Diffusion Neuroimaging of Speech Acquisition in Infants

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We utilize diffusion MRI (dMRI) data from the Baby Connectome Project to longitudinally characterize white matter tract maturation across motor, auditory, visual, ventral language, and dorsal language pathways in infants from birth to 24 months of age. Our analysis reveals three primary insights into the neural basis of early speech acquisition. First, association tracts (arcuate fasciculus and superior

longitudinal fasciculus) exhibit marked immaturity at birth but undergo rapid maturation paralleling motor tracts (corticospinal and thalamo-precentral tract). By 24 months, these association tracts approach maturity levels comparable to primary sensory tracts (acoustic and optic radiation), and the maturation of these motor and association tracts consistently correlate with infants' comprehension of gesture-based phrases. Second, these rapidly maturing association tracts correlate with nearly all developmental domains, including motor skill, social interaction, emotional regulation, living skill, and speech. Conversely, complex speech behaviors correlate broadly across nearly all examined tracts, underscoring extensive neural integration characterized by nonlinear mappings between neural substrates and developmental outcomes. Third, exploratory longitudinal mediation analyses suggest an asymmetric loop of communicative interactions in early infancy: gross-motor skill indirectly facilitates speech development through enhanced social interactions; while social interaction facilitates speech development by refining fine-motor skill. Collectively, these findings highlight motor development as a major developmental driver in early infancy and advocate an integrative, experience-dependent, and dynamic model of early speech acquisition. This study points to future research avenues focused on elucidating how social interactions function as a pivotal catalyst, aligning infants' neural and behavioral development — from spontaneous, undifferentiated actions toward socially adaptive behaviors.

Infants are exceptional learners, continuously adapting — both physically and mentally — to rapidly changing environments, strikingly exemplified by their immediate transition from an aquatic womb to terrestrial life at birth (*1, 2*). Their first cry signals the onset of postnatal communicative interactions (*3, 4*), which are intially motor-based. Newborns may not immediately recognize these vocalizations as mouth-produced (*5*), and caregivers often find them ambiguous and challenging to interpret. This necessitates careful observation and responsive behavior (*6, 7*), guided by contextual information (*8, 9*). Over time, sustained reciprocal interactions between the developing neural

substrates and cumulative experiences progressively align infants with their social environment (*10, 11, 1*), establishing a critical foundation for acquiring increasingly complex cognitive skills, notably speech (*12, 13*).

Speech acquisition represents one of the most complex cognitive processes undertaken by the developing brain (*14*), illustrating infants' extraordinary *learning efficiency*, which surpasses that observed in adults, other animals, and artificial intelligence systems (*15, 16, 17*). Investigating the neural mechanisms underlying speech acquisition provides a unique window into understanding how the brain matures and organizes itself to efficiently process noisy, dynamic, real-world information. This line of research may offer transformative insights for developing brain-inspired, energy-efficient artificial intelligence systems. Crucially, infants' exceptional learning capabilities are closely linked to the formation of *network-level efficiency* (*18, 19*). However, the fundamental question of how early-life experiences shape structural connectivity and functional integration during early neurodevelopment remains unresolved.

From contemporary perspectives, infants' exceptional *learning efficiency* is particularly associated with neonatal imitation — a social learning mechanism traditionally viewed as an inborn capacity enabling direct copy of observed gestures without requiring postnatal experiences (*20, 5*). The strongest evidence supporting this interpretation comes from neonatal imitation of tongue protrusion (*21*), a perceptually opaque behavior, as newborns lack direct visual experiences of their own facial gestures and thus cannot readily map observed actions onto self-produced gestures (*22*). Despite its prevalence (*23*), this interpretation has remained controversial over the past four decades, partly due to inconsistent replication of neonatal imitation behaviors (*24, 25, 26, 27*). Advances in functional neuroimaging have provided insights into neural mechanisms underlying imitation, particularly involving the mirror neuron system, which responds to both sensory and motor stimuli in the mature brain (*28, 29, 30*). However, neuroimaging evidence regarding these neural mechanisms in neonates remains contradictory. For example, a magnetoencephalography (MEG) study indicate that Broca's area — a core component of the mirror neuron system crucial for vocal imitation — does not exhibit activation in response to speech stimuli in newborns (*31*). Intriguingly, an alternative method — near-infrared spectroscopy (NIRS) — combined with different syllable contrasts has revealed distinct activation patterns (*32*). Collectively, these findings indicate that the neural developmental mechanisms underpinning neonatal speech learning are likely far more complex and

dynamic than previously recognized.

The complexity underpinning speech processing has recently been recognized as an emergent property of the brain connectome (*33, 18*). Correspondingly, neonatal brains undergo extensive development, initially involving proliferation of neural connections, followed by selective pruning to form sparse yet efficient white matter connections (*34, 35*), resulting in a mature brain characterized primarily by *network-level efficiency* (*36, 37*). Typically, through shaping white matter tracts within and across multiple segregated brain systems — such as motor, auditory, and visual systems involved in speech acquisition (*38, 39, 40*) — the refined neural networks facilitate functional integration (*41*). This functional integration contributes to intrinsic complexity of speech processing, progressing typically from simple to complex capacities during prolonged developmental periods. Such complexity makes it particularly challenging to isolate and examine single mechanism under strictly controlled experimental conditions (*42, 43*). A more specific question here is: How are associations across sensory and motor systems established — specifically, are they innate or experience-dependent?

Non-invasive diffusion MRI (dMRI) now provides an exceptional window into understanding functional integration (*19, 44*). This neuroimaging approach offers distinct advantages, including the task-free setting, suitability for longitudinal assessment, and the comprehensive examination of white matter tracts linking multiple brain systems (*45, 46*). White matter connections critically influence fundamental aspects of cognitive processes, such as the speed of neural signal transmission and oscillatory synchronization among brain regions, exhibiting plasticity continuously shaped by postnatal experiences (*47, 48, 49*). Therefore, longitudinal assessment of changes in white matter tracts attributes is crucial for elucidating mechanisms underlying *network-level efficiency* and thus *learning efficiency*. Although numerous studies have utilized dMRI to chart developmental trajectories, clear behavioral correlations involving major tracts within and across multiple systems remain unclear (*50, 51*). This limitation arises primarily from difficulties in reliably collecting behaviral and dMRI data from infants, compounded by difficulties in accurately extracting tracts across multiple brain systems during early developmental periods (0–24 months), which are characterized by significant variability (*52, 50*). These obstacles constrain the full methodological potential of dMRI in clarifying developmental mechanisms underlying speech acquisition. In this study, we leverage the largest-ever behavioral and dMRI dataset from the Baby Connectome Project (BCP) (*53*), overcom-

ing these methodological barriers (*54*), to comprehensively characterize developmental trajectories of white matter tracts within and across motor, auditory, and visual systems. Our results provide insights into early neural integration mechanisms underpinning speech acquisition, inform ongoing theoretical debates, and highlight valuable yet underexplored avenues for future research.

Neural mechanisms underlying sensory-motor interactions during speech acquisition

Speech acquisition involves dynamic interactions between neural substrates and postnatal experiences (*13*), reflected in plastic changes in both structural and functional connectivity (*41*). Throughout the prolonged development period, speech development undergoes a series of critical periods, which denote cascading time windows of maximal sensitivity to specific speech stimuli, progressing from simple to complex (*55*). Recent evidence further indicates that this sensitivity is not limited to the acoustic domain but fundamentally extends into motor domains (*56, 57, 58, 59, 60*). To elucidate these mechanisms, diverse neuroimaging techniques have been employed to characterize the neural basis associated with speech acquisition.

Noninvasive neuroimaging techniques, including electroencephalography or event-related potentials (EEG or ERPs) (*61*), NIRS (*32*), functional magnetic resonance imaging (fMRI) (*62*), MEG (*31*), and dMRI (*63*), have been widely utilized to investigate speech acquisition mechanisms from fetal stages through early infancy (*44*). These techniques are particularly informative for capturing subtle infant responses to speech stimuli, enabling characterization of speech-related neural activity as early as the prenatal period (*64, 65*). Prenatal development of the motor and auditory systems, characterized by synaptogenesis and myelination, has been extensively documented through histological analyses and structural MRI (sMRI) studies (*66, 67, 68*). Prenatal brain maturation reaches a level sufficient to support basic motor responses, such as fetal movements and heart rate alterations elicited by acoustic stimuli (*69, 70, 71, 72*). Moreover, fetal MEG and fMRI studies have demonstrated clear activations in auditory cortices in response to external acoustic stimuli, providing direct neural evidence of fetal auditory processing capabilities (*73, 74*). Additionally, critical speech-related white matter tracts, including arcuate fasciculus (AF) and superior

longitudinal fasciculus (SLF), have been successfully identified from fetal dMRI data (*75, 76*).

Prenatal interaction patterns, characterized by fetal motor responses to auditory stimuli, exemplify an asymmetric communicative pattern — acoustic-in, motor-out — highlighting the fetal brain capability for functional integration across sensory and motor systems. Similarly, initial postnatal communications, such as crying and other motor activities, are initially vague but gradually become attuned and integrated with vocal-based speech systems (*6, 8*). Although these early motor behaviors often convey information challenging for adults to interpret, they represent crucial precursor to more explicit speech-based communicative exchanges (*65*).

After birth, infants progressively refine their responses to ambient stimuli, transitioning from the first cry to cooing, babbling, and eventually producing their first recognizable words around 12 months of age (*77*). Concurrently, infants become increasingly adept at discriminating phonemes, syllables, phonological patterns, and morphemic cues, demonstrating substantial improvements by approximately 24 months of age (*78*). This developmental progression has been widely conceptualized as a cascading spectrum characterized by critical periods (*79, 80, 55*). Through these critical periods, infants become progressively sensitive to specific regularity patterns (*81, 82*). By approximately one year of age, infants shift from sensitivity to universal phonetic contrasts toward selective recognition of contrasts specific to their native linguistic environment, a process termed *perceptual attunement* (*10, 83*).

Crucially, speech perception is not limited solely to auditory development; rather, integration with the motor system also critically influences it (*84, 85*). During development, speech perception and production systems become highly integrated, which involves sensory, motor, and sensorimotor experiences (*86, 87*). At the brain-region level, Broca's area, associated primarily with motor functions, can also be activated by speech stimuli (*88*), highlighting its key role in sensory-motor integration (*89*). Given the multimodal nature of speech, dMRI data hold significant promise for elucidating the integrative mechanisms underlying the development of white matter tracts that coordinate sensory and motor systems (*46, 18*). In the following sections, we comprehensively characterize developmental trajectories of white matter tracts across multiple pathways (Sections Functional categorization of white matter tracts and Asynchronous and synchronous maturation of white matter tracts across multiple brain systems) and explore their correlations with the cascading development of motor skills, social interaction, and speech (Sections Relative immaturity of association tracts at

birth and Rapid postnatal maturation of association tracts).

Functional categorization of white matter tracts

Previous studies on infant speech acquisition have predominantly focused on white matter tracts within the classical dual-stream pathways (ventral language and dorsal language) (*90, 51*), despite recognizing that speech processing involves extensive interactions across multiple brain networks (*33, 18*). However, comprehensive analyses of speech acquisition have been hindered by substantial challenges associated with acquiring, processing, and analyzing infant data, largely due to significant data variability across development periods (*52, 46*). To address these challenges, the Baby Connectome Project (BCP) now offers a large-scale longitudinal dataset comprising high-quality multi-shell high angular resolution diffusion imaging (HARDI), alongside extensive behavioral assessments covering motor skill, social interaction, emotional regulation, living skill, and speech (*53*). Additionally, our group has developed robust AI-based processing and analysis tools (*91, 92, 93, 94*), specifically enabling accurate extraction of auditory tracts spanning peripheral, subcortical, and cortical regions in infants (*54*). Building upon these advancements, the current study extends tract extraction capabilities to consider multiple brain systems, including motor, sensory (auditory, visual), and their associated domains (auditory-motor, visual-motor, and auditory-visual-motor).

We defined white matter tracts based on established protocols derived from the high-quality Human Connectome Project (HCP) dataset (*95, 96*) and extracted these tracts from the longitudinal BCP dMRI data spanning neonatal to 24-month-old infants (Table S1). These extracted tracts were categorized into five distinct functional groups — **motor**, **auditory**, **visual**, **ventral** language, and **dorsal** language, and each represented consistently by distinct colors across the text, trajectory curves, and figure legends in this manuscript.

- **Motor** group includes **corticospinal tract** (**CST**), **thalamo-precentral tract** (**T-PREC**), and **corpus callosum anterior midbody** (**CC_4**), each connecting to primary **motor** cortex (precentral gyrus).

- **Auditory** group comprises tracts spanning peripheral, subcortical, and cortical regions,

delineated based on established anatomical criteria (*97*). However, peripheral auditory tracts were excluded from subsequent analyses due to substantial noise in their microstructural measures.

- **Visual** group includes the **optic radiation** (**OR**), **middle longitudinal fasciculus** (**MLF**), and **superior longitudinal fasciculus II** (**SLF II**). Although traditionally classified within ventral (**MLF**) and dorsal (**SLF II**) language pathways (*33*), we reclassified them into the visual group, given their established roles in **auditory**-**visual**-**semantic** integration (**MLF**) (*98, 99*) and visual-motor processing (**SLF II**) (*100*).

- **Ventral** language group comprises the **uncinate fasciculus** (**UF**), **inferior fronto-occipital fasciculus** (**IFOF**), and **inferior longitudinal fasciculus** (**ILF**). Notably, the **IFOF**, closely implicated in **visual** processing (*33*), is distinctly highlighted in **yellow** in Fig. 1 (maintained consistently across subsequent figures), underscoring its dual roles in **visual** and semantic processing (*101*).

- **Dorsal** language pathway includes **AF** and **SLF III**, both prominently associated with speech articulation (*102*).

Fig. 1 illustrates the extracted tracts across developmental stages from neonatal to 24-month of age, arranged on the eight faces of an octahedron. These tracts demonstrate notable variability in maturation rates, consistent with their diverse functional specializations. For instance, **ILF** and **UF** exhibit relatively slower size growth, aligning with their prolonged developmental course for processing semantic meaning. In contrast, **AF** shows one of the most rapid maturation among all examined tracts. Notably, our results reveal that the neonatal **AF** already connects to Brodmann's area 44 (BA 44), as explicitly shown in Fig. S2. This finding contrasts with earlier studies that failed to detect such neonatal connectivity (*103, 104, 105*), likely due to previous limitations in data resolution and tract extraction methodologies. Our observations thus underscore the importance of employing high-quality data and robust methods for accurate tract extraction (*106*). Collectively, these results provide compelling anatomical evidence supporting the existence of early-established neural connectivity between superior temporal and inferior frontal cortices from birth, supporting the early integration of sensory and motor regions critical to the primordial speech networks.

Asynchronous and synchronous maturation of white matter tracts across multiple brain systems

The infant brain undergoes dramatic development during the first two postnatal years (*107*), coinciding with rapid structural and functional reorganization essential for the emergence of speech capacities (*77, 83*). To characterize underlying neurodevelopmental processes, we employed neurite density index (NDI), derived from the neurite orientation dispersion and density imaging (NODDI) model (*108*). Mean NDI values were computed for each tract, and population-level developmental trajectories were modeled using linear mixed-effects models (LMMs) (*109*). The overall NDI trajectories are presented in Fig. 2, with detailed tract-specific trajectories provided in Fig. S3. These trajectory curves were color-coded according to their functional category — **motor**, **auditory**, **visual**, **ventral** language, and **dorsal** language — demonstrating patterns of increase broadly consistent with previously documented volumetric growth and maturation in infant white matter (*107, 110, 45, 49*).

