

The role of focused attention in learning from early childhood to late adolescence: Implications of neonatal brainstem compromise following preterm birth

Or Burstein¹  | Maya Sabag^{1,2}  | Lea Kurtzman¹ | Ronny Geva^{1,2} 

¹Department of Psychology, Bar Ilan University, Ramat Gan, Israel

²The Gonda Multidisciplinary Brain Research Center, Bar Ilan University, Ramat Gan, Israel

Correspondence

Ronny Geva, Department of Psychology, Gonda Multidisciplinary Brain Research Center, Bar Ilan University, Ramat Gan 5290002, Israel.
Email: ronny.geva@biu.ac.il

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Abstract

This comprehensive longitudinal study explored for the first time the interrelations between neonatal brainstem abnormalities, focused attention (FA), and learning—following a preterm cohort ($N=175$; 46.3% female; predominantly White) from birth (2003–2006) to 17 years. The findings indicated that FA during early childhood was associated with language outcomes in toddlerhood ($n=131$) and academic and attention self-report indices in late adolescence ($n=44$). Pilot assessments indicated that FA at 17 years ($n=25$) was also associated with concurrent academic and attention functioning. Structural equation modeling analyses revealed that neonatal brainstem functioning, manifested in auditory brainstem response patterns, was associated with early-life FA competence, which affected learning development. Implications underscore the essential role of early brainstem function and FA in shaping childhood learning trajectories.

The ability to effortfully focus attention to explore the environment is a gateway to cognitive development (Gibson, 1988). This ability, termed *focused attention* (FA), signifies a level of engagement that enables goal-driven learning rather than mere orienting to external cues (Ruff & Rothbart, 2001). Importantly, its initial operational phases are already evident in young toddlers (Oakes et al., 2002). However, there are major literature gaps concerning the development of FA, these include: What neurobiological factors scaffold or impede FA development? And what are the long-term interrelations between FA and learning? In this study, we investigated the association between FA and neurocognitive development—from infancy to late adolescence—and placed particular emphasis on the possible involvement of early-evolving brainstem substrates that play a major role in autonomic and sensory regulation. We explored their possible role in the context of prematurity—a factor

known to be related to an increased risk for attention and learning difficulties.

Development of FA

“Are you listening?! Did you hear what I said?,” a parent may ask their child who gazes directly at them but seems phased away. Attention research delves into the question of what it looks like when the child's attention is really channeled for learning and not merely wandering around (Kruschke, 2003; Masek et al., 2021). For instance, a child may look at a given toy or deal with an academic task without being engaged and, therefore, not learn much. We suggest that a prominent missing ingredient is FA.

Holly Ruff (1986) typified FA in early life as a state in which the child is actively exploring. FA is typically first observed at around 6 months and becomes more prevalent

Abbreviations: ABR, auditory brainstem evoked response; ADHD, attention deficit hyperactivity disorder; BDI, Beck Depression Inventory; BORIS, Behavioral Observation Research Interactive Software; BSID-II, Bayley Scales of Infant and Toddler Development–II; CBF, compromised brainstem function; FA, focused attention; GA, gestational age; ICC, intra-class correlation coefficient; IVH, intraventricular hemorrhage; MDI, Mental Development Index; NBF, normal brainstem function; NBRIS, Neurobiologic Risk Score; NICU, neonatal intensive care unit; PVL, periventricular leukomalacia; RDLS, Reynell Developmental Language Scales; SEM, structural equation modeling; SSWQ, Student Subjective Wellbeing Questionnaire.

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thereafter (Oakes et al., 2002; Ruff et al., 1992; Ruff & Capozzoli, 2003). The important role of FA in learning is evident in infants' use of it when encountering a novel object (Oakes & Tellinghuisen, 1994; Ruff et al., 1992) and by a reduction in distractibility while exercising it (Oakes & Tellinghuisen, 1994; Ruff & Capozzoli, 2003). Previous studies found that FA ability in early childhood reinforces language acquisition (MacRoy-Higgins & Montemarano, 2016) and predicts subsequent cognitive development in early childhood (Johansson et al., 2015; Kochanska et al., 2000; Ruff & Lawson, 1990), thus accentuating the importance of FA in learning.

