

A subset of brain regions within adult functional connectivity networks demonstrate high reliability across early development

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Highlights

- Specialized functional networks in the human cerebral cortex, evident in resting-state fMRI, support sensory, motor, cognitive, and affective functions and evolve throughout the lifespan.
- Existing studies have focused on age-specific networks for infants, but less on to what extent adult networks can describe infant functional connectivity (FC).
- Analysis revealed a subset of areas in infants showing adult-like network organization, with within-network FC exhibiting less variation across age and higher reliability across scans.
- These areas are posited near locations with low variability in functional network identity in adults, suggestive of the relationship between developmental sequence and interindividual variability in functional network organization.

Keywords

fMRI, functional connectivity, system, network, infant, resting state

43 **Abstract**

44 The human cerebral cortex contains groups of areas that support sensory, motor,
45 cognitive, and affective functions, often categorized as functional networks. These areas
46 show stronger internal and weaker external functional connectivity (FC) and exhibit
47 similar FC profiles within rather than between networks. Previous studies have
48 demonstrated the development of these networks from nascent forms present before
49 birth to their mature, adult-like topography in childhood. However, analyses often still
50 use definitions based on adult functional networks. We aim to assess how this might
51 lead to the misidentification of functional networks and explore potential consequences
52 and solutions.

53 Our findings suggest that even though adult networks provide only a marginally
54 better than-chance description of the infant FC organization, misidentification was
55 largely driven by specific areas. By restricting functional networks to areas showing
56 adult-like network clustering, we observed consistent within-network FC both within and
57 across scans and throughout development. Additionally, these areas were spatially
58 closer to locations with low variability in network identity among adults. Our analysis
59 aids in understanding the potential consequences of using adult networks "as is" and
60 provides guidance for future research on selecting and utilizing functional network
61 models based on the research question and scenario.

62 **1. Introduction**

64 At the meso-scale, the human cerebral cortex consists of specialized functional
65 modules (Power et al., 2011; Yeo et al., 2011) that work together as large-scale
66 functional networks to support sensory, motor, higher-cognitive, and affective functions
67 (Petersen & Sporns, 2015; Wig, 2017). In adult humans, these large-scale networks
68 exhibit relatively consistent spatial topographies across both acquisition paradigms (task
69 and resting states) and individuals (Gratton et al., 2018), and are disrupted by disease
70 (Fornito et al., 2015; Fox & Greicius, 2010). The modular composition of the brain
71 serves to segregate information processing between distinct sensory modalities or
72 cognitive domains (Grayson & Fair, 2017; Petersen & Sporns, 2015).

73 Prior research has demonstrated that these functional networks develop across
74 the lifespan from infancy through old age (Grayson & Fair, 2017; Sun et al., 2023; Wig,
75 2017), paralleling the development of complex behavior functions (Grayson & Fair,
76 2017; Petersen & Sporns, 2015). Preliminary forms of adult functional networks are
77 already present in utero (Moore et al., 2024; Thomason et al., 2013; Turk et al., 2019).
78 In addition, the existence of robust, bilateral segregated networks for somatomotor,
79 primary auditory, primary visual, and extrastriate visual cortex have also been confirmed
80 (Eyre et al., 2021; Fransson et al., 2007; Gao, Alcauter, Elton, et al., 2015, 2015;
81 Smyser et al., 2010). Higher-order resting-state networks appear to be less mature in
82 early infancy (Gao, Alcauter, Elton, et al., 2015; Gao et al., 2009). By the age of 1-2
83 years, the default mode network becomes more adult-like in some studies (Gao,
84 Alcauter, Elton, et al., 2015; Gao, Alcauter, Smith, et al., 2015; Gao et al., 2009) but
85 remains localized in other studies (Eggebrecht et al., 2017; Kardan et al., 2022; Marrus
86 et al., 2018; F. Wang et al., 2023).

87 Due to these observations, researchers conducting analysis on infant
88 neuroimaging data often face a dilemma of choosing a proper representation model for

89 their data. Some researchers used the adult network models when describing the
90 relationships between functional connectivity (FC) in the brain and behavioral
91 phenotypes in infants (Nielsen et al., 2022; Rudolph et al., 2018; Tooley et al., 2023) or
92 when comparing between infants and adults (Yates et al., 2023). One argument for this
93 choice is to encourage biological interpretability and facilitate communication across
94 groups by adopting the same terminology across developmental stages. However,
95 defining the functional networks using the exact adult topography may be inaccurate
96 and cause the mixing of fMRI BOLD signals across different sub-networks (Smith et al.,
97 2011), thus lowering statistical power. Furthermore, some of the differences in FC might
98 be confounded by the differences in network topography or network identity
99 (Bijsterbosch et al., 2018, 2019).

100 An alternative approach is to derive data-driven functional networks for specific
101 developmental stages (Eggebrecht et al., 2017; Kardan et al., 2022; Marrus et al., 2018;
102 Wheelock et al., 2019). While this would potentially mitigate the problem of poor FC
103 representation within functional networks and help improve reproducibility, the utility and
104 interpretability of those results are less apparent. Ultimately, the choice should be
105 dependent on the research goal, but it is also important to understand how poorly the
106 adult network topography fits data from infants – presumably, if the adult functional
107 network topography is dramatically different from that in infants, then the application of
108 the adult functional networks to infant studies would likely result in low reliability (Marek
109 et al., 2022). Here, we aim to delve deeper into this problem, and examine to what
110 extent the infant networks are similar to and different from the adult networks in terms of
111 describing the underlying modular structure in their FC.

112 In addition, converging evidence from different modalities suggests that the
113 human cortex does not develop in a spatially uniform manner. Rather, regions within
114 primary sensory and motor cortex mature earlier in their biological properties than
115 regions in higher order association cortex (Ahmad et al., 2023; Flechsig, 1901; Garcia et
116 al., 2018; Grayson & Fair, 2017; Hill et al., 2010; Sydnor et al., 2021; Truzzi & Cusack,
117 2023). When the areas mature earlier, it leaves little room for future plasticity (Hill et al.,
118 2010), and hence may result in less interindividual variability or reduced susceptibility to
119 environmental influences (Gao et al., 2017) and psychopathological factors (Sydnor et
120 al., 2021). We hypothesized that some areas would demonstrate early signs of adult-
121 like organization, especially towards the sensorimotor end of the functional hierarchy
122 (Gao, Alcauter, Elton, et al., 2015; Sydnor et al., 2021). We further hypothesized that
123 areas with adult-like organization would overlap with areas of low interindividual
124 variability in functional network assignments (Dworetzky et al., 2021; Gordon, Laumann,
125 Adeyemo, et al., 2017; Gratton et al., 2018; Hermosillo et al., 2024; Kong et al., 2019;
126 Langs et al., 2016; Seitzman et al., 2019).

127 In the present work, we used one adult resting-state fMRI dataset with 120
128 participants (aged 19-32 years) and one typically developing infant resting-state fMRI
129 dataset with 181 participants (aged 8-60 months) to quantify how well the infant and
130 adult networks can describe the modular structure in the adult and infant FC. In
131 addition, we quantified the fit of the networks in each area and mapped out the spatial
132 distribution of the strength of misidentification. Furthermore, we analyzed the age effect
133 on within-network FC using all areas versus only the subset of areas with a stronger
134 association to other areas in the same network than alternative networks to

135 demonstrate the potential consequences of model choice. Lastly, we compared the
136 spatial distribution of our area subset to the spatial distribution of locations with the
137 greatest group convergence in functional network identity across individuals. Our
138 findings will help researchers working with infant neuroimaging data understand the
139 pros and cons of using adult and infant functional network models, appreciate the
140 current results in the literature, and provide recommendations for future research.

141

142 **2. Materials and Methods**

143

144 **2.1. Data Collection**

145

146 **2.1.1. Washington University 120 (WU 120)**

147 This dataset has been previously described in detail (Power et al., 2017). Briefly,
148 data were collected from 120 healthy young adult subjects during relaxed eyes–open
149 fixation (60 females, mean age = 25 years, age range = 19–32 years). All subjects were
150 native speakers of English and right-handed. Subjects were recruited from the
151 Washington University community and were screened with a self-report questionnaire to
152 ensure that they had no current or previous history of neurological or psychiatric
153 diagnosis, as well as no head injuries resulting in a loss of consciousness for more than
154 5 minutes. Informed consent was obtained from all subjects. The study was approved
155 by the Washington University School of Medicine Human Studies Committee and
156 Institutional Review Board.

157 Structural and functional MRI data were obtained with a Siemens MAGNETOM
158 Trio Tim 3.0-T Scanner (Erlangen, Germany) and a Siemens 12-channel Head Matrix
159 Coil. A T1-weighted sagittal magnetization-prepared rapid acquisition gradient-echo
160 (MP-RAGE) structural image was obtained [time echo (TE) = 3.08 ms, time repetition,
161 TR (partition) = 2.4 s, time to inversion (TI) = 1000 ms, flip angle = 8°, 176 slices with 1
162 × 1 × 1 mm voxels]. An auto-align pulse sequence protocol provided in the Siemens
163 software was used to align the acquisition slices of the functional scans parallel to the
164 anterior commissure–posterior commissure plane of the MP-RAGE and centered on the
165 brain. This plane is parallel to the slices in the Talairach atlas (Talairach & Tournoux,
166 1988).

167 During functional MRI data acquisition, subjects were instructed to relax while
168 fixating on a black crosshair that was presented against a white background. Functional
169 imaging was performed using a BOLD contrast-sensitive gradient-echo echo-planar
170 imaging (EPI) sequence (TE = 27 ms, flip angle = 90°, in-plane resolution = 4 × 4 mm).
171 Whole-brain EPI volumes (MR frames) of 32 contiguous, 4-mm-thick axial slices were
172 obtained every 2.5 s. A T2-weighted turbo spin-echo structural image (TE = 84 ms, TR
173 = 6.8 s, 32 slices with 1 × 1 × 4 mm voxels) in the same anatomical planes as the BOLD
174 images was also obtained to improve alignment to an atlas. Anterior→Posterior (AP)
175 phase encoding was used for fMRI acquisition. The number of volumes collected from
176 subjects ranged from 184 to 724 (mean = 336 frames, 14.0 min).

177

178 **2.1.2. Baby Connectome Project (BCP)**

179 Full-term (gestational age of 37-42 weeks) infants free of any major pregnancy
180 and delivery complications were recruited as part of the Baby Connectome Project

181 (Howell et al., 2019). All procedures were approved by the University of North Carolina
182 at Chapel Hill and the University of Minnesota Institutional Review Boards. Informed
183 consent was obtained from the parents of all participants. In the final cohort used
184 following fMRI data quality control (described below), we retained 313 MRI sessions
185 from 181 individuals (95 females, 8-60 months, mean 19.1 months and standard
186 deviation 8.3 months) (Supplementary Figure 1).

187 All MRI images were acquired on a Siemens 3T Prisma scanner with a 32-
188 channel head coil at the University of Minnesota and at the University of North Carolina
189 at Chapel Hill during natural sleep without the use of sedating medications. T1-weighted
190 (TR=2400 ms, TE=2.24 ms, 0.8 mm isotropic; flip angle = 8°), T2-weighted images
191 (TR=3200 ms, TE=564 ms, 0.8 mm isotropic), spin echo field maps (SEFM) (TR=8000
192 ms, TE=66 ms, 2 mm isotropic, MB=1), and fMRI data (TR=800 ms, TE=37 ms, 2 mm
193 isotropic, MB=8) were collected. A mixture of Anterior→Posterior (AP) and
194 Posterior→Anterior (PA) phase encoding directions was used for fMRI acquisition in
195 each session, but they were concatenated into one time series. An early subset of data
196 was collected with a 720-ms TR (N = 95). The number of low-motion volumes collected
197 from subjects ranged from 840 to 2100 (mean = 1306 frames, 16.9 min).

198

199 **2.2. fMRI analysis**

200

201 **2.2.1. MRI data preprocessing**

202

203 **2.2.1.1. MRI data preprocessing – WU120**

204 Functional images were first processed to reduce artifacts including (1)
205 Correction of odd versus even slice intensity differences attributable to interleaved
206 acquisition without gaps, (2) correction for head movement within and across runs, and
207 (3) across-run intensity normalization to a whole-brain mode value of 1000. Atlas
208 transformation of the functional data was computed for each individual using the MP-
209 RAGE scan. Each run was then resampled to an isotropic 3-mm atlas space (Talairach
210 & Tournoux, 1988), combining movement correction and atlas transformation in a single
211 cubic spline interpolation (Lancaster et al., 1995).