These trajectories comprehensively illustrate early white matter maturation patterns relevant to speech acquisition, enabling detailed analyses of asynchronous and synchronous development within and across multiple neural systems (*111*). As depicted in Fig. 2, tracts from different groups generally exhibit distinct NDI values, indicating variable maturation during the first two postnatal years. For instance, tracts such as the **CST**, **AR**, **OR**, **UF**, and **AF** demonstrate pronounced variability in maturity at birth, suggesting developmental asynchrony established prenatally. Furthermore, the subsequent maturation rates of these tracts differ markedly — the **AF** matures more rapidly compared to the primary sensory tracts, **AR** and **OR**. Despite these initial differences, tracts such as **AR**, **OR**, **SLF II**, **AF**, and **SLF III** converge toward comparable maturation level by 24 months. This convergence highlights a critical developmental milestone at which the transmission efficiency of association tracts reaches parity with primary sensory tracts, underscoring the increasing capacity for integrated sensory-motor processing essential for speech (*38, 112*).

In parallel with these asynchronous patterns, several tracts exhibit notably synchronous developmental trajectories, which may underpin the emergence of functional synchronization (*113*). Specifically, the visually related **SLF II** dorsal language tracts (**AF** and **SLF III**) demonstrate closely overlapping NDI trajectories throughout the entire 24-month period. Although consistently

parallel to the **CST** and **T-PREC**, these association tract trajectories exhibit relatively lower maturity compared to both. This synchronous developmental pattern suggests coordinated maturation mechanisms potentially driven by shared postnatal experiences that simultaneously engage multiple tracts (*41, 114, 64*). Given the clear structure-function relationships, examining these asynchronous and synchronous developmental patterns may provide critical insights into how early-life experiences shape neural development.

The functional relevance of these synchronous maturation patterns is further evidenced by significant correlations between tract-specific NDI values and infant behavioral scores. Considering the rapid and advanced maturation of motor tracts, we first emphasize the correlations between tract maturation and gesture-based communication. As detailed in Table 1, the NDI values of $\mathbf{CST_L}$, $\mathbf{T\text{-}PREC_L}$, $\mathbf{SLF\ II_R}$, and $\mathbf{AF_L}$ consistently and significantly correlate with infants' comprehension of gesture phrases, as measured by the MacArthur-Bates Communicative Development Inventories (CDI) - Words and Gestures (W & G) (*115*). These findings support that parallel maturation across **motor** and these association tracts are consistently synchronized by early gestured based interactions. Furthermore, as shown in Table 2, NDI values of **MLF** exhibit significant correlation with the total number of words understood by infants, aligning well with prior evidence emphasizing its role in semantic comprehension, despite ongoing controversy (*33*).

Considering that the CDI - W & G primarily assesses early gesture-based communication, we extended our analysis to investigate broader correlations between tract maturation and performance across ten additional behavioral assessments (detailed in Supplementary Materials, Section Data acquisition and participates). These assessments cover critical domains of infant development, including motor skill, social interaction, visual awareness, emotional regulation, living skill, and speech. Our analysis revealed a total of 367 significant correlations, detailed in supplementary files `1_significant_relationships_t_b_ordered_by_behavior.csv` and `1_significant_relationships_t_b_ordered_by_tract.csv`. In general, tract maturation significantly correlated with diverse early behavioral performances. Specifically, individual tracts, such as the **AF**, exhibited significant correlations with a broad range of functional domains, encompassing nearly all assessed behavioral categories. Conversely, complex behaviors, such as receptive language, correlated significantly with nearly all investigated tracts. Collectively, these observations indicate that the integrative relationships between tracts and complex behaviors resemble nonlinear

one-to-many and *many-to-one* mappings (*116*).

To clarify the functional role of the **MLF**, which remains incompletely understood, we examined its potential hemispheric lateralization and observed intriguing differences. Specifically, we found that the left **MLF** predominantly correlated with receptive and expressive language, whereas the right **MLF** primarily correlated with **motor** skill. However, as depicted in their developmental trajectories in Fig. 2, hemispheric differences in maturation were subtle. Both hemispheres initially exhibited maturation levels comparable to other association tracts, **AF**, **SLF II**, and **SLF III** at birth but demonstrated significantly slower maturation rates thereafter. Notably, by three months of age, the developmental trajectory of the **MLF** closely aligned with that of **ILF**, supporting its integration role in semantic processing. These semantically relevant tracts, including **ILF**, **MLF**, and **UF**, consistently displayed slower maturation throughout the first two postnatal years — a developmental pattern known to extend over decades to achieve proficient semantic processing (*77*).

We also observed that tract maturation commonly exhibited positive correlations with relatively simple skills, such as motor behaviors (including gestures, gross-motor, fine-motor, and fine domains) and gesture phrase comprehension. In contrast, negative correlations were observed between tract maturity and complex speech skills, such as receptive language, expressive language, and communication domain, consistent with the previous finding (*117*). These results provide evidence *that the maturation of individual tracts does not directly facilitate complex speech capacities, which require extensive integration*. Rather, motor and gesture-based communication skills may serve the precursors that scaffold the emergence of complex speech capabilities (*118, 119, 120*). Nevertheless, considerable complexity persists in identifying the specific precursors involved, and ongoing research continues to debate these relationships (*16, 2, 65, 87, 5*).

Relative immaturity of association tracts at birth

During gestation, fetuses sequentially develop initial capabilities in **motor**, **auditory**, and **visual** domains, typically beginning with **motor**, followed by **auditory**, and subsequently **visual** functions (*121, 65*). This early development enables fetal sensory-motor behaviors, such as limb movements, particularly in response to acoustic stimuli (*69, 70, 71, 72*). This results in uneven maturity across these sensory and motor tracts at birth (*46*). As illustrated in Fig. 2, the primary **visual** tract (**OR**) is

notably less mature than the primary **auditory** tract (**AR**), which demonstrates considerably lower maturity than the **motor** tracts (**CST** and **T-PREC**). These results thus empirically substantiate the sequential prenatal development of sensory and motor systems at the white matter level.

At birth, the observed asynchrony in tract maturation provides insights beyond the prenatal developmental course of the **motor**, **auditory**, and **visual** systems. Notably, association tracts such as **SLF II**, **AF**, **SLF III**, and **MLF** consistently exhibit the lowest initial maturity among all examined tracts. These findings indicate that, although isolated **motor**, **auditoy**, and **visual** systems attain relatively advanced prenatal maturation, their functional integration remains comparatively immature at birth, no matter **auditory**-**motor**, **visual**-**motor**, or **auditory**- **visual**-**motor** tracts. This connectivity immaturity significantly restricts effective inter-system signal transmission. In general, neonatal brain systems remain underdeveloped, necessitating extensive postnatal structural and functional maturation before reaching the adult-level efficiency required to support sophisticated behaviors such as proficient speech communication. Nevertheless, this initial immaturity endows the neonatal brain with maximal neural plasticity, enabling rapid and incremental learning from postnatal experiences (*114*) through relatively minor adjustments or reorganization (*48*).

Immediately after birth, pre-wired neural substrates support a basic repertoire of behaviors. Neonatal behaviors — such as the first cry — ensure survival, facilitate the transition from the intrauterine to the external environment (*122,4*), and postnatal experiences progressively shape both neural and behavioral development, based on the rudimentary structural and functional connectivity (*64, 114*). During development, association tracts (*i.e.*, the **SLF II**, **AF**, and **SLF III**) exhibit rapid maturation parallel to motor tracts (**CST** and **T-PREC**) over the first postnatal year, underpinning swift development of motor and sensory-motor capacities. A pivotal question thus arises: What specific experiences shape these developmental trajectories?

To address this question, we conducted a cross-sectional mediation analysis examining ternary correlations among seven developmental domains — 1) white matter tracts, 2) motor skill, 3) social interaction, 4) visual & cognitive awareness, 5) emotional regulation, 6) living skill, and 7) speech — using 11 behavioral assessments from the BCP (categorization criteria detailed in Supplementary Materials, Section Behavioral assessments and categorization). The results reveal 849 potential pathways from 74, 409 possible ones, as detailed in Table S6 and supplementary file (`2_combined_results_with_fdr_and_mediation.csv`), which implied two key insights. First,

we identified significant positive correlations between tract maturation and motor skill, as well as visual & cognitive awareness, both of which also positively correlated with speech performance. These results suggest an indirect pathway between tract maturation and speech development, mediated by abovementioned factors. Second, among these identified mediation pathways linking tracts to speech performance, motor skill (*i.e.*, gross-motor, fine-motor, and fine subdomain) prominently served as the dominant mediator (111 out of 118 pathways identified with tract maturation as the predictor), underscoring their pivotal role in early speech acquisition.

Considering recent evidence highlighting the critical role of both social interaction and sensorimotor (or fine-motor) experiences (*11, 123, 124, 60, 87*), we further explored mediation pathways using social interaction and motor skill as predictors (X), with language performance as the outcome (Y). Our mediation analysis revealed 731 statistically significant pathways involving mediators (M), including visual & cognitive awareness, living skill, emotional regulation, motor skill, and social interaction. These findings highlight two aspects of complexity in speech acquisition. First, speech development likely depend on broad functional domains rather than exclusively sensory, motor, and social interaction experiences alone. Second, we identified dynamic reciprocal relationships, where social interaction and motor skill alternately served as *motor* → *social and social* → *motor* pairs, and mediators in the two pairs significantly correlated with speech outcomes.

These findings align with recent discoveries highlighting the facilitating role of synergistic, multimodal sensorimotor experiences in learning (*5*), rather than isolated **motor**, **auditory**, or **visual** experiences but rather on (*125, 126*). Given that social interaction provides sensorimotor experiences of high quality and quantity (*86, 127*), which prominently involve the fine-motor skills (*128, 129*), clarifying the relationship between motor skill and social interaction in the context of speech acquisition is crucial for understanding the socilized developmental transition.

Rapid postnatal maturation of association tracts

Fetuses and neonates can primarily respond to external stimuli through motor activities, but these responses are often ambiguous to caregivers, exemplified by the apparent randomness of neonatal resonses (*26*). Nonetheless, such neonatal motor-based behaviors, even in foetuses, reveal communicative competence (*8, 130*), fundamentally shaping the neural substrates of both infants and

their mothers during extensive care-soliciting interactions in early infancy (*114, 131, 6*). As illustrated in Fig. 2, motor and association tracts (**CST**, **T-PREC**, **SLF II** , **AF**, and **SLF III**) exhibit notably rapid and synchronous maturation throughout the first postnatal year. The rapid maturation of **motor** tracts can be attributed to those abundant motor experiences; however, the mechanisms by which similar to motor experiences promote the parallel maturation of association tracts remain unclear.

To investigate potential mechanisms underlying the maturation of motor and association tracts, we further conducted longitudinal mediation analyses focusing on the relationship between motor skill and social interaction within the context of speech acquisition. Specifically, we explored two alternative mediation pathways: 1) *motor* → *social* → *speech*, in which motor skill at the 4-6 month window was employed to predict social interaction performance at the 12-14 month window, which subsequently predicted speech outcomes at the 24-26 month window; and 2) *social* → *motor* → *speech*, similar to pathway 1) but with predictor and mediator switched. The results are presented in Tables 3 and 4, with more detailed information provided in supplementary files (`3_mediation_results_m_s_l.xlsx` and `3_mediation_results_s_m_l.xlsx`). Both analyses identified multiple significant pathways, collectively revealing a distinct and intriguing developmental cascade.

In the *motor* → *social* → *speech* pathway, predictors were predominantly associated with gross-motor skill, which effectively predicted mediators related to social interaction. This finding aligns with existing evidence emphasizing the communicative role of early gross-motor skill in facilitating social interaction during early infancy (*132, 118, 120*). In contrast, in the *social* → *motor* → *speech* pathway, predictors involving social interaction primarily predicted mediators related to fine-motor rather than gross-motor skill. This pattern confirms that social interaction may foster infants' execution and refinement of fine-motor skills, which require intricate coordination aross sensory and motor systems (*133, 127, 5*). Collectively, these findings highlight the mediating roles of both social interaction and fine-motor experiences contributing to the early development, typically the speech acquisition.

Both the motor → social → speech and social → motor → speech pathways prominently involved *interpersonal* and *socialization* elements within the social interaction domain, as illustrated in Table 3 and 4, suggesting a broader integrative developmental loop. Specifically, gross-motor

activities elicited by external stimuli may initially facilitate social interactions between infants and caregivers, particularly when infants cannot produce explicit speech contents (*8, 118*). In turn, these social interactions offer sensorimotor experiences of high quality and quantity, facilitating the development of imitation, which critically depends on the sensory-motor integration (*42, 134, 5, 124*). Social interactions effectively capture infants' attention, motivate their actions, and transform perceptually opaque behaviors into transparent, imitable actions, substantially enriching infants' experiences for speech acquisition (*11, 135, 136*).

This extended loop does not suggest that postnatal skills are acquired through a strictly linear or sequential manner; rather, it highlights a nonlinear, interactive process continueously interacting with neural substrates (*41, 64, 114, 137*). Within this extended loop, rudimentary communication and its subsequent refinement may develop synchronously, generating both motor and sensorimotor experiences. Considering that association tracts responsible for transmitting sensory signals to **motor** cortices strongly correlate with sensorimotor skill performance (*138, 139*), and that ongoing sensorimotor practice dynamically refines experiential learning and the microstructural properties of these tracts (*79, 137*), the extended loop may explain why association tracts (**AF**, **SLF II**, and **SLF III**) exhibit rapid and synchronous maturation trajectories alongside motor tracts (**CST** and **T-PREC**). Association tracts, driven by such dense early communicative interactions with both motor and sensorimotor experiences, mature rapidly and in parallel with motor tracts. By approximately 24 months, the association tracts reach maturity levels comparable to primary sensory tracts (**AR** and **OR**) which signifies a critical developmental milestone at which neural systems begin transmitting sensory stimuli to motor cortices with efficiency comparable to intrinsic sensory pathways. Collectively, early-life social interactions provide essential learning opportunities, reciprocally shaping and refining both neural and functional connectivity, and profoundly influencing individual development.

Concluding remarks

An integrative, experience-dependent, and dynamic model of speech acquisition

Speech is one of the most complex and uniquely human abilities (*140, 14*), increasingly viewed as an emergent property arising from dynamic interactions across widely distributed neural systems (*33, 18*). Our findings strongly support this emergent perspective by demonstrating extensive correlations between early speech behaviors and virtually all examined white matter tracts spanning **motor**, **auditory**, **visual**, **ventral**, and **dorsal** language pathways. At birth, although the neonatal brain is structurally prewired, functionally segregated systems remain immature and inefficiently interconnected, as indicated by underdeveloped primary sensory and association tracts compared to motor tracts (**CST** and **T-PREC**). During the first 12 months of development, these association tracts exhibit remarkably rapid maturation, with developmental trajectories closely paralleling those of the **motor** tracts, highlighting the critical role of early **motor** development. This observation provides support for underlying motor mechanisms associated with early behaviors, such as speech perception (*141, 125, 87*).

To explore the driving factors behind rapid **motor** development, we conducted a two-stage exploratory mediation analysis — initially *cross-sectional*, followed by *longitudinal* — revealing a developmental cascade involving social interaction, gross-motor, and fine-motor skills. In the first stage, cross-sectional mediation analyses identified multiple mediators (M), including motor skill, social interaction, visual awareness, emotional regulation, and living skill, highlighting the indirect and complex pathways through which neural substrates or other experiences (X) influence speech performance (Y). These results further support the integrative nature of speech by demonstrating its close associations across multiple developmental domains. In the second stage, our longitudinal mediation analyses further specified two temporal sequences or directional influences involving social interaction and motor skill: 1) gross-motor skill at the 4-6 month window primarily supported social interactions at the 12-14 month window; 2) social interaction at the 4-6 month window significantly facilitated fine-motor skill at the 12-14 month window. Ultimately, these identified mediators — social interaction and fine-motor skill at the 12-14 month window — robustly promoted

speech abilities at the 24-26 month window.

Besides social interaction, these postnatal experiences fundamentally shape neural substrate maturation. Notably, we identified extensive correlations between tract maturity and a wide range of early developmental behaviors, addressing a critical gap concerning detailed behavioral implications of white matter maturation (*50, 51*), though recent studies have clarified neural correlations between language pathways and early cognitive performance (*142, 143, 51*). The observed structural-functional relationship demonstrated complexity and nonlinearity (*116, 19*), revealing *one-to-many* and *many-to-one* mappings between tracts and behavioral outcomes. These findings advocate a cautious perspective when interpreting cascading precursors to the complex speech — including motor skill, visual skill, social interaction, emotional regulation, and living skill — as no single developmental factor may dominate the influence alone. From a systems view, speech emerges as a property of whole-brain interactions, wherein the whole fundamentally differs from the sum of its parts (*144, 18*); and complex brain functions cannot be adequately understood through isolated aspects. Therefore, our work advocates a holistic rather than reductionist perspective to avoid overlooking the critical redundancy and resilience provided by integrative neural systems (*145*), established through long-term developmental integrations. This holistic perspective questions strategies aiming to understand speech perception or semantic processing solely by focusing on isolated brain system or regions (*146, 147*).

More profoundly, our work points to aspects that extend the classical dual-stream model by explicitly incorporating additional sensory and motor circuits. Rather than merely focusing on *sound-to-articulator* and *sound-to-semantic* mappings, this extension emphasizes dynamic interactions among neural substrates, motor skill, and social interaction as integral components for elucidating speech acquisition. Immediately after birth — and even prenatally in fetuses (*130*) — motor-based behaviors such as crying and gestures constitute primary means for newborns to respond to external stimuli (*3*). Early communication thus exhibits an asymmetric pattern characterized by two synergistic loops: an *infant-arouses-caregiver-support* loop, wherein infants' ambiguous yet expressive signals solicit caregiving responses; and a complementary *caregiver-arouses-infant-learning* loop, wherein caregivers' motor actions actively capture infants' attention and elicit imitation. These two loops converge within the domain of social interaction, resonating with social learning theories (*11, 127, 119*) that highlight the pivotal role of social interactions in the developmental transition

from gross-motor-based (gesture) to fine-motor-based (speech) communication. Collectively, our empirical findings support an integrative, experience-dependent, and dynamic model of speech acquisition.

Imitation: innate or learned?

While our results advocate the experience-dependent nature of speech acquisition, they inevitably intersect with ongoing controversies surrounding neonatal imitation (*148, 136, 149, 150, 151, 23*). The intense controversy regarding innate imitation primarily arises from replication failures (*24, 25, 152, 153, 154*). Neonatal responses to external stimuli seemingly appear random, as illustrated by studies comprehensively implementing eleven types of adult-modeled stimuli and longitudinally assessing infant responses (*26*). Over periods ranging from 1 to 9 weeks, newborns consistently showed no greater frequency of anticipated responses compared to control responses across four separate time points, demonstrating *one-stimulus-to-many-responses* or *many-stimuli-to-one-response* patterns. Consequently, the investigators recommend caution when interpreting these seemingly random responses as supportive evidence for innate neonatal imitation (*155, 156, 27*). A critical consideration here is that, although neonatal prewired networks can transmit signals from primary auditory cortices to Broca's area and elicit motor responses (*69, 32, 70, 71, 72*), the sensorimotor regularities necessary for robust imitation remain immature and under develpment.

At birth, speech-specific syllables do not necessarily activate Broca's area (*31*). Neonates may not initially be aware of their own facial articulators, owing to the perceptual opacity, until they have learned to establish associations across **motor**, **auditory**, and **visual** systems through social interactions (*5*). Social interactions — particularly those involving caregivers imitating infants — provide high-quality and high-quantity sensorimotor experiences facilitating infant learning (*127*). These experiences continuously and nonlinearly interact with prewired neural systems, gradually enabling efficient processing of stimuli exhibiting regular patterns and frequently appeared (*22, 2, 157, 116, 41, 114, 137*). Consequently, efficient learning mechanisms may emerge as early as birth, guiding neonates to establish correspondances among domains of their unseen facial gestures and those of others (*158, 159*), a foundational step toward imitation and directly copying caregivers' behaviors. Nevertheless, despite uncertainty regarding the precise timing at which infants form these

sensorimotor correspondences, existing evidence sufficiently supports the notion that imitation is gradually acquired — from simple to complex — through experience-dependent processes, which may commence immediately after birth.

From an information-theoretic perspective, these findings suggest that neonatal brains develop according to a maximum entropy principle. (*160, 161*). Characterized by highly redundant synaptic proliferation and by infants' seemingly random and nonspecific behavioral responses to environmental stimuli, these unsettled brain-behavior correlations initially allow maximal flexibility in establishing associations. During development, neural networks progressively undergo synaptic pruning, eliminating redundant or less useful connections, for reducing entropy and prediction errors through refining functional specialization and integration (*162*). Concurrently, human behaviors shift from stochastic, voluntary, undifferentiated responses to highly predictable and socially adaptive activities (*116, 1*). This behavioral attunement coincides neural reorganization could be observed in existing literature. For examples, speech-specific syllables initially activate broader cortical regions around the Sylvian fissure during the neonatal stage, but such activations become progressively confined to superior temporal regions by 12 months (as shown in Fig. 1 (a) 3rd row) (*31*), demonstrating increased neural specialization. In parallel, infants' initially broad perceptual sensitivities gradually specialize to efficiently process only native or ambient language(s) by one year of age (*163*). Overall, correspondence between observed and executed perceptually opaque gestures are established through postnatal experiences, and the regularity and frequency of these experiences fundamentally affect neural efficiency and reorganization, subsequently influencing motor skill, social interaction, and speech acquisition.

Revisiting speech acquisition: hierarchical organization, dynamic interaction, and intervention strategies

By emphasizing integrative and dynamic aspects of speech acquisition, our results reveal a potential hierarchical organization of speech acquisition rooted in motor-based gestures rather than acousticial patterns (*16, 164*). This highlights the communicative function of early motor activities alongside speech or language (*8, 165*), connects prenatal and postnatal development cascades (*65, 130*), and underscores the pivotal role of social interaction in facilitating learning (*166, 123*). Our correlation

analyses using CDI - W & G assessments revealed that **motor** and association tracts exhibited positive correlations with gesture-based phrases, whereas the **MLF** showed negative correlation with noun-based vocabulary. The difference between gesture-based phrase and noun-based vocabulary further support existence of a hierarchy in early speech acquisition.

We propose a hypothesis: the hierarchy in speech acquisition may correlate with both the developmental sequence of neural systems and the extent of neural integration across multiple brain systems. Acquisition tasks engaging fewer, more mature neural systems may be easier to accomplish. Given the higher maturity of the **motor** and **auditory** systems, initial alignment of internal motor commands with regular acoustic stimulus encodings may be easier, facilitating the establishment of associations necessary for acquiring more complex experiences (*167, 5*). Consequently, supportive effects from **motor**, **auditory**-**motor**, and **visual**-**motor** tracts may directly facilitate the acquisition of gesture-based phrases. In contrast, the **auditory**-**visual**-**semantic** integration tract (**MLF**) indirectly supports semantic comprehension of noun-based vocabulary, requiring more extensive integration of contextual regularities to categorize perceptual stimuli (*116*). Intuitively, gesture-based gesture phrases such as '*give me a hug*' are easier for infants to comprehend compared to noun-based vocabulary like '*vacuum*' (CDI - W & G). Additionally, differences in syllable acquisition may reflect variability in activation patterns within Broca's area. Neonatal activation in Broca's area is less readily observed for voiceless syllables such as the bilabial-plosive /pa/ and alveolar-plosive /ta/ (*31*), compared to voiced syllables like /ba/ and /ga/ (*32*). This difference likely arises because voiced syllables place lower demands on airflow control and neuromuscular coordination, making them easier for infant to acquire.

The **motor** system may further underlie speech perception, both neurally and behaviorally (*141, 84, 89, 85, 168, 112, 40*), although lesions in **motor** cortices do not always impair speech perception (*169, 146*). Therefore, more comprehensive theoretical models are needed (*170*). Given the extensive neural integration underpinning speech processing (*38, 87*), it is crucial to understand how early-life experiences evolve from rudimentary, isolated forms into increasingly sophisticated and integrated structures (*16, 140, 163*). This developmental progression gradually shapes neural systems, establishing the structural-functional correspondences critical for efficient information processing (*19*).

Communicative interactions via **motor** activities initiate prenatally (*130*), exhibiting asymmet-

ric patterns that extend into early infancy. Both the *infant-arouses-caregiver-support* and *caregiver-arouses-infant-learning* loops constitute an integrated, reciprocal framework, highlighting that early-life communication initially relies on separate mechanisms for perception and response. These early interactive loops between caregivers and infants not only solicit cares but also provide abundant, high-quality sensorimotor experiences (*148, 118, 5*), facilitating the maturation of motor and association tracts and fundamentally shaping more efficient neural networks. During development, spontaneous and undifferentiated gross-motor-based gestures gradually transition toward socially adaptive fine-motor-based speech, ultimately aligning with the ambient social context. However, our proposed theoretical hypothesis remains speculative and requires further rigorous investigation. Future studies should examine detailed patterns, including correlations between maternal sensitivity and gesture frequency, maternal vocal imitation and activation patterns in Broca's area, early social-interaction aspirations and fine-motor skill performance, and even the long-term developmental impacts of these interactions.

Besides these theoretical insights into speech acquisition, our works may also contribute valuable perspectives toward understanding developmental disorders. Neonates initially communicate via ambiguous motor behaviors long before acquiring speech. These subtle yet significant early behaviors — including crying and gross motor movements — center around the critical developmental task of establishing correspondences across sensory and motor domains (*128, 87, 5*), aiding infants in transforming perceptually opaque actions into transparent ones (*22*). Such early behaviors profoundly influence white matter tract maturation, significantly correlating with skills across various cognitive domains. Conversely, developmental disorders may stem from difficulties in establishing these fundamental correspondences due to insufficient or inadequate experiences necessary for establishing integrated, efficient neural pathways. More profoundly, such developmental variability may originate from ambient social context (*7*), which should be addressed first. Thus, effective interventions should aim to progressively restore and maintain active communicative interactions within the dynamic developmental loops — particularly by emphasizing timely responsiveness to infants' motor signals, encouraging infants' active engagement with caregivers, and clearly imitating infants' vocalization and gestures. These approaches generate eriched, high-quality sensorimotor experiences, assisting infants in returning mentally and physiologically to normative trajectories.

Such interventions might be particularly challenging for infants with cochlear implants (CI)

or auditory brainstem implants (ABI) (*171, 172*). Although caregiver imitation benefits infant vocalizations (*173*), infants with CI or ABI may encounter greater obstacles, since acoustic signals transmitted through artificial devices substantially differ from those processed via natural auditory pathways. Nonetheless, these barriers could potentially be overcome by identifying and utilizing multimodal correspondences beyond auditory cues alone. Specifically, caregivers could imitate infants by aligning their responses across multiple sensory, motor, and somatosensory domains rather than relying exclusively on vocal imitation.

Limitations and unresolved questions

Our study offers significant methodological advancements by applying advanced tract-extraction techniques to the largest-ever high-quality infant diffusion MRI and behavioral dataset. These techniques, combined with comprehensive multi-stage statistical analyses, were specifically designed to robustly identify developmental cascades. Theoretically, our findings highlight motor system maturation as a dominant event during early development, with social interaction serving as a pivotal catalyst, facilitating infants' communicative transition from gross-motor-based to fine-motor-based, and ultimately to socialized speech behaviors. However, several limitations remain.

First, our longitudinal mediation analysis relied on age windows rather than precise time points, potentially introducing artifacts that may obscure subtle developmental patterns. Nevertheless, given the rapid developmental pace during the first two years and considerable variability across individuals, such artifacts are unlikely to substantially distort our overall consistent findings, especially as age effects were adjusted at each measurement window to preserve the longitudinal structure. Caution is warranted, as finer-grained temporal analyses requiring precise experimental settings would be beneficial. Second, the behavioral assessments employed were relatively coarse and general-purpose, not specifically-designed to capture detailed behavioral markers relevant to early gross-motor, social interaction, fine-motor, and other specific skills. Although our analyses provided meaningful correlations between broad behaviors and white matter tracts, it did not explicitly clarify the hierarchical structure of speech acquisition like the visual grouping rules (*174*). Future studies utilizing more targeted, fine-grained behavioral assessments could significantly uncover detailed developmental cascades underlying speech acquisition. Lastly, our works exclusively

employed diffusion MRI. Multimodal neuroimaging approaches (*e.g.*, incorporating sMRI, fMRI, and E/MEG) would enrich insights into the neural foundations of cognitive functions. Collectively, longitudinal studies integrating precise behavioral assessments, narrower developmental windows, and multimodal neuroimaging methodologies will substantially advance our understanding of the complex mechanisms underpinning early speech acquisition.

In this work, by highlighting the unique advantages of diffusion neuroimaging in uncovering neural maturation underlying speech acquisition, our study provides a holistic framework for interpreting key aspects of emergent and integrative speech acquisition. Our findings suggest potential directions for further understanding developmental cascades beginning in prenatal periods. Several intriguing questions arise, warranting future investigation:

1. *Ethical considerations*: Given that early-life experiences foundationally influence developmental trajectories (*e.g.*, timing of initial sucking behaviors (*122*)), how can researchers effectively minimize potential adverse impacts of experimental manipulations on infants, particularly when the long-term consequences of altering early behaviors remain uncertain?

2. *Speech hierarchy*: Given that articulatory gestures (*i.e.*, distinctive features) fundamentally shape produced acoustic patterns (*175*), does the difficulty infants experience in controlling specific speech articulators (*e.g.*, lips, tongue, vocal cords) directly correlate with their difficulty in producing and perceiving the corresponding phonemes or syllables? Conversely, and more intriguingly, does mastering simpler phonemic acoustic regularities (in both production and perception) facilitate infants' awareness of correspondences between their own vocal gestures and those of their caregivers (*127, 5*)?

3. *Acoustic variability*: Given the substantial acoustic variability inherent in human speech (*176*), does the functional linkage across motor, auditory, and visual systems provide the neural basis or encoding dimensions through which infants leverage contextual regularities to effectively categorize perceptual stimuli (*116*)?

4. *Correspondence establishment*: Given that neonates learn through establishing correspondences involving a range of spontaneously elicited neonatal behaviors (*5*), how can researchers determine the earliest developmental time point at which infants reliably establish correspondences between their own vocal gestures and those observed in caregivers?

5. *Energy-efficient learning architectures*: Given that early learning depends on multimodal associations (*5, 17*), which may represent and compute external dynamic environments more efficiently with contextual regularities using the nonlinear (one-to-many and many-to-one) mappings (*116, 19*), how can researchers design artificial neural network architectures that model such nonlinear biological computational processes, thereby reducing the storage and energy demands of current large-scale models (*177, 178, 179*)?

Table 1: Significant correlations between tract maturation and total number of phrases understood from the CDI - W & G assessment.

Total number of phrases understood	p**-value**	r^2
$\mathbf{AF_L}^{**}$	0.006	0.838
$\mathbf{SLF\ II_R}^{**}$	0.006	0.848
$\mathbf{CST_L}^{**}$	0.006	0.851
$\mathbf{T\ PREC_L}^{**}$	0.006	0.829

Table 2: Significant correlations between tract maturation and total number of words understood from the CDI - W & G tests.

Total number of words understood	p**-value**	r^2
$\mathbf{MLF_L}^{*}$	0.045	0.927

Table 3: Summary of longitudinal mediation pathways (Motor → Social → Speech)

Predictor (Motor)	**Mediator (Social)**	**Outcome (Speech)**	**Motor → Social**			**Social → Speech**		
			Estimate	*Std. Error*	p-value	*Estimate*	*Std. Error*	p-value
grosssubdomain Raw	interpersrelationsubdom Raw	mcg vc totcom	0.711	0.238	0.003^{**}	8.535	4.343	0.049^{*}
grosssubdomain Raw	interpersrelationsubdom Raw	mcg vc totpr	0.711	0.238	0.003^{**}	18.566	7.190	0.010^{*}
grosssubdomain Raw	interpersrelationsubdom Raw	Receptive Language Raw	0.644	0.227	0.005^{**}	0.562	0.230	0.014^{*}
grosssubdomain Raw	interpersrelationsubdom Raw	Receptive Language T	0.644	0.227	0.005^{**}	1.552	0.672	0.021^{*}
grosssubdomain Raw	interpersrelationsubdom Raw	receptivesubdomain Raw	0.620	0.219	0.005^{**}	0.475	0.235	0.043^{*}
grosssubdomain Raw	interpersrelationsubdom Raw	receptivesubdomain v Scale	0.620	0.219	0.005^{**}	0.289	0.146	0.048^{*}
motorskillsdomain Domain Standard	interpersrelationsubdom Raw	mcg vc totpr	0.121	0.036	0.001^{***}	16.542	7.516	0.028^{*}
motorskillsdomain v Scale	interpersrelationsubdom Raw	mcg vc totpr	0.443	0.125	0.0004^{***}	16.653	7.603	0.028^{*}
grosssubdomain Raw	interpersrelationsubdom v Scale	mcg vc totcom	0.574	0.176	0.001^{**}	11.610	5.923	0.050^{*}
grosssubdomain Raw	interpersrelationsubdom v Scale	mcg vc totpr	0.574	0.176	0.001^{**}	23.284	9.956	0.019^{*}
grosssubdomain Raw	interpersrelationsubdom v Scale	Receptive Language Raw	0.493	0.172	0.004^{**}	0.634	0.312	0.043^{*}
grosssubdomain v Scale	interpersrelationsubdom v Scale	mcg vc totcom	0.397	0.195	0.042^{*}	11.704	5.439	0.031^{*}
grosssubdomain v Scale	interpersrelationsubdom v Scale	mcg vc totpr	0.397	0.195	0.042^{*}	20.824	9.133	0.023^{*}
grosssubdomain Raw	socializationdomain Domain Standard	mcg vc totpr	2.110	0.781	0.007^{**}	5.741	2.277	0.012^{*}
motorskillsdomain Domain Standard	socializationdomain Domain Standard	mcg vc totpr	0.338	0.120	0.005^{**}	4.877	2.322	0.036^{*}
motorskillsdomain v Scale	socializationdomain Domain Standard	mcg vc totpr	1.269	0.418	0.002^{**}	4.912	2.349	0.037^{*}

Note: Significance levels indicated by: $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$. Predictor, mediator, and outcome variables are assessed approximately at 6, 12, and 24 months respectively.

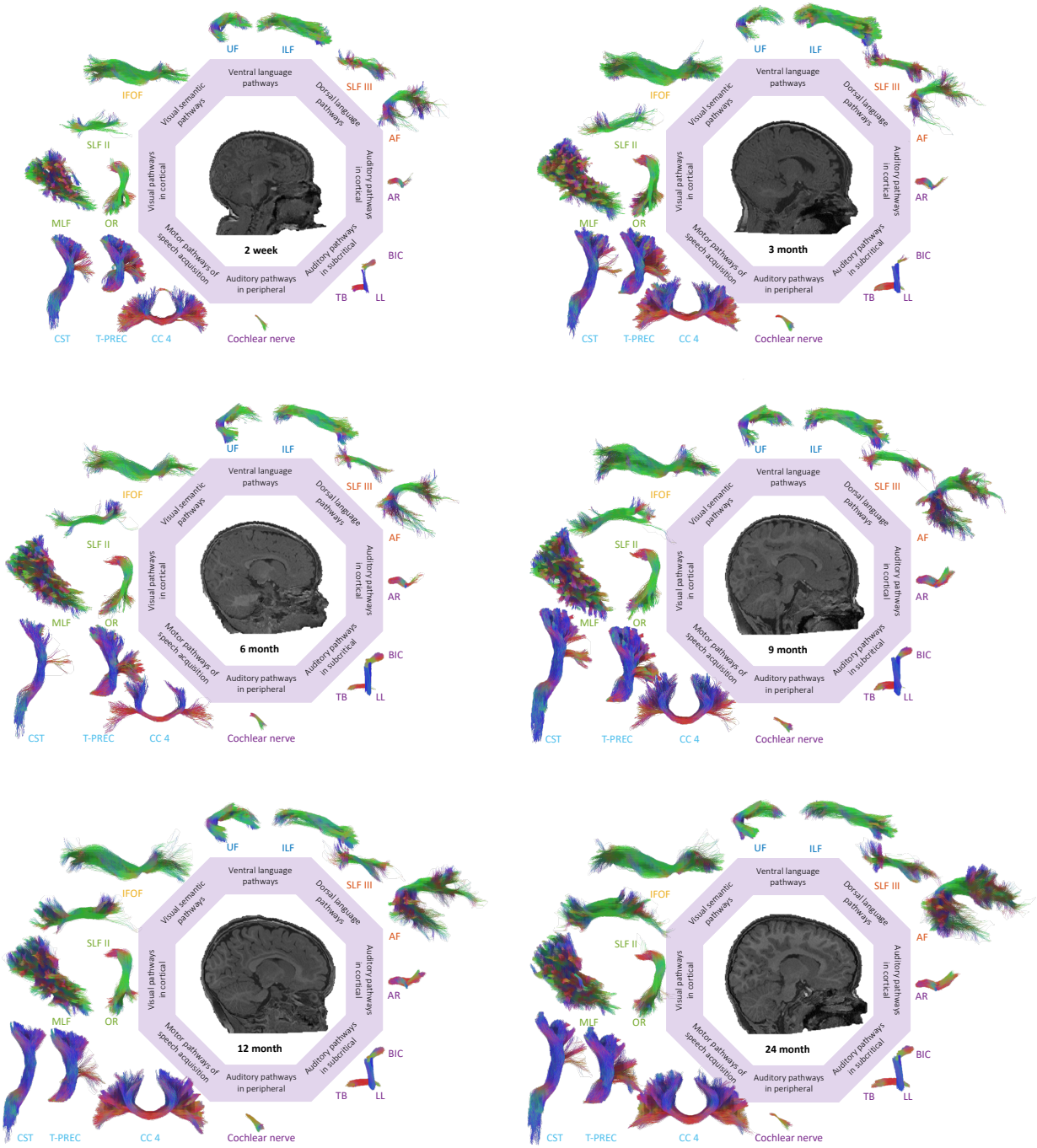

Figure 1: Extracted tracts of speech pathways in left hemisphere[1].

TB: **trapezoid body**; **LL**: **lateral lemniscus**; **BIC**: **brachium of the inferior colliculus**; **AR**: **acoustic radiation**; **AF**: **arcuate fasciculus**; **SLF III**: **superior longitudinal fasciculus III**; **ILF**: **inferior longitudinal fasciculus**; **IFOF**: **inferior fronto-occipital fasciculus**; **UF**: **uncinate fasciculus**; **OR**: **optic radiation**; **SLF II**: **superior longitudinal fasciculus II**; **MLF**: **middle longitudinal fasciculus**; **CST**: **corticospinal tract**; **T-PREC**: **thalamo-precentral**; and **CC_4**: **corpus callosum anterior midbody** (**primary motor**).

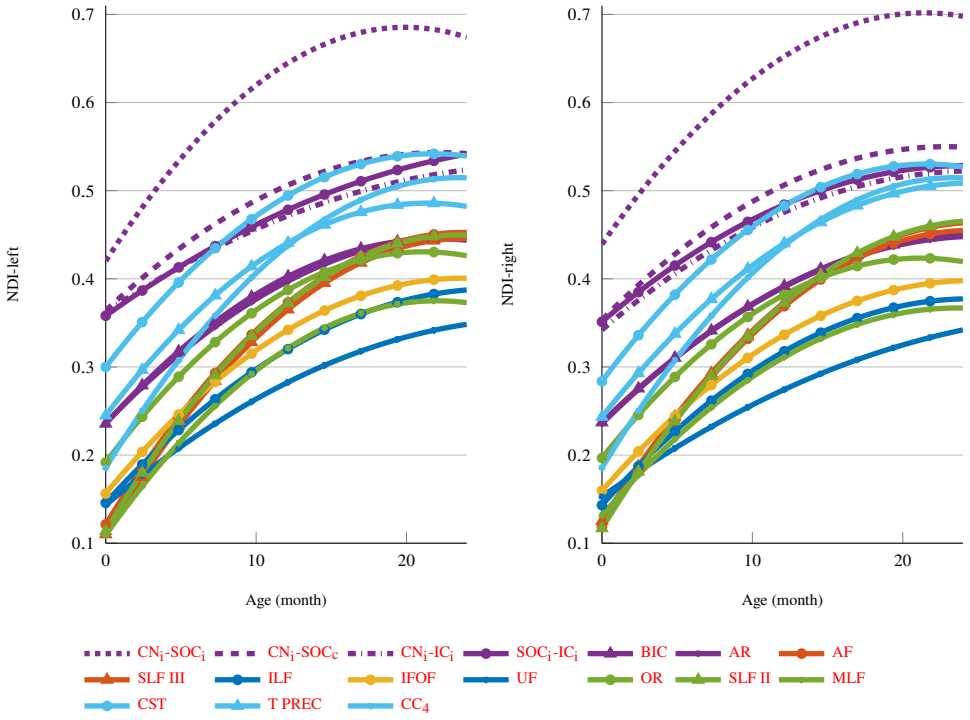

Figure 2: Synaptogenesis characterization with NDI in both hemispheres. (CN: cochlear nucleus; SOC: superior olivary complex; and IC: inferior colliculus)

Table 4: Summary of longitudinal mediation pathways (Social → Motor → Speech)

Predictor (Social)	**Mediator (Motor)**	**Outcome (Speech)**	**Social → Motor**			**Motor → Speech**		
			Estimate	*Std. Error*	p-value	*Estimate*	*Std. Error*	p-value
interpersrelationsubdom Raw	mcg lg total	Expressive Language Raw	0.790	0.355	0.026^{*}	0.401	0.146	0.006^{**}
interpersrelationsubdom Raw	mcg lg total	Expressive Language T	0.790	0.355	0.026^{*}	1.018	0.370	0.006^{**}
interpersrelationsubdom Raw	mcg lg total	mcg vc totpr	0.927	0.331	0.005^{**}	7.597	3.676	0.039^{*}
interpersrelationsubdom Raw	mcg tg total	Expressive Language Raw	0.923	0.448	0.039^{*}	0.318	0.114	0.005^{**}
interpersrelationsubdom Raw	mcg tg total	Expressive Language T	0.923	0.448	0.039^{*}	0.808	0.287	0.005^{**}
interpersrelationsubdom Raw	motorskillsdomain Domain Standard	mcg ph total	1.255	0.536	0.019^{*}	0.073	0.035	0.038^{*}
interpersrelationsubdom v Scale	mcg lg total	Expressive Language Raw	1.199	0.583	0.040^{*}	0.375	0.147	0.011^{*}
interpersrelationsubdom v Scale	mcg lg total	Expressive Language T	1.199	0.583	0.040^{*}	0.959	0.371	0.010^{*}
interpersrelationsubdom v Scale	mcg lg total	mcg vc totpr	1.356	0.522	0.009^{**}	7.209	3.602	0.045^{*}
interpersrelationsubdom v Scale	motorskillsdomain Domain Standard	mcg ph total	1.808	0.902	0.045^{*}	0.077	0.035	0.025^{*}
playleisuretimesubdom Raw	finesubdomain v Scale	Receptive Language Raw	0.483	0.156	0.002^{**}	0.646	0.309	0.037^{*}
playleisuretimesubdom Raw	finesubdomain v Scale	Receptive Language T	0.483	0.156	0.002^{**}	1.799	0.903	0.046^{*}
playleisuretimesubdom Raw	motorskillsdomain Domain Standard	Receptive Language Raw	1.925	0.961	0.045^{*}	0.121	0.050	0.015^{*}
playleisuretimesubdom Raw	motorskillsdomain Domain Standard	Receptive Language T	1.925	0.961	0.045^{*}	0.337	0.145	0.020^{*}
playleisuretimesubdom v Scale	Fine Motor T	Expressive Language Raw	1.043	0.485	0.031^{*}	−0.263	0.130	0.043^{*}
playleisuretimesubdom v Scale	Fine Motor T	Expressive Language T	1.043	0.485	0.031^{*}	−0.709	0.327	0.030^{*}
playleisuretimesubdom v Scale	finesubdomain v Scale	Receptive Language Raw	0.379	0.124	0.002^{**}	0.620	0.308	0.044^{*}
playleisuretimesubdom v Scale	motorskillsdomain Domain Standard	Receptive Language Raw	1.564	0.764	0.041^{*}	0.118	0.050	0.017^{*}
playleisuretimesubdom v Scale	motorskillsdomain Domain Standard	Receptive Language T	1.564	0.764	0.041^{*}	0.328	0.145	0.024^{*}
socializationdomain Domain Standard	Fine Motor T	Expressive Language T	0.282	0.127	0.026^{*}	−0.710	0.332	0.032^{*}
socializationdomain Domain Standard	motorskillsdomain Domain Standard	Receptive Language Raw	0.359	0.182	0.048^{*}	0.113	0.049	0.022^{*}
socializationdomain Domain Standard	motorskillsdomain Domain Standard	Receptive Language T	0.359	0.182	0.048^{*}	0.311	0.144	0.032^{*}
socializationdomain v Scale	Fine Motor T	Expressive Language T	0.832	0.373	0.026^{*}	−0.707	0.332	0.033^{*}
socializationdomain v Scale	motorskillsdomain Domain Standard	Receptive Language Raw	1.103	0.538	0.040^{*}	0.114	0.049	0.022^{*}
socializationdomain v Scale	motorskillsdomain Domain Standard	Receptive Language T	1.103	0.538	0.040^{*}	0.312	0.145	0.031^{*}

Note: Significance levels indicated by: $^{*}p < 0.05$, $^{**}p < 0.01$. Predictor, mediator, and outcome variables are assessed approximately at 6, 12, and 24 months respectively.

