# Automated processing pipeline for neonatal diffusion MRI in the developing Human Connectome Project

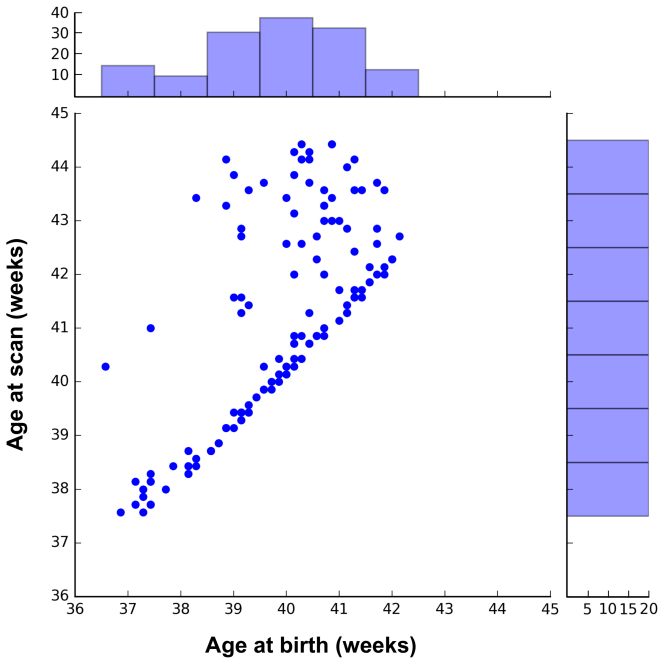

## Authors:

*Matteo Bastiani[1], Jesper Andersson[1], Lucilio Cordero-Grande[2], Maria Murgasova[2], Jana Hutter[2], Anthony N. Price[2], Antonios Makropoulos[3], Sean P. Fitzgibbon[1], Emer Hughes[2], Daniel Rueckert[3], Suresh Victor[2], Mary Rutherford[2], A. David Edwards[2], Steve Smith[1], Jacques-Donald Tournier[2], Joseph V. Hajnal[2], Saad Jbabdi[1], Stamatios N. Sotiropoulos[1,4]*

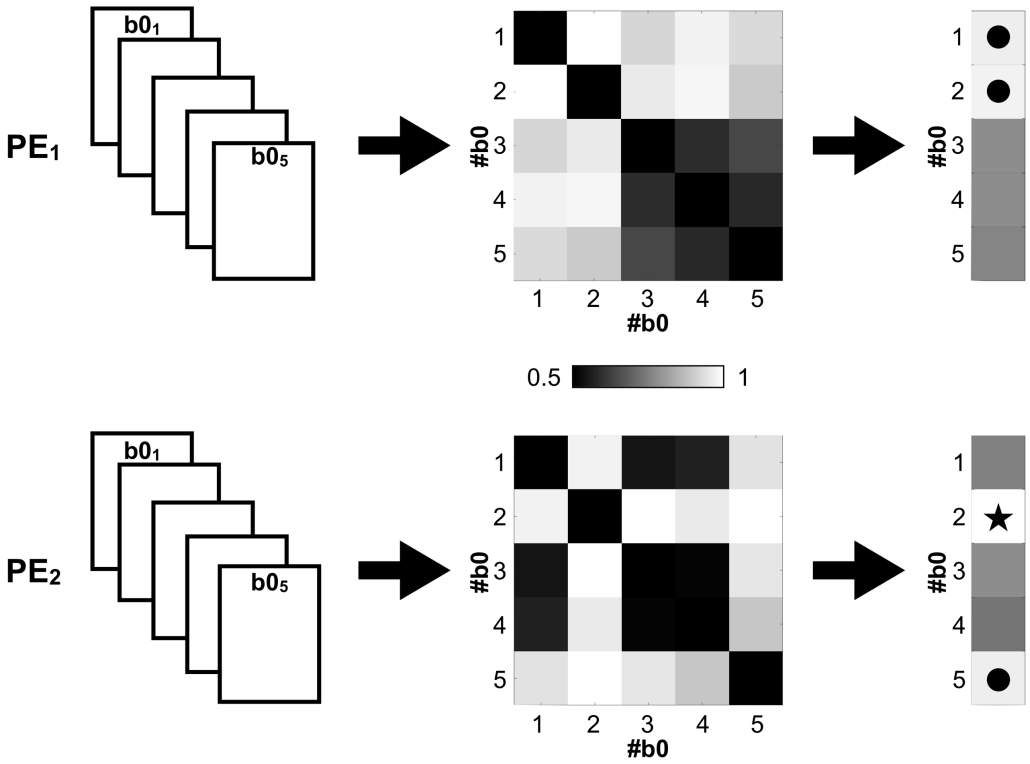
[1] Wellcome Centre for Integrative Neuroimaging - Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB), University of Oxford, UK
[2] Centre for the Developing Brain, King's College London, UK
[3] Department of Computing, Imperial College London, UK
[4] Sir Peter Mansfield Imaging Centre, School of Medicine, University of Nottingham, UK


## Supplementary Material

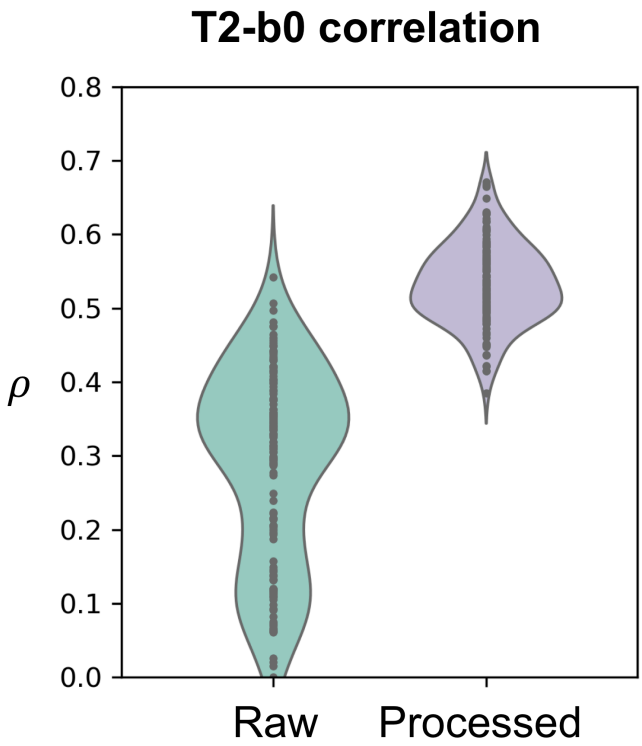
*Supplementary figures*



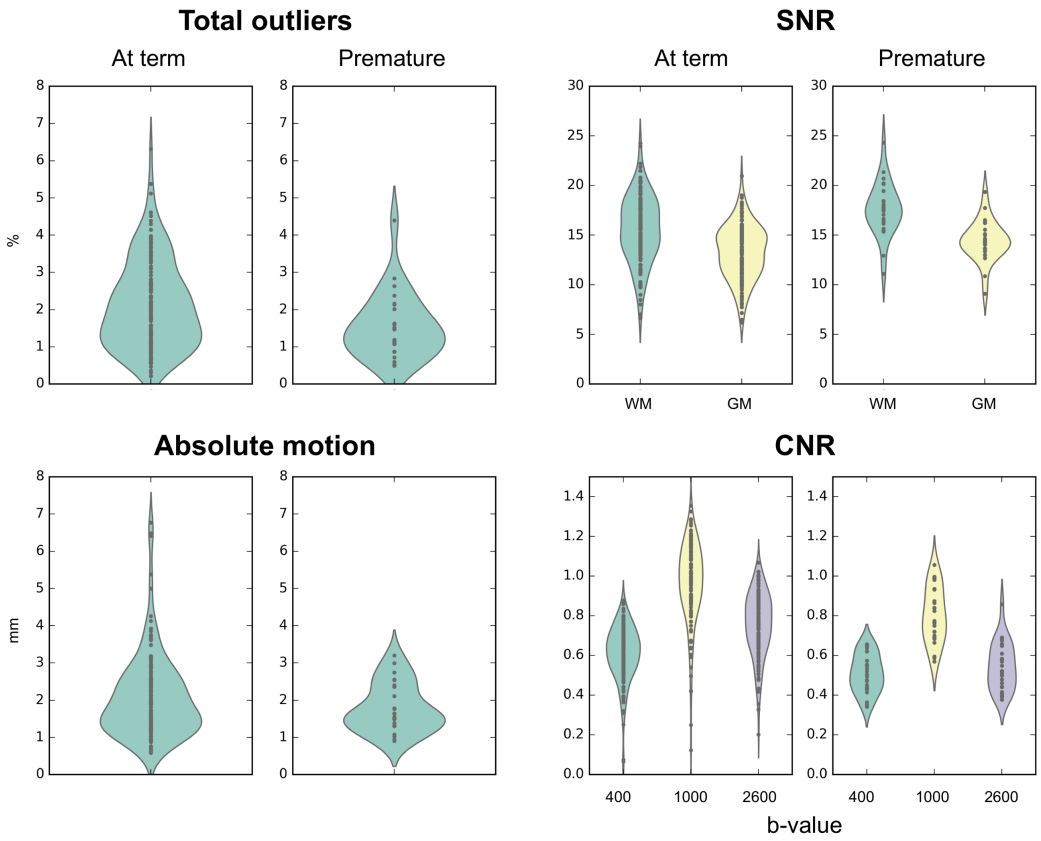

**Supplementary figure 1**: Age at birth and at scan distributions for the 140 subjects used in this work. The scatter plot shows the individual relation between age at scan and age at birth. Most neonates were scanned shortly after birth, with a median difference between age at scan and age at birth of 0.5 weeks.



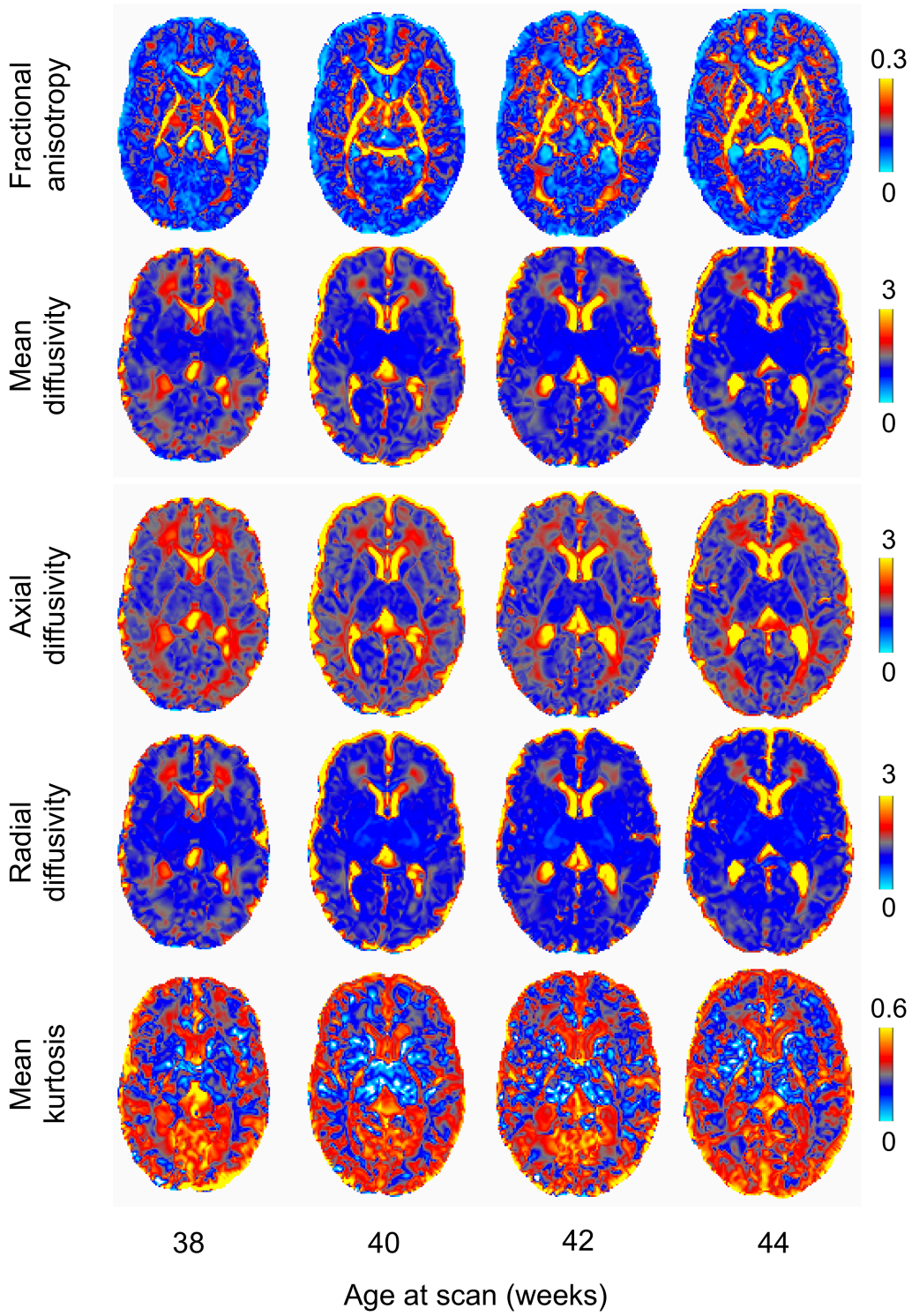

**Supplementary figure 2**: Selection of the best b0 volumes and reference scan. For each PE direction, the correlations between each pair of b0 volumes are computed after rigid alignment (6 DOFs). The b0 volumes showing the highest average correlation (i.e., excluding the diagonal values) are then chosen (black dots). The b0 volume with the highest correlation amongst all acquired PE directions is chosen as the reference volume (black star).



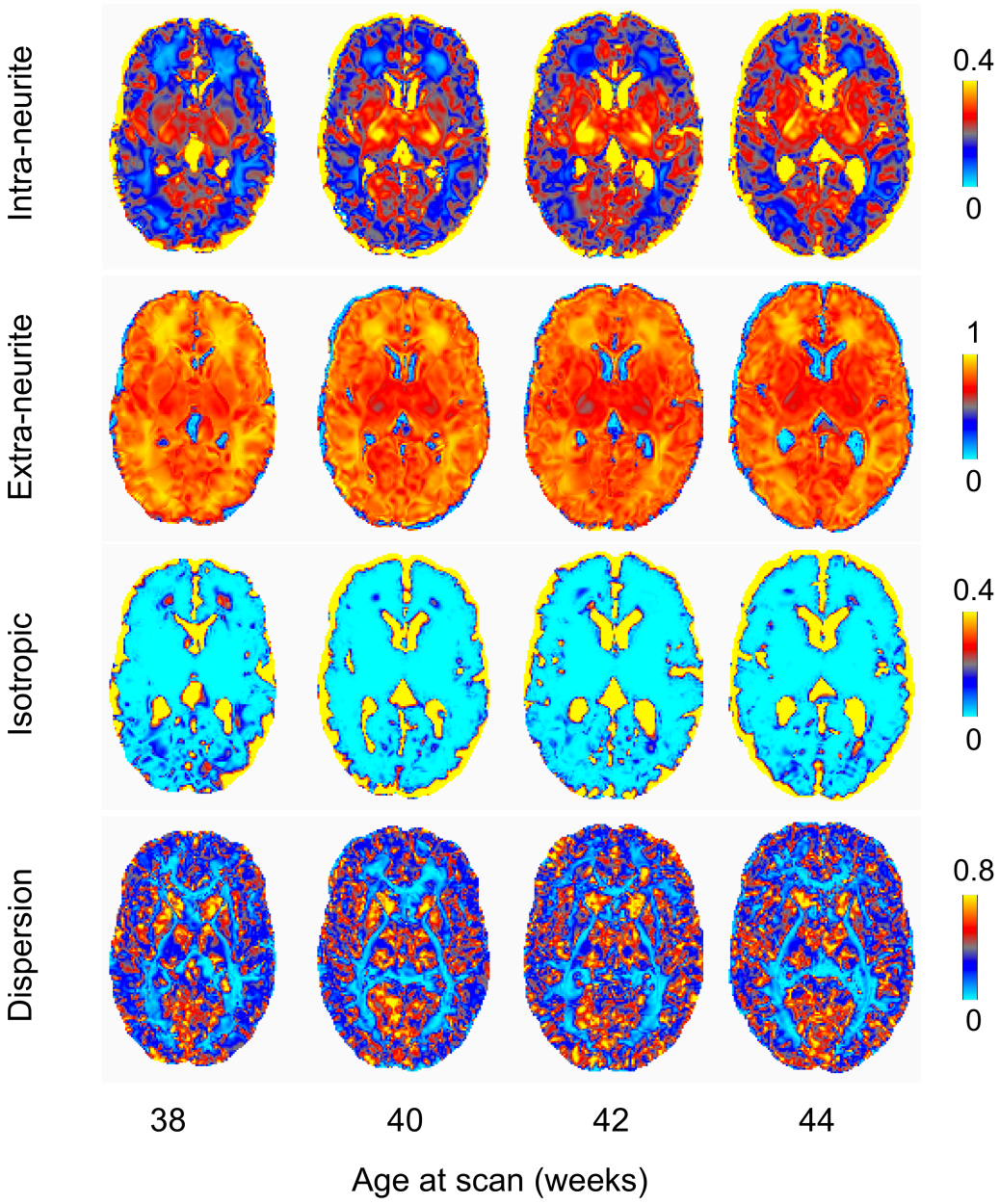

**Supplementary figure 3**: Quantitative assessment of processing and registration performances. The correlation between the high-resolution T2-weighted volume and the averaged b0 volume shows a significant improvement between processed and raw data (median correlations for 140 at term newborns: 0.33 for raw and 0.53 for processed data).



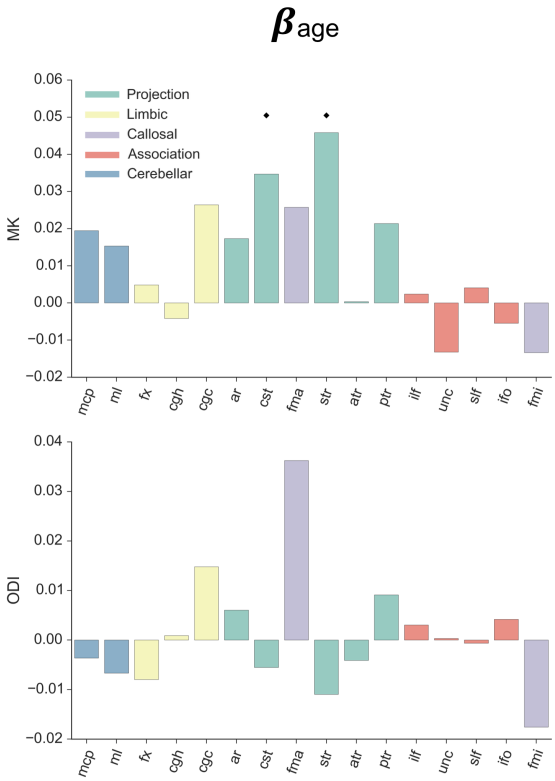

**Supplementary figure 4**: QC metrics comparison between preterm and born at term infants. The distributions were derived from the 140 at term subjects used throughout the article and from 25 infants born preterm (age at scan range: 29 to 35 weeks. Median values and distributions overlap nicely for total outliers, average motion and SNR in both tissue types. Diffusion CNR values are slightly lower in the preterm infants because of a reduced anisotropy and higher water content in the brain.




**Supplementary figure 5**: Output of the dMRI processing pipeline showing single-subject DT-derived microstructural measures from 38-44 weeks. Diffusivities are expressed in $\mu m^2/ms$.




**Supplementary figure 6**: Output of the dMRI processing pipeline showing single-subject NODDI metrics from 38 to 44 weeks post-menstrual age.




**Supplementary figure 7:** Linear regression analysis coefficients for tract-specific microstructural indices (MK and ODI). Maturational speed (i.e., slopes) indicated as $\beta_{age}$. Slopes are normalised by the tract-specific scalar value averaged across ages, to facilitate comparison. Values in bar plots are sorted according to the FA magnitudes. Diamonds indicate that microstructural measures and age-at-scan were significantly, i.e., $p < 0.05$ corrected related for a specific tract. See table 2 in the main text for abbreviations.

*Supplementary tables*

| **Index** | **Tracts** | **$\beta_0$** | **$\beta_{age}$** | **$\beta_{tbv}$** |
|---|---|---|---|---|
| FA | ar | 0.2124 | 0.0060 | -0.0001 |
| | atr | 0.1854 | 0.0096** | -0.0002 |
| | cgc | 0.1854 | 0.0050 | -0.0002 |
| | cgh | 0.1458 | 0.0038 | -0.0001 |
| | cst | 0.2722 | 0.0077* | -0.0002 |
| | fma | 0.2281 | 0.0081* | -0.0003 |
| | fmi | 0.1729 | 0.0172** | -0.0003 |
| | fx | 0.1746 | 0.0032 | -0.0002 |
| | ifo | 0.1783 | 0.0144** | -0.0002 |
| | ilf | 0.1857 | 0.0117** | -0.0002 |
| | mcp | 0.1837 | 0.0022 | -0.0001 |
| | ml | 0.1985 | 0.0030 | 0.0001 |
| | ptr | 0.2127 | 0.0118** | -0.0002 |
| | slf | 0.1768 | 0.0121** | -0.0003 |
| | str | 0.2423 | 0.0095** | -0.0003 |
| | unc | 0.1642 | 0.0103** | -0.0002 |

| | | | | |
|---|---|---|---|---|
| MD | ar | 0.0013 | 0.0000** | 0.0000 |
| | atr | 0.0013 | -0.0001** | 0.0000** |
| | cgc | 0.0013 | 0.0000 | 0.0000 |
| | cgh | 0.0013 | 0.0000** | 0.0000 |
| | cst | 0.0012 | 0.0000** | 0.0000 |
| | fma | 0.0014 | 0.0000** | 0.0000 |
| | fmi | 0.0015 | -0.0001** | 0.0000* |
| | fx | 0.0017 | 0.0000 | 0.0000** |
| | ifo | 0.0015 | -0.0001** | 0.0000 |
| | ilf | 0.0014 | 0.0000** | 0.0000 |
| | mcp | 0.0013 | 0.0000 | 0.0000 |
| | ml | 0.0011 | 0.0000** | 0.0000 |
| | ptr | 0.0013 | 0.0000** | 0.0000 |
| | slf | 0.0014 | 0.0000** | 0.0000 |
| | str | 0.0012 | 0.0000** | 0.0000* |
| | unc | 0.0014 | -0.0001** | 0.0000 |
| MK | ar | 0.2759 | 0.0048 | -0.0001 |
| | atr | 0.2832 | 0.0001 | 0.0002 |
| | cgc | 0.2423 | 0.0064 | 0.0002 |
| | cgh | 0.2794 | -0.0012 | 0.0001 |
| | cst | 0.3433 | 0.0119** | -0.0001 |
| | fma | 0.3238 | 0.0083 | -0.0001 |
| | fmi | 0.3142 | -0.0042 | 0.0002 |
| | fx | 0.3950 | 0.0019 | 0.0001 |
| | ifo | 0.2870 | -0.0016 | 0.0001 |
| | ilf | 0.2766 | 0.0007 | 0.0001 |
| | mcp | 0.4316 | 0.0084 | 0.0000 |
| | ml | 0.4543 | 0.0070 | -0.0003 |
| | ptr | 0.2796 | 0.0060 | 0.0000 |
| | slf | 0.2221 | 0.0009 | 0.0001 |
| | str | 0.2979 | 0.0137** | -0.0001 |
| | unc | 0.2546 | -0.0034 | 0.0000 |
| INTRA | ar | 0.1817 | 0.0086** | -0.0002 |
| | atr | 0.2082 | 0.0138** | -0.0003 |
| | cgc | 0.1636 | 0.0077** | -0.0002 |
| | cgh | 0.2004 | 0.0060* | 0.0000 |
| | cst | 0.2491 | 0.0111** | -0.0002 |
| | fma | 0.1860 | 0.0100** | -0.0002 |
| | fmi | 0.1440 | 0.0156** | -0.0002 |
| | fx | 0.2720 | 0.0027 | 0.0006* |
| | ifo | 0.1373 | 0.0132** | -0.0002 |
| | ilf | 0.1421 | 0.0107** | -0.0002 |
| | mcp | 0.2944 | 0.0056 | 0.0001 |
| | ml | 0.3675 | 0.0053 | -0.0001 |
| | ptr | 0.1752 | 0.0120** | -0.0002 |

| | | | | |
|---|---|---|---|---|
| | slf | 0.1233 | 0.0108** | -0.0003* |
| | str | 0.2171 | 0.0127** | -0.0004** |
| | unc | 0.1513 | 0.0116** | -0.0002 |
| ISO | ar | 0.0101 | -0.0020 | 0.0000 |
| | atr | 0.0160 | -0.0067 | 0.0002** |
| | cgc | 0.0033 | 0.0001 | 0.0000 |
| | cgh | 0.0283 | -0.0033 | 0.0002 |
| | cst | 0.0158 | -0.0011 | 0.0001 |
| | fma | 0.0752 | -0.0068 | 0.0003 |
| | fmi | 0.0431 | -0.0135** | 0.0004* |
| | fx | 0.2373 | -0.0073 | 0.0010** |
| | ifo | 0.0407 | -0.0123** | 0.0004** |
| | ilf | 0.0248 | -0.0061** | 0.0002* |
| | mcp | 0.0932 | -0.0013 | 0.0001 |
| | ml | 0.0661 | -0.0044** | 0.0000 |
| | ptr | 0.0278 | -0.0045** | 0.0002** |
| | slf | 0.0128 | -0.0049** | 0.0001* |
| | str | 0.0027 | -0.0008* | 0.0000 |
| | unc | 0.0143 | -0.0058** | 0.0001 |
| ODI | ar | 0.1706 | 0.0010 | 0.0000 |
| | atr | 0.2508 | -0.0010 | -0.0002 |
| | cgc | 0.1999 | 0.0030 | -0.0001 |
| | cgh | 0.3193 | 0.0003 | 0.0001 |
| | cst | 0.1509 | -0.0008 | 0.0000 |
| | fma | 0.1211 | 0.0044 | 0.0000 |
| | fmi | 0.1212 | -0.0021 | 0.0000 |
| | fx | 0.1466 | -0.0012 | 0.0001 |
| | ifo | 0.1220 | 0.0005 | 0.0000 |
| | ilf | 0.1260 | 0.0004 | 0.0000 |
| | mcp | 0.2384 | -0.0009 | 0.0002 |
| | ml | 0.2920 | -0.0019 | -0.0001 |
| | ptr | 0.1476 | 0.0013 | 0.0000 |
| | slf | 0.1550 | -0.0001 | 0.0001 |
| | str | 0.1728 | -0.0019 | 0.0000 |
| | unc | 0.1733 | 0.0001 | 0.0000 |

**Supplementary table 1:** Linear regression coefficients for tract-specific microstructural analysis. **: $p < 0.01$ (Bonferronicorrected), *: $p < 0.05$ (Bonferroni corrected).