212 Additional preprocessing steps were applied to the functional data to reduce the
213 effect of high-motion frames. This was performed in two iterations. In the first iteration,
214 the processing steps were (1) demeaning and detrending, (2), multiple regression
215 including: whole-brain, ventricular cerebrospinal fluid (CSF), and white matter signals,
216 and motion regressors derived by Volterra expansion and (3) a band-pass filter (0.009
217 Hz < f < 0.08 Hz). Following the initial FC preprocessing iteration, temporal masks were
218 created to flag motion-contaminated frames. Motion-contaminated volumes were
219 identified by framewise displacement (FD), defined as the squared sum of the motion
220 vectors (Power et al., 2012). Volumes with FD > 0.2 mm and segments of data lasting
221 fewer than 5 contiguous volumes were censored.

222 The data were then reprocessed in a second iteration, incorporating the temporal
223 masks described above. This reprocessing was identical to the initial processing stream
224 but ignored censored data. Data were interpolated across censored frames using least
225 squares spectral estimation (Power et al., 2014) of the values at censored frames, so
226 that continuous data could be passed through the band-pass filter (0.009 Hz < f < 0.08

227 Hz) without contaminating frames near high motion frames. Censored frames were
228 ultimately ignored during functional connectivity matrix generation.

229 Individual surfaces were generated from the structural images and the functional
230 data was sampled to surface space (Glasser et al., 2013). First, following volumetric
231 registration, anatomical surfaces for the left and right hemispheres were generated from
232 each subject's MP-RAGE image using FreeSurfer's default recon-all processing pipeline
233 (v5.0)(Fischl, 2012). This pipeline included brain extraction, segmentation, generation of
234 white matter and pial surfaces, inflation of the surfaces to a sphere, and surface shape-
235 based spherical registration of the subject's "native" surface to the fsaverage surface.
236 The fsaverage-registered left and right hemisphere surfaces were then brought into
237 register with each other (Van Essen et al., 2012), resampled to a resolution of 164000
238 vertices using Caret tools (Van Essen et al., 2001) and subsequently down sampled to
239 a 32492 vertex surface (fs_LR 32k). The BOLD volumes were sampled to each
240 subject's individual "native" midthickness surface (generated as the average of the white
241 and pial surfaces) using the ribbon-constrained sampling procedure available in
242 Connectome Workbench (v0.84) and then deformed and resampled from the
243 individual's "native" surface to the 32k fs_LR surface. Finally, the time courses were
244 smoothed along the 32k fs_LR surface using a Gaussian smoothing kernel ($\sigma = 2.55$
245 mm).

246

247 **2.2.1.2. MRI data preprocessing – BCP**

248 MRI data were processed using the DCAN-Labs infant-abcd-bids-pipeline
249 (v0.0.22) largely following steps described previously (Feczko et al., 2021). Structural
250 MRI data underwent HCP-style processing (Feczko et al., 2021; Glasser et al., 2013),
251 including ANTS N4 bias correction, ANTS denoising, T1/T2 distortion
252 correction/registration, and finally ANTS SyN algorithm deformation alignment to an
253 infant MNI template. In addition, a refined brain mask was generated from data that was
254 segmented using in-house age-specific templates via Joint Label Fusion (JLF). The
255 toddler-specific mask and segmentation were substituted into the FreeSurfer (Fischl,
256 2012) pipeline and used to refine the white matter segmentation and guide the
257 FreeSurfer surface delineation. The native surface data were then deformed to the
258 fsaverage LR32k template via a spherical registration.

259 For functional MRI preprocessing, a scout image (frame 16 in each run) was
260 selected from the fMRI time series. The scout was distortion-corrected via spin-echo
261 field maps, served as the reference for motion correction via rigid-body realignment
262 (Feczko et al., 2021), and was registered to the native T1. Across-run intensity
263 normalization to a whole-brain mode value of 10,000 was then performed. These steps
264 were combined in a single resampling with the MNI template transformation from the
265 previous step, such that all fMRI frames were registered to the infant MNI template.
266 Manual inspection of image quality of structural and functional data was conducted to
267 exclude sessions with bad data quality.

268 To prepare the functional data for FC analysis, further processing steps were
269 applied after sampling the BOLD data to the fsLR_32k surface space using steps
270 described in 2.2.1.1. First, functional data were demeaned and detrended in time.
271 Denoising was then performed using a general linear model with regressors including
272 signal and motion variables. Signal regressors included mean CIFTI gray-ordinate time

273 series, Joint Label Fusion (JLF)-defined white matter, and JLF-defined CSF. Motion
274 regressors included volume-based translational and rotational components and their 24-
275 parameter Volterra expansion. The movement of the head was measured by FD and an
276 age-specific respiratory notch filter (0.28-0.48 Hz) was applied to the FD traces and
277 motion parameter estimates to mitigate the effects of factitious head motion due to
278 infant respiration (Fair, 2020; Kaplan et al., 2022). Frames were censored during
279 demeaning/detrending if their post-respiratory filtering FD value exceeded 0.3 mm to
280 generate the denoised beta values in the general linear model. Bandpass filtering was
281 applied using a second-order Butterworth filter (0.008–0.09 Hz). To preserve the
282 temporal sequence and avoid aliasing caused by missing time points during bandpass
283 filtering, interpolation was used to replace missing frames, and residuals were acquired
284 from the denoising general linear model. In addition, zero-padding was applied to both
285 ends of the BOLD data prior to filtering to minimize the distortions in the edges of the
286 time series. The data were originally minimally spatially smoothed with a geodesic 2D
287 Gaussian kernel ($\sigma = 0.85$ mm). A further smoothing with a geodesic 2D Gaussian
288 kernel ($\sigma = 2.40$ mm) was applied to give a final effective smoothing of $\sigma = 2.55$ mm to
289 match the smoothing used in the adult dataset (WU 120). Finally, the timeseries were
290 concatenated across all complete and partially completed scan runs with good data
291 quality. The first 7 frames from each run, frames with > 0.2 mm FD post-respiratory
292 filtering (Kaplan et al., 2022) and outlier frames whose across-vertex standard deviation
293 was more than 3 median absolute deviations from the median of the low FD frames
294 were censored and ignored for functional connectivity matrix construction.

295

296 **2.2.2. Functional Connectivity Matrix Construction**

297 The preprocessed BOLD timeseries data of each session were parcellated into
298 333 non-overlapping areas using the Gordon parcellation (Gordon et al., 2016). This
299 choice of parcellation was justified by recent work by our group that demonstrated that
300 the Gordon parcellation had the best fit among a set of adult parcellations and
301 performed comparably to most available infant parcellations in data from infants aged
302 around 8-30 months (Tu et al., 2023). After that, a total number of frames equivalent to
303 7.2 minutes of data (560 frames for TR = 0.72 and 600 frames for TR = 0.8) were
304 randomly sampled from the full censored timeseries in each fMRI session. The
305 Pearson's correlation between the parcellated timeseries was computed to create a 333
306 x 333 functional connectivity (FC) matrix. This matrix was then Fisher-Z-transformed.
307 The group-average FC matrix was calculated as the mean FC across fMRI sessions.

308

309 **2.3. Infant and Adult Functional Networks Schemes**

310 We used the Gordon network assignments (Gordon et al., 2016) for “Adult
311 Networks” (Figure 1A) and Kardan network assignments (Kardan et al., 2022) for “Infant
312 Networks” (Figure 1B). These networks were derived at the 333 area level using the
313 same Infomap community detection algorithm (Rosvall & Bergstrom, 2010) optimized
314 for identifying networks in FC data (Power et al., 2011). Among the 333 areas, some
315 were originally assigned in communities fewer than 5 areas and considered unassigned
316 (named “None” and “Unspecified”). These areas commonly fall under locations
317 subjected to the biggest susceptibility artifact (Ojemann et al., 1997). We removed them

318 from all analyses and had 286 areas left for the adult networks (“Gordon”) and 328
319 areas left for the infant networks (“Kardan”).

320 The 12 Gordon networks include the auditory (Aud), cingulo-opercular (CON),
321 parietal memory (PMN), default mode (DMN), dorsal attention (DAN), fronto-parietal
322 (FPN), retrosplenial temporal (RTN), somatomotor hand (SMN hand), somatomotor
323 mouth (SMN mouth), salience (Sal), ventral attention (VAN), and visual (Vis) networks.
324 The 10 Kardan networks include somatomotor (SMN), temporal (Tem), posterior
325 frontoparietal (pFPN), posterior default mode (pDMN), lateral visual (lVis), medial visual
326 (mVis), dorsal attention (DAN), anterior fronto-parietal (aFPN), anterior default mode
327 (aDMN).

328

329 **2.4. Functional Network Overlap**

330 The overlap between a network in the Gordon networks and a network in the
331 Kardan networks can be measured with the Dice coefficient, with 0 indicating no overlap
332 and 1 indicating complete overlap. For this analysis, each network is represented with a
333 333 x 1 vector with 1 for the areas in the network and 0 for the areas outside the
334 network.

335

336 **2.5. Silhouette Index Calculation**

337 Following prior procedures in the literature (Rousseeuw, 1987; Yeo et al., 2011),
338 we calculated the silhouette index (SI) for each area with the correlation distance using
339 the spatial similarity between the FC profiles (without the diagonal elements which refer
340 to the meaningless self-connectivity):

341

$$342 \quad SI = \frac{b - a}{\max(a, b)} \quad (\text{Equation 1})$$

343

344 where b is the mean between-network correlation distance of the FC profiles, and a is
345 the mean within-network correlation distance of the FC profiles. FC profiles here refer to
346 the FC from each area to all other areas (i.e., one row in the FC matrix).

347 Intuitively, the SI ranges from +1 to -1 with the sign indicating whether the area
348 has a more similar FC profile to areas in its own network (+) or to areas in an alternative
349 network (-). The magnitude indicates the confidence of this assignment, with a higher
350 magnitude suggestive of strong confidence. The average SI for the FC in a network
351 scheme was defined as the average SI across all areas.

352 By default, the silhouette index compares the current network to the best
353 alternative network, which also depends on the quality of alternatives. However, other
354 researchers have chosen to use a similar metric that compares the average within-
355 network similarity to the average between-network similarity across all alternative
356 networks, rather than just the best alternative (Ji et al., 2019). This approach tends to be
357 less conservative and generally results in a higher silhouette index when calculated in
358 this manner. We also calculated the silhouette index with the average of all networks
359 rather than just the alternative network in the Supplementary Materials.

360 In order to obtain a confidence interval for the average SI across individual
361 sessions, we used a bootstrap 95% confidence interval estimate in 1000 random draws

362 of individual sessions from the full sample (N = 120 for WU120 and N = 313 for BCP)
363 with replacement.

364

365 **2.6. Identify the Subset of Areas with Similar Network Organization to the Gordon** 366 **Networks in Infants**

367 A positive SI indicates that the area has a more similar FC profile to areas in its
368 own network. We obtained the subset of areas that had a similar network organization
369 to other areas defined in the Gordon network scheme in infants by only retaining the
370 areas with a positive SI in the group-average infant FC. We refer to this set of positive
371 SI areas as ‘Gordon Subset’.

372

373 **2.7. Distance Between High Consensus Regions of Interests (ROIs) and the** 374 **“Gordon Subset” Areas**

375 To quantify the spatial distribution similarity between the locations of low
376 interindividual variability and the “Gordon Subset” areas, we calculated the Euclidean
377 distance between the high consensus cortical ROIs and the centers of the Gordon
378 areas. We used published coordinates of 153 high consensus ROIs calculated
379 previously by identifying locations that demonstrated consistent network assignment
380 across a large majority (i.e. $\geq 75\%$) of subjects in the Dartmouth dataset (N = 69
381 subjects, 56 female, average age 20.2 years)(Gordon et al., 2016) when a template-
382 matching procedure (Gordon, Laumann, Adeyemo, et al., 2017) was applied to identify
383 individual network assignments (Dworetsky et al., 2021).

384 For each of the “high consensus” ROIs, we found their distance to the nearest
385 “Gordon Subset” area and their distance to an alternative Gordon area. An average of
386 this difference was recorded and named “distance difference”. A negative distance
387 difference indicates that on average, the high consensus regions were closer to the
388 “Gordon Subset” area centers than to the alternative Gordon areas. To account for the
389 potential effect of differences in number of areas between the “Gordon Subset” areas (N
390 = 166) and the alternative areas not in the subset (N = 120), we randomly assigned the
391 166 out of 286 areas a label of “Gordon Subset” and repeated the analysis above 1000
392 times to obtain a null distribution.

393

394 **2.8. Moving Average Analysis Across Age**

395 To examine the FC fit to different network schemes across infancy, we used a
396 moving average analysis across age. For this analysis, we limited our data to the 281
397 sessions collected at the age of 8-27 months because the data became very sparse and
398 less evenly distributed after 27 months (Supplementary Figure 1). We first sorted the
399 fMRI sessions by age at scan. Sessions were arranged chronologically by age, and FC
400 averages were computed for consecutive windows of 20 sessions, with each window
401 representing the mean age within it. This window was then shifted by one session at a
402 time until all 281 sessions were accounted for. Subsequently, we calculated the average
403 similarity index (SI) using the same method.

404

405 **2.9. Age effect of within-network FC**

406 To test the hypothesis that the subset of areas has relatively stable within-
407 network FC across chronological age in infants, we compared the age effect on within-

408 network FC when the networks include only the subset versus full set of areas. The age
409 effect of within-network FC was quantified with a Spearman's correlation (ρ). The
410 significance of the difference between the correlation between chronological age and
411 within-network FC in the subset versus full set of areas is calculated with a Z-test on
412 Fisher-Z-transformed r values.

413

414 **2.10. Intraclass Correlation Coefficient**

415 To assess the differences in reliability of within-network edges for using the
416 Gordon networks with all areas versus the subset of areas. We quantified the test-retest
417 reliability of FC with intraclass correlation coefficient (ICC). We assessed the
418 consistency among measurements under the fixed levels of the session factor (Tozzi et
419 al., 2020), referred to as ICC 'C-1' (McGraw & Wong, 1996) or ICC (3,1) (Shrout &
420 Fleiss, 1979).

421 For this analysis, we re-calculated the FC matrices for each individual with two
422 non-overlapping time windows of data from each session. "Test" and "re-test" were
423 defined as the first 6 min and last 6 min of low-motion data, separated by at least 1.2
424 min low motion data in between to reduce the impact of temporal autocorrelation (i.e.
425 total > 13.2 min low-motion data). Only 167 sessions had enough low-motion data for
426 this analysis. First, the FC values in the upper triangle of each subject's connectivity
427 matrix were entered as rows in two large matrices (one matrix for "test" and another for
428 "re-test", one row per subject in each matrix). Then, the corresponding columns of these
429 matrices were compared to obtain an ICC value for each edge. The mean and standard
430 error of the mean of the ICCs within each of the Gordon networks were calculated for
431 the full and subset of the areas.

432

433 **2.11. Group consistency and differential power of FC edges**

434 Prior studies suggested that it was possible to identify individuals using FC in
435 infants from the BCP dataset (Hu et al., 2022; Kardan et al., 2022). To assess which FC
436 edges (i.e. connections between a pair of areas) are more consistent across individuals
437 versus distinct across individuals, we calculated the group consistency (ϕ) and
438 differential power (DP) measures (Finn et al., 2015). We aim to describe the distribution
439 of highly consistent edges and highly differentiating edges with respect to adult and
440 infant network models. For this analysis, we only use the one session from each of the
441 115 unique subjects with at least 13.2 min low-motion data. Given two sets of
442 connectivity $[X_i^{R1}]$, $[X_i^{R2}]$ obtained from the two resting scan windows ($R1$ and $R2$) after
443 z-score normalization, the edgewise product vector φ_i was computed as

444

$$445 \varphi_i(e) = X_i^{R1}(e) * X_i^{R2}(e), e = 1, \dots, M \text{ (Equation 2)}$$

446

447 where i indexed the subject, e indexed the edge, and M indexed the total number of FC
448 edges. The sum of φ_i over all edges is the correlation between $[X_i^{R1}]$, $[X_i^{R2}]$. The group
449 consistency ϕ was computed as the mean of φ_i across all subjects. We defined the
450 edges with the top 10% ϕ values to be "highly consistent".

451 Similarly, the edgewise product vector φ_{ij} was calculated between patterns from
452 different subjects, for example:

$$453 \varphi_{ij}(e) = X_i^{R1}(e) * X_j^{R2}(e), e = 1, \dots, M, i \neq j \text{ (Equation 3)}$$

$$P_i(e) = P|\varphi_{ij}(e) > \varphi_{ii}(e) \text{ or } \varphi_{ji}(e) > \varphi_{ii}(e)| \text{ (Equation 4)}$$

$$DP(e) = \sum_i \{-\ln(P_i(e))\} \text{ (Equation 5)}$$

We defined the edges with the top 10% DP values as “highly differentiating”.

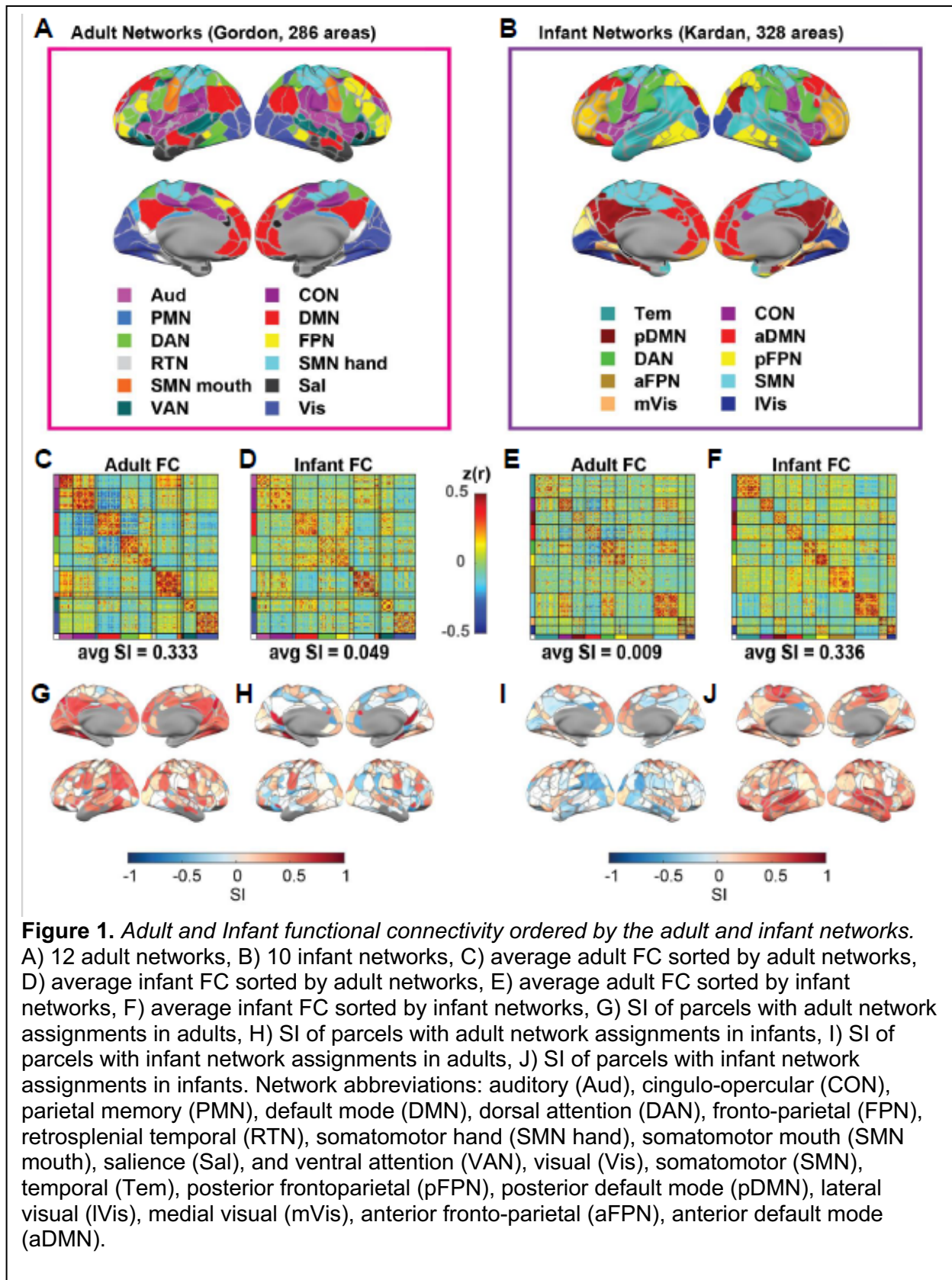
3. Results (currently 1643 words)

3.1. Adult and Infant functional connectivity clustering were best described by the adult and infant network assignments respectively

Gordon networks (adult) (Figure 1A) and Kardan networks (infant) (Figure 1B) assignments demonstrate a reasonable degree of agreement: Normalized Mutual Information (NMI) = 0.5 for the overlapping 281 areas after excluding the “None”/ “Unspecified” network in both adult and infant network assignments. The CON, pDMN, aDMN, SMN, mVis and IVis networks in the Kardan networks tend to have a large dice overlap with a single Gordon network, but Tem, DAN, pFPN, aFPN have a match to multiple Gordon networks (Supplementary Figure 2).

Next, we asked how closely the network assignments matched the similarity of FC profiles within and between different networks and quantified it with the silhouette index (SI; Rousseeuw, 1987; Yeo et al., 2011). We used the average FC across 120 adult sessions and the average FC across 313 infant sessions. We found that adult FC had a more modular organization (Figure 1C) when grouping into adult networks (Figure 1A) than infant networks (Figure 1E). The average SI for areas assigned to adult networks in adult FC (0.333, 95% bootstrap CI = [0.3088, 0.3417]) was much higher than the average SI for areas assigned to infant networks in adult FC (0.009, 95% bootstrap CI = [-0.0015, 0.0168]). In contrast, the opposite was observed for infant FC, with a higher average SI for areas assigned to infant networks in infant FC (0.336, 95% bootstrap CI = [0.3280, 0.3397], Figure 1F) than the average SI for areas assigned to adult networks in infant FC (0.049, 95% bootstrap CI = [0.0406, 0.0560], Figure 1D). Furthermore, the results were also qualitatively validated across individual sessions, with a much higher SI of adult networks than infant networks on adult FC (Cohen’s $d = 1.215$, $p < 0.001$) (Supplementary Figure 3C), and a much higher SI of infant networks than adult networks on infant FC (Cohen’s $d = 2.744$, $p < 0.001$) (Supplementary Figure 4C). Taken together, the adult networks better describe the modular organization in adult FC than infant FC, and the infant networks better describe the modular organization in infant FC than adult FC. However, the SI is comparable for adult FC and infant FC using the best network model, suggesting the presence of the modular organization in both cohorts.

Notably, some areas tend to have a positive SI for areas assigned to adult networks regardless of the FC age group (Figure 1G & I). Since the spatial distribution of SI across sessions (Supplementary 3A-B & 4A-B) was relatively consistent, it is unlikely that the low SI magnitude in infants was purely driven by high interindividual variability.



497 **3.2. A subset of areas demonstrates adult-like network organization throughout** 498 **development**

499 An SI above zero for an area indicates that its FC profile more closely resembles
500 those of other areas in the same network than those in any alternative network within a
501 given network scheme (e.g., adult Gordon networks). Therefore, we selected the subset
502 of areas with an SI above zero when the adult networks were applied to the infant FC
503 (166 areas in total, Figure 2A). These areas fell into all 11 out of the 12 Gordon
504 networks (i.e., all except for PMN), with the whole RTN, SMN mouth and Sal networks
505 retained, and the remaining 8 networks partially retained (Figure 2B). We validated that
506 the areas with SI above zero are highly consistent across bootstrap samples, with 156
507 out of the 166 areas having SI above zero in at least 950 out of 1000 bootstraps
508 (Supplementary Figure 6).

509 As expected, the average SI for areas assigned to adult networks in infant FC
510 was much higher using the subset of areas than all areas (0.388, 95% bootstrap CI =
511 [0.3792, 0.3925]; Figure 2C). The average SI for areas assigned to adult networks in
512 adult FC was also marginally higher using the subset (0.419, 95% bootstrap CI =
513 [0.3925, 0.4300]) (Supplementary Figure 7A), suggesting that this subset captured the
514 areas that are most coherently organized into the adult networks in both infants and
515 adults. Compared to “Gordon Full” (286 areas, Figure 1A), “Gordon Subset” was
516 disproportionately enriched in the SMN networks (SMN hand and SMN mouth) (Figure
517 2D). As expected, the within-network FC was significantly higher across infant sessions
518 (paired t-test, FDR-corrected $p < 0.05$) for all 8 partially retained networks compared to
519 full networks, with little change in variability (Figure 2E). Similarly, the within-network FC
520 was significantly higher across adult sessions (paired t-test, FDR-corrected $p < 0.05$) for
521 all seven out of eight partially retained networks, and significantly lower across adult
522 sessions for FPN. In general, the within-network FC differences between “Gordon Full”
523 and “Gordon Subset” were larger in infants than in adults (Table 1).

524
525 **Table 1.** *Cohen’s d of the within-network FC differences in Gordon Full V.S. Gordon*
526 *Subset.*

	Aud	CON	DMN	DAN	FPN	SMN hand	VAN	Vis
Infant FC	-2.41	-0.29	-1.80	-2.23	-1.54	-2.81	-2.64	-2.91
Adult FC	-1.13	-0.31	-0.46	-1.47	0.70	-1.09	-1.53	-2.10

527
528 It was implied from the results above that the difference in within-network FC
529 between adults and infants would be smaller when using the “Gordon Subset”
530 compared to the “Gordon Full”. We tested this directly using a two-sample t-test (Figure
531 3, Table 2). We found that in seven out of the eight partially retained Gordon networks
532 the adult FC was significantly higher (FDR-corrected $p < 0.05$) than the infant FC with
533 the “Gordon Full” area set (Figure 3A). On the other hand, only five out of the eight still
534 demonstrated significantly higher within-network FC (FDR-corrected $p < 0.05$) in adults
535 compared to infants, and two out of the eight demonstrated significantly lower within-
536 network FC (FDR-corrected $p < 0.05$) (Figure 3B).