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Author contributions: F.L. designed the research, wrote the code, and drafted the manuscript. F.L., J.L., and J.G. collected and processed the dataset. F.L. and X.C. provided statistical analysis and interpretation of the data. F.L., Y.W., Z.W., and H.W. made contributions in the areas of anatomical delineation and data analysis. F.L., J.F., H.Z., and D.S. coordinated and supervised the whole work. All authors were involved in critical revisions of the manuscript, and have read and approved the final version.

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Data and materials availability: Baby Connectome Project (BCP) are publicly available (*53*), on URL https://www.humanconnectome.org/study/lifespan-baby-connectome-project.

Supplementary materials

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0_summary_matched_t_b_item_number.csv

1_significant_relationships_t_b_ordered_by_behavior.csv

1_significant_relationships_t_b_ordered_by_tract.csv

2_combined_results_with_fdr_and_mediation.csv

3_mediation_results_m_s_l.xlsx

3_mediation_results_s_m_l.xlsx

Supplementary Materials for

Diffusion Neuroimaging of Speech Acquisition in Infants

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Materials and Methods

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Supplementary files:

The following supplementary files provide detailed tract-level and behavior-level statistical results:

`0_summary_matched_t_b_item_number.csv` — *Summary of the number of matched tract–behavior item pairs across* 11 *assessments*

`1_significant_relationships_t_b_ordered_by_behavior.csv` — *Significant tract–behavior associations, sorted by behavioral variable names*

`1_significant_relationships_t_b_ordered_by_tract.csv` — *Same as above, sorted by tract variable names*

`2_combined_results_with_fdr_and_mediation.csv` — *Comprehensive cross-sectional mediation results across all* 19 *pathway models*

`3_mediation_results_m_s_l.xlsx` — *Longitudinal mediation results for the motor → social → speech pathway*

`3_mediation_results_s_m_l.xlsx` — *Longitudinal mediation results for the social → motor → speech pathway*

Materials and Methods

Data acquisition and participates

We utilized the Baby Connectome Project (BCP) dataset, which currently represents the largest high-quality, longitudinal infant neuroimaging dataset available, accompanied by extensive behavioral assessments (*53*). After performing quality control (QC) procedures as previously described in (*54*), we retained a total of 246 data samples from 164 infants for analysis. The distribution of samples by age (in months) is detailed in Table,1.

For the primary statistical analyses, we focused on 5 behavioral assessments that provided the highest number of matched tract–behavior pairs, as detailed in Section Statistical Analysis and Behavioral assessments and categorization. Behavioral scores were included only if obtained within a one-month interval of the corresponding dMRI scan. Fig. S1 illustrates the distribution of matched subjects for the MacArthur-Bates Communicative Development Inventories (CDI) – Words and Gestures (W & G), comprising 90 data samples from 74 infants (37 females and 37 males). A small subset of infants older than 24 months was included to fully utilize the available longitudinal follow-up data.

Detailed descriptions of BCP data acquisition protocols are provided in (*53*). Briefly, both T1-weighted (T1w) and diffusion MRI (dMRI) data were acquired using a 3T Siemens Prisma scanner. T1w data were collected using a magnetization-prepared rapid gradient-echo (MPRAGE) sequence with the following parameters: repetition time (TR) = 2400 ms; echo time (TE) = 2.24 ms; flip angle = 8 degrees, matrix size = 320×320, field of view (FOV) = $256 \times 256\,\text{mm}^2$; and isotropic voxel size = $0.8\,\text{mm}^3$. The dMRI data were acquired using a multiband spin-echo echo-planar imaging (EPI) sequence with the following parameters: TR = 2640 ms; TE = 88.6 ms; flip angle = 78 degrees; matrix size = 140×105, FOV = $210 \times 210\,\text{mm}^2$; and isotropic voxel size = $1.5\,\text{mm}^3$. The diffusion acquisition included six diffusion weighting shells (b-values = 500, 1000, 1500, 2000, 2500, and 3000 s/mm^2), comprising 144 diffusion-weighted directions and 6 b_0 volumes. To ensure longitudinal compatibility with data from the HCP Lifespan Pilot Project (*180*), two specific shell (b-values = 1500 and 3000 s/mm^2) were explicitly included. Tractography was performed utilizing both T1w and dMRI data from all subjects, as detailed in Section Data Processing and Tract Extraction.

Data Processing and Tract Extraction

Infant structural MRI (sMRI) and dMRI data were processed using our multimodal MRI processing toolbox (*93*), which integrates well-established neuroimaging toolboxes, including FSL (*181*), ANTs (*182*), and MRtrix3 (*183*). Brain tissue segmentation and region-of-interest (ROI) parcellation were conducted using our recently developed deep-learning–based algorithms, specifically optimized to ensure longitudinal consistency across infant imaging data (*92, 91, 94*). These processing outputs subsequently facilitated accurate co-registration of sMRI and dMRI data (*184*), estimation of fiber orientation distribution functions (fODFs) (*185*), and tractography (*186*).

Building upon our recently introduced tract extraction toolbox — NeoAudi Tract (NAT) (*54*) — originally designed for individualized extraction of auditory tracts from infant dMRI data, we extended its capability to systematically extract white matter tracts across multiple brain systems. These included the **motor**, **auditory**, **visual**, **ventral** language, and **dorsal** language pathways. The extracted tracts allowed comprehensive characterization of developmental trajectories, reflecting underlying synaptogenesis and myelination processes.

To achieve systematic extraction of white matter tracts across **motor**, **visual**, **ventral** language, and **dorsal** language pathways, we constructed a tract atlas from a subset of 105 well-annotated adult subjects from the high-quality Human Connectome Project (HCP) dataset (*95, 187*). Following procedures previously validated for auditory tract extraction across peripheral, subcortical, and cortical regions (*54*), we first generated a coarse atlas of speech-related tracts by averaging anatomically aligned adult tracts (*188*). This initial atlas was iteratively refined through repeated tract extraction and realignment, progressively producing a high-resolution adult reference tract atlas. The refined atlas was subsequently warped to individual infant dMRI data using NAT's dual-branch registration framework, specifically designed to ensure accurate alignment across both cortical and subcortical regions.

Statistical Analysis

After tract extraction, we averaged microstructural attributes within each tract and modeled their developmental trajectories using linear mixed-effects models (LMMs) (*109*). To determine the best-fitting model for developmental trajectories of the neurite density index (NDI), we compared

linear, logarithmic, and quadratic models, as commonly used in developmental neuroimaging investigations (*189, 190, 50*). All three models demonstrated statistically significant fits across tracts (all p-values < 0.001), as summarized in Tables S2, S3, and S4. However, the quadratic model consistently provided superior fits, yielding higher r^2 values and lower Akaike Information Criterion (AIC) scores compared to the other models. Additionally, the logarithmic model occasionally predicted negative values at birth, which are physiologically implausible given that NDI value range between 0 and 1. Therefore, we adopted the quadratic model to fit NDI trajectories across infancy.

To examine associations between tracts and behaviors, and identify potential mediators, we implemented a three-stage analysis pipeline: *1*) tract–behavior correlation analysis, *2*) cross-sectional mediation analysis, and *3*) longitudinal mediation analysis. In stage *1*) and *2*), we applied LMMs (*109*), incorporating quadratic age effects when tract variables were included. For stage *3*, we used standard linear models, consistent with longitudinal mediation analysis methods (*127*). Subjects with missing data for variables of interest were excluded in stages *1*) and *3*). In contrast, in stage *2*), we adopted a more flexible missing data strategy: individuals missing at most one of the three variables (predictor (X), mediator (M), or outcome (Y)) were retained, with missing values imputed using the `mice` package in `R`, generating 100 imputed datasets. Model parameters were estimated separately for each dataset and subsequently pooled using Rubin's rules (*191*), accounting for both within- and between-imputation variability. Pooled p-values were derived from t-statistics calculated using the combined standard errors and degrees of freedom from Rubin's combination formula.

In both cross-sectional and longitudinal mediation analyses (stages *2* and *3*), we employed piecewise structural equation modeling using `psem` package in `R` (*192*). Each mediation model consisted of two linear (mixed-effects) submodels: one predicting M from the X, and the other predicting Y from both X and M. For cross-sectional mediation analysis (stage *2*), both submodels were formulated as LMMs, included age and sex as fixed-effect covariates and subject identity as a random intercept to account for repeated measures. When tract variables were included as predictors (X), we additionally incorporated a quadratic term (X^2) to model nonlinear age effects.

For longitudinal mediation analysis (stage *3*), we employed a two-step linear modeling framework to estimate indirect pathways between early predictors and mediators to later outcomes.

Specifically, we first modeled M (measured at the 12-14 month window) as a function of X (measured at 4-6 month window), controlling for age of both time points. Subsequently, we modeled Y (measured at the 24–26 month window) as a function of both earlier X and M, again controlling for age at each time point. These two models were jointly analyzed using `psem` to estimate standardized path coefficients and mediation effects. This approach preserved the longitudinal data structure while adjusting for age effects at each measurement window, approximating a temporally ordered mediation framework within the constraints of real-world data collection.

Behavioral assessments and categorization

We employed 11 behavioral assessments from the BCP dataset, which were categorized into two groups — *Primary* and *Supplementary* — as detailed in Table S5. The *Primary* group comprised 5 assessments consistently used across all analytical stages: *1*) tract–behavior correlation analysis, *2*) cross-sectional mediation analysis, and *3*) longitudinal mediation analysis. Each primary assessment provided over 70 samples with valid matches to tract data. In contrast, the *Supplementary* group included 6 additional assessments used exclusively for tract–behavior correlation analyses due to limited matched sample sizes. The number of matched tract–behavior item pairs per assessment is provided in the supplementary file *0_summary_matched_t_b_item_number.csv*. Matching was performed using a consistent criterion: only behavioral scores collected within a one-month window of the corresponding dMRI scan were retained for analysis. Statistical significance (p-values < 0.05) was determined after adjusting for multiple comparisons across 33 tracts using the Benjamini-Hochberg false discovery rate (FDR) correction procedure (*193*). The significant results following correction are provided in supplementary files `1_significant_relationships_t_b_ordered_by_behavior.csv` and `1_significant_relationships_t_b_ordered_by_tract.csv`, differing only in their ordering based on *tract* or *behavior* variables.

In stage *(2)*, we formulated 19 theoretical hypotheses, each corresponding to a unique pathway model, as presented in Table S6. Each model followed a three-variable structure — Predictor (X) $\rightarrow$ Mediator (M) $\rightarrow$ Outcome (Y) — with variables selected from behavioral assessments categorized into seven functional domains. A complete list of variables under each domain is provided in Tables S7, S8, S9, S10, S11, S12, and S13. Across these 19 pathway models, a total of 74, 276 valid $X \rightarrow M \rightarrow Y$ combinations were identified. After applying FDR correction across all 74, 276

combinations, we identified 849 statistically significant mediation pathways, defined as those with both $X \rightarrow M$ and $M \rightarrow Y$ yielded FDR-adjusted p-values < 0.05. These results are detailed in the supplementary file `2_combined_results_with_fdr_and_mediation.csv`.

The number of significant mediation pathways for each model, reported in Table S6, can be categorized into two primary groups: *(1)* models with tract variables as predictors, and *(2)* models with behavioral variables (e.g., social or motor skills) as predictors. In the first group, motor variables consistently emerged as the most effective mediators, yielding the highest number of significant results. Conversely, pathways involving emotional regulation or social interaction as mediators rarely yielded significant outcomes. In the second group, we focused on behavioral predictors — mainly social and motor factors — and their mediated effects on language outcomes through other developmental domains. Given that variables related to living skill exhibited limited correlations with tract-level measures in the first group, our results suggest neural substrates preferentially support motor skill development, which subsequently facilitates broader developmental domains, including speech acquisition. visual–cognitive variables also served as effective mediators, possibly reflecting early perceptual processes such as observing articulator movements during caregiver–infant interactions, rather than later-developing literacy skills (*e.g.*, reading or writing). Settings for stage (*3*) are detailed in Section Mediation pathway analysis.

Mediation pathway analysis

Given our observations suggesting that social interactions may reciprocally facilitate motor skill development, we further explored their relationship to clarify the development sequence linking tract maturation, motor, and social development. To this end, we conducted a longitudinal mediation analysis examining two alternative developmental pathways: *1*) a *motor* → *social* → *speech* model, and *ii*) a *social* → *motor* → *speech* model.

Specifically, in the first pathway (*motor* → *social* → *speech*), motor skill measured during the 4-6 month window was used to predict social interaction performance at 12-14 months, which in turn predicted speech outcomes at 24–26 months. In the second pathway (*social* → *motor* → *speech*), early social interactions at 4–6 months predicted subsequent motor skill development at 12–14 months, which then influenced speech outcomes at 24–26 months. Due to the targeted analysis involving a limited number of theoretically predefined mediation paths,

we did not apply the Benjamini-Hochberg false discovery rate (FDR) correction (*193*) at this stage. Instead, uncorrected p-values were reported to individually assess the significance of each mediation pathway. Detailed results from these analyses are provided in supplementary files `3_mediation_results_m_s_l.xlsx` (motor → social → speech) and `3_mediation_results_s_m_l.xlsx` (social → motor → speech).

Supplementary Text

Additional Results

As part of our preliminary analyses, we also evaluated standard diffusion tensor imaging (DTI)-derived metrics — namely, radial diffusivity (RD), mean diffusivity (MD), and fractional anisotropy (FA) — to investigate their potential associations with early language development. These metrics were examined alongside neurite density index (NDI) to ensure a comprehensive characterization of tract microstructure. However, RD values of white matter tracts showed no significant correlation with MacArthur–Bates Communicative Development Inventories (CDI) – Words and Gestures (W & G) scores. This lack of correlation likely arises from intrinsic limitations of the DTI model, which inadequately resolves crossing fibers, introducing bias particularly into FA and RD metrics.

Notably, as depicted by FA trajectories in Fig. S7 (Fig. S9 for detailed illustrations), auditory brainstem tracts (*e.g.*, **CN–IC** and **SOC–IC**) appeared less mature than the acoustic radiation (**AR**), a result inconsistent with established neuroanatomical and histological evidence (*69*). Similarly, MD trajectories as shown in Fig. S6 (Fig. S8 for detailed illustrations), closely mirrored the FA trajectories (Fig. S7); while RD trajectories demonstrate better maturation of **BIC** than **AR**, as shown in Fig. S4 (Fig. S5 for detailed illustrations). These inconsistencies further underscore the limitations inherent to traditional DTI-based metrics in the context of infant tract development. Given these methodological constraints, we primarily employed NDI, which offers a more robust and biologically interpretable characterization of tract maturation relevant to early speech acquisition.

