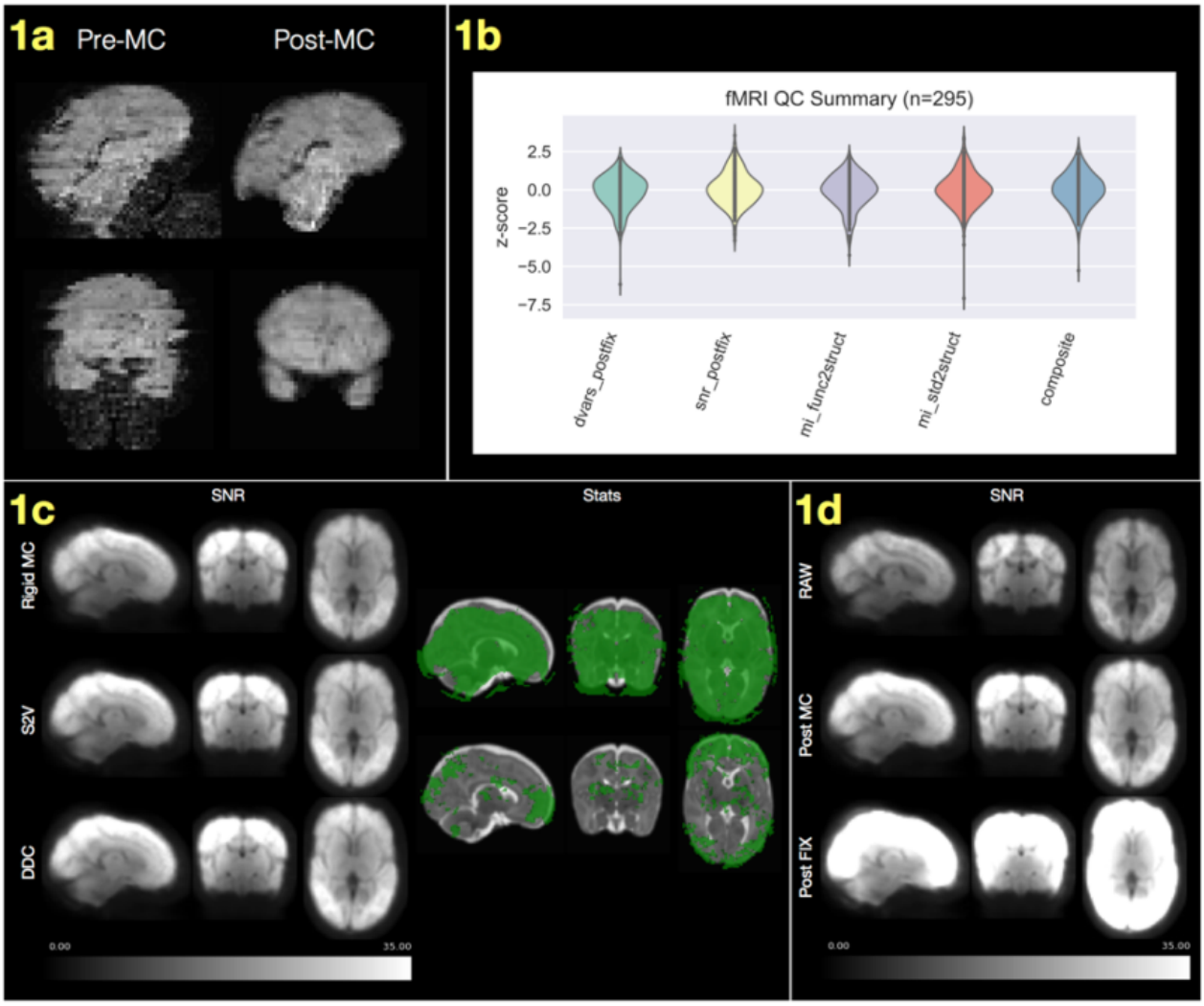


**Figure 1 (1a)** Exemplar single-volume of an EPI from a single-subject with intravolume movement before (Pre-MC) and after S2V correction (Post-MC) **(1b)** fMRI QC group summary metrics for 295 subjects. Any z-scores more negative than -3 are flagged as outliers for manual inspection. **(1c)** Left: mean SNR (N=40) for rigid-body motion correction (Rigid-MC), slice-to-volume motion correction (S2V), and S2V + dynamic distortion correction (DDC). Right: p-values ($p<0.001$) for S2V SNR minus Rigid-MC SNR (upper) and DDC SNR minus S2V SNR (lower). **(1d)** Mean SNR (N=40) for raw (RAW), motion and distortion corrected (post-MC) and the ICA-denoised (Post-FIX) functional. Post-MC SNR is significantly > RAW, and post-FIX SNR is significantly > post-MC at most brain voxels ($p<0.001$).

**Conclusions:**

Processing refinements integrated into the dHCP fMRI framework provide substantial reduction in movement related distortions, resulting in significant improvements in SNR, and detection of high quality RSNs from neonates. Ongoing analyses are probing the fine structure of these networks, and their variability across subjects and age, with the aim of defining a multi-modal time-varying map of the neonatal connectome.

**Imaging Methods:**

BOLD fMRI [2]

**Lifespan Development:**

Normal Brain Development: Fetus to Adolescence [1]

**Modeling and Analysis Methods:**

Methods Development
Motion Correction and Preprocessing

**Keywords:**

Development
FUNCTIONAL MRI

[1|2]Indicates the priority used for review

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**Please indicate which methods were used in your research:**

Functional MRI

**For human MRI, what field strength scanner do you use?**

3.0T

**Which processing packages did you use for your study?**

FSL

**Provide references using author date format**

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