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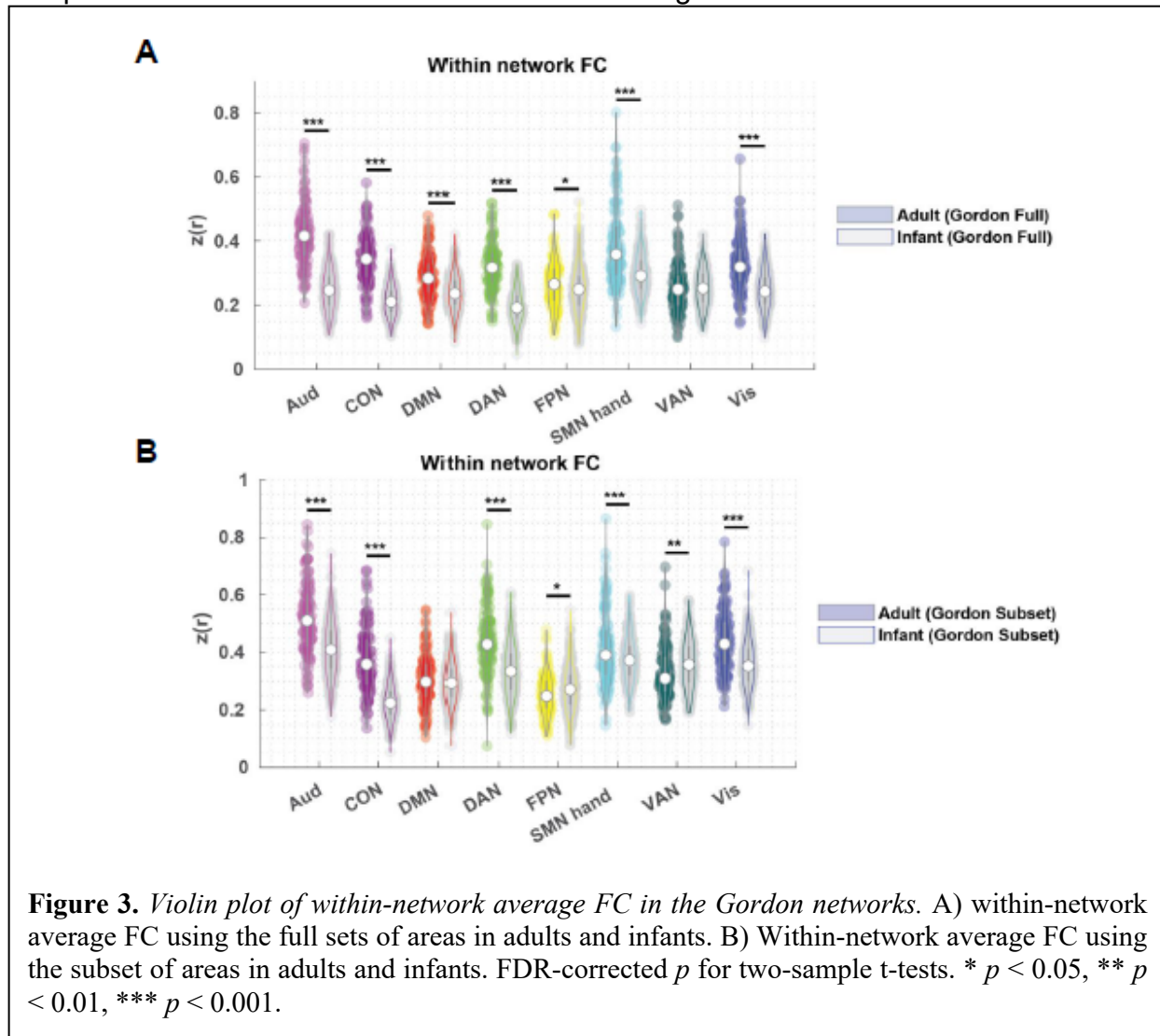
Table 2. Cohen's *d* of the within-network FC differences in adults V.S. infants

	Aud	CON	DMN	DAN	FPN	SMN hand	VAN	Vis
Gordon Full	2.35	2.35	0.80	2.11	0.23	1.04	0.03	1.22
Gordon Subset	1.04	1.88	0.13	1.04	-0.26	0.43	-0.34	0.94

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Additionally, we found that the effect of chronological age on within-network FC within the infant cohort was also reduced when the “Gordon Subset” was used in place of “Gordon Full” (Supplementary Figure 8). The details are reported in the Supplementary Materials.

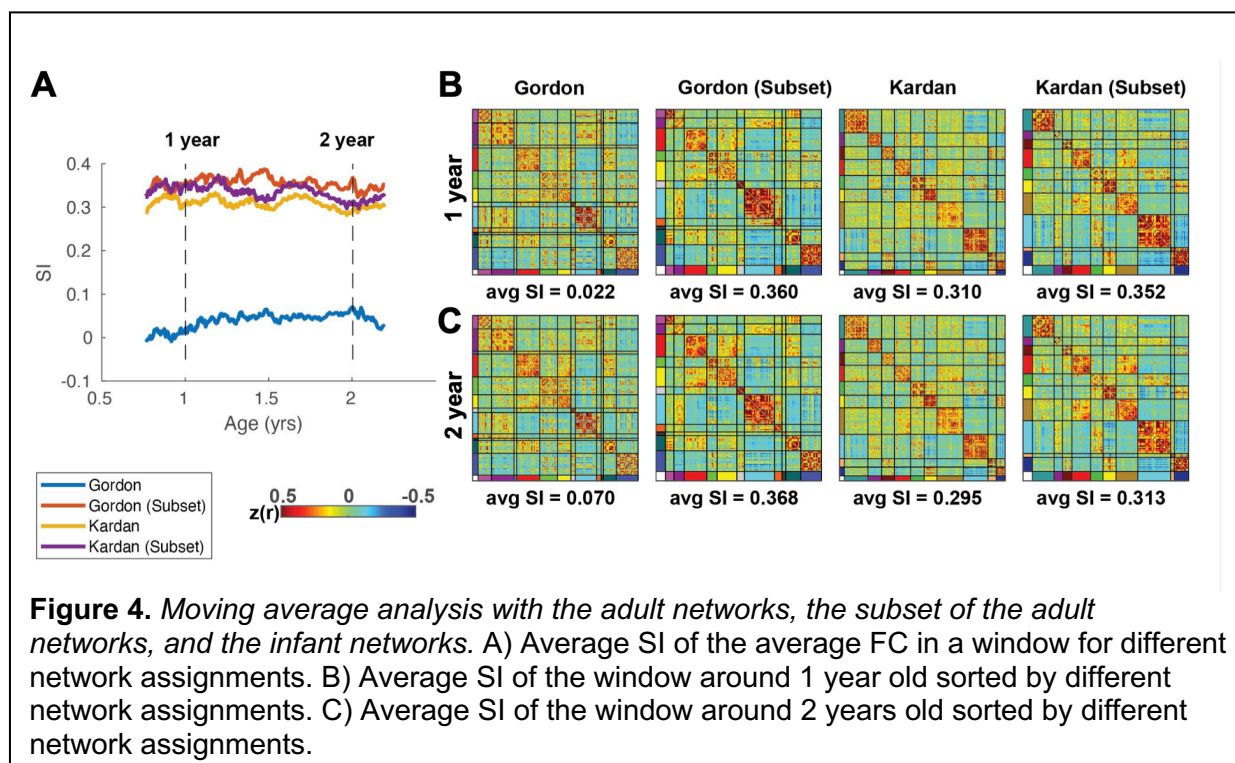
Taken together, this suggested that while the within-network FC within “Subset” was higher than within “Full” in both infant and adult datasets, using the “Subset” compared to “Full” reduced the difference across age.



547

548 3.4. Adult versus infant network across 1-2-year-olds

549 Next, we asked whether there was any variation between how the different
 550 network schemes fit the infant FC at various stages between 1 to 2 years (Gordon adult
 551 networks and Kardan infant networks). In addition, we also applied the Gordon and
 552 Kardan network sorting on the subset of 166 areas in Figure 2A. Using a moving
 553 average approach across infant ages, we found a consistent order of the network
 554 schemes, with the Gordon (Subset), Kardan and Kardan (Subset) having a similar
 555 average SI, and Gordon networks having a much lower average SI (Figure 4A). When
 556 comparing 1 year (Figure 4B) and 2 years (Figure 4C). We found a marginal increase in
 557 the average SI for the Gordon networks, even though the 95% bootstrap confidence



558 interval across 1000 bootstraps did not overlap (Supplementary Figure 9).

559 3.5. The subset of areas with adult-like network organization is in spatial 560 proximity to the high consensus regions across adult individuals

561 To quantify the spatial distribution similarity between the locations of low
 562 interindividual variability in network identity (“high consensus cortical ROIs”) (Dworetzky
 563 et al., 2021) and the “Gordon Subset” areas, we calculated the Euclidean distance
 564 between the centers of the “Gordon Subset” areas (Figure 5A) and the alternative “not
 565 Gordon Subset” areas (Figure 5B) by 3.9 mm (~1 voxel). To rule out the possibility that
 566 this difference was driven by the differences in the number of areas, we repeated the
 567 same analysis by permuting “Gordon Subset” (N = 166) versus “not Gordon Subset” (N
 568 = 120) labels 1000 times to generate a null distribution. We found that the actual
 569 difference (3.9 mm) was significantly higher than the null ($p < 0.001$, permutation
 570 testing) (Figure 5C).

571

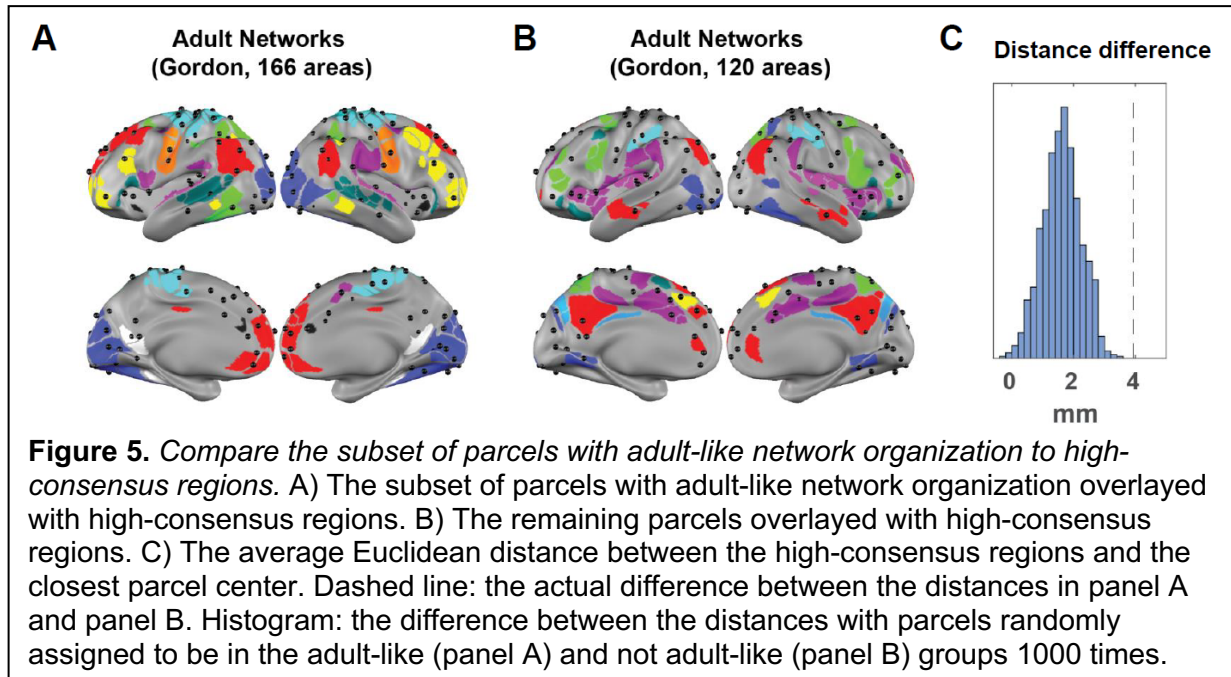


Figure 5. Compare the subset of parcels with adult-like network organization to high-consensus regions. A) The subset of parcels with adult-like network organization overlaid with high-consensus regions. B) The remaining parcels overlaid with high-consensus regions. C) The average Euclidean distance between the high-consensus regions and the closest parcel center. Dashed line: the actual difference between the distances in panel A and panel B. Histogram: the difference between the distances with parcels randomly assigned to be in the adult-like (panel A) and not adult-like (panel B) groups 1000 times.

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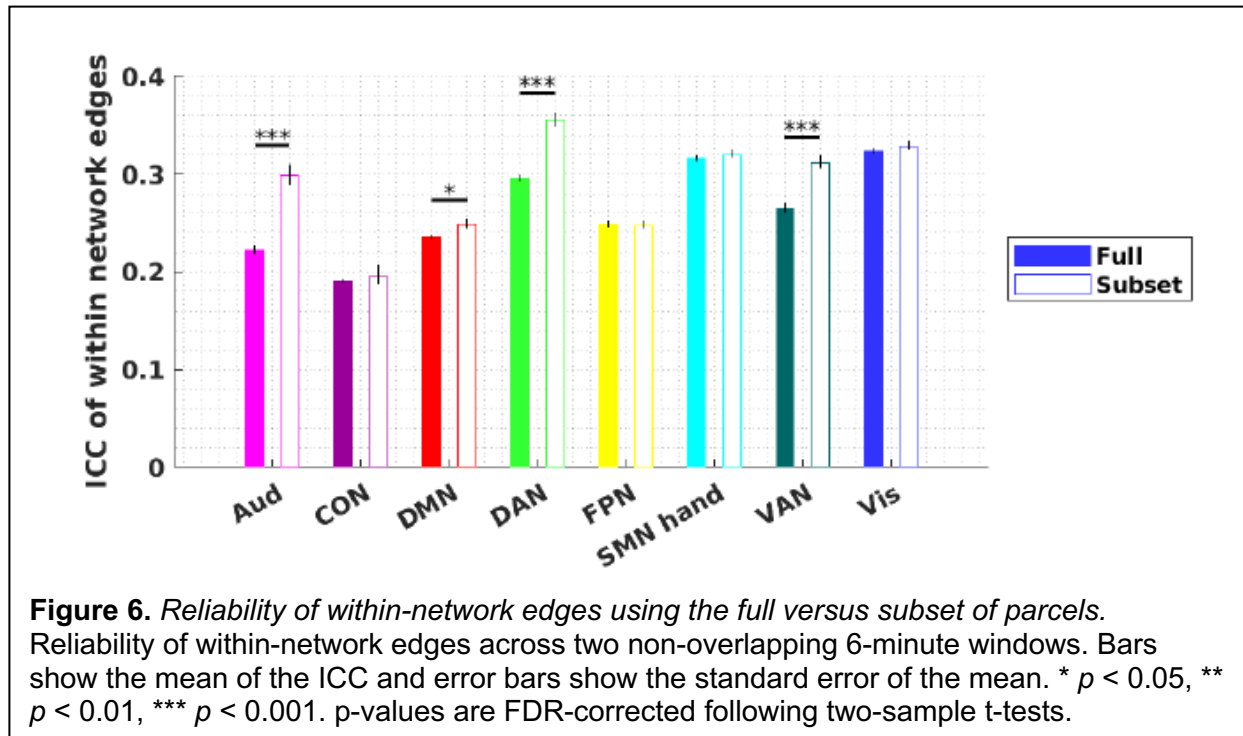
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3.6. Within-network FC edges in the subset of areas has a higher test-retest reliability and a higher consistency across subjects

Comparing FC computed from non-overlapping time windows in the same session demonstrated that the subset parcels had significantly higher within-session reliability than the full parcel set. In particular, the four out of eight networks with partially retained parcels exhibited higher average ICC with the parcel subset than the full parcel set (two-sample t-test, FDR-corrected $p < 0.05$): Aud (Cohen's $d = 0.68$), DMN (Cohen's $d = 0.13$), DAN (Cohen's $d = 0.55$), and VAN (Cohen's $d = 0.43$) (Figure 6)

To examine whether the contribution of FC edges to individual identification varied across the within- and between-network blocks by the three network schemes, we also quantified the FC group consistency (ϕ) and differential power (DP) (Finn et al., 2015). Consistent with previous literature, we observed that a large percentage (~50%) of FC edges in the within-network blocks tend to be highly consistent in all three network schemes, as opposed to between-network blocks (~6%) (Supplementary Figure 10; Supplementary Table 1). The sensorimotor networks especially had a large proportion of highly consistent within-network FC edges (Supplementary Table 1-2). Moreover, using adult networks defined by the subset of areas ("Gordon Subset"), the percentage of high consistent edges within network increased dramatically for all eight partially retained networks (Supplementary Table 2), suggesting that the adult network spanned by our subset over-represented areas with highly consistent FC between them.

On the other hand, within-network blocks tend to have only a slightly larger percentage of highly differentiating FC edges (~15%) than between-network blocks (~10%) (Supplementary Table 3), with both increased and decreased proportion of highly differentiating edges when using the "Gordon Subset" instead of "Gordon Full".



598 4. Discussion

599

600 4.1. Infant FC has a modular structure distinct from adult FC

601 We observed that for infants at 8-60 months, brain areas did exhibit some degree
602 of clustering in average FC profiles according to the adult network assignments (average
603 $SI > 0$), although much weaker than that in adult FC. This observation is consistent with
604 prior literature where a modular organization of FC was detected in preterm-born (Cao et
605 al., 2017; van den Heuvel et al., 2015) and *in utero* fetal baby brains (Thomason et al.,
606 2014; Wheelock et al., 2019), with a decent degree of similarity to the modular
607 organization in the adult FC (van den Heuvel et al., 2015). Furthermore, it seemed that
608 instead of being less modular and more random, the infant FC data were better described
609 with notably different but related modular organization, including fragmented anterior and
610 posterior segments of higher-order association networks (Eggebrecht et al., 2017; Eyre
611 et al., 2021; Kardan et al., 2022; Marrus et al., 2018).

612

613 4.2. Identification of functional network cores that are stable across development

614 We found that a subset of the areas tended to exhibit more of an adult-like network
615 FC clustering pattern, forming the “network cores” of adult networks. While the unique
616 and evolving modular organization in infant FC has been an interesting and important
617 topic of study (F. Wang et al., 2023; Wen et al., 2019, 2020), it is also desirable to note
618 their similarities to older children and adults (Fransson et al., 2007; Gao, Alcauter, Elton,
619 et al., 2015). The difference in within-network FC across ages was reduced when this
620 subset was used instead of the full set of brain areas. The FC within this subset of regions
621 was also more consistent across sessions and individuals. These areas likely form the
622 early scaffold for what will eventually become the adult networks (Grayson & Fair, 2017).

623

624 **4.3. The role of childhood experience in shaping the development of functional** 625 **networks**

626 Our results hinted that interindividual variability in functional network topography
627 might have a developmental origin. To a first approximation, the spatial topography of the
628 network cores we found resembled that of the locations with low interindividual variability
629 in network identity (Dworetzky et al., 2021; Gordon, Laumann, Gilmore, et al., 2017;
630 Hermsillo et al., 2024), while the areas that are subject to misidentification in infants
631 resembled integration zones with a high degree of network overlap (Hermsillo et al.,
632 2024) and network hubs with a high participation coefficient (Power et al., 2013).

633 One potential explanation for this observation is that some parts of the brain
634 matured *in utero* and, thus, showed limited plasticity after birth, while other parts continue
635 to develop throughout childhood. In line with this, mature synaptic density, cortical
636 thickness, and gray matter density were reached earlier in low-expanding regions (e.g.
637 V1 and Heschl's gyrus) than in high-expanding regions (DLPFC) (Hill et al., 2010). There
638 might be biological or evolutionary reasons to have parts of the adult networks maturing
639 later, such as to limit the prenatal resources on regions most important for early survival
640 and increase the influence of postnatal experience on other regions (Hill et al., 2010). In
641 addition, the regional variability of network stability might also be linked to variability in
642 the expression of excitatory and inhibitory features across the cortex (Sydnor et al., 2021).
643 The idea that areas with higher FC variability had more behavioral significance is further
644 reinforced by research demonstrating that behavioral and cognitive domain features could
645 be better predicted from FC in cortical areas with high FC variability (Mueller et al., 2013).
646 Recognition of the regional variability in functional network stability across development
647 in future research is important, as they may become useful biomarkers for
648 psychopathology (Sydnor et al., 2021), as well as therapeutic targets for brain stimulation
649 interventions (Correll et al., 2021).

650 We did not observe a strong over-representation of sensorimotor networks
651 compared to association networks in our stable network cores, despite the literature
652 suggesting that sensorimotor networks mature early than association networks (Gao,
653 Alcauter, Elton, et al., 2015; Sydnor et al., 2021). The network cores spanned both
654 sensorimotor and association networks along the functional hierarchy of the neocortex
655 (Flechsfig, 1901; Mesulam, 1998; Sydnor et al., 2021). One potential limitation is that our
656 infant cohort was older than eight months and significant earlier neurodevelopmental
657 changes along the sensorimotor-association hierarchy might have happened before eight
658 months (Bethlehem et al., 2022; Flechsfig, 1901). Another possibility is that the
659 sensorimotor functional networks definition was inaccurate, e.g. the auditory network
660 might incorporated parts of secondary somatosensory regions (Raju & Tadi, 2024),
661 making the areas within the network less similar in their FC profile.

662 663 **4.4. Using a subset of areas to improve statistical power and interpretability**

664 There are pros and cons of using a pre-existing functional network model and a
665 data-driven functional network model for infant neuroimaging research. Studies of
666 functional networks in infants have often implemented unsupervised methods (i.e.
667 clustering or similar types of community detection algorithms) to find age-specific modules
668 and called them "functional networks" (Eggebrecht et al., 2017; Kardan et al., 2022;
669 Marrus et al., 2018; Molloy & Saygin, 2022; Myers et al., 2024; Sylvester et al., 2022; F.

670 Wang et al., 2023; Wen et al., 2019, 2020). These identified modules were by definition
671 a good representation of the organizational structure in the data and may help address
672 the problem of reproducibility in brain-wise association studies (Hermosillo et al., 2024;
673 Marek et al., 2022). However, unlike the adult networks that have been extensively
674 validated with behavioral task data to corroborate their “functional” roles (Power et al.,
675 2011; Wig, 2017; Yeo et al., 2011), those age-specific modules often lack biological
676 support for their functions, making the relevance to a broader developmental context less
677 obvious. On the other hand, using the adult-network topography directly on infants
678 neglects the infant-specific organizational features and risks including spurious variability
679 in measurements (be they from fMRI, EEG, or fNIRS), leading to reduced effect size and
680 power (Hermosillo et al., 2024), or an exaggerated difference across development. For
681 example, our results in section 3.2 suggested that differences in within-network FC across
682 age groups might be partially attributed to the misspecification of functional network
683 identity.

684 Here, we proposed an alternative strategy that used a subset of areas representing
685 the stable “network cores” across infancy and adulthood for studying trajectories of FC
686 during development. This approach strikes a balance between
687 interpretability/comparability across cohorts, and reliability/reproducibility. This idea of
688 using a subset of the brain areas to define ROIs as an approach to improve statistical
689 power has been proposed in the literature (Dworetzky et al., 2021; Hermosillo et al., 2024).
690 However, instead of focusing the subset of brain areas with interindividual variability, we
691 focused on excluding the subset of brain areas that had a network misidentification in the
692 infant cohort. Alternatively, depending on the research question at hand, one might be
693 interested in focusing on the areas that are unstable across development, which may
694 have behavioral or clinical significance as mentioned in section 4.3.

695 696 **4.5. Precision Functional Mapping in Developmental Cohorts Using Adult Group** 697 **Priors Needs to Be Practiced with Caution**

698 As demonstrated in our results, on average the adult functional networks did not
699 well represent the organization of infant FC into internally similar clusters, which might
700 have important implications for research using an adult functional network model to
701 generate individual-specific functional networks in the developmental cohort. Recent
702 research has recognized idiosyncratic details and reliable features in functional network
703 topography across human individuals qualitatively different from group-average estimates
704 (Gordon et al., 2015; Gordon, Laumann, Gilmore, et al., 2017; Gratton et al., 2018;
705 Laumann et al., 2015). Those features are stable across sessions (Seitzman et al., 2019),
706 as well as task versus rest states (Kraus et al., 2021). The individual differences in
707 association network topography also predict individual differences in executive function
708 (Cui et al., 2020). However, reliable identification of individualized functional networks
709 with unsupervised clustering or community detection procedures requires extended data
710 acquisition. For example, with the Infomap algorithm (Power et al., 2011; Rosvall &
711 Bergstrom, 2008), more than 90 minutes of data is required to achieve an average
712 network overlap dice coefficient of > 0.75 (Gordon, Laumann, Gilmore, et al., 2017).
713 Therefore, several semi-supervised methods have been developed to derive individual
714 functional networks (Cui et al., 2020; Gordon, Laumann, Adeyemo, et al., 2017; Hacker
715 et al., 2013; Kong et al., 2019; D. Wang et al., 2015) using adult networks as priors.

716 However, those approaches generally assumed that the individual functional networks
717 were highly similar to the adult group average. This assumption might not be suitable for
718 developmental cohorts: as we demonstrated here, on average, the adult functional
719 networks poorly represented the organization of the infant FC into internally coherent
720 clusters. Two unwanted consequences might arise from this observation. First, the
721 network templates generated by averaging the FC profiles within a poorly defined network
722 might be noisy and inaccurate. Second, the algorithms may incorrectly force a categorical
723 label for locations that poorly matched all available networks. Future studies using adult-
724 based priors in developmental cohorts should keep those limitations in mind and develop
725 strategies to mitigate them.

726

727 **4.6. Limitations and Future Directions**

728 Our infant fMRI data were collected during natural sleep while adult networks were
729 derived from awake resting state data. Since sleep and the level of arousal are known to
730 modify the FC structure in adults (Chang et al., 2016; Mitra et al., 2017; Tagliazucchi et
731 al., 2012), and that FC patterns in asleep 6 and 12 months old infants more closely
732 resemble FC patterns in asleep adults (Mitra et al., 2017), the difference in modularity
733 and hence in the quality of clustering as measured by the silhouette index between adult
734 and infant FC using the adult Gordon network might be smaller if the infant fMRI data
735 were collected during an awake state. Other differences in the acquisition and processing
736 of the two datasets might introduce confounds, too. Additionally, while we observed little
737 age effect on within-network FC, this could be due to the narrow age range of our sample
738 (mostly between 1 and 3 years). Moreover, we used an adult area parcellation (Gordon
739 et al., 2016) for the adult (Gordon et al., 2016) and infant (Kardan et al., 2022), which was
740 slightly inferior to an age-specific parcellation for the toddler group to describe the local
741 area organization at this age based on our preliminary analysis. The mixing of fMRI
742 signals within the ill-defined areas might contributed to some of the low SI observed in
743 those areas. In the future, the same analysis strategy could be applied directly to
744 vertex/voxel level data for higher precision.

745 Future studies could examine the cellular, molecular, and genetic properties of the
746 areas that have already developed an adult-like organization in infancy to fully understand
747 the biological underpinning of our observation. Furthermore, given that we expect that
748 using the subset of areas that form relatively stable network organization across
749 development would improve statistical power for brain-wide association studies (Marek
750 et al., 2022) using FC, future studies with larger samples and well-defined behavior
751 measures with reliability tests used in prior literature can be used to test this hypothesis
752 (Hermosillo et al., 2024; Marek et al., 2022). Moreover, it would be interesting to
753 investigate whether the same “network cores” exist in subcortical structures, such as the
754 thalamus. One plausible hypothesis is that the topography and diversity of thalamocortical
755 projection may relate to the variability of functional network stability across the neocortex.

756

757 **4.7. Conclusion**

758 We found that despite the large differences in FC organization between infants
759 and adults on average, there existed a subset of cortical areas whose FC profiles
760 demonstrated adult-like network organization even in infants. These areas were spatially
761 closer to previously locations of high consensus in network identity across adult

762 individuals than alternative areas. Additionally, within-network FC defined with the subset
763 of areas was higher in magnitude and more reliable across scans, individuals, and
764 development. We proposed the use of adult networks defined by the subset of areas with
765 an adult-like network relationship as a complementary approach of studying infant FC
766 than using age-specific functional networks derived from data-driven methods. This would
767 strengthen reliability, yet at the same time encourage interpretability and comparability
768 across developmental stages. The biological basis of the regional variability of functional
769 network stability, as well as its psychopathological and behavioral impacts may become
770 interesting topics for future research.

771

772 **Author Contributions**

773 JCT conceptualized the project. JCT and YW conducted a formal analysis. OK, OM,
774 TKMD, CMS, DD, XW, and YW processed/curated the data. MDW, JCT, JTE were
775 responsible for funding acquisition. JCT and MDW wrote the original draft. Everyone
776 contributed to the review and editing of the final manuscript.

777

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783

784 **Declaration of Competing Interests**

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

787

788 **Data and Code Availability**

789 The WU 120 data can be downloaded from

790 <https://legacy.openfmri.org/dataset/ds000243/>.

791 The BCP data can be downloaded from the National Institute of Mental Health
792 Data Archive (NDA) at https://nda.nih.gov/edit_collection.html?id=2848. The
793 preprocessing scripts are available at [https://github.com/DCAN-Labs/dcan-infant-](https://github.com/DCAN-Labs/dcan-infant-pipeline)
794 [pipeline](https://github.com/DCAN-Labs/dcan-infant-pipeline). The analysis scripts used to generate the results and figures are available on
795 <https://github.com/cindyhfls/Tu-2024-GordonSubset-DCN>.

796 The test for the difference between correlations were implemented from the
797 function [corr_rtest](#) downloaded from MATLAB central. The Intraclass Correlation
798 Coefficient (ICC) was calculated from the function [ICC](#) downloaded from MATLAB
799 central.

800

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804 helped with the collection, processing, and curation of the data.

805

806 **Declaration of generative AI and AI-assisted technologies in the writing process**

807 During the preparation of this work the authors used ChatGPT in order to
808 improve sentence structure and language precision. After using this tool/service, the
809 authors reviewed and edited the content as needed and take full responsibility for the
810 content of the publication.

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1164 **Supplementary Materials**

1165

1166 **Supplementary Results**

1167 **S1. Silhouette index of adult networks in infant FC with the mean in all alternative**
1168 **networks**

1169 When the SI was calculated with respect to the mean in all alternative networks
1170 rather than the mean of the best alternative network, they were still moderately
1171 correlated with the SI reported in the main results (Pearson's $r = 0.74$, $p < 0.001$).
1172 However, since the mean of similarity to all alternative networks (especially to the ones
1173 spatially distant from the area in question) would tend to be lower than the best
1174 alternative, the SI is positively shifted with almost all parcels having $SI > 0$
1175 (Supplementary Figure 5).

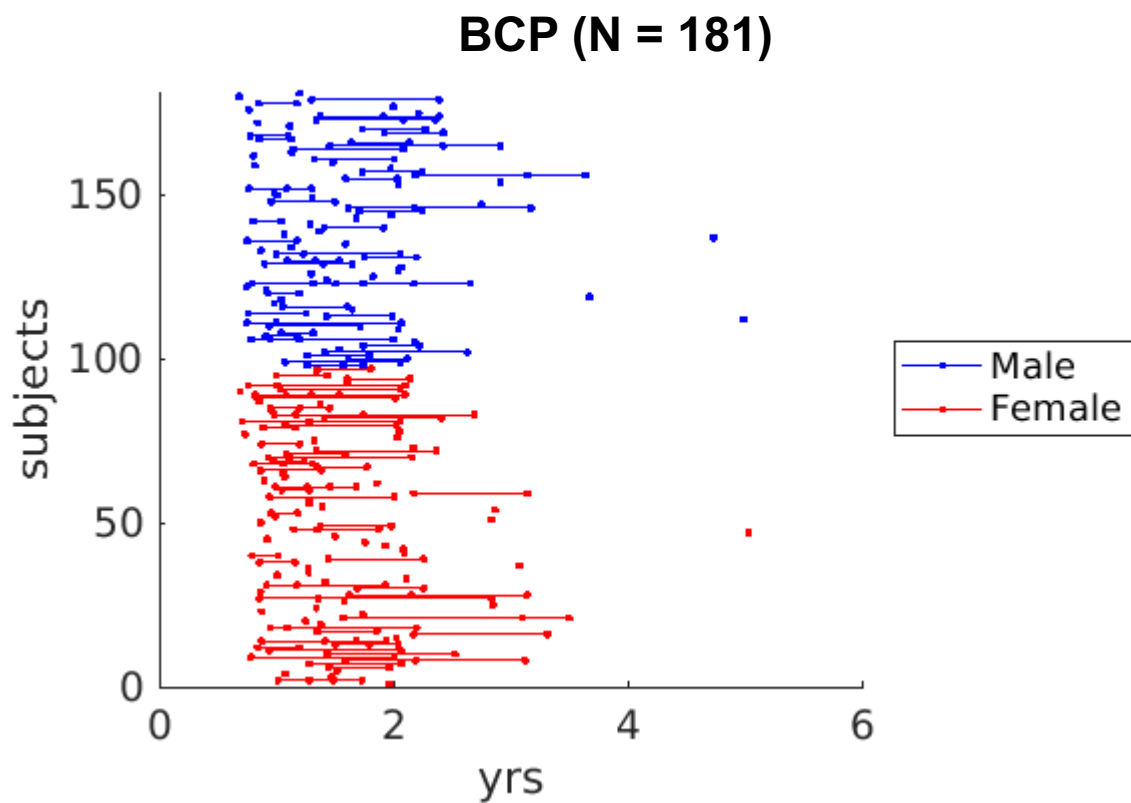
1176 **S2. Age effect on within-network FC is smaller in magnitude with the subset of**
1177 **areas in the Gordon network**

1178 If the subset of areas with adult-like network configuration tends to be more
1179 stable across infant development, then they will have a relatively stable within-network
1180 FC across chronological age. We computed within-network FC across age using full
1181 versus subset of areas. For the eight networks that were partially retained, five networks
1182 demonstrated a significant correlation between within-network FC and age ($p < 0.05$,
1183 Spearman's ρ): the within-network Aud, SMN hand and Vis networks were negatively
1184 correlated with age and the within-network FC in DAN and the FPN were positively
1185 correlated with age. The age effect was greater in magnitude with the full set of areas
1186 (Figure 3A) than with only the partially retained areas (Figure 3B) for the SMN hand
1187 network, although not significant when comparing the Fisher-Z-transformed ρ values (Z
1188 $= 1.588$, one-sided $p = 0.056$). Similar results were found for other networks, where the
1189 age effect was less negative for Aud, SMN hand and Vis networks, and less positive for
1190 DAN and FPN, but none of them had a significant ($p < 0.05$) Z-test. To examine the
1191 robustness of our result to the selection of data samples, we generated 1000
1192 bootstrapped samples of the infant sessions. We found that the sign of the difference
1193 was consistent across bootstrap samples (i.e., on average the networks using the
1194 subset of areas were less correlated with age than the full set of areas) (Figure 3C). The
1195 mean and 95% confidence interval for the bootstrap showed a mean difference in
1196 Fisher-Z-transformed ρ values for full versus subset was -0.1139 [-0.1721, 0.0129] for
1197 Aud, -0.1386 [-0.1684, -0.0814] for SMN hand, 0.0020 [-0.0887, 0.0348] for Vis, -0.0205
1198 [-0.0120, 0.1439] for DAN and 0.0089 [0.0071, 0.0511] for FPN (Figure 3C).

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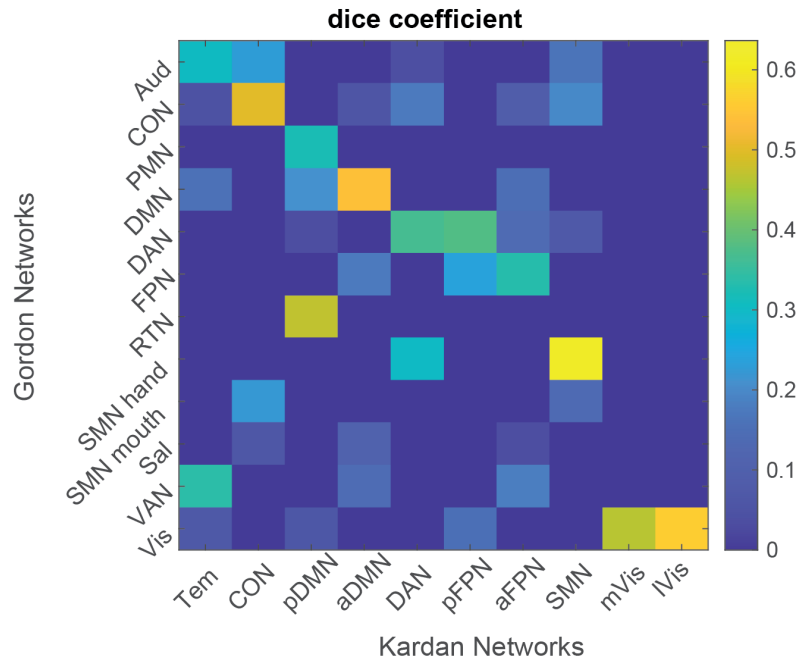
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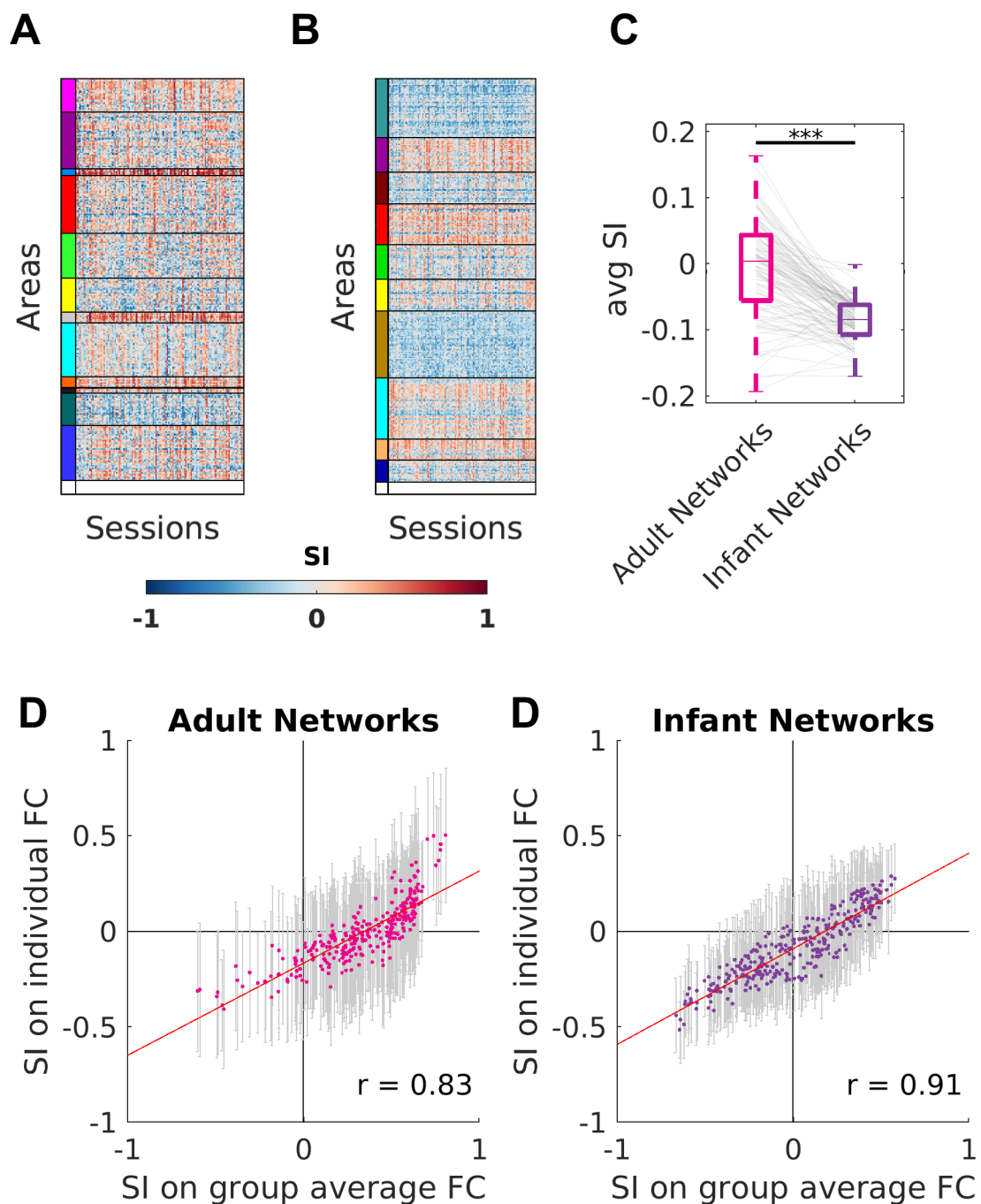
Supplementary Figure 1. *Distribution of age and sex*

1202



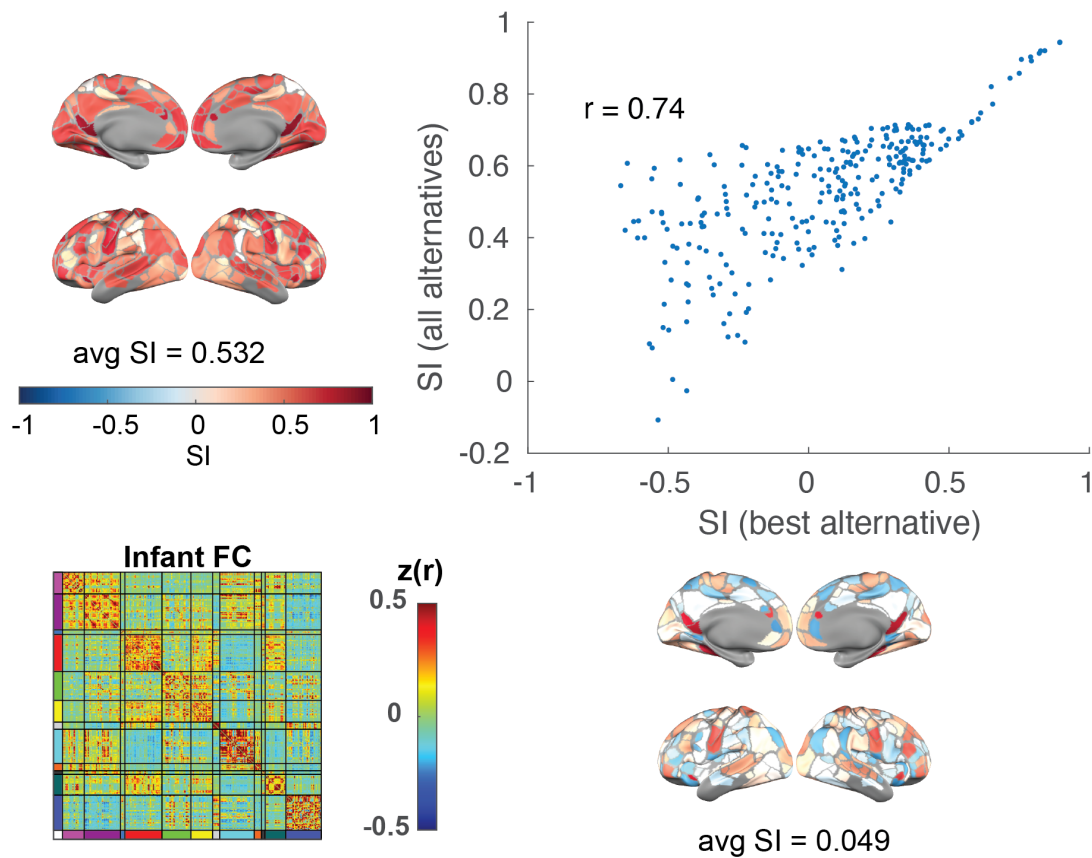
Supplementary Figure 2. Dice overlap between the Gordon Networks (Adult) and the Kardan Networks (Infant). Network abbreviations: auditory (Aud), cingulo-opercular (CON), parietal memory (PMN), default mode (DMN), dorsal attention (DAN), fronto-parietal (FPN), retrosplenial temporal (RTN), somatomotor hand (SMN hand), somatomotor mouth (SMN mouth), salience (Sal), and ventral attention (VAN), visual (Vis), somatomotor (SMN), temporal (Tem), posterior frontoparietal (pFPN), posterior default mode (pDMN), lateral visual (IVis), medial visual (mVis), anterior fronto-parietal (aFPN), anterior default mode (aDMN).

1203



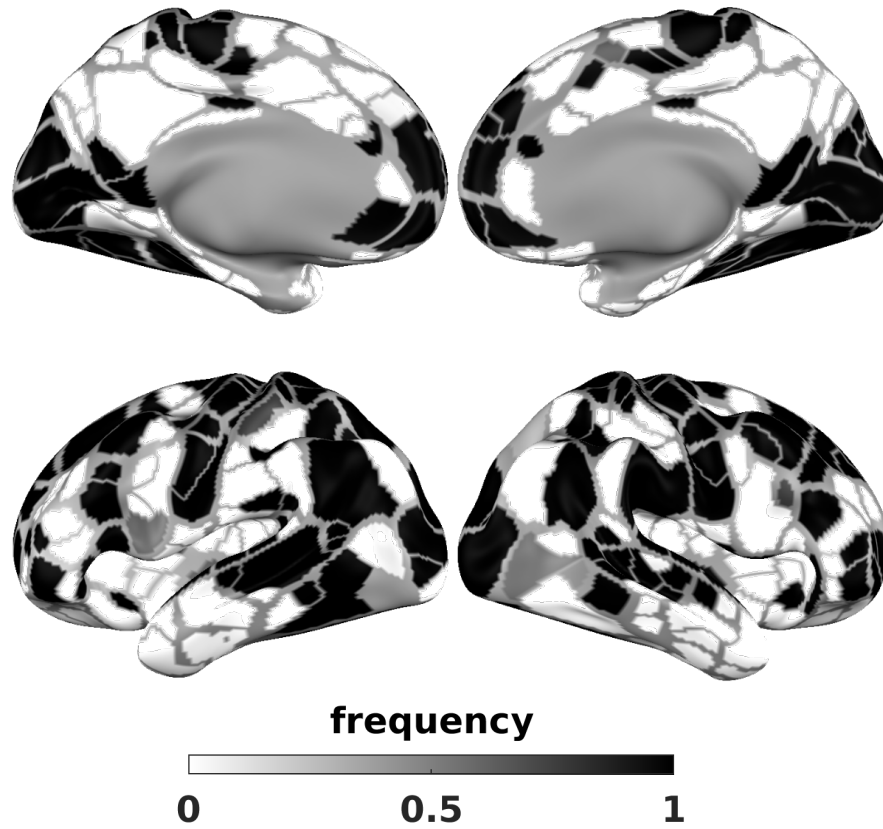
Supplementary Figure 3. *Silhouette index (SI) of adult and infant networks on individual adults' FC.* A) SI across adult networks (Gordon, 286 areas). B) SI across infant networks (Kardan, 328 areas). C) average SI of adult and infant networks across areas on individual adults' FC. *** $p < 0.001$ in paired t-test. D) Pearson's correlation of SI of adult networks on group average FC and the mean of SI on individual FC across 286 areas. E) Pearson's correlation of SI of infant networks on group average FC and the mean of SI on individual FC across 328 areas.

1204



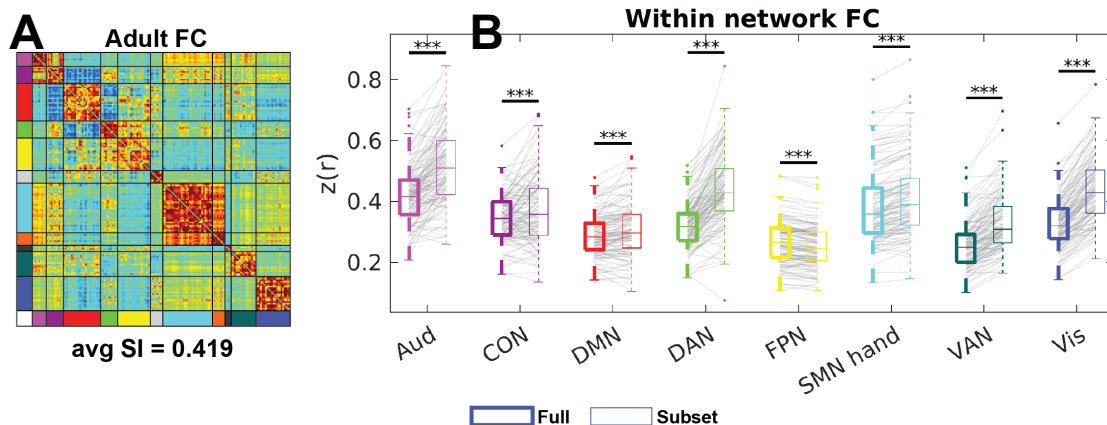
Supplementary Figure 5. Correlation between silhouette index calculated with the best network or with all alternative networks.

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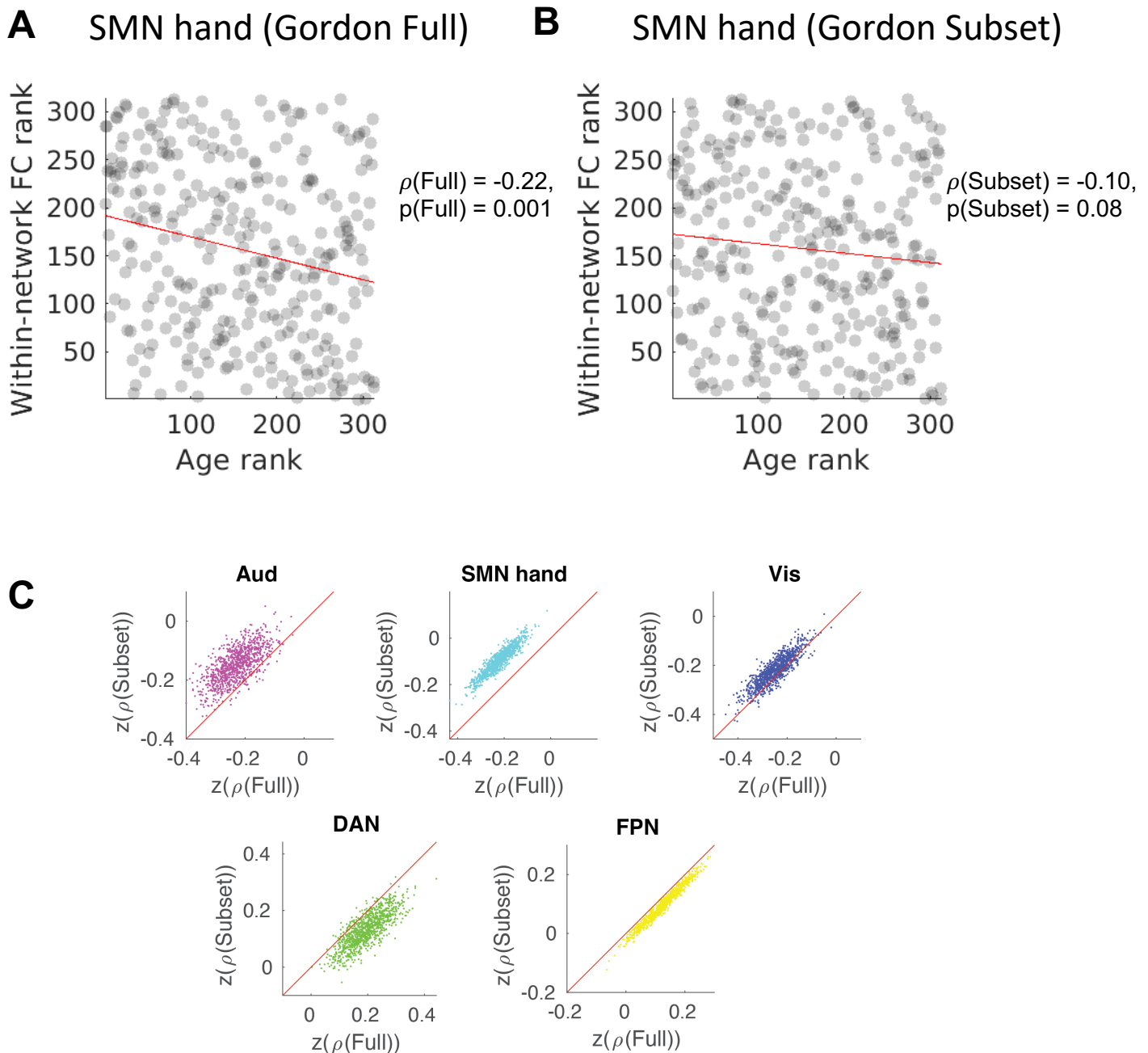
Supplementary Figure 6. *Frequency of $SI > 0$ across 1000 bootstraps.*

1206



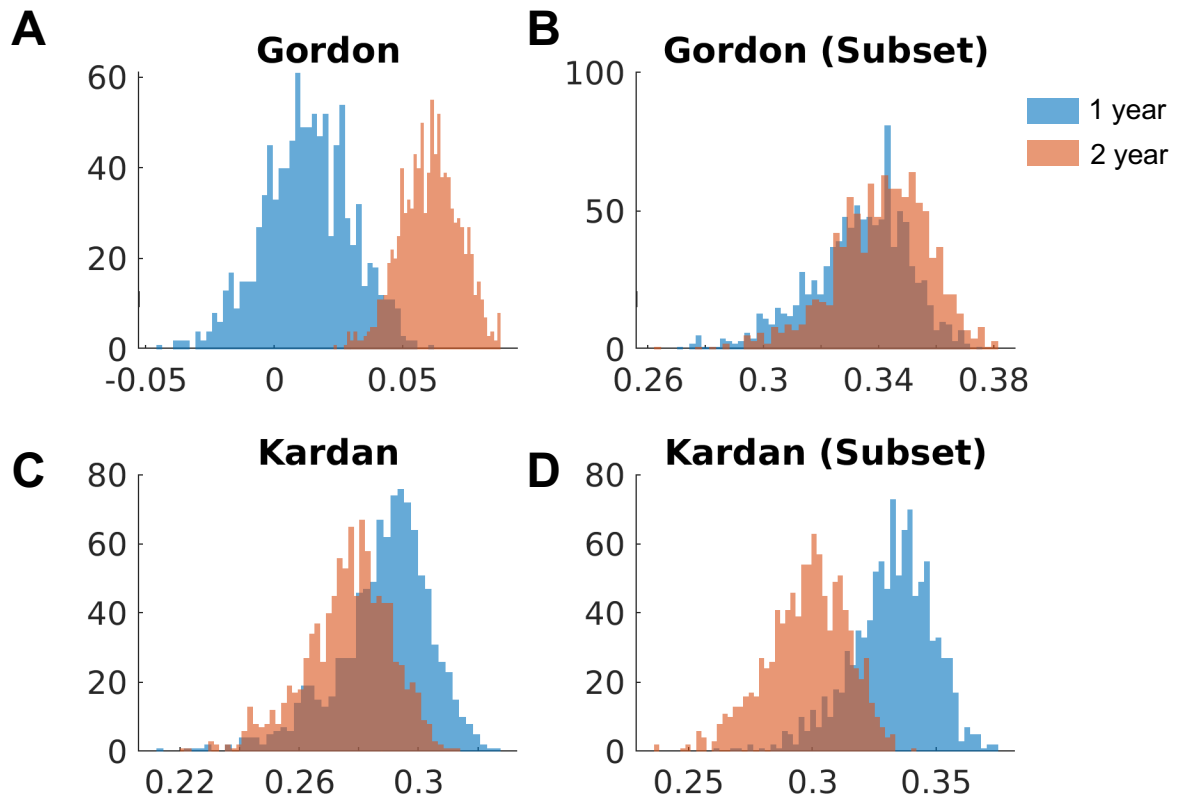
Supplementary Figure 7. Adult FC using the Gordon Subset. A) The sorted average FC in infants with the subset of areas. B) The average within-network FC with full (left) versus subset (right) across sessions.

1207

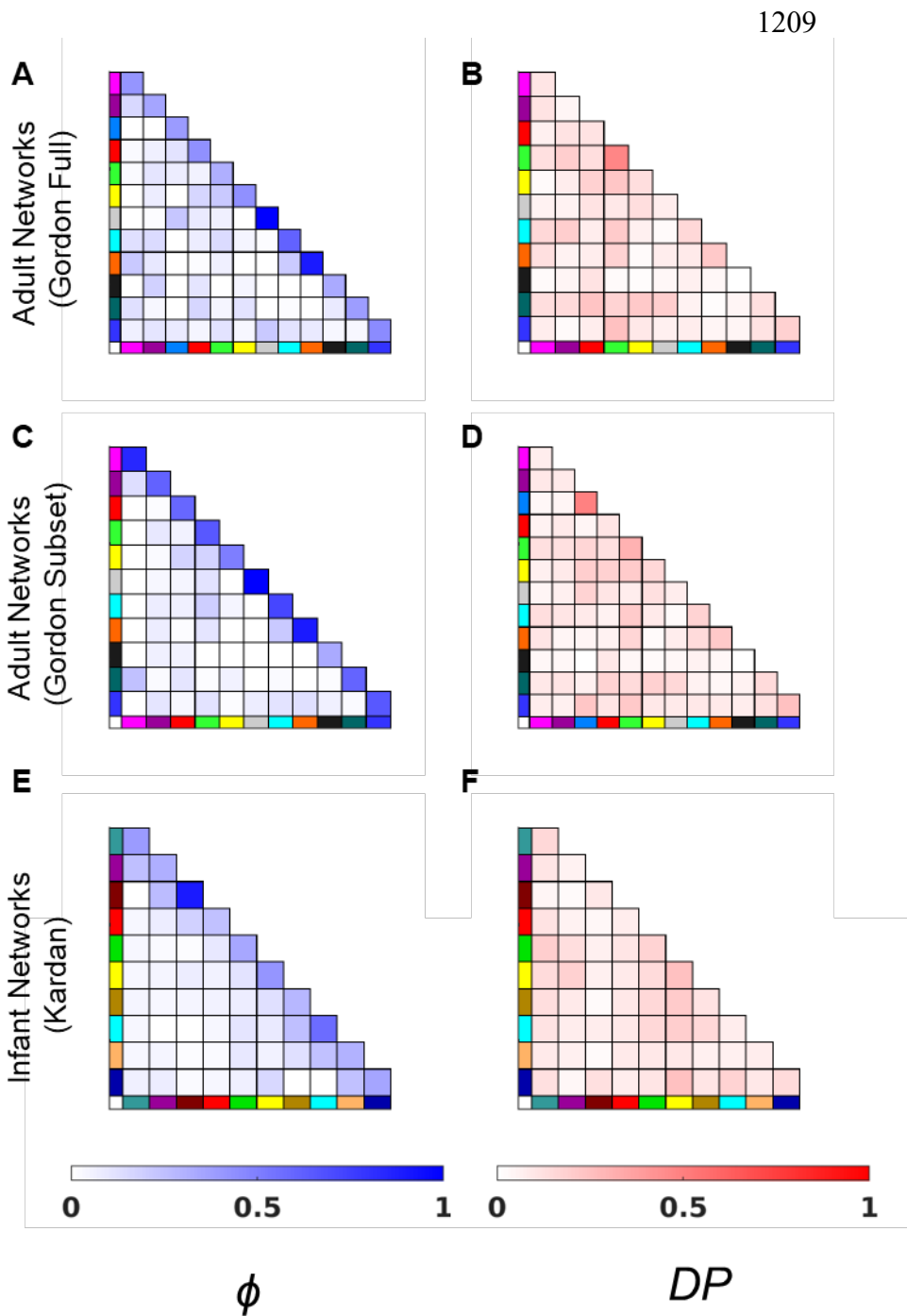


Supplementary Figure 8. Correlation between age and within-network FC in using the subset of areas versus the full set of areas. A) Scatter plot of within-network FC versus age for SMN hand network defined with the full set of areas. B) Scatter plot of within-network FC versus age for SMN hand network defined with the subset set of areas. C) The within-network FC for three networks is negatively correlated with age (Aud, SMN hand, Vis), and the within-network FC for two networks is positively correlated with age (DAN, FPN). The x-axis is the Fisher-Z-transformed Spearman's correlation (ρ) between within-network FC using the full set of areas and age. The y-axis is the Fisher-Z-transformed Spearman's correlation (ρ) within-network FC using the subset of areas and age). Each data point represents a bootstrap sample of sessions ($N = 1000$). Red line shows the line of least-squared fit in A-B and the line of identity in C.

1208



Supplementary Figure 9. *Bootstrapped distributions of average silhouette Index at 1 year and 2 years ($N = 1000$ bootstrapped samples). A) Gordon networks. B) Gordon networks but with the subset of areas in Figure 2A. C) Kardan networks. D) Kardan networks but with the subset of areas in Figure 2A.*



Supplementary Figure 10. Fraction of high consistency (ϕ) and high differential power (DP) edges (top 10%) across Gordon Full (A-B), Gordon Subset (C-D), Kardan (E-F).

1210

Supplementary Table 1. Percentage of highly consistent (ϕ) edges across different network assignment schemes

	Gordon Full	Gordon Subset	Kardan
within-network	44.1%	63.1%	49.5%
between-network	8.3%	6.5%	5.4%

1211

Supplementary Table 2. Percentage of highly consistent (ϕ) edges across different network assignment schemes. The eight partially retained networks were bolded and had an asterisk.

within-network	Gordon Full	Gordon Subset
Aud*	41.30%	84.21%
CON*	35.64%	61.73%
PMN	40.00%	/
DMN*	43.17%	59.07%
DAN*	31.45%	65.17%
FPN*	43.12%	50.84%
RTN	100%	100%
SMN hand*	61.45%	72.82%
SMN mouth	89.29%	89.29%
Sal	33.33%	33.33%
VAN*	38.34%	60.94%
Vis*	45.89%	65.17%

1212

Supplementary Table 3. Percentage of high differential power (*DP*) edges across different network assignment schemes.

	Gordon Full	Gordon Subset	Kardan
within-network	16.50%	14.73%	12.79%
between-network	10.81%	10.98%	9.93%

1213

Supplementary Table 4. Percentage of high differential power (*DP*) edges across different network assignment schemes. The eight partially retained networks were bolded and had an asterisk.

within-network	Gordon Full	Gordon Subset
Aud*	7.97%	10.53%
CON*	8.33%	4.94%
PMN	50.00%	/
DMN*	10.73%	11.59%
DAN*	30.24%	47.19%
FPN*	15.58%	13.91%
RTN	7.14%	7.14%
SMN hand*	17.92%	15.82%
SMN mouth	21.43%	21.43%
Sal	0%	0%
VAN*	14.62%	12.02%
Vis*	24.97%	18.43%