Current theories of attention have not yet addressed FA comprehensively. Still, the attentional networks framework suggested by Posner and colleagues (Posner & Rothbart, 2023) points to some of its vital ingredients by noting the difference between cue-driven orienting behavior using the orienting network (Posner, 2016), activation of the alerting network to increase attentiveness to salient stimuli (Bast et al., 2018; Minzenberg et al., 2008), or being able to detect and deliberately focus at a target even in a conflictual context by using the executive attention network (Neta et al., 2016; Posner & Rothbart, 2023).

The executive attention network is responsible for top-down cognitive processes including signal detection, monitoring, response inhibition, conflict resolution, and goal-driven sustained attention (Petersen & Posner, 2012). This network substantially buds from the end of the first year of life (Conejero & Rueda, 2017) and continues to develop throughout childhood (Posner & Rothbart, 2023), coinciding with the development of FA ability (Fisher, 2019; Xie et al., 2019). Functionally, FA involves operations of the executive attention network including detecting, monitoring, and sustaining attention by inner volition, but also calls for timely participation of the other networks. The neuroscience literature has suggested thus far that FA relies on the activation of executive brain centers (Brefczynski-Lewis et al., 2007; Manna et al., 2010), which modulate alertness via the brainstem (Cheng et al., 2019; Vestergaard-Poulsen et al., 2009) to maintain orienting toward the desired stimulus (Ozaki & Ogawa, 2009). Based on these notions, FA could be characterized as a multifaceted skill contingent on integrating functions from all three attention networks—the alerting and orienting networks orchestrated by the executive network (Posner & Rothbart, 2023). Atypical developmental patterns in these networks and learning difficulties have been documented following preterm birth, pointing to this population as an interesting source for exploring FA and the mechanisms affecting its development.

Attention and learning development following preterm birth

Preterm birth, defined as a live birth before 37 weeks of gestation (World Health Organization, 2023),

represented 9.9% of all live births worldwide in 2020 (Lawn et al., 2023). It is associated with persistent attention deficits (Anderson et al., 2021; Burstein et al., 2021) and a higher likelihood of learning and academic problems (McBryde et al., 2020). It has been suggested that early deficits in attention organization might be a precursor of the ensuing cognitive and academic difficulties (Rose et al., 2011) such that attention orienting deficits in infancy predict executive attention abnormalities in toddlerhood in ways that negatively affect preterm children's verbal intelligence and reading proficiency (Blankenship et al., 2019). Importantly, preterm birth is associated with increased susceptibility to abnormalities in all three attentional networks. These include delayed latency to fixate and visual following (*orienting network*) in early life (Burstein et al., 2021), diminished intrinsic control of arousal in attention tasks (*alerting network*) in the preschool years (Jaeger et al., 2021), and, eventually, impaired functioning of the *executive network* (e.g., error monitoring, conflict resolution, response inhibition) that stand out compared to the other networks in the early school years (Leclercq et al., 2006; Pizzo et al., 2010). This presents prematurity as a candidate factor for understanding the prerequisites for effective FA development (Burstein et al., 2021).

Learning and cognitive development theories suggest that less conspicuous difficulties in rudimentary cognitive or sensorimotor operations incurred early in development may instigate a “domino” effect, leading to more robust difficulties in mastering more complex skills (Bayley, 1955; Fletcher et al., 2019; Frostig, 1972; Piaget, 1952). As such, studies have suggested that the higher likelihood of adverse cognitive sequelae of preterm birth may be related to earlier dysfunctions in autonomic and sensorimotor facets (Doussard-Roosevelt et al., 1997; Geva et al., 2014, 2016; Weinstein et al., 2014). This notion is highly related to FA as an ability contingent on integrating attention orienting and autonomic regulation. Notably, these primary functions are known to be processed by brainstem hubs and pathways (Burstein & Geva, 2021). Therefore, it seems vital to consider the integrity of early maturing pathways traversing the brainstem when exploring FA development, particularly following preterm birth.