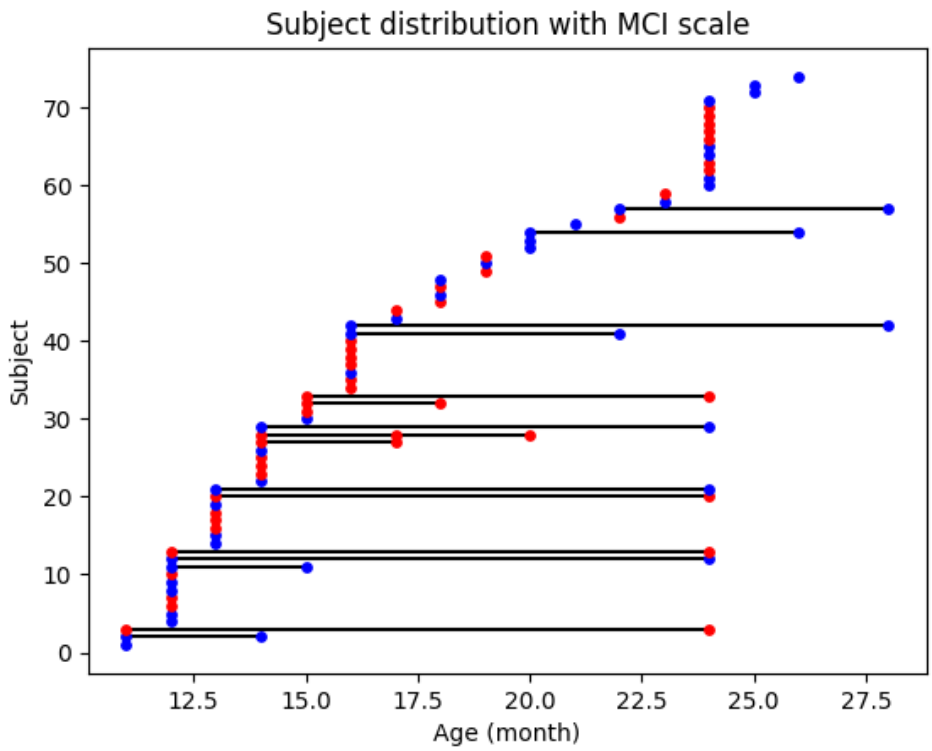

Figure S1: The paired CDI - W & G sores and longitudinal scans of participants with different ages. For each male subject, each scan is demonstrated as a blue point, while red point denotes female infants. The scans from the same subjects are connected by a horizontal black line.

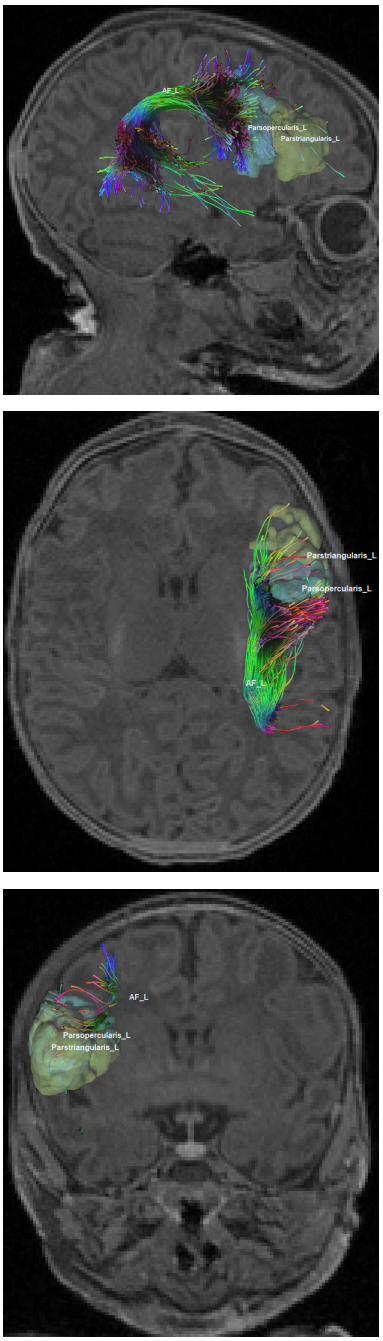

Figure S2: The extracted **AF** in the left hemisphere of a neonate reaches BA 44 (Parsopercularis_L, denoted by light blue) and BA 45 (Parstriangularis_L denoted by light green).

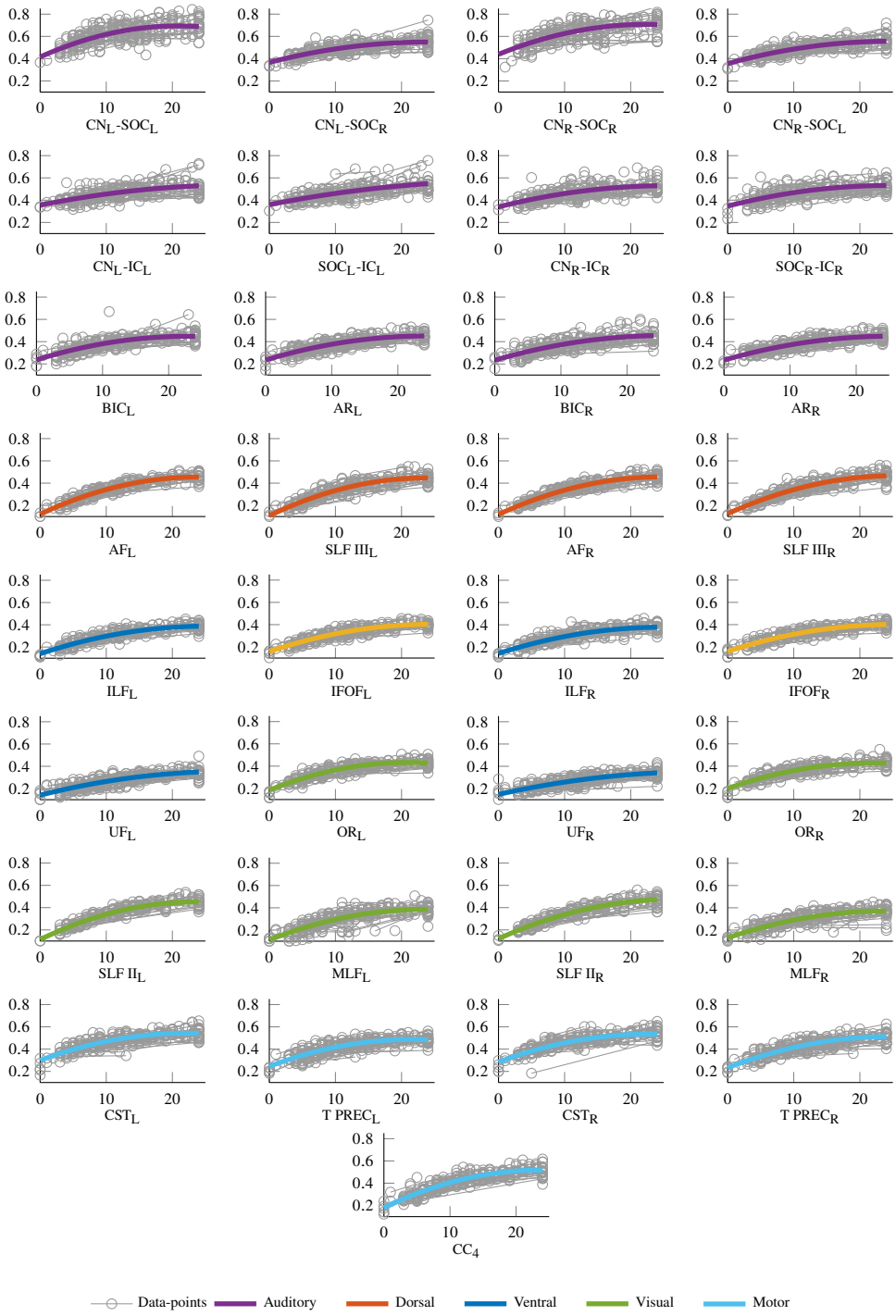

Figure S3: NDI dots of both hemispheres.

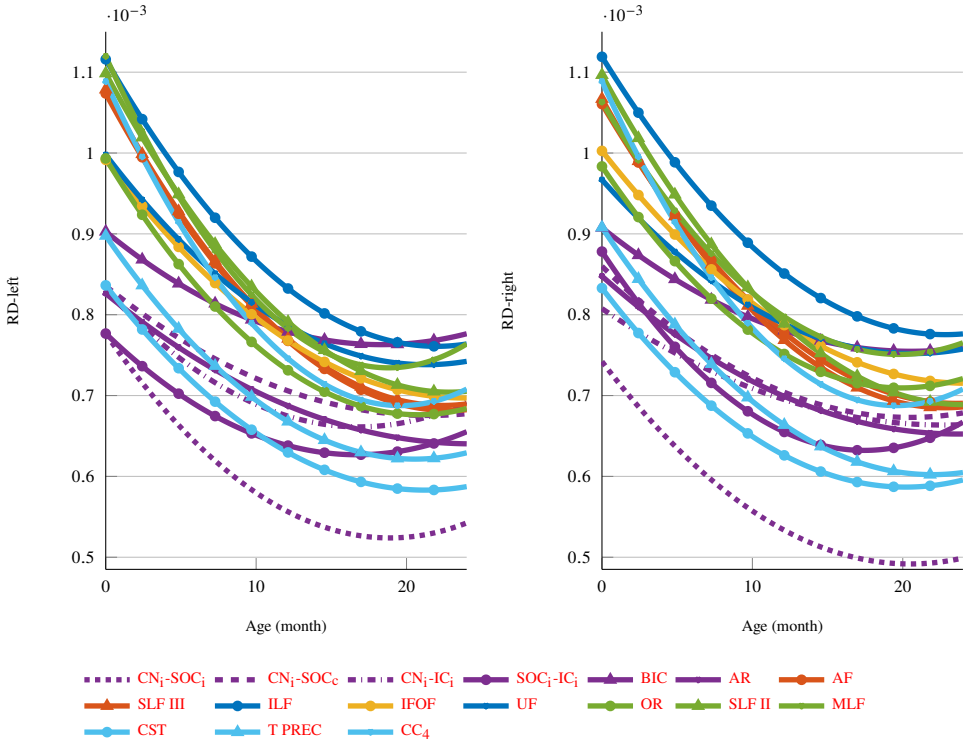

Figure S4: White matter microstructural characterization with RD in both hemispheres.

Table S1: Summary of infant dMRI data samples employed.

Age	**2 wk**	**1 mo**	**2 mo**	**3 mo**	**4 mo**	**5 mo**	**6 mo**	**7 mo**	**8 mo**	**9 mo**	**10 mo**	**11 mo**	**12 mo**
Sample size (N)	5	2	1	9	9	17	14	10	14	17	7	13	17
Age		**13 mo**	**14 mo**	**15 mo**	**16 mo**	**17 mo**	**18 mo**	**19 mo**	**20 mo**	**21 mo**	**22 mo**	**23 mo**	**24 mo**
Sample size (N)		10	10	15	10	5	8	7	6	5	5	6	24

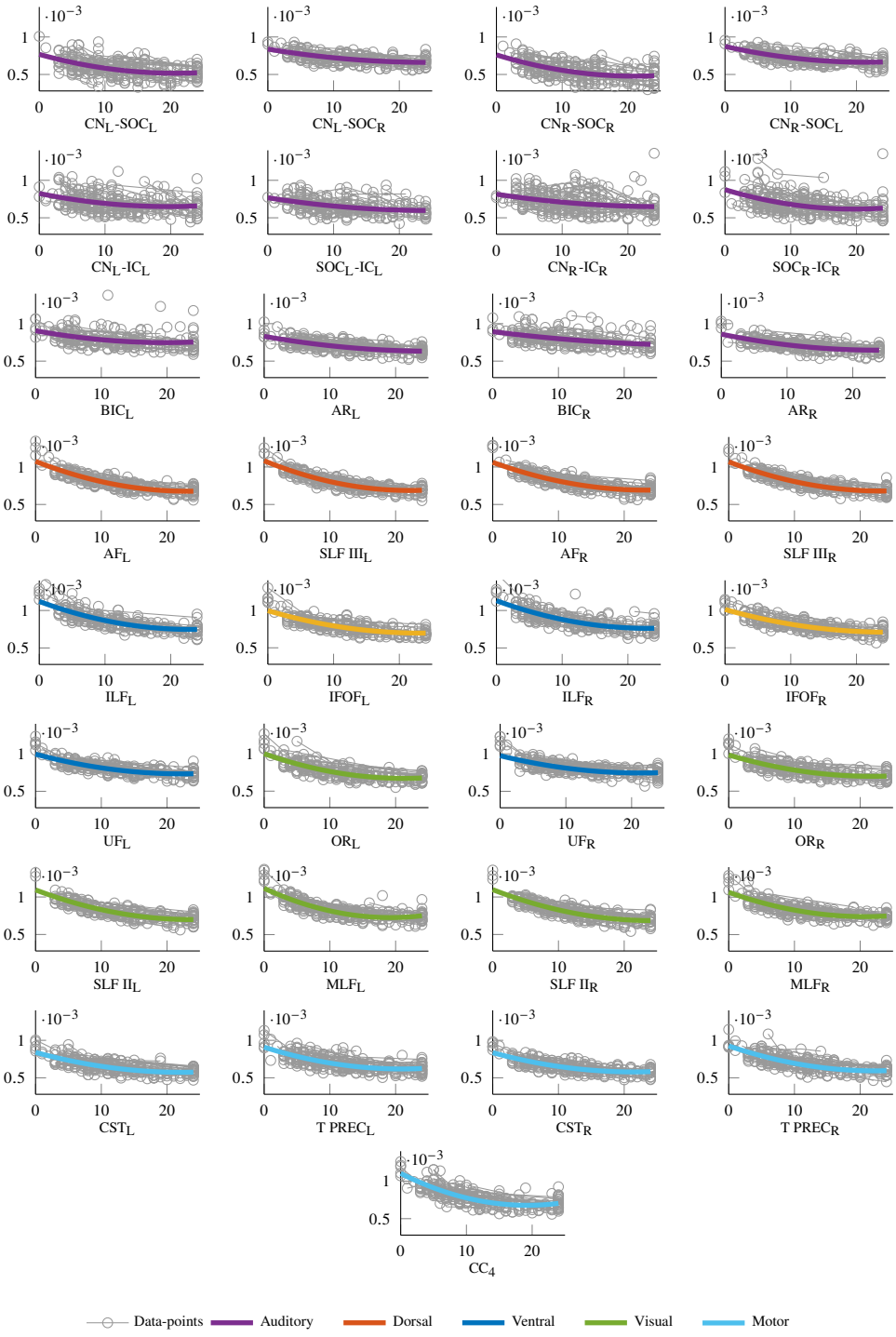

Figure S5: RD dots of both hemispheres.

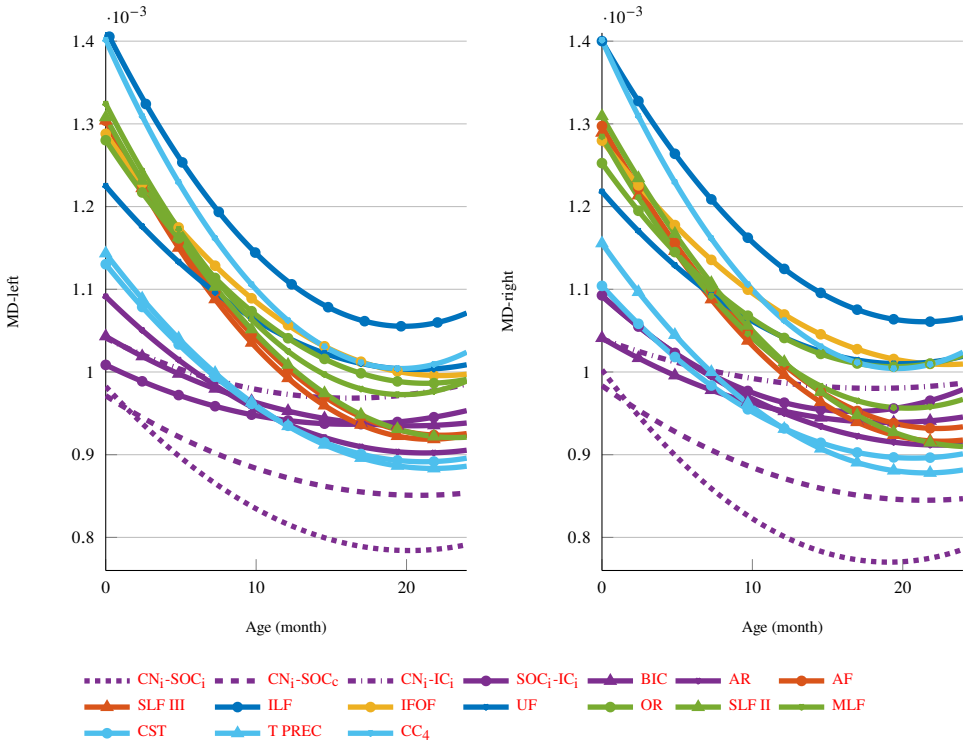

Figure S6: White matter microstructural characterization with MD.

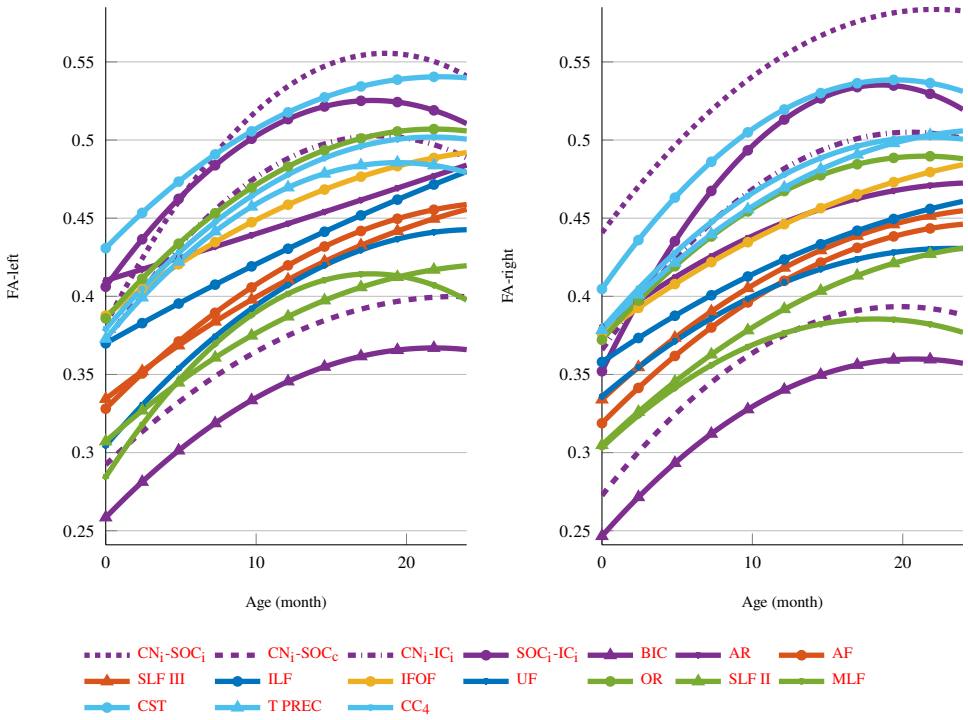

Figure S7: White matter microstructural characterization with FA.

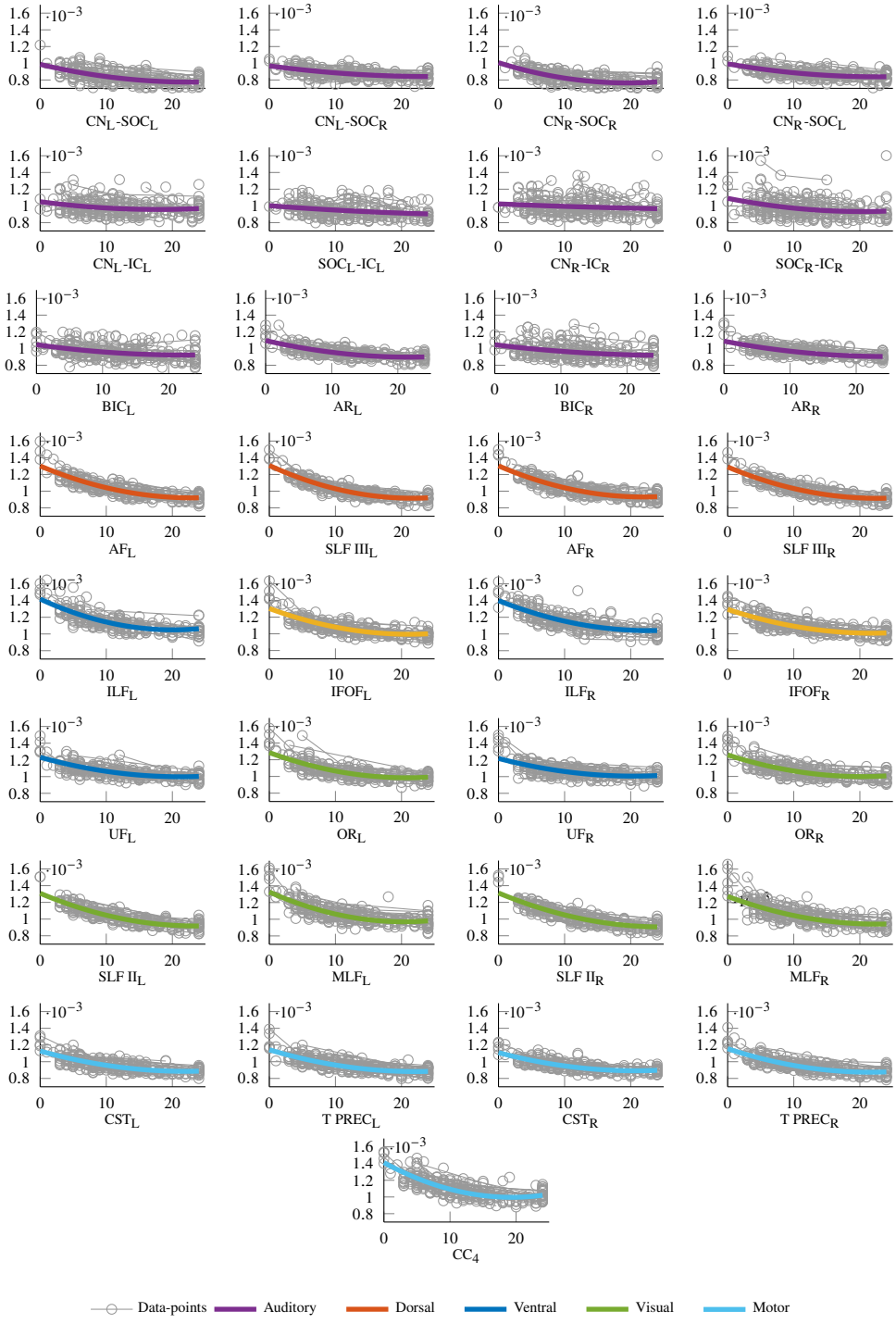

Figure S8: MD dots of both hemispheres.

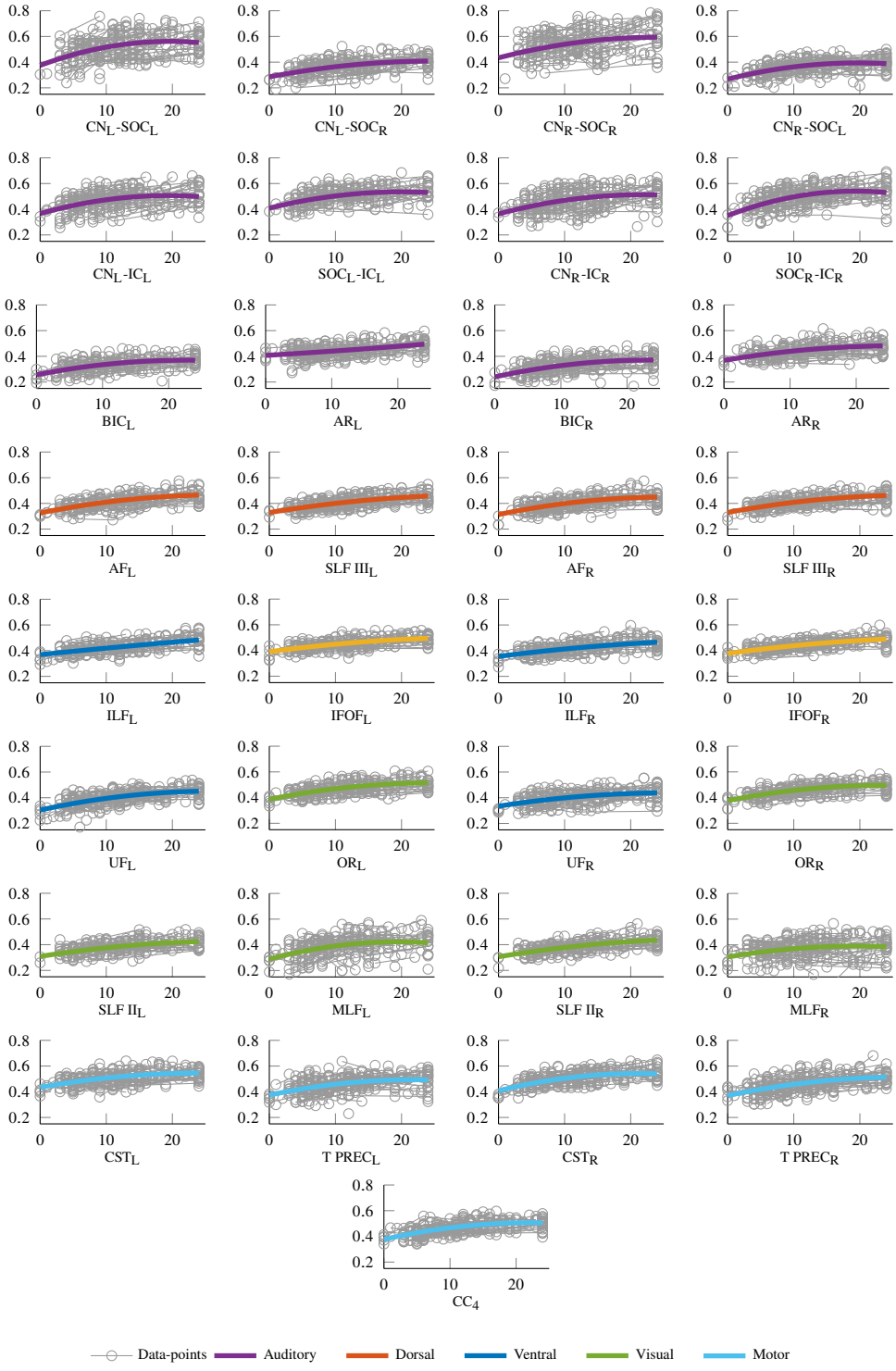

Figure S9: FA dots of both hemispheres.

Table S2: Comparison of linear, logarithmic, and quadratic models in LMMs based on adjusted r-squared and AIC performance among for auditory tracts.

Tract name		CN_L-SOC_L	CN_L-SOC_R	CN_R-SOC_R	CN_R-SOC_L	CN_L-IC_L	SOC_L-IC_L	CN_R-IC_R	SOC_R-IC_R	BIC_L	AR_L	BIC_R	AR_R
Linear	p	4.79e-26	1.89e-35	1.70e-26	3.05e-41	1.47e-27	1.69e-33	1.44e-33	6.43e-28	3.71e-41	6.47e-56	2.03e-41	1.48e-60
	$r^2 \uparrow$	0.7140	0.8796	0.8074	0.8909	0.8818	0.7923	0.7408	0.7946	0.9068	0.8892	0.9011	0.8476
	AIC $\downarrow$	-514.23	-816.07	-519.94	-836.21	**-716.33**	**-718.99**	-694.47	-694.17	-770.46	-874.04	-747.59	-871.90
Logarithm	$p \downarrow$	5.04e-36	3.79e-46	8.38e-39	2.30e-53	2.21e-27	3.49e-31	4.74e-31	1.37e-36	3.23e-43	1.83e-56	4.35e-39	2.93e-55
	$r^2 \uparrow$	0.7812	0.8794	0.8318	0.8580	0.8395	0.7609	**0.7758**	0.7900	0.9072	0.9113	**0.9141**	0.8895
	AIC $\downarrow$	**-555.17**	**-847.69**	**-561.43**	**-857.30**	-707.14	-712.44	**-703.52**	**-722.32**	**-795.78**	**-906.62**	**-764.61**	**-896.21**
Quadratic	p	6.90e-17	2.00e-19	3.39e-12	3.65e-24	1.64e-09	6.97e-08	3.17e-12	9.87e-11	2.90e-25	3.28e-26	1.43e-16	7.84e-26
	$r^2 \uparrow$	**0.8211**	**0.9319**	**0.8747**	**0.9032**	**0.9013**	**0.8110**	0.7675	**0.8038**	**0.9410**	**0.9254**	0.9055	**0.8950**
	AIC $\downarrow$	-524.66	-820.68	-528.20	-838.97	-704.00	-698.70	-683.24	-690.49	-793.89	-900.76	-750.89	-890.55

AIC=akaike information criterion; L=left; R=right; **CN=cochlear nucleus**; **SOC=superior olivary complex**; **IC=inferior colliculus**; **BIC=brachium of the inferior colliculus**; **AR=acoustic radiation**.

Table S3: Comparison of linear, logarithmic, and quadratic models in LMMs based on adjusted r-squared and AIC performance for major tracts in left hemisphere.

Tract name		AF	SLF III	ILF	IFOF	UF	OR	SLF II	MLF	CST	T PREC	CC 4
Linear	p	8.38e-81	2.25e-72	7.59e-63	1.11e-71	1.75e-57	1.47e-49	3.70e-78	6.63e-51	8.66e-46	4.49e-46	2.85e-66
	$r^2 \uparrow$	0.9515	0.9426	0.9469	0.9530	0.9549	0.9256	0.9669	0.8200	0.9125	0.7691	0.9193
	AIC $\downarrow$	-832.38	-751.84	-867.01	-909.85	-896.60	-834.53	-810.49	-652.56	-776.55	-771.07	-735.43
Logarithm	p	1.90e-90	3.62e-77	2.67e-67	2.21e-75	4.83e-48	3.56e-76	1.42e-100	6.21e-43	1.34e-68	2.58e-55	2.21e-67
	$r^2 \uparrow$	0.9807	0.9747	**0.9561**	**0.9708**	0.9443	0.9565	0.9932	0.8935	0.9236	0.8223	**0.9635**
	AIC $\downarrow$	-936.45	-818.96	**-908.26**	-963.81	-880.99	**-949.98**	-943.79	-672.10	**-850.82**	**-828.91**	-797.66
Quadratic	p	1.10e-71	2.80e-53	7.62e-42	1.48e-47	3.18e-20	1.12e-52	3.65e-71	1.36e-22	1.32e-27	7.00e-32	2.05e-45
	$r^2 \uparrow$	**0.9809**	**0.9837**	0.9233	0.9647	**0.9797**	**0.9628**	**0.9959**	**0.9027**	**0.9379**	**0.8250**	0.9534
	AIC $\downarrow$	**-961.34**	**-833.29**	-904.68	**-979.13**	**-907.79**	-937.37	**-966.21**	**-673.90**	-819.47	-816.58	**-807.99**

AIC=akaike information criterion; **AF**: **arcuate fasciculus**; **SLF III**: **superior longitudinal fasciculus III**; **ILF**: **inferior longitudinal fasciculus**; **IFOF**: **inferior fronto-occipital fasciculus**; **UF**: **uncinate fasciculus**; **OR**: **optic radiation**; **SLF II**: **superior longitudinal fasciculus II**; **MLF**: **middle longitudinal fasciculus**; **CST**: **corticospinal tract**; **T PREC**: **thalamo-precentral**; and **CC 4**: **corpus callosum anterior midbody** (**primary motor**).

Table S4: Comparison of linear, logarithmic, and quadratic models in LMMs based on adjusted r-squared and AIC performance for major tracts in right hemisphere.

Tract name		AF	SLF III	ILF	IFOF	UF	OR	SLF II	MLF	CST	T PREC	CC 4
Linear	p	1.15e-86	1.87e-85	2.48e-63	1.17e-68	6.98e-53	3.54e-50	1.40e-88	1.26e-49	1.15e-86	1.70e-62	2.85e-66
	$r^2 \uparrow$	0.9494	0.9386	0.9208	0.9354	0.9410	0.9688	0.9766	0.9211	0.9279	0.8413	0.9193
	AIC $\downarrow$	-873.23	-827.82	-843.14	-918.38	-912.78	-839.25	-865.23	-793.70	-776.44	-774.12	-735.43
Logarithm	p	3.03e-94	9.26e-85	9.14e-63	3.21e-70	2.48e-44	1.56e-77	3.32e-93	2.53e-51	3.03e-94	1.78e-59	2.21e-67
	$r^2 \uparrow$	0.9769	**0.9694**	**0.9348**	0.9613	0.9127	0.9584	0.9848	0.9229	0.9197	0.9256	**0.9635**
	AIC $\downarrow$	-963.30	-882.94	-869.48	-962.88	-888.58	**-923.97**	-924.86	**-820.15**	**-837.81**	-811.35	-797.66
Quadratic	p	2.27e-66	4.00e-52	3.82e-40	1.94e-40	4.15e-15	5.15e-37	8.98e-60	4.04e-31	2.27e-66	3.70e-27	2.05e-45
	$r^2 \uparrow$	**0.9774**	0.9686	0.9207	**0.9726**	**0.9812**	**0.9751**	**0.9878**	**0.9580**	**0.9543**	**0.9462**	0.9534
	AIC $\downarrow$	**-981.34**	**-899.23**	**-877.80**	**-968.36**	**-916.90**	-897.93	**-946.34**	-818.08	-822.88	**-816.36**	**-807.99**

AIC=akaike information criterion; **AF**: **arcuate fasciculus**; **SLF III**: **superior longitudinal fasciculus III**; **ILF**: **inferior longitudinal fasciculus**; **IFOF**: **inferior fronto-occipital fasciculus**; **UF**: **uncinate fasciculus**; **OR**: **optic radiation**; **SLF II**: **superior longitudinal fasciculus II**; **MLF**: **middle longitudinal fasciculus**; **CST**: **corticospinal tract**; **T PREC**: **thalamo-precentral**; and **CC_4**: **corpus callosum anterior midbody** (**primary motor**).

Table S5: Eleven behavioral assessments used in this study

Assessment	Postfix abbreviation in tables	Usage in Analysis
MacArthur-Bates Communicative Development Inventories – Words and Gestures Form (*194*)	_mci_wg	Primary in all analyses
Mullen Scales of Early Learning (*195*)	_mullen	Primary
Vineland Adaptive Behavior Scales (*196*)	_vine	Primary
Infant-Toddler Social and Emotional Assessment (*197*)	_itsea	Primary
Repetitive Behavior Scale–Revised (*198*)	_rbsr	Primary
Child Behavior Checklist (*199*)	_cbcl	Supplementary only in tract - behavior analysis
Dimensional Joint Attention Assessment (*200*)	_djaa	Supplementary
Early Childhood Behavior Questionnaire (*201*)	_ecbq	Supplementary
Infant Behavior Questionnaire (*202*)	_ibq	Supplementary
Minnesota Executive Function Scale (*203*)	_mefs	Supplementary
Rating of Reciprocal Social Behavior (*204*)	_rrsb	Supplementary

Table S6: Summary of pathway models with theoretical hypotheses

ID	Pathways Model	Number of Combinations	Number of Passed Pathways	Purpose and Theoretical Hypothesis
A1	Tract → Motor → Language	6,006	44	Does Tracts support Motor then Language?
A2	Tract → Social → Language	5,148	0	Does Tracts support Social then Language?
A3	Tract → Visual & Cognitive → Language	1,287	7	Does Tracts support Visual then Language?
B1	Tract → Social → Motor	5,544	0	Does Tracts support Social then Language?
B2	Tract → Motor → Social	5,544	42	Does Tracts support Motor then Social?
B3	Tract → Motor → Emotional & Regulatory	7,854	0	Does Tracts support Motor then Emotion?
B4	Tract → Social → Emotional & Regulatory	6,732	0	Does Tracts support Social then Emotion?
B5	Tract → Motor → Living Skills	5,082	24	Does Tracts support Motor then Living skills?
B6	Tract → Social → Living Skills	4,356	0	Does Tracts support Social then Living skills?
C1	Tract → Emotional & Regulatory → Language	7,293	0	Does Tracts support Emotion then Language?
C2	Tract → Living Skills → Language	4,719	1	Does Tracts support Living skills then Language?
D1	Motor → Visual & Cognitive → Language	546	80	Does Motor support Visual then Language?
D2	Social → Visual & Cognitive → Language	468	3	Does Social support Visual then Language?
D3	Motor → Emotional & Regulatory → Language	3,094	4	Does Motor support Emotion then Language?
D4	Social → Emotional & Regulatory → Language	2,652	1	Does Social support Emotion then Language?
D5	Motor → Living Skills → Language	2,002	171	Does Motor support Living skills then Language?
D6	Social → Living Skills → Language	1,716	164	Does Social support Living skills then Language?
E1	Social → Motor → Language	2,184	145	Does Social support Motor then Language?
E2	Motor → Social → Language	2,184	163	Does Motor support Social then Language?
	$74,409$ **Combinations in Total**		849 **out of** $74,276$ **potential pathway using FDR correction**	

Table S7: Group 1: Tract Variables

Variable	Source
avg_AF_l	Tract Extraction (NDI mean)
avg_AF_r	Tract Extraction (NDI mean)
avg_SLF3_l	Tract Extraction (NDI mean)
avg_SLF3_r	Tract Extraction (NDI mean)
avg_ILF_l	Tract Extraction (NDI mean)
avg_ILF_r	Tract Extraction (NDI mean)
avg_IFO_l	Tract Extraction (NDI mean)
avg_IFO_r	Tract Extraction (NDI mean)
avg_UF_l	Tract Extraction (NDI mean)
avg_UF_r	Tract Extraction (NDI mean)
avg_OR_l	Tract Extraction (NDI mean)
avg_OR_r	Tract Extraction (NDI mean)
avg_SLF2_l	Tract Extraction (NDI mean)
avg_SLF2_r	Tract Extraction (NDI mean)
avg_MLF_l	Tract Extraction (NDI mean)
avg_MLF_r	Tract Extraction (NDI mean)
avg_CST_l	Tract Extraction (NDI mean)
avg_CST_r	Tract Extraction (NDI mean)
avg_TPREC_l	Tract Extraction (NDI mean)
avg_TPREC_r	Tract Extraction (NDI mean)
avg_CC_4	Tract Extraction (NDI mean)
avg_roi1toroi4	Tract Extraction (NDI mean)
avg_roi2toroi3	Tract Extraction (NDI mean)
avg_roi1toroi5	Tract Extraction (NDI mean)
avg_roi2toroi6	Tract Extraction (NDI mean)
avg_roi5toroi7	Tract Extraction (NDI mean)
avg_roi6toroi8	Tract Extraction (NDI mean)
avg_roi7topacl	Tract Extraction (NDI mean)
avg_roi8topacr	Tract Extraction (NDI mean)
avg_roi1toroi3	Tract Extraction (NDI mean)
avg_roi2toroi4	Tract Extraction (NDI mean)
avg_roi3toroi5	Tract Extraction (NDI mean)
avg_roi4toroi6	Tract Extraction (NDI mean)

Table S8: Group 2: Language Variables

Variable	Source
mcg ph total mci wg	MacArthur-Bates CDI - W & G
mcg vc totcom mci wg	MacArthur-Bates CDI - W & G
mcg vc totpr mci wg	MacArthur-Bates CDI - W & G
Receptive Language T Score	Mullen Scales of Early Learning
Expressive Language T Score	Mullen Scales of Early Learning
Receptive Language Raw Score	Mullen Scales of Early Learning
Expressive Language Raw Score	Mullen Scales of Early Learning
receptive subdomain Raw Score	Vineland Adaptive Behavior Scales
expressive subdomain Raw Score	Vineland Adaptive Behavior Scales
receptive subdomain v Scale Score	Vineland Adaptive Behavior Scales
expressive subdomain v Scale Score	Vineland Adaptive Behavior Scales
communication domain Domain Standard Score	Vineland Adaptive Behavior Scales
communication domain v Scale Score	Vineland Adaptive Behavior Scales

Table S9: Group 3: Social Variables

Variable	Source
interpersrelationsubdom v Scale Score	Vineland Adaptive Behavior Scales
playleisuretimesubdomain v Scale Score	Vineland Adaptive Behavior Scales
interpersrelationsubdom Raw Score	Vineland Adaptive Behavior Scales
playleisuretimesubdomain Raw Score	Vineland Adaptive Behavior Scales
socializationdomain v Scale Score	Vineland Adaptive Behavior Scales
socializationdomain Domain Standard Score	Vineland Adaptive Behavior Scales
Competence domain compliance mean raw score	Infant-Toddler Social and Emotional Assessment
Competence domain imitation play mean raw score	Infant-Toddler Social and Emotional Assessment
Competence domain empathy mean raw score	Infant-Toddler Social and Emotional Assessment
Internalizing domain inhibition to novelty mean raw score	Infant-Toddler Social and Emotional Assessment
Social relatedness item cluster mean raw score	Infant-Toddler Social and Emotional Assessment
Hours spend with other children weekly	Infant-Toddler Social and Emotional Assessment

Table S10: Group 4: Motor Variables

Variable	Source
mcg eg total mci wg	MacArthur-Bates CDI - W & G
mcg lg total mci wg	MacArthur-Bates CDI - W & G
mcg tg total mci wg	MacArthur-Bates CDI - W & G
Gross motor T Score	Mullen Scales of Early Learning
Fine Motor T Score	Mullen Scales of Early Learning
Gross Motor Raw Score	Mullen Scales of Early Learning
Fine Motor Raw Score	Mullen Scales of Early Learning
gross subdomain Raw Score	Vineland Adaptive Behavior Scales
fine subdomain Raw Score	Vineland Adaptive Behavior Scales
gross subdomain v Scale Score	Vineland Adaptive Behavior Scales
fine subdomain v Scale Score	Vineland Adaptive Behavior Scales
motorskills domain v Scale Score	Vineland Adaptive Behavior Scales
motorskills domain Domain Standard Score	Vineland Adaptive Behavior Scales
Repetitive Motor Mean frequency score	Repetitive Behavior Scale-Revised

Table S11: Group 5: Visual & Cognitive Variables

Variable	Source
Visual Reception T Score	Mullen Scales of Early Learning
Visual Reception Raw Score	Mullen Scales of Early Learning
Cognitive T Score Sum	Mullen Scales of Early Learning

Table S12: Group 6: Daily Living Skills Variables

Variable	Source
personal subdomain Raw Score	Vineland Adaptive Behavior Scales
domestic subdomain Raw Score	Vineland Adaptive Behavior Scales
community subdomain Raw Score	Vineland Adaptive Behavior Scales
coping skills subdomain Raw Score	Vineland Adaptive Behavior Scales
personal subdomain v Scale Score	Vineland Adaptive Behavior Scales
domestic subdomain v Scale Score	Vineland Adaptive Behavior Scales
community subdomain v Scale Score	Vineland Adaptive Behavior Scales
coping skills subdomain v Scale Score	Vineland Adaptive Behavior Scales
living skills domain v Scale Score	Vineland Adaptive Behavior Scales
living skills domain Domain Standard Score	Vineland Adaptive Behavior Scales
Sum of Domain Standard Scores	Vineland Adaptive Behavior Scales

Table S13: Group 7: Emotional and Regulatory Behavior Variables

Variable	Source
Total Competence T Score	Infant-Toddler Social and Emotional Assessment
Dysregulation domain sleep mean raw score	Infant-Toddler Social and Emotional Assessment
Dysregulation domain eating mean raw score	Infant-Toddler Social and Emotional Assessment
Competence domain mastery motivation mean raw score	Infant-Toddler Social and Emotional Assessment
Externalizing domain mean raw score	Infant-Toddler Social and Emotional Assessment
Internalizing domain mean raw score	Infant-Toddler Social and Emotional Assessment
Externalizing domain activity impulsivity mean score	Infant-Toddler Social and Emotional Assessment
Internalizing domain depression withdrawal mean score	Infant-Toddler Social and Emotional Assessment
Externalizing domain aggression defiance mean raw score	Infant-Toddler Social and Emotional Assessment
Externalizing domain peer aggression mean raw score	Infant-Toddler Social and Emotional Assessment
Competence domain prosocial peer relations mean raw score	Infant-Toddler Social and Emotional Assessment
Maladaptive item cluster mean raw score	Infant-Toddler Social and Emotional Assessment
Atypical item cluster mean raw score	Infant-Toddler Social and Emotional Assessment
Self Directed Self Injurious Mean frequency score	Repetitive Behavior Scale-Revised
Restricted Behavior Mean frequency score	Repetitive Behavior Scale-Revised
Ritual Routine Behavior Mean frequency score	Repetitive Behavior Scale-Revised
Composite Score Mean frequency score	Repetitive Behavior Scale-Revised