

Short-timescale fluctuation asymmetry precedes chronnectome growth transitions and behavioral development in early infancy

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Article

Keywords: infancy, functional connectome development, dynamic functional connectivity, visually guided behavior, fluctuation asymmetry ratio, longitudinal MRI

Posted Date: August 21st, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10638172/v1>

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Additional Declarations: There is **NO** Competing Interest.

1 **Short-timescale fluctuation asymmetry precedes chronnectome growth**
2 **transitions and behavioral development in early infancy**

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15

16 **Abstract**

17 Early infancy is characterized by rapid, nonlinear reorganization of the functional
18 connectome, yet its dominant growth modes and relationship to short-timescale brain
19 dynamics remain unclear. Using a densely sampled longitudinal multimodal dataset
20 collected across the first six postnatal months, we estimated days-scale trajectories of
21 whole-brain functional connectivity growth and visually guided behaviors. We identify
22 a growth-mode transition in the functional connectome at approximately 2-4 months,
23 marked by a shift from predominantly local strengthening toward increasingly
24 distributed integration. This developmental reorganization was preceded by changes in
25 the fluctuation asymmetry ratio (FLARe), a measure of asymmetry in recurring short-
26 timescale co-fluctuation states. Across individuals, FLARe predicted subsequent
27 change rates of functional connectivity and visually guided behaviors. These findings
28 identify short-timescale fluctuation asymmetry as a previously unrecognized
29 prospective signal of later days-scale connectome and behavioral change, and provide
30 a cross-timescale framework for linking functional brain dynamics unfolding over
31 seconds to developmental change emerging over weeks to months.

32 **Keywords:** infancy, functional connectome development, dynamic functional
33 connectivity, visually guided behavior, fluctuation asymmetry ratio, longitudinal MRI

34

35 **Introduction**

36 The first months of life are marked by rapid reorganization of large-scale functional
37 brain networks ^{1,2}. Unimodal networks, including visual, auditory, and sensorimotor
38 systems, are established early and undergo rapid refinement within the first postnatal
39 months, whereas long-range and multimodal connectivity, essential for flexible
40 cognition, develops more gradually ³⁻⁵. This early reorganization can be understood in
41 terms of the brain's functional growth mode, defined as the dominant pattern by which
42 functional connections strengthen or weaken to shape network architecture over
43 developmental time. A predominantly local-modular growth mode, in which
44 developmental changes are dominated by increasing short-range connectivity and
45 network segregation, is well documented prenatally ⁶⁻⁸. In contrast, longitudinal studies
46 beginning around 4 months reveal a shift toward a more distributed growth mode,
47 characterized by developmental changes that increasingly emphasize long-range, cross-
48 network integration over local strengthening ⁹⁻¹². Because longitudinal fMRI studies
49 from birth to ~3 months are scarce, it remains unknown whether early postnatal
50 functional connectome development remains dominated by local strengthening or
51 whether a shift toward increasingly distributed growth has already begun.

52 Behavior similarly undergoes rapid reorganization during early infancy as sensory,
53 motor, cognitive, and social behaviors become increasingly coordinated over the first
54 postnatal months ^{13,14}. For example, eye movements become increasingly coordinated
55 with head and body movements ¹⁵, while visual attention is deployed with increasing
56 flexibility according to social context in addition to the perceptual properties of stimuli
57 ¹⁶. Early behaviors are thought to be supported primarily by interactions among
58 subcortical systems and early-developing cortical networks, with increasingly
59 coordinated behaviors recruiting progressively broader interactions among distributed
60 cortical systems ^{17,18}. This developmental progression parallels the hypothesized
61 transition in functional growth mode, in which developmental change shifts from local
62 patterns of organization toward increasingly distributed interactions across the
63 functional connectome ^{11,17,18}. Pinpointing when and how this functional reorganization

unfolds is therefore critical for understanding how the developing functional connectome supports increasingly coordinated behavior.

Equally important is understanding the mechanisms that drive this early reorganization of the functional connectome. Resting-state connectivity is dynamically organized over seconds, forming a functional chronnectome composed of recurring modes of network interaction¹⁹. Hebbian plasticity provides a compelling framework for linking these short-timescale dynamics to longer-term developmental change: repeated, patterned co-fluctuations tend to bias synaptic strengthening or weakening over time²⁰⁻²⁴. On this view, recurring patterns of seconds-scale network co-fluctuation—often studied using dynamic functional network connectivity—should systematically influence longer-term trajectories of days-scale functional connectivity change and, ultimately, emerging behavior. Supporting this cross-timescale relationship, alterations in seconds-scale dynamics in preterm infants, such as reduced mean synchronization, accompany delays in network maturation and atypical cognitive and motor outcomes^{25,26}. These observations suggest that spontaneous dynamic activity is not merely a reflection of current network state but may be a driver of subsequent developmental change.

To test whether fast dynamics shape longer-term development, we introduce a dynamic measure—fluctuation asymmetry ratio (FLARe)—that quantifies how asymmetrically the brain expresses recurring patterns of second-scale network co-fluctuation. Dynamic functional connectivity analyses have shown that resting-state activity is organized into a small number of recurring co-fluctuation states, each representing a characteristic pattern of coordinated fluctuations among large-scale brain networks²⁷⁻³⁰. Brain states can be expressed in two opposing forms that represent opposite fluctuations of the same underlying co-fluctuation^{27,31}. FLARe quantifies the asymmetry between these opposing state expressions, with its magnitude indicating the degree to which one expression predominates over the other and its sign indicating which expression predominates. We hypothesized that states exhibiting greater asymmetry would exert a stronger influence on subsequent days-scale connectivity change because repeated

expression of one state configuration provides more consistent opportunities for activity-dependent strengthening or weakening³²⁻³⁴.

Guided by this framework, we tested two hypotheses in a densely sampled longitudinal cohort with repeated resting-state fMRI and behavioral measures across the first six postnatal months. First, we hypothesized that the infant functional connectome undergoes a growth mode transition during this period, with the predominant pattern of developmental change shifting from local strengthening toward distributed integration. Second, we hypothesized that seconds-scale dynamics, indexed by FLARe, predict days-scale changes in functional connectivity and behavior during this period. We focused on oculomotor control and social visual engagement because these behaviors mature rapidly during early infancy and depend on coordinated activity across visual, motor, attentional, and social brain systems, making them sensitive behavioral indicators of the large-scale functional connectome reorganization occurring during this developmental period³⁵⁻³⁷. Together, these analyses test both the presence and timing of a growth-mode transition and the dynamic mechanisms that may drive functional connectome reorganization.

We identify a brief but marked transition in growth mode around 2-4 months, shifting from localized strengthening to increasingly distributed integration. We further show that FLARe exhibits a developmental shift that precedes the growth-mode transition and prospectively predicts changes in both functional connectivity and visual behavior. These findings reveal a mechanistic pathway linking spontaneous dynamics to both neural and behavioral development, demonstrating how seconds-scale dynamic activity helps shape the early architecture of the human functional connectome and the developmental trajectories of emerging behaviors. More broadly, they highlight a dynamic signature with potential utility as an early indicator of functional connectome and behavioral trajectories during a period of exceptional plasticity and vulnerability.

Results

We analyzed longitudinal resting-state fMRI (n=128 sessions; up to 3 sessions per infant) and eye-tracking data (n=168 sessions; up to six sessions per infant) collected from 71 typically developing infants sampled across the first six postnatal months (see Methods, “Participants for inclusion/exclusion criteria and ‘Dataset and preprocessing’ for quality-control procedures). Across all participants, the sample yielded dense coverage throughout early infancy, allowing developmental trajectories to be estimated across the full 0-6-month window (see **Fig. 2a** and **Supplementary Figure S1** for sampling distribution). Visual behaviors included measures of oculomotor control (indexed as percentage of visual targets reached) and social visual engagement (indexed as percentage of time spent looking at the eyes of others) derived from eye-tracking assessments (see Methods ‘Dataset and preprocessing’).

Functional connectivity was characterized using static functional network connectivity (sFNC) among 53 networks³⁸ (**Fig. 1a**, see Methods “Individual static functional network connectivity”), with developmental change in connectivity and visual behavior quantified as change rates (CRs; see Methods ‘Change-rate trajectories and zero-crossing points’). We additionally characterized infant whole-brain co-fluctuation patterns and their seconds-scale dynamics using FLARe (see Methods ‘Identification of seconds-scale brain states and axes from spontaneous dynamic connectome’ and ‘Fluctuation asymmetry ratio of state co-fluctuation patterns’). Finally, we tested whether individual differences in FLARe prospectively predicted subsequent days-scale changes in functional connectivity and visual behavior (see Methods ‘Prediction of days-scale change rates from seconds-scale fluctuation asymmetry’).

Static functional connectivity trajectories reveal a growth-mode transition

We hypothesized that the first six postnatal months contain a transition in functional growth mode, with CRs more positive for short- than long-range connections early in infancy and more positive for long- than short-range connections later in infancy. Such

a transition would be reflected by clustered zero-crossings in distance-stratified CR trajectories.

To test this hypothesis, we computed CR trajectories for 1,378 unique pairwise connections between the 53 networks and examined how these trajectories varied as a function of inter-network distance, defined as the Euclidean distance between network peak coordinates (see Methods ‘Individual static functional network connectivity’). When pairwise connectivity CRs were averaged within connectivity-length bins (Fig. 2b), short-range connections (10-40 mm) showed positive CRs in early life that became negative by approximately four months, whereas long-range connections (80-110 mm) exhibited the opposite pattern, transitioning from negative to positive CRs over the same interval. Connections at intermediate distances showed trajectories that fell between these two extremes. Zero-crossings of distance-stratified CR trajectories clustered between postnatal days 71 and 133, defining a growth-mode transition window separating an early stage (Stage 1; prior to day 71) from a later stage (Stage 2; after day 133). A similar transition window was observed when CR trajectories were estimated at the individual rather than population level (**Supplementary Fig. S2**).

This transition period was also evident at the level of functional domains (**Fig. 2c**). Across auditory (AUD), sensorimotor (SM), visual (VS), cognitive-control (CC), default-mode (DM), and cerebellar (CB), and subcortical (SC) domains, a substantial proportion (39.3%) of within- and between-domain CR trajectories crossed zero within the same 71-133-day window. Because domain-level connections vary in their spatial distances (**Supplementary Fig. S3**), we highlight two representative domain pairs that predominantly reflect short-range (VS-VS; mean distance=35.2 mm) and long-range (CC-CB; mean distance=82.5 mm) connectivity. VS-VS crossed zero at day 127, and CC-CB crossed at day 77 (**Fig. 2c**), consistent with the distance-dependent transitions observed at the pairwise connection level (**Fig. 2b**).

Change rate trajectories for eye-tracking measures showed a similar temporal pattern (**Fig. 2d**). Both oculomotor control and preferential attention to eyes exhibited their highest change rates during the first four postnatal months, followed by a marked

174 slowing thereafter (eye-looking CR crossed zero at day 167; CR trajectory for
175 oculomotor function did not cross zero). Thus, rapid behavioral development
176 characterized Stage 1 and progressively slowed as the functional connectome
177 underwent its growth-mode transition.

178 **Stage-dependent reorganization of connectivity growth dynamics**

179 Having identified a transition window based on clustered zero-crossings in change-rate
180 trajectories, we next tested whether the organizing principle governing connectivity
181 change differed between the two developmental stages defined by this window.
182 Because the hypothesized growth-mode transition expects distinct distance-dependent
183 patterns of connectivity change, we first examined whether the relationship between
184 connectivity change and inter-network distance differed between Stage 1 and Stage 2.

185 During Stage 1, connectivity length was negatively correlated with CR ($r = -0.16, p <$
186 0.001), with a zero-crossing at ~ 60 mm, indicating stronger increases in short- than
187 long-distance connections (**Fig. 3a**, left). In contrast, during Stage 2, this relationship
188 reversed: connectivity length was positively correlated with CR ($r = 0.23, p < 0.001$),
189 with a zero-crossing at ~ 56 mm (**Fig. 3a**, right), indicating stronger increases in long-
190 than short-distance functional connections¹¹. Thus, functional connectivity does not
191 change in a single uniform direction across development but instead follows different
192 organizational patterns before and after the transition period, shifting from a local-
193 modular to a more distributed organizing principle.

194 Multiple domains showed reversals in the direction of CRs from Stage 1 to Stage 2,
195 indicating that stage-dependent differences in connectivity change were broadly
196 distributed across functional domains, rather than confined to specific systems (**Fig.**
197 **3b**). Among 28 domain connectivity pairs, 11 of these exhibited a reversal in the
198 direction of change, indicating that the transition in functional connectivity growth
199 mode was widespread rather than restricted to a small number of functional systems
200 (**Supplementary Fig. S6**). For example, connectivity within the visual domain (VS-
201 VS) showed positive CRs in Stage 1 (mean CR = 2.04) but negative CRs in Stage 2

(mean CR = -0.88), whereas sensorimotor-cognitive control connectivity (CB-CC) showed the opposite pattern, transitioning from negative CRs in Stage 1 (mean CR = -1.44) to positive CRs in Stage 2 (mean CR = 1.06). Although some domains showed more extensive shifts than others—for example, multiple visual connections reversed directions, whereas relatively fewer default mode connections did—the high proportion of direction reversals across domain pairs indicates that the transition in functional connectivity growth mode is widespread rather than domain-specific.

Finally, we examined whether the dynamics of connectivity growth—its overall magnitude and direction—differed across stages. Growth magnitude, defined as the mean absolute change rate ($|CR|$) across connections (**Fig. 3c**, see Methods ‘Magnitude and direction of change-rate pattern in functional connectome’), decreased across Stage 1 (-30.8%), indicating a slowing of connectivity change during early infancy, but increased across Stage 2 (+25.1%), reflecting faster rates of change following the transition. To quantify changes in the direction of growth, we measured the angle of cosine similarity between CR patterns at the beginning and end of each stage. Larger angular change indicates greater reorientation of the overall connectivity growth pattern. Notably, the transition period was characterized by relatively low growth magnitude yet exhibited the largest change in growth direction (1.47°/day), exceeding that observed in Stage 1 (0.66°/day) and Stage 2 (0.70°/day). Together, these findings indicate that Stage 1 is characterized by slowing but directionally stable connectivity change, the transition window by low overall change magnitude coupled with the largest shift in growth direction, and Stage 2 by renewed acceleration of connectivity change under a different growth mode. In other words, the system slows as it reorients before accelerating under a newly established growth mode.

Seconds-scale dynamic states are associated with the growth-mode transition.

We next examined how seconds-scale dynamics relate to days-scale changes in FNC²⁰. First, we tested the edge-wise correspondence between dynamic connectivity modes or states derived from dFNC and stage-specific static FNC change-rate patterns. Such correspondence, while not required for FLARe to predict subsequent connectivity

change, would provide connectome-level specificity by showing that short-timescale states preferentially involve the same connections that strengthen or weaken over development. Second, we asked how the identified dynamic states jointly account for the evolving pattern of connectivity change across development. Finally, at the population level, we tested whether reorganization of the dynamic states preceded the growth-mode transition observed in static functional connectivity. Temporal precedence would be consistent with a role for changing seconds-scale dynamics in the emergence of subsequent connectivity growth patterns.

To characterize seconds-scale dynamics, we identified five dynamic states from dynamic functional network connectivity (dFNC) using spatial independent component analysis (spatial ICA; **Fig. 4A**; see Methods ‘Identification of seconds-scale brain states and axes from spontaneous dynamic connectome’ and **Supplemental Fig. S8**). Individual state timeseries were then estimated using spatially constrained ICA, allowing us to quantify the expression of each state in every infant and scan. All five states showed high reliability across ICA runs (ICASSO IQ > 0.8; **Supplementary Fig. S9**). To summarize the network organization of each state, we extracted the dominant eigenvector of the state pattern (**Fig. 4B**). The sign of the eigenvector loadings separated networks into two groups that fluctuated in opposite directions, which were further summarized at the functional-domain level (**Fig. 4C**).

Identified five states includes two forms: 1) segregated form characterized by stronger within-group and weaker cross-group co-fluctuation, and 2) integrated form (sign-reversed segregated form), characterized by weaker within-group and stronger cross-group co-fluctuation. All five states exhibited a modular organization consisting of two network groups, indicating a main fluctuation axis that was captured by the first eigenvector of the state pattern. For example, State 1 comprised two network groups (SM-AUD-SC and VS-DM-CB), fluctuating along a previously described sensorimotor-visual functional gradient (Neuromaps³⁹ cortical similarity with Axis 1, $|r|=0.65$). Larger fluctuation amplitudes along this dominant axis were associated with the segregated form of the state (mean Pearson’s $r=0.43$, **Fig. 4D**), because higher/lower

amplitude of axis fluctuation will be more likely to increase/reduce brain transient synchronized activity along this axis, showing dynamic within-group and cross-group state patterns in the dFNC. This organization provides the basis for interpreting brain dynamics using segregated and integrated network configurations.

To test whether seconds-scale states involved the same connections undergoing days-scale growth, we compared the spatial loading pattern (segregated form) of each dynamic state (**Fig. 4A**) with the mean stage-specific connectivity CR pattern derived from static FNC (**Fig. 5a**) and found strong stage-dependent correspondence between the five state patterns and days-scale connectivity CR patterns (**Fig. 5b**). Growth patterns in Stage 1 and Stage 2 show highly overlaps in connections that are co-fluctuated in the state segregated and integrated forms.

Having established that the spatial patterns of individual dynamic states correspond to stage-specific patterns of connectivity growth, we next asked how the five states jointly account for the evolving pattern of connectivity change over development. We therefore decomposed the days-scale connectivity CR trajectories using the five dynamic state patterns as spatial priors (**Fig. 5A**; see Methods, "Contribution trajectories of state co-fluctuation patterns"). This analysis estimated a state-specific contribution trajectory for each state, reflecting how strongly that state accounted for the observed connectivity CR pattern at each developmental time point (**Fig. 5C**). Together, the five states explained 80.0% of the temporal variance in connectivity CR trajectories, with State 2 accounting for the largest share (55.2%). State-specific contribution trajectories remained relatively stable throughout Stage 1, shifted during the transition period, and reached a new equilibrium during Stage 2. Notably, the trajectories exhibited a pronounced convergence period, characterized by reduced variability in the relative contributions of the five states, centered around day 91 and spanning approximately days 69-131. This convergence closely overlapped the growth-mode transition window identified in the static connectivity analysis (**Fig. 3**), suggesting that the growth-mode transition is accompanied by a redistribution of the relative contributions of the five dynamic states to connectivity growth.

To determine whether seconds-scale dynamics reorganize before the observed growth-mode transition, we next examined developmental trajectories of each state's fluctuation asymmetry ratio (FLARe; **Fig. 5D**, see Methods "Fluctuation asymmetry ratio of state co-fluctuation patterns"). As introduced above, FLARe quantifies the asymmetry between the two opposing expressions of a dynamic state, providing a measure of how consistently one state expression is favored over the other. Across the 0-6-month period, the mean state FLARe remained modestly positive (approximately 0.24, **Fig. 5d**), indicating a slight overall bias toward the segregated form of the identified states. State-specific FLARe trajectories converged toward this mean between approximately days 51 and 113, with maximal convergence around day 77 (**Fig. 5d**). A MANOVA revealed significant differences in FLARe before versus after this convergence window for States 1, 2, 3 and 5 (Wilks' lambda, $F = 2.48$, $p < 0.05$; $n_1 = 72$, $n_2 = 72$), demonstrating coordinated developmental changes across multiple dynamic states (**Fig. 5e**). Specifically, State 1 and State 5 showed increasingly positive FLARe over development, reflecting increasing dominance of their segregated forms, whereas State 2 showed negative FLARe, indicating increasing dominance of its integrated form. Critically, convergence of the FLARe trajectories preceded convergence of days-scale connectivity CRs by approximately 14 days. Moreover, state-specific FLARe trajectories closely tracked the corresponding state contribution trajectories derived from the connectivity decomposition (mean $r=0.728$ using a 14-day delay correlation), indicating that changes in seconds-scale asymmetry were temporally aligned with changes in each state's association with days-scale connectivity growth. Although temporal precedence alone does not establish causality, this ordering is consistent with a model in which reorganization of structured seconds-scale co-fluctuation asymmetry precedes, and potentially contributes to, the subsequent changes in static functional connectivity.

State-specific fluctuation asymmetry predicts future connectivity growth at the individual level

We next directly tested the central prediction of our cross-timescale framework: whether seconds-scale FLARe predicts subsequent days-scale connectivity growth at the individual level. Specifically, we used individual FLARe values at an earlier timepoint (T1) to predict connectivity CRs at a later timepoint (T2), up to 60 days later (T1 age range: 15-148 days; mean T1-T2 interval: 50.3 ± 9.2 days), using 1,000 trials of subject-separated cross-validation (**Fig. 6a**). The 60-day T1-T2 interval was selected to capture downstream connectivity changes following the approximately 14-day lead of FLARe reorganization relative to the growth-mode transition. Mean CRs for 10 of the 28 domain pairs were significantly predicted by earlier FLARe values (FDR-corrected $p < 0.001$; r CIs > 0 ; full statistics in **Supplementary Tables S1 and S2**). Notably, these 10 domain pairs accounted for 81.1% of the total variance in developmental connectivity trajectories across all 28 domain pairs (**Supplementary Figure S4b**), indicating that predictive relationships were concentrated within the principal modes of connectome development. As a temporal specificity control, we repeated the analysis in the reverse direction, asking whether T2 FLARe predicted T1 connectivity CRs. In contrast, only 3 of 28 domain pairs were significantly predicted, together accounting for just 6.05% of the variance. For significant prospective predictions (T1-to-T2), associations between state FLARes and subsequent days-scale CRs were either linear or quadratic. Because the magnitude of FLARe indicates how strongly one state expression predominates and the sign indicates which expression predominates, the predicted direction of connectivity change depended on whether the domain pair belongs to the same or opposing state-defined network groups (**Fig. 4c**). This relationship is illustrated by representative examples for VS-SM and VS-CB domain pairs (**Fig. 6b, c**). For the VS-SM domain pair, days-scale CR showed a significant quadratic relationship with State 3 FLARe (quadratic term, partial $r=0.27$, FDR-corrected $p<0.05$), with the strongest effects observed for negative FLARe values. Because VS and SM belong to opposing groups in State 3 (**Fig. 4c**), negative FLARe

indicates greater dominance of the integrated form, which is characterized by stronger cross-group co-fluctuation. Thus, preferential expression of the integrated form of State 3 predicted subsequent strengthening of negative VS-SM connectivity. For the VS-CB domain pair, days-scale CR showed a significant positive linear association with State 4 FLARe (linear term, partial $r=0.28$, FDR-corrected $p<0.05$). Because VS and CB belong to the same group in State 4 (**Fig. 4c**), positive FLARe indicates greater dominance of the segregated form, characterized by stronger within-group co-fluctuation. Thus, preferential expression of the segregated form of State 4 predicted subsequent strengthening of VS-CB connectivity. Additional state-wise associations are shown in **Supplementary Figure S10**).

Notably, significant predictions were not uniformly distributed across the connectome: all involved primary sensory or sensorimotor, subcortical, or cerebellar domains (AUD, VS, SM, SC and CB), whereas connectivity growth involving only higher-order cortical domains (CC and DM) was not significantly predicted.

State-wise fluctuation asymmetry predicts subsequent changes in visual behavior at the individual level

We next tested whether FLARe also predicts subsequent changes in visual behaviors. Using the same ≤ 60 -day prediction framework, we examined whether individual FLARe values at T1 predicted subsequent CRs in oculomotor control and preferential attention to eyes at T2 (T1 age range: 58-160 days; mean T1-T2 interval: 30.6 ± 8.9 days). T2 CRs in oculomotor control (percentage of visual targets reached) were significantly predicted by T1 FLARe values (mean $r = 0.212$, CIs [0.167, 0.257], $p < 0.001$, $df = 999$), whereas T2 FLARe values did not significantly predict T1 behavior change (mean $r=-0.164$, CIs [-0.218, -0.109], $p=1$, $df=999$; **Fig. 6d**). Exploratory state-wise analyses suggested nominal associations between oculomotor CRs and States 4 and 5 FLARe (**Supplementary Fig. S11**), although neither survived FDR correction. State 4 showed a quadratic association (quadratic term, partial $r=-0.24$), whereas State 5 showed a negative linear association.

CR in preferential attention to eyes at T2 was predicted more strongly by T1 FLARe values (mean $r = 0.402$, CIs $[0.363, 0.440]$, $p < 0.001$, $df = 999$) than by T2 FLARe values (mean $r = -0.155$, CIs $[-0.208, -0.101]$, $p = 1$, $df = 999$; **Fig. 6d, f**). State-wise analyses revealed that CR in preferential attention to eyes showed a positive linear association with State 2 FLARe (partial $r = 0.31$, FDR-corrected $p < 0.05$) and a negative linear association with State 5 FLARe (partial $r = -0.31$, FDR-corrected $p < 0.05$; **Fig. 6e**). Greater dominance of the segregated form of State 2 and the integrated form of State 5 was each associated with larger subsequent increases in preferential attention to eyes during the first six postnatal months. State 2 separates visual and cerebellar systems (VS, CB) from cognitive control networks (CC), whereas State 5 separates auditory, sensorimotor, and subcortical systems (AUD, SM, SC) from visual, cognitive control, and cerebellar systems (VS, CC, CB) (**Fig. 4c**).

Discussion

Here, we identify a growth-mode transition in the infant functional connectome during the first six postnatal months and show this transition is preceded and partly predicted by seconds-scale co-fluctuation dynamics. The dominant pattern of functional connectivity change shifted from early local strengthening to later long-range strengthening, with a transition period around 2-4 months after birth. Importantly, FLARe, a measure of asymmetry in recurring seconds-scale co-fluctuation states, predicted future connectivity change and subsequent visually guided behaviors. Together, these findings show that short-timescale functional brain dynamics contain prospective information about functional connectome organization and behavioral development.

We identified a previously unrecognized transition in the dominant mode of functional connectome growth during early infancy, consistent with our hypothesis that postnatal development comprises temporally distinct phases of network maturation. Rather than following a monotonic local-to-distributed developmental principle from birth onward, early postnatal development was characterized by two distinct growth modes. During

Stage 1, developmental change was dominated by strengthening local connections; following a transition period around 2-4 months, the predominant pattern of change shifted toward longer-range connectivity. In interpreting this transition, it is important to note that growth modes describe the dominant pattern of change across the developing connectome rather than the trajectories of individual connections. A distributed growth mode therefore does not imply cessation of local strengthening, but rather a shift in the overall organization of connectivity change. These findings refine developmental models proposing that functional brain organization progresses from local specialization toward increasingly distributed network architecture^{6,11}, suggesting that this progression occurs through a distinct transition period rather than a gradual, monotonic process⁴⁰. Resolving this transition was made possible by longitudinal sampling that provided dense temporal coverage across infants during the first six postnatal months, a period of especially rapid functional connectome development.

The timing of the identified growth-mode transition coincides with one of the most dynamic periods of behavioral change during infancy. During the first postnatal months, infants rapidly acquired increasingly coordinated visual, motor, and social behaviors⁴¹⁻⁴⁴. For example, visual orienting becomes more efficient and flexible, eye movements become increasingly coordinated with head and body movements, and visual attention and smiling are progressively incorporated into reciprocal social interactions with caregivers⁴⁵⁻⁴⁸. Dynamic systems perspectives propose that these developmental advances emerge through interactions among multiple developing systems rather than independent maturation of individual functions^{49,50}. In this context, the growth-mode transition identified here may represent a connectome-level correlate of this broader developmental reorganization, as the dominant pattern of functional connectivity growth shifts toward longer-range integration during the same developmental window.

Beyond identifying the transition in functional connectome growth, our findings demonstrate that this developmental reorganization can be largely accounted for the organization of short-timescale co-fluctuation dynamics. At the group level, the five identified recurring co-fluctuation states explained approximately 80% of the temporal

variance in connectivity growth trajectories, and both their relative contributions and state-specific FLARe trajectories underwent coordinated reorganization around the growth-mode transition period, with FLARe changes preceding the transition by approximately two weeks. At the individual level, FLARe—a measure of the directional asymmetry with which recurring co-fluctuation states are expressed—predicted for subsequent rates of functional connectivity growth. Together, these findings suggest that seconds-scale co-fluctuation dynamics anticipate future large-scale connectome development rather than simply reflecting contemporaneous functional organization. Extending prior work linking dynamic functional connectivity to age, cognitive state, behavior, and developmental maturity⁵¹⁻⁵⁴, we show that short-timescale co-fluctuation dynamics also contain prospective information about the subsequent trajectory of functional connectome maturation.

The functional significance of these predictive dynamics is underscored by their ability to anticipate subsequent behavioral development. FLARe predicted not only subsequent rates of functional connectivity growth but also subsequent rates of change in both oculomotor control and, more strongly, preferential attention to the eyes of others. State-specific analyses provided additional insight into the network interactions that predict subsequent increases in preferential attention to others' eyes. Greater dominance of the segregated form of State 2, characterized by stronger co-fluctuation within the visual and cerebellar network group and within the cognitive control group than between them, and the integrated form of State 5, characterized by stronger co-fluctuation between the auditory, sensorimotor, and subcortical group and the visual, cerebellar, and cognitive control group, each predicted larger subsequent increases in preferential attention to eyes. Although State 2 and State 5 represent distinct interactional configurations, both repeatedly implicated visual, cerebellar, and cognitive control systems. This suggests that the predictive information resides not simply in which functional systems are engaged, but in how interactions among those systems are dynamically organized. This interpretation is consistent with developmental accounts in which functional specialization emerges through changing

patterns of interaction among brain regions¹⁸, as well as cascading models of early visual development, which propose that visual orienting and social attention emerge through interactions among developing visual, attentional, oculomotor, motor, and learning systems¹⁴. The recurring network interactions identified in our analyses are consistent with both neural systems supporting early visually guided behavior and broader patterns of functional network reorganization during infancy. Subcortical pathways are thought to support early visual orienting and attention to socially relevant stimuli⁵⁵, while recent work demonstrates progressive refinement of cerebellar interactions with visual and sensorimotor systems together with increasing incorporation of cognitive-control networks during infancy^{56,57}, closely paralleling the visual, sensorimotor, cerebellar, subcortical, and cognitive control systems implicated in our state-specific prediction analyses.

The finding that short-timescale co-fluctuation dynamics prospectively predict both connectome and behavioral development have broader implications for understanding how functional brain dynamics relate to developmental change across temporal scales. Conceptually, FLARe quantifies asymmetry in transient, state-specific co-fluctuation patterns, whereas connectivity change rates capture the direction and magnitude of longer-term, static functional connectome development. Static and dynamic functional connectivity are often treated as related signatures of the same underlying neural process^{51,54}, yet how seconds-scale co-fluctuation dynamics relate to subsequent developmental change has remained largely unknown. Here, we demonstrate that short-timescale fluctuation asymmetry along the principal functional axes of recurring co-fluctuation states prospectively guide the dominant growth modes (temporal derivative) of longer-term functional connectome, which together account for the majority of developmental variance across the connectome, as well as subsequent visual behaviors. These findings establish short-timescale fluctuation asymmetry as a prospective marker of longer-term developmental change, revealing a predictive link between functional brain dynamics unfolding over seconds and developmental change emerging over weeks to months.

One possible explanation for these predictive relationships comes from activity-dependent models of brain development, in which repeated patterns of neural coactivation contribute to refinement of developing circuits through Hebbian mechanisms. Animal studies have established that endogenous spontaneous activity plays a fundamental role in formation and refinement of developing neural circuits, while human developmental studies have linked early electrophysiological activity to subsequent structural brain growth and maturation of neonatal functional networks⁵⁸⁻⁶². A complementary perspective comes from scaffold-based models of brain organization, in which spontaneous dynamics are constrained by the brain's existing structural and functional architecture⁶³⁻⁶⁵. Consistent with this view, the recurring co-fluctuation states identified here aligned closely with established functional gradients, suggesting that spontaneous fluctuations preferentially occur along the brain's existing large-scale organizational axes. Within this scaffold-constrained repertoire, persistent directional asymmetries in state expression may capture signatures of activity-dependent processes, linking existing functional architecture to subsequent connectivity refinement. Although FLARe is not a direct measure of neuronal plasticity, these findings provide a conceptual bridge between scaffold-based and activity-dependent models and offer a framework for future multimodal longitudinal studies investigating how structural maturation, functional dynamics, and activity-dependent plasticity interact during early brain development.

Several limitations warrant consideration. First, although the present findings establish a prospective relationship between spontaneous dynamics and subsequent brain and behavioral development, they do not establish causality or identify the biological mechanisms underlying this relationship. Second, FLARe is a systems-level measure derived from BOLD fMRI and therefore provides an indirect index of the neuronal processes underlying activity-dependent plasticity. Third, while the dense sampling across participants during the first six postnatal months enabled characterization of rapid developmental change during a period of heightened neuroplasticity, it remains unclear whether similar coupling between spontaneous dynamics and subsequent

connectome development is observed across other developmental periods. Addressing these questions will require future multimodal longitudinal studies spanning broader stages of development.

Together, these findings identify short-timescale co-fluctuation dynamics as a previously unrecognized source of prospective information about early functional connectome and behavioral development. By linking functional brain dynamics unfolding over seconds to developmental change emerging over weeks to months, this work provides a framework for investigating how intrinsic brain activity shapes early brain development. Beyond advancing our understanding of normative development, these findings raise the possibility that dynamic brain states may provide early indicators of developmental trajectories before stable behavioral differences emerge.

Materials and Method

Participants

Participants were typically developing infants (43 males and 31 females) enrolled in an ongoing prospective longitudinal study of infants at low- and elevated-likelihood for autism spectrum disorder (ASD). Typicality was ascertained by the absence of factors associated with increased likelihood of developmental disability: all infants had uncomplicated deliveries (mean gestational age = 39.2 weeks, SD=1.34 weeks), had no family history of ASD in first, second, or third degree relatives, no developmental delays in first degree relatives, no pre- or perinatal complications, no history of seizures, no known medical conditions or genetic disorders, and no hearing loss or visual impairment. Participants had no contraindications for MRI. The research protocol was approved by the Emory University Institutional Review Board and legal guardians provided informed consent for their infant's participation. All ethical regulations relevant to human research participants were followed.

Dataset and Preprocessing

1 Functional MRI Data

MRI data collection: Infants were scheduled to undergo MRI scans at up to three pseudorandom timepoints between birth and 6 months to optimize scan coverage over the first six postnatal months. Across all participants, sessions were separated by a mean of 1.4 days during the first six months. MRI scans were acquired at Emory University's Center for Systems Imaging Core on a 3T Siemens Tim Trio or a 3T Siemens Prisma scanner, using a 32-channel head coil. All infants were scanned during natural sleep. Functional MRI data were acquired using a multiband echo planar imaging (EPI) sequence. The acquisition parameters for the Tim Trio/Prisma scanner were TR = 720/800 ms, TE = 33/37 ms, flip angle = 53°/52°, FOV = 208 × 208 mm, and 2.5/2 mm isotropic spatial resolution. A total of 290 scans were acquired across imaging sessions, with each session comprising an average of 2.07 scans; each scan lasted approximately 6 minutes.

fMRI preprocessing: Data were preprocessed as in ⁶⁶. The first 16 volumes were discarded to allow the MR signal to reach magnetization equilibrium. Head motion correction was performed using the 'mcflirt' function in FSL (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL>), aligning all volumes to the first one. To correct for distortion in the multi-band resting-fMRI (rs-fMRI) data, single-band data acquired with phase encoding in both the AP and PA directions were used to estimate the susceptibility-induced off-resonance field. Following distortion correction, slice timing correction was applied. A two-step normalization process was employed to align the infant datasets into a common Montreal Neurological Institute (MNI) space. The first step involved normalizing the infant fMRI data to the 3-month UNC/UMN baby connectome project (BCP) T1 template ⁶⁷. In the second step, the output from the first normalization was further aligned to the SPM EPI template ⁶⁸. Finally, a 6 mm Gaussian kernel was applied to smooth the spatially normalized fMRI images.

Quality control for excluding cases: Individual resting-state fMRI scans were excluded if they (1) showed poor normalization to MNI space, assessed by comparing individual brain masks with the group mask (n=16); (2) contained fewer than 100 usable volumes (n=34); or (3) exhibited excessive head motion (mean framewise displacement > 0.65

mm) (n=18). After quality control, 222 resting-state fMRI scans from 128 imaging sessions in 71 infants (31 female, 40 male) were retained. Overall, 39.4%, 40.8%, and 19.7% of infants contributed data from one, two, and three longitudinal visits, respectively. When multiple resting-state fMRI scans from the same imaging session passed quality control, they were treated as repeated measures in subsequent analyses.

2 Eye-tracking Data

Eye-tracking data collection: Eye-tracking data were collected and analyzed as described in previous studies^{36,69}. Infants completed up to six eye-tracking sessions between birth and seven months. Eye-tracking data were acquired using an ISCAN eye-tracking system based on the pupil–corneal reflection method and sampled at 60 Hz.

Prior to the start of data collection, experimenters calibrated infant gaze position based on the image of the right eye using a five-point calibration procedure³⁶. Each point was individually validated by experimenters. Calibration accuracy was assessed throughout each session using automated presentation of a five-point calibration target sequence, and the resulting calibration measurements were used to correct gaze coordinates during post-processing. During eye-tracking sessions, infants watched pre-recorded videos of actresses engaging them in an infant-directed manner with simple speech, songs, and/or gestures. The videos were filmed against a classroom-like backdrop to represent an infant-friendly environment. Eye-tracking sessions lasted approximately 40 minutes depending on the extent of infant participation and were ended early by experimenters in cases where infants were fussy or fell asleep. Of the 71 infants with resting-state fMRI data, 64 also contributed valid eye-tracking data, yielding a total of 168 eye-tracking sessions.

Eye-tracking Preprocessing: Eye movement analysis and fixation coding were performed using custom software written in MATLAB (MathWorks). The first stage of processing automatically identified non-fixation data, including blinks, saccades, and fixations directed away from the stimulus presentation screen. Saccades were identified using an eye velocity threshold of 30°/s, blinks were detected as previously described

⁷⁰, and off-screen fixations were identified based on fixation coordinates falling outside the stimulus presentation screen.

Remaining eye movements classified as fixations were assigned to one of four regions of interest (ROIs) defined for every frame of each video: eyes, mouth, body (neck, shoulders, and contours surrounding the eyes and mouth, including hair), and objects (surrounding inanimate stimuli). ROIs were manually traced for every video frame and stored as binary bitmaps using custom MATLAB software. Fixation coding was then performed automatically by comparing each participant's fixation coordinates with the corresponding ROI bitmaps to determine fixation time within each region.

Measure of oculomotor control - Percentage of visual targets reached: The percentage of targets ‘hit’ during each automated calibration check was calculated as an index of oculomotor control. A ‘hit’ was determined as gaze coordinates falling within a radius of 5° of visual angle of the calibration target. Five targets (upper left, upper right, center, bottom left, bottom right) were presented in randomized order during each test, the percentage of hits was measured as a value out of 5. The average performance across multiple trials in one session was calculated.

Measure of Social Visual Attention - Percentage of fixation time on eyes: The percentage of fixation time on eyes was calculated as the number of frames spent fixating to eyes divided by the total number of recorded fixations for each video in the session.

Individual static functional network connectivity

We first implemented the NeuroMark framework via GIFT fMRI toolbox (<http://trendscenter.org/software/gift>) to capture individual intrinsic connectivity networks (ICNs) from fMRI scans ⁷¹⁻⁷³. This pipeline is capable of capturing subject-specific variability within brain functional networks and maintains comparability across participants. In this study, we used the NeuroMark_fMRI_1.0 template (available in GIFT and at <http://trendscenter.org/data>) as the spatial priors for estimating functional networks for each participant. This NeuroMark template includes

53 replicable ICNs³⁸ arranged into seven functional domains: subcortical (SC), auditory (AUD), sensorimotor (SM), visual (VS), cognitive-control (CC), default-mode (DM), and cerebellar (CB) domains. The timeseries of ICNs were postprocessed to remove residual noise, including: 1) detrending linear, quadratic, and cubic trends, 2) multiple regression of the six realignment parameters and their derivatives, 3) removal and replacement of detected outliers, and 4) band-pass filtering with a cutoff frequency of 0.01 Hz–0.15 Hz.

Static functional network connectivity (sFNC) was estimated by calculating Pearson correlation coefficients between the time courses of each pair of intrinsic connectivity networks (ICNs), yielding a 53×53 connectivity matrix. Connectivity strength (CS) in sFNC was corrected using Fisher-Z transformation. Since the sFNC matrix is symmetric, only the 1378 unique connections in the upper triangle portion of the matrix were used for subsequent analyses. Domain-level functional connectivity was summarized in a 7*7 matrix by averaging sFNC values for all connections within and between the seven functional domains. Inter-network distance was defined as the Euclidean distance between the peak coordinates of each pair of ICNs in the 3-month BCP T1 template. Peak coordinates were obtained by mapping the NeuroMark v1.0 atlas (<https://trendscenter.org/data/>) from the SPM EPI template to the 3-month BCP template.

Change-rate trajectories and zero-crossing points

We estimated change rates for both static functional connectivity and eye-tracking-derived behaviors during the first six postnatal months. Change rate was defined as the temporal derivative of each measure. Because estimating developmental change requires different trade-offs between population-level reliability and individual-level precision, change rates were calculated differently for the population- and individual-level analyses, as described below.

1) Population change rate: Population-level CRs were estimated by taking the temporal derivative of the fitted developmental trajectory for each measure. Estimating

CRs from the fitted trajectories leverages all available longitudinal observations, providing more robust estimates than derivatives computed from individual scan pairs. For functional connectivity, developmental trajectories were estimated independently for each of the 1,378 unique functional connections. The change rate at timepoint t is calculated as the value in the derivative of FNC trajectory at timepoint t , i.e. $sFNC_{i,j}(t + 1) - sFNC_{i,j}(t)$.

2) Individual change rate: Individual-level change rates (CRs) were estimated from pairs of consecutive visits within the same infant. For each measure, CR was calculated as the difference between values at the two visits divided by the corresponding difference in age, providing an estimate of the infant's mean daily change over that interval:

$$CR_{i,j}^n\left(\frac{t_2 + t_1}{2}\right) \approx \frac{sFNC_{i,j}^n(t_2) - sFNC_{i,j}^n(t_1)}{t_2 - t_1}, \quad (1)$$

in which $sFNC_{i,j}$ is the functional connectivity between the i th and j th network, and t_2 and t_1 are corrected ages for time 1 (T1) and time 2 (T2) visits for each participant n . Based on Lagrange's Mean Value Theorem⁷⁴, for a continuous function (e.g. developmental trajectory), at least one point c between t_1 and t_2 where the instantaneous change rate equals the mean change rate over the whole period. In this study, this mean change rate over the whole period approximates the instantaneous change rate at the midpoint $(t_2 + t_1)/2$ of this period. To reach a relatively accurate measurement, we excluded samples with a time interval greater than two months.

Change rates for oculomotor control and eye-looking were calculated using the same derivative-based framework. CR trajectories for each functional connection and behavioral measure were estimated using generalized additive models (GAMs; see 'Trajectory estimation via generalized additive model'). Zero-crossing points were defined as the ages at which a fitted CR trajectory crossed zero, indicating a transition from increasing to decreasing growth (or vice versa). Accordingly, the zero-crossing point marks the age at which the developmental direction changes.

3) Magnitude and direction of connectome change-rate patterns. At each age, the upper triangular portion of the functional connectivity CR matrix (1,378 unique connections) was represented as a high-dimensional vector describing the pattern of developmental change across the connectome. We quantified two complementary properties of this vector. First, its magnitude was defined as the mean absolute CR across all 1,378 connections, reflecting the overall rate of connectome reorganization. Second, its direction was characterized by the angle between the CR vectors at the beginning and end of each developmental stage, computed from their cosine similarity. Larger angles indicate greater changes in the relative pattern of connectivity development across the connectome. The cosine similarity is computed as below:

$$\cos \theta = \frac{CR(t_1) * CR(t_2)}{|CR(t_1)| * |CR(t_2)|}, \quad (2)$$

in which $CR(T1)$, $CR(T2)$ present CR patterns at the beginning and end of a stage, and $| \quad |$ is the norm of a vector. The cosine similarity ranges from -1 to 1. Larger θ per day indicates a greater change in growth direction.

Trajectory estimation via generalized additive model

The trajectory of a connection was estimated via a linear generalized additive model using the ‘pygam’ packages⁷⁵. For a linear GAM model, the response variable y can be formulated as a linear combination of age-related spline basis functions and covariates:

$$y = \beta_0 + \sum_{j=1}^p f_i(x_j) + \beta_1 \cdot G + \beta_2 \cdot M + \beta_3 \cdot S + \epsilon, \quad (3)$$

in which β_0 represents the intercept, β_1, β_2 and β_3 the covariation parameter, p indicates the predictor number, $f_i(x)$ is the i th smooth function of age x , and ϵ is error term. The linear GAM uses a set of spline basis functions (defaulted as cubic functions) to represent the smooth functions $f_i(x_j)$. The number of basis functions determines the model’s flexibility. In our study, the spline parameter is set with the spline number = 10 and cubic spline function to control the complexity of the model. For connectivity,

sex (G), head motion (M) and scanner (S) information were computed as linear covariates in the GAM with coefficients β_1 , β_2 and β_3 . For behavior, only sex (G) was included as a covariate. A regularization in the fitting model was used to penalize the roughness of the smooth functions. A large regularization could reduce overfitting and avoid small noise fluctuations⁷⁶. A built-in grid search based on generalized cross-validation was used for optimal regularization within the range from 1 to 1000 with logarithmic intervals. Since individual change rate is computed by numerical differentiation, which is known to amplify measurement noise⁷⁷, the optimal regularization parameter for the change rate was searched starting with a large value of 10. To avoid overrepresenting imaging sessions with multiple fMRI scans, each scan was weighted by the inverse of the number of scans acquired from the same infant at that visit during GAM fitting. This ensured that each imaging session contributed equally to trajectory estimation. All other GAM parameters were left at their default values.

Identification of seconds-scale brain states and axes from spontaneous dynamic connectome

Seconds-scale brain states were identified from chronnectome using independent component analysis (ICA) (GIFT, <http://trendscenter.org/software/gift>; see Supplementary Fig. S7 for pipeline)^{27,31}. First, individual dynamic functional network connectivity (dFNC) was computed via a sliding window approach, which calculated the Pearson correlation coefficient between the timeseries of two ICNs within a 45s window slide in increments of 1 TR. Previous work has shown that 30s to 1 min windows capture reliable brain dynamics⁷⁸. Dynamic connectivity values were normalized using a Fisher-z transformation. Then we removed the dFNCs mean connectivity over time for each participant to focus on dynamic fluctuations above static FNC. Next the dFNCs across all participants in all visits were concatenated along the temporal dimension to form a large matrix. Finally, blind ICA with ‘infomax’ optimization was applied to this large matrix to obtain N brain state patterns. This procedure was performed 100 times, and the most central solution was chosen as the

optimal one. The reliable state number N here was chosen based on the independent component analysis with stability analysis (ICASSO) index quality above 0.8⁷⁹. After the identification of the brain states, we applied spatially constrained ICA (scICA)⁸⁰ to each participant to obtain participant-specific brain state patterns and their corresponding state timeseries.

The first eigenvector of each state pattern was extracted to characterize its dominant functional axis. For visualization, eigenvector loadings exceeding an absolute threshold of 0.1 were mapped back to MNI space using a winner-take-all assignment and projected onto the fsaverageRL32k cortical surface using the *pyvista* Python package⁸¹. The resulting functional axis was summarized by averaging network loadings within each of the seven functional domains, yielding two opposing groups of domains with positive and negative loadings. To quantify expression of each functional axis at the individual level, spatially constrained ICA (scICA)⁸⁰ was applied to each subject's 53-network time series to obtain subject-specific axis time series. Axis amplitude was calculated as the absolute value of the axis time series after smoothing with a 45-s sliding window.

Fluctuation asymmetry ratio of state co-fluctuation patterns

Brain states summary multi-variable co-fluctuations in the time-varying functional connectome. Each co-fluctuation state comprised two complementary configurations corresponding to positive and negative excursions of its time series. Positive value in the state timeseries represents a strengthened and weakened couplings in the state spatial pattern, whereas negative amplitudes represent its sign-reversed counterpart, with strengthened and weakened couplings exchanged.

To quantify the relative expression of these two configurations, we defined the fluctuation asymmetry ratio (FLARe) for each state and scan. FLARe was calculated as the logarithm of the ratio between the mean fluctuation power during positive excursions of a state time series and the mean fluctuation power during negative excursions (Equation 4). Positive FLARe values indicate stronger expression of the

positive co-fluctuation configuration, whereas negative values indicate stronger expression of the sign-reversed configuration.

$$FLARe = \log \left[\frac{\frac{1}{N_{pos}} \sum S_{pos}^2}{\frac{1}{N_{neg}} \sum S_{neg}^2} \right] \quad (4)$$

in which S_{pos}^2 and N_{pos} represented the square of positive fluctuations and the number of positive timepoints in a state time series, and S_{neg}^2 and N_{neg} for negative fluctuations. Positive and negative values of a state's time series correspond to the integrated and segregated forms of its co-fluctuation pattern, respectively. FLARe quantified the relative expression of these two forms by comparing the fluctuation power of positive and negative state excursions. Positive FLARe values indicated greater expression of the segregated form, whereas negative values indicated greater expression of the integrated form. Across states, the segregated form was associated with larger functional-axis amplitudes. In addition, the magnitude of FLARe ($|FLARe|$) reflected the degree to which spontaneous neural fluctuations were biased toward either the integrated or segregated form, with larger absolute values indicating stronger preferential expression of one configuration.

Contribution trajectories of state co-fluctuation patterns

Days-scale connectivity CR trajectories (1378 connections-by-171 days) were decomposed using spatially constrained ICA (scICA) ⁸⁰, with the co-fluctuation state patterns serving as spatial priors (Equation 5). The resulting temporal coefficients quantified the contribution of each co-fluctuation pattern to the developmental trajectory of functional connectivity change.

$$CR_{i,j}^t \approx \sum_{k=1}^K \alpha_{i,j,k} Contri_k^t, \quad (5)$$

Where $CR_{i,j}^t$ were the change rate of connectivity between network i and network j at age t ; $\alpha_{i,j,k}$ was the (i th, j th) element in the k co-fluctuation pattern; $Contri_k^t$ was the

contribution of the k th co-fluctuation pattern at age t . Positive values indicated greater contributions of the integrated co-fluctuation form to days-scale connectivity change, whereas negative values indicated greater contributions of the segregated form.

Prediction of days-scale change rates from seconds-scale fluctuation asymmetry.

Prediction models used FLARe measured at an earlier visit(T1) to estimate subsequent connectome and behavioral CRs (T2) from the same infant. Assuming the relationship function $f(FLARe_k^{t-\tau})$ is nonlinear, we model delayed effects (τ) with state-specific lag influence via a quadratic term. Specifically, we used random forest⁸² as the prediction model using ten state features ($FLARe_i$ and $FLARe_i^2, i = 1, \dots, 5$) with ten-fold cross validation. To avoid information leaking from multiple fMRI scans of the same subject in the cross validation, we randomly split available subjects rather than fMRI scans into the training and testing datasets. The performance of a model in one trial was evaluated by Pearson's coefficient between predicted changes and observed changes which was concatenated with ten validation folds. The number of estimators in random forest was set to 50. Each prediction was tested 1000 times to check the significance by Nadeau–Bengio corrected k-fold t-test⁸³. The significance was further corrected by the Benjamini-Hochberg FDR method. A significance prediction should satisfy two requirements: 1) the confidence interval of r should be all positive and 2) the corrected p-corrected 0.001.

The FLARe prediction of visual behaviors followed the same analytic procedures as the connectome CR prediction. Because eye-tracking and fMRI data were not always collected on the same day, we computed behavioral CR only when both eye-tracking sessions fell within ≤ 2 months of the corresponding fMRI scan. If there were more than two eye-tracking sessions within this interval, CRs were computed separately between two continuous sessions. The prospective prediction analyses included 112 connectivity CR samples and 75 behavioral CR samples, both restricted to T1-T2 intervals of ≤ 60 days.

To characterize potentially quadratic or linear associations between a single state FLARE and a days-scale change rate, we calculated the partial correlation of all features with CRs. Specifically, we fitted a second-order polynomial regression model $y = \beta_0 + \beta_1 x + \dots + \beta_n x_n + \varepsilon, n = 1, \dots, 10$, where β_0 was the intercept, β_n was the coefficient of x_n , and ε denotes residual errors. Model parameters were estimated by ordinary least squares, minimizing the sum of squared residuals. Coefficient significance was assessed using two-sided t-tests on the OLS estimates (null hypotheses: $\beta_1=0$ and $\beta_2=0$), and p-values were FDR-corrected across terms with significance threshold at $\alpha=0.05$.

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1009 **Acknowledgments**

1010 We greatly appreciate the families and their infants who volunteered to participate in
1011 this research study. We would also like to thank the research coordinators, assistants,
1012 and fellows at the Marcus Autism Center, Brittney Sholar, Carly Reineri, Joannna
1013 Beugnon, Lindsey Evans, Jordan Pincus, Jennifer Gutierrez, Tristan Ponzo, and
1014 Adriana Mendez, and the MRI Techs at the Emory Center for Systems Imaging Core,
1015 Michael White, Sarah Basadre, and Samira Yeboah, for their data collection efforts.

1016 **Funding**

1017 The National Institute of Mental Health, USA (K01MH108741, 2P50MH100029 to
1018 S.S., R01MH118285 to S.S., R01MH119251 to S.S. and A.I.); the National Institute
1019 of Biomedical Imaging and Bioengineering, USA (R01EB027147 to S.S. and V.C.);
1020 funds from the Whitehead and Marcus Foundations (to S.S. and V.C.).

1021 **Contributions**

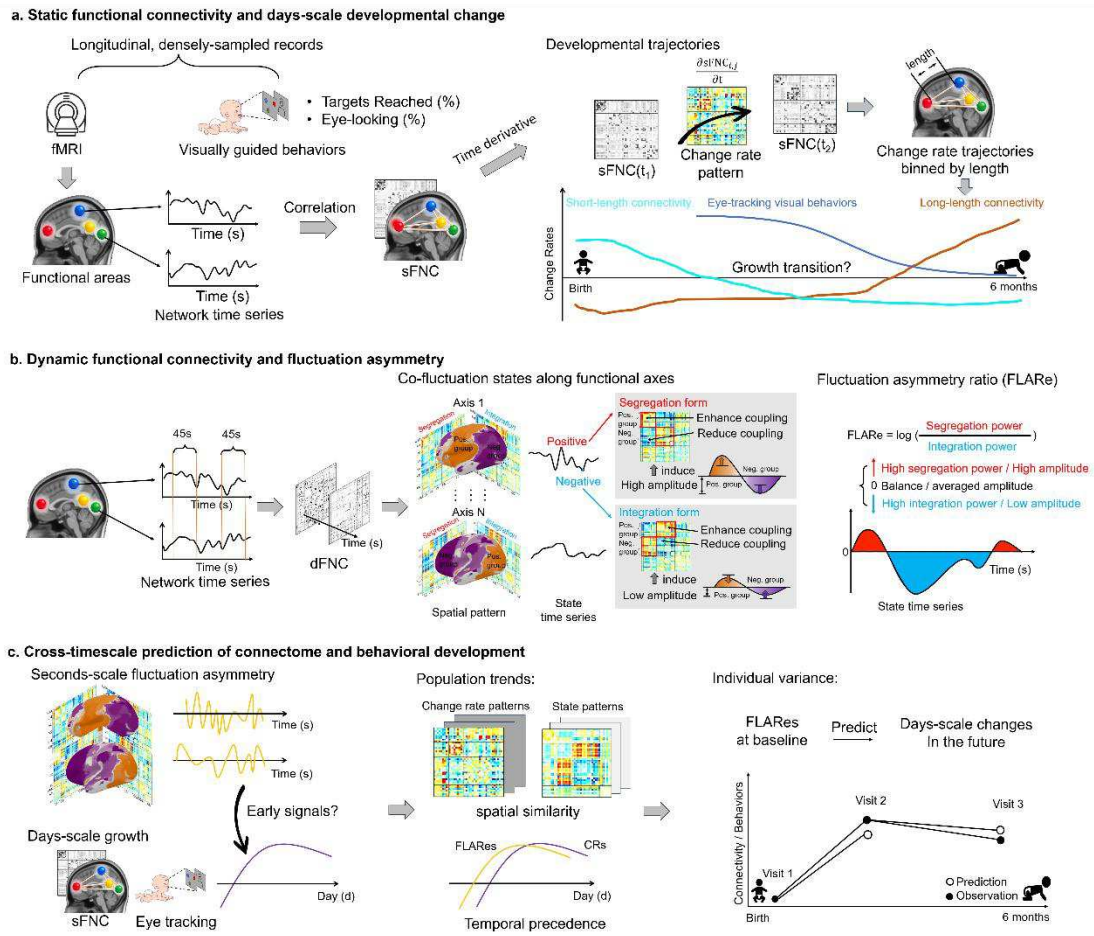
1022 L.M., S.S. and V.D.C. designed the study; S.S. supervised collection of the fMRI
1023 dataset. A.F. analyzed the infant eye-tracking data; Z.F. preprocessed the fMRI data;

1024 L.M., performed formal analysis; L.M., S.S. and V.D.C. interpreted the data. L.M.
1025 and S.S. wrote the manuscript, and L.M., S.S., A.F., and V.D.C. critically revised the
1026 manuscript. Z.F., J.S., A.I. M.S. and Q.L. help interpretate results; All co-authors
1027 helped refine the manuscript.

1028 **Competing Interests**

1029 The authors declare no competing interests.

1 Figures



2

Figure 1. Analysis framework for predicting days-scale functional connectivity and behavioral development from seconds-scale brain dynamics. (a) Static functional connectivity and days-scale developmental change. Static FNC (sFNC) is calculated by correlating resting-state network time series. The growth of sFNC is quantified using connectivity change rates (CR), a derivative between two continuous timepoints. CR trajectories are binned by inter-network distance to test for a distance-dependent transition in functional growth mode from local-modular to distributed organization. (b) Dynamic functional connectivity and fluctuation asymmetry. Dynamic FNC is calculated using a sliding-window approach. Recurring co-fluctuation states were identified using spatial independent component analysis, and the principal functional axis of each state was defined by its first eigenvector. Fluctuation asymmetry ratio (FLARe) quantifies the directional imbalance between the two opposing expressions (integrated and segregated forms) of each co-fluctuation state, with magnitude reflecting the degree of asymmetry and sign indicating the predominant expression. (c) Cross-timescale prediction of connectome and behavioral development. Seconds-scale co-fluctuation state organization and FLARe were used to characterize population-level trajectories of days-scale functional connectivity change and to predict future individual changes in functional connectivity and behavior, testing whether short-timescale brain dynamics prospectively predict connectome and behavioral development.

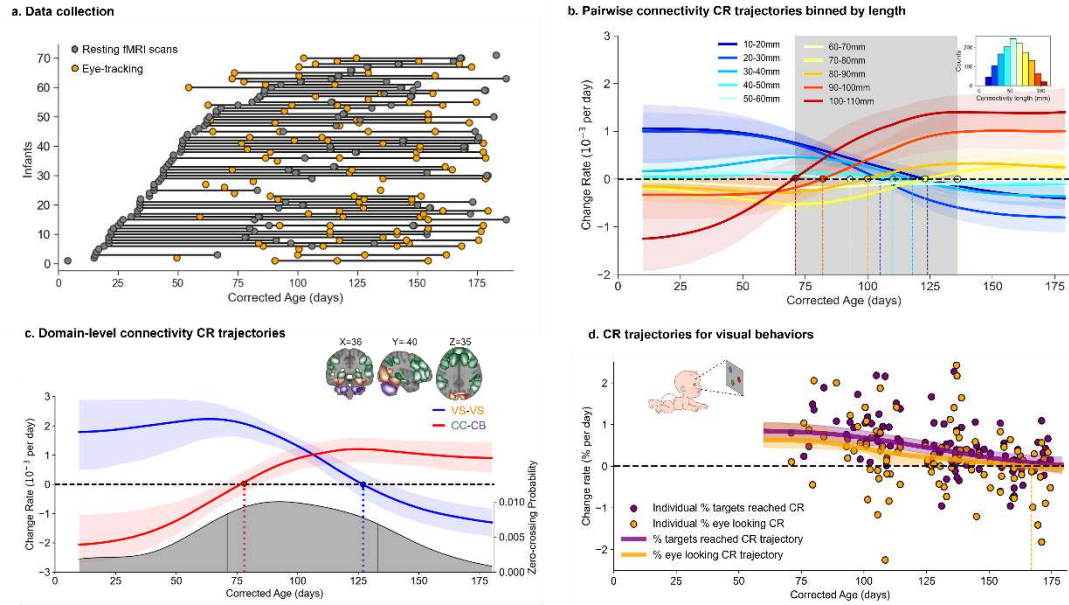


Figure 2. Change-rate trajectories of connectivity and visual behavior during the first six postnatal months. (a) Longitudinal sampling of resting-state fMRI and eye-tracking assessments across infants as a function of corrected age. Each row represents one infant; dots indicate assessment sessions, connected by lines within infant. (b) Pairwise connectivity CR trajectories binned by connectivity length (10-110 mm; 10mm bins). Dotted vertical lines mark zero-crossings for each distance bin. The shaded region (days 71-133) denotes the transition window defined by zero-crossings. Inset shows the distribution of connectivity lengths across all 1,378 connections. (c) Domain-level connectivity CR trajectories illustrating representative short- and long-range connectivity. Short-range within-visual connectivity (VS-VS; mean distance=35.2mm) and long-range cognitive control-cerebellar connectivity (CC-CB; mean distance=82.5mm) exhibit zero-crossings within the same window, consistent with the distance-dependent pattern observed in (b). (d) CR trajectories for visual behaviors (percentage of visual targets reached and percentage of fixation time on eyes). Behavioral change rates are highest before ~4 months and slow thereafter, coinciding with the transition window. Shaded regions in (b-d) indicate 95% confidence intervals estimated from 1,000 bootstrapped samples.

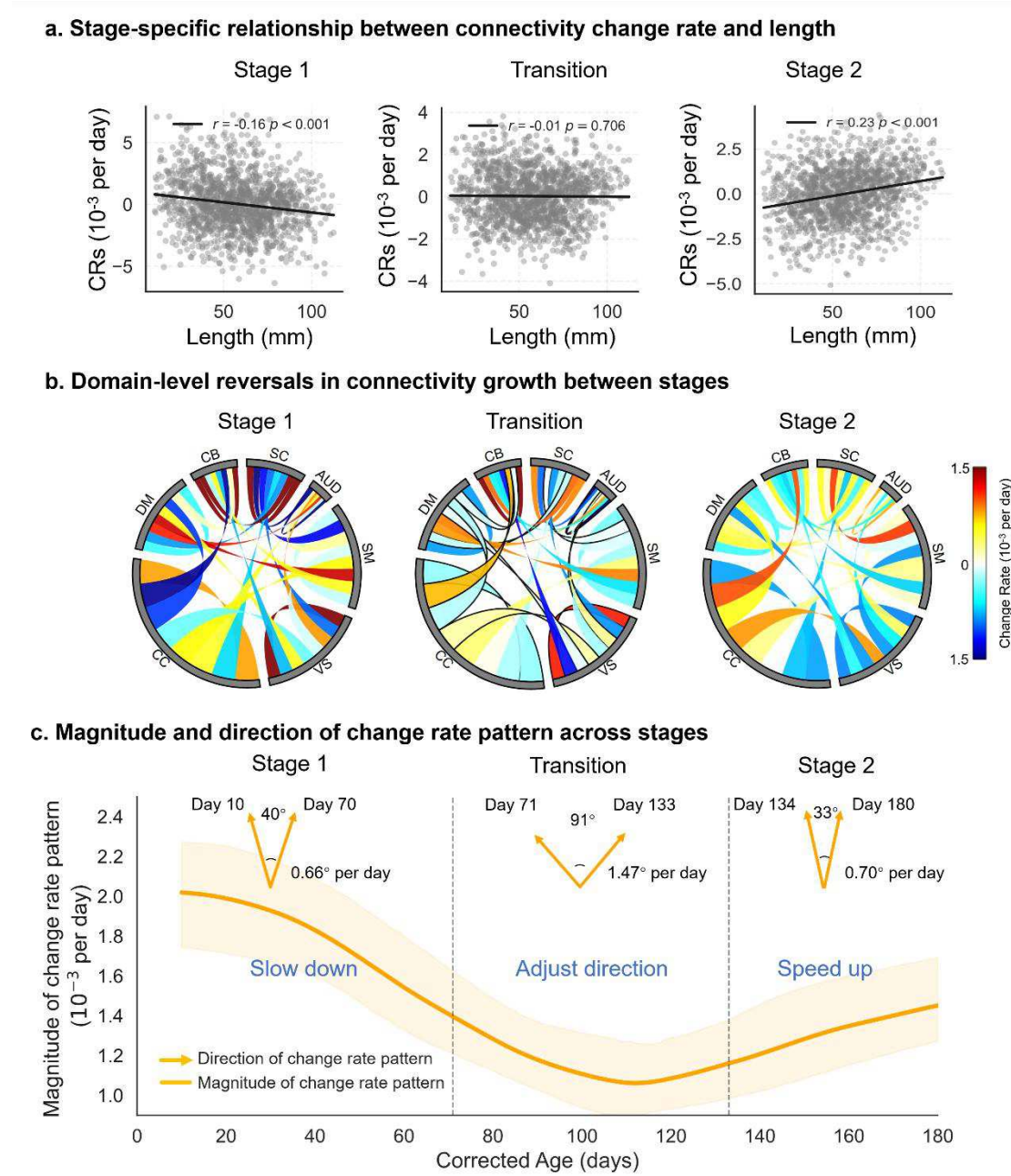


Figure 3. Stage-dependent reorganization of connectivity growth. (a) Relationship between change rate (CR) and connectivity length across 1,378 connections in Stage 1, the transition period, and Stage 2. Connectivity length was defined as the Euclidean distance between peak coordinates of two connected networks. (b) Functional domain-level differences in connectivity CR between stages. Linkage colors represent mean CRs within domain-level connectivity. Black edges indicate there is a significant transition in its CR trajectory during transition period. Criteria: the zero-crossing points of mean trajectory should fall within the transition period and its confidence bounds have at least one zero-crossing point. (c) Magnitude and direction of connectivity CR across stages. Shaded regions indicate 95% confidence intervals estimated from 1,000 bootstrap samples.

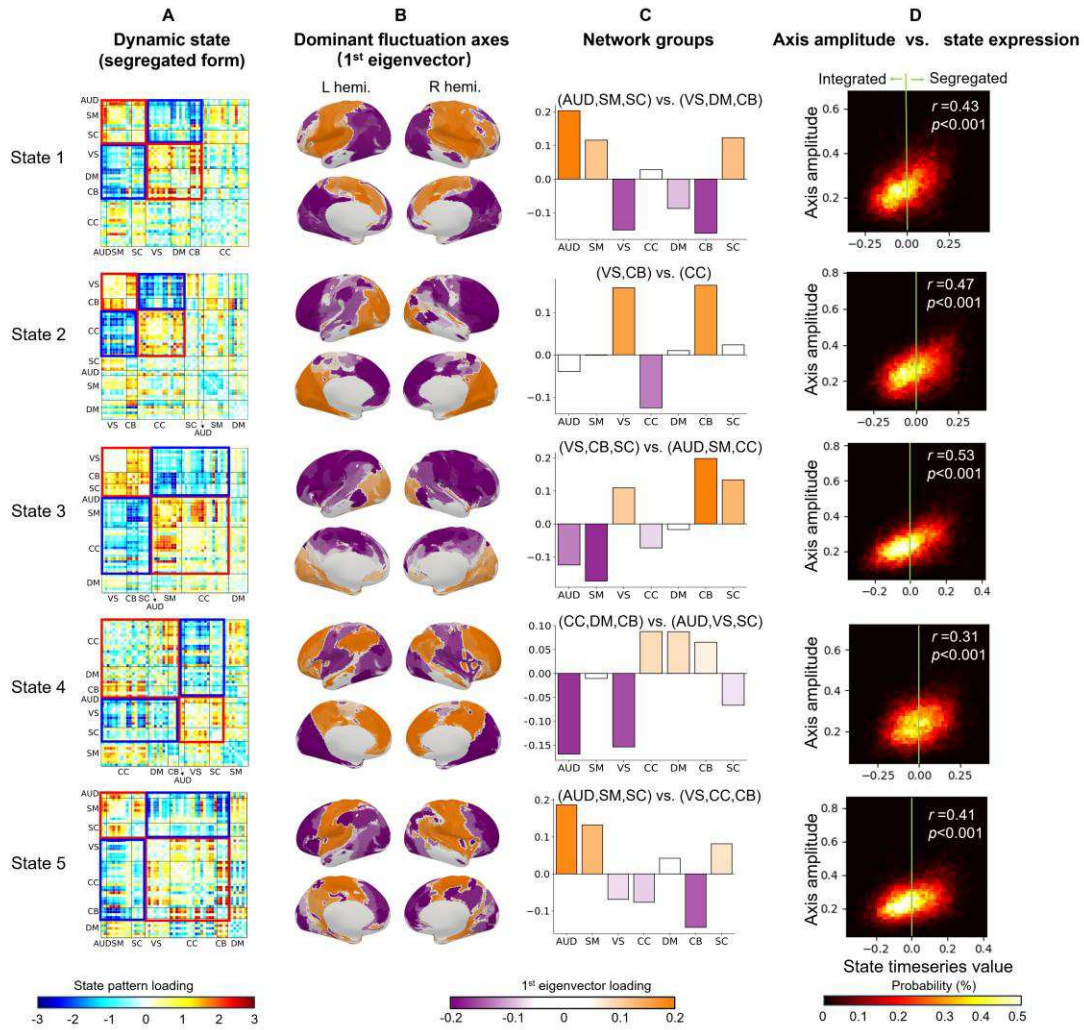
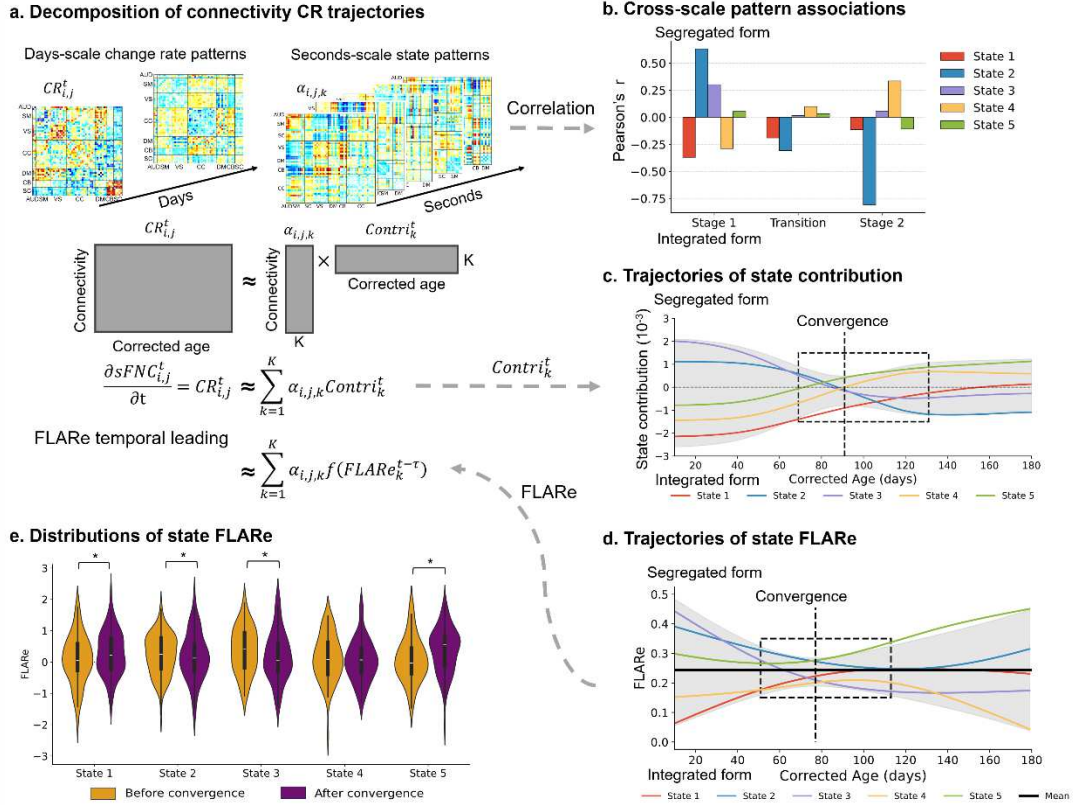
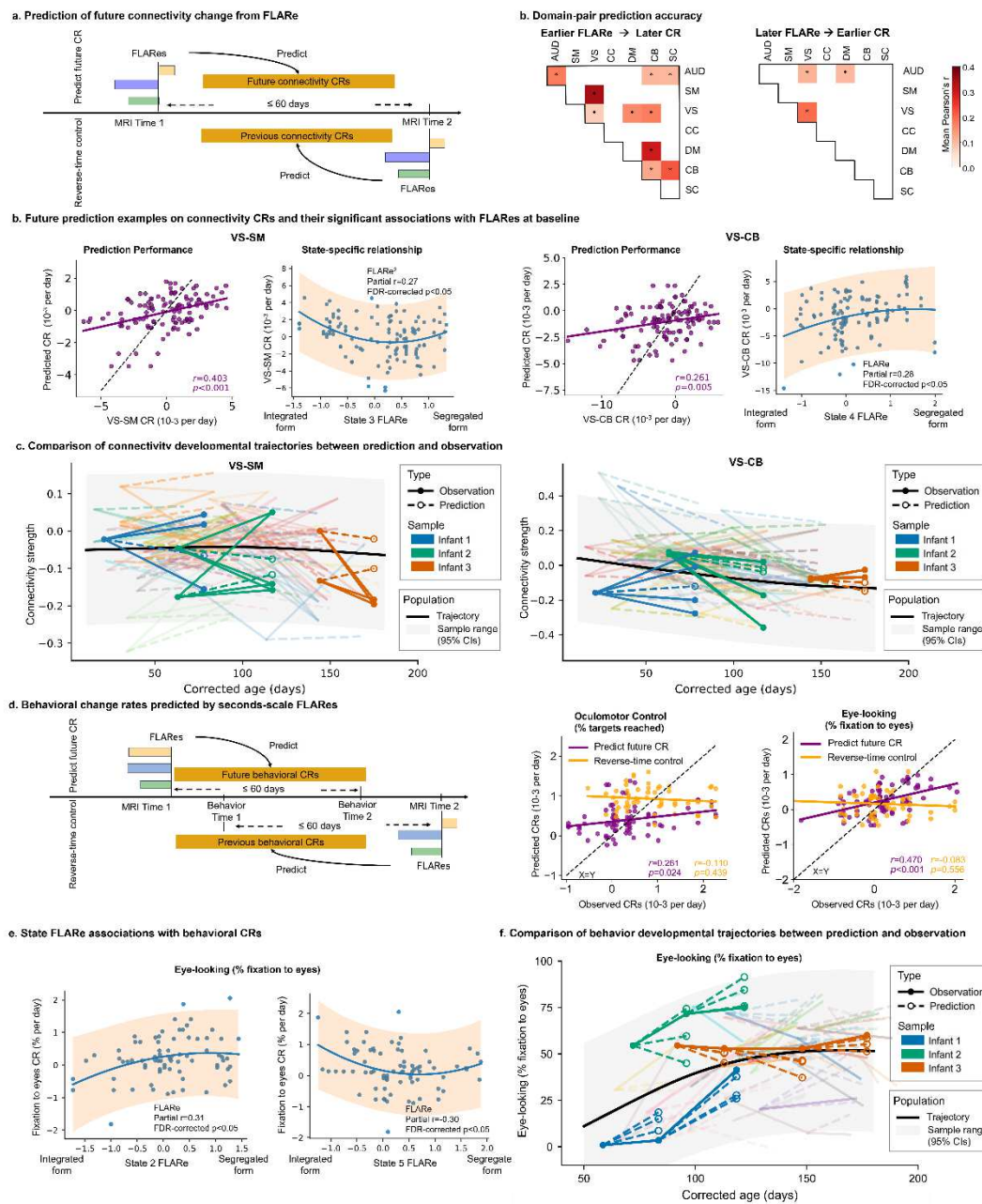


Figure 4. Five dynamic states and their opposing integrated and segregated forms. (A) State pattern loading matrices, shown in the segregated form. Color indicates the loading of the ICA-derived state pattern; large absolute values indicate stronger perturbations on connection. Networks are ordered according to the state-defined groups shown in C. In the segregated form, positive loadings predominantly occur within network groups, whereas negative loadings predominantly occur between groups, corresponding to stronger within-group and weaker cross-group coupling relative to the mean connectivity pattern. The integrated form is the sign-reversed version of the same state. (B) Dominant eigenvector maps for each state. Color indicates eigenvector loading, with opposite colors denoting networks that fluctuate in opposite directions within the state. (C) Domain-averaged eigenvector loadings, summarizing how functional domains separate into the two network groups that define each state. (D) Relationship between axis amplitude and state form across all infant fMRI scans. Larger axis amplitudes were associated with the segregated form of each state, whereas lower axis amplitudes were associated with the integrated form.



68

69 **Figure 5. Relationship between seconds-scale dynamics and days-scale**
70 **connectivity growth.** (a) Schematic illustrating the analytic framework linking
71 seconds-scale dynamic states to days-scale connectivity change rate trajectories. Spatial
72 patterns of five seconds-scale co-fluctuation states (Fig. 4a) were compared with stage-
73 specific days-scale CR patterns. The CR tensor (171 timepoints x 1,378 connections)
74 was further decomposed using spatially constrained ICA with state patterns as priors to
75 estimate state-specific contribution trajectories. (b) Spatial correspondence between
76 dynamic state patterns and Stage 1 and Stage 2 CR patterns. Positive correlations
77 indicate greater correspondence with the segregated form of a state, whereas negative
78 correlations indicate greater correspondence with its integrated form. (c) State-specific
79 contribution trajectories, indexing the relative contribution of each dynamic state to the
80 observed connectivity CR pattern over development. Reduced cross-state variability
81 marks a convergence window centered at approximately day 91, corresponding to the
82 growth-mode transition identified in static connectivity analyses (Fig. 3). (d) FLARE
83 trajectories for each state. A convergence window between approximately days 51-113
84 reflects reduced between-state variability. (e) Statistical comparison of FLARE values
85 before and after the convergence period. In subplot c, d, the gray band denotes ± 1.5
86 standard deviations across state trajectories. Convergence periods are defined as the
87 contiguous window (of equal length to the growth-mode transition period) with the
88 lowest across-state standard deviation. Boxed dotted lines indicate the convergence
89 period, and the vertical dotted line marks the transition point.



90

91 **Figure 6. State-wise FLARE predicts subsequent connectivity and behavioral**
 92 **change at the individual level.** (a) Prediction of future connectivity CRs from earlier
 93 state FLARE values (left) and reverse-time control analyses predicting previous CRs
 94 from later FLARE values (right) within ≤ 60 -day intervals. Heat maps show cross-
 95 validated prediction performance for connectivity pairs; asterisks denote FDR-
 96 corrected significant predictions (Nadeau-Bengio corrected k-fold t-test, 1000
 97 iterations of subject-independent 10-fold cross-validation; $n=112$ infants). (b)
 98 Representative examples illustrating prediction performance (left; predicted versus
 99 observed connectivity CR; black line denotes perfect prediction) and corresponding
 100 state-specific FLARE-CR associations (right) for the VS-SM and VS-CB domain pairs.
 101 (c) Comparison of connectivity developmental trajectories between observation and

102 predicted trajectories using state FLARes; left: VS-SM; right: VS-CB. (d) Prediction
103 of future behavioral CRs from earlier state FLARes (purple line) and reverse-time
104 control analyses using later FLARes values (orange line) within $\leq$ 60-day intervals
105 (n=75 infants). (e) State-specific associations between FLARes and subsequent
106 behavioral change rates for eye looking behavior. (f) Comparison of observed behavior
107 developmental trajectories with reconstructed trajectories using predicted CRs of eye
108 looking behavior.

109

Supplementary Files

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- [2026MaDynamicPredictionOfInfantDevelopmentsupp.pdf](#)