Prematurity, brainstem function, and FA

Substantial morphological changes in the brainstem occur during the gestation and neonatal periods to sustain vital cardiorespiratory reflexes, parasympathetic functions, and sensory processing (O'Rahilly & Müller, 2006). Accordingly, early extrauterine exposure is associated with an increased risk of anatomical and neurochemical abnormalities in the brainstem's development (Schmidbauer et al., 2019; Wu et al., 2020). One sign of early compromised brainstem function (CBF)

following preterm birth is delayed neural transmission in the auditory pathways, evident by the auditory brainstem evoked response (ABR) test (Stipdonk et al., 2016).

The ABR measures neuro-electrical activity following exposure to standardized auditory stimulations. Its waveform is typically organized in five peaks along the auditory brainstem pathway, reflecting the responsiveness of the auditory vestibular nerve, cochlear nuclei, superior olive, lateral lemniscus, and inferior colliculus (Wilkinson & Jiang, 2006). The ABR test is commonly used as a screener for hearing deficits (Levit et al., 2015). However, it has been shown that subtle delays in ABR latencies may be associated with difficulties in cognitive, attention, and social development (Burstein & Geva, 2021; Geva et al., 2014, 2017; Miron et al., 2021; Wang et al., 2020). A previous study (Wang & Jiang, 2015) found a prevalence of 22.4% for abnormal ABR latencies indicating CBF in neonates born very preterm (i.e., before 32 gestational weeks).

Neurodevelopmental frameworks help clarify how developmental cascades materialize at the neural level. A previous model suggests that early brainstem development has vast implications for the integrity of later-evolving cortical functions (Geva & Feldman, 2008; Tucker et al., 2000), including executive attention operations (Geva et al., 2017). More specifically, brainstem involvement in FA is suggested to be first evident in noradrenergic projections from the locus coeruleus that increase phasic readiness and regulate the level of alertness needed to attend to the environment (Bast et al., 2018; Minzenberg et al., 2008). When developed properly, these functions are integrated with the later maturing executive network that coordinates arousal and orienting (Pozuelos et al., 2014), enabling infants to transform looking behavior into learning. However, neonatal CBF might destabilize arousal regulation and instigate protracted effects on later maturing executive neural networks that facilitate effortful control of attention. Here, we explore whether neonatal CBF following preterm birth might interfere with the neurodevelopmental processes that sustain FA in infancy and late adolescence and whether such interference—specifically manifested in FA (rather than mere orienting)—might then be associated with the child's learning proficiency. The exploration is focused on the involvement of brainstem functions in higher-order cognitive capacities (i.e., FA) that facilitate language development and academic achievements.

Current study

The current study investigated the possible links between early brainstem functioning and attention and academic development by using an extensive longitudinal design. We followed a cohort of preterm children from birth to late adolescence to assess whether (1) FA, rather than basic orienting behavior, has significant involvement in language, attention, and academic development, both in early

childhood and late adolescence; (2) within-subject stability is evident in FA development; (3) brainstem integrity near birth is associated with FA ability in the short and long-term; (4) which in turn relate to language acquisition in the early years; and (5) this trajectory might extend into late adolescence and be expressed in academic proficiency.

METHODS

Participants

A sample of 175 infants, born between gestational age (GA) of 30 to 35 weeks, were recruited from the Level III neonatal intensive care unit (NICU) at Sheba Medical Center in Israel for a prospective longitudinal study. Infant exclusion criteria included severe brain injury identified in neonatal cranial ultrasound (i.e., intraventricular hemorrhage [IVH]>grade 2, periventricular leukomalacia [PVL]), severe neurosensory impairment (e.g., deafness, blindness), and metabolic or genetic diseases. Parental inclusion criteria included maternal age of at least 21 years at childbirth and no use of psychoactive drugs or psychiatric medications peripartum. Based on educational and occupational national standards, all families were in the middle-class socioeconomic bracket (Harlap et al., 1977). Infants were born between the years 2003 and 2006. Overall, 70% of the families approached in the NICU consented and were enrolled in the study. The presented data were collected during the NICU stay and ages 16 months and 17 years. We used corrected ages for scheduling assessments during the first 2 years of life (D'Agostino, 2010). The retention rate at 16m was 82.9% (145 out of 175). Sixteen years after enrollment, efforts were made to contact all former participants. Thirty-nine infants (17.6%) withdrew from the initial cohort in earlier phases. Of the remaining participants, we traced 51.5% (70 of 136), and, finally, 47 adolescents (representing 26.9% of the initial cohort) took part at age 17 years, at which time the participants and their parents reaffirmed their informed consent. There were no significant differences between participants who dropped from the study and those who participated at 16m and 17y, apart from more singleton toddlers who participated in 16m and a less severe mean medical risk score for participants at 17y (Tables S1 and S2). Table 1 provides the characteristics of the entire cohort. The Institutional Review Board of Sheba Medical Center and the Bar Ilan University Ethics Committee approved the study (Approval #2021/14).

Assessments

NICU assessment

Preterm neonates underwent an ABR assessment by a trained audiologist using the Bio-logic Navigator

TABLE 1 Sample characteristics ($N=169$).

Characteristic	Mean (SD) n (%)		p
	NBF	CBF	
n	118	51	
Infant			
GA at birth (weeks)*	33.0 (1.33)	32.5 (1.52)	.031
ABR post-conceptual age (weeks)	35.0 (1.41)	34.9 (1.40)	.706
Birthweight (g)	1711 (349)	1720 (328)	.871
Female**	63 (53.4%)	15 (29.4%)	.004
Cesarean section	81 (69.2%)	33 (64.7%)	.564
Singleton	65 (55.1%)	29 (56.9%)	.831
Apgar 1'	8.48 (1.03)	8.12 (1.29)	.052
Apgar 5'	9.68 (0.60)	9.53 (0.83)	.185
NBRS	2.21 (1.89)	2.58 (2.07)	.265
Hospitalization (days)	30.1 (12.7)	32.3 (16.0)	.339
RDS	33 (28.4%)	17 (33.3%)	.526
Sepsis	9 (7.8%)	5 (9.8%)	.660
Hyperbilirubinemia	73 (62.9%)	32 (62.7%)	.982
IVH grade I–II	8 (6.9%)	4 (7.8%)	.827
NEC	5 (4.3%)	1 (2.0%)	.452
16m participation*	87 (73.7%)	45 (88.2%)	.036
16m corrected age (years)	1.36 (0.26)	1.33 (0.28)	.495
17y participation	33 (28.0%)	11 (21.6%)	.384
17y age (years)	17.2 (0.90)	17.6 (0.45)	.231
Mother			
Maternal age at childbirth (years)	33.5 (5.05)	32.3 (3.97)	.179
Maternal education (first degree or more)	86 (76.1%)	39 (79.6%)	.627
Postpartum maternal BDI score	5.81 (5.05)	6.15 (4.20)	.682

Note: Missing values do not exceed 4 observations per characteristic, except for maternal education with 7 missing values, and maternal BDI score with 8 missing values.

Abbreviations: ABR, auditory brainstem evoked response; BDI, Beck Depression Inventory; CBF, compromised brainstem function; GA, gestational age; IVH, intraventricular hemorrhage; NBF, normal brainstem function; NBRS, Neurobiologic Risk Score; NEC, necrotizing enterocolitis; RDS, respiratory distress syndrome.

* $p < .05$; ** $p < .01$.

Pro (model 907; Natus, CA, USA). ABR assessments were conducted during the first 5 weeks of postnatal life (Mdn=1.89 weeks; post-conceptual age in weeks: $M=35.0$, $SD=1.40$), during a sensitive period in which the brainstem pathways undergo rapid developmental spurts, as previously described (Geva et al., 2013, 2017). ABR data were missing for six infants due to technical problems. The criterion for CBF was based on delayed latencies of more than 1.5SDs of the III–V or I–V interpeak intervals from the previously established post-conceptual age-adjusted norms (Karmel et al., 1988). Routine ABR assessments before NICU discharge

ensured that all participants were without hearing impairments. Of the 169 infants, 51 infants with ABR data were classified with CBF. Figure 1 depicts the standardized differences in ABR latencies between the normal brainstem function (NBF) and CBF groups. All experimenters and coders, at all phases of the study, were blind to participants' neonatal ABR group classification.

Ante- and post-natal data were obtained from the hospital's records. Neonatal medical risk was assessed using the Neurobiologic Risk Score (NBRS; Brazy et al., 1991). Parents filled out an additional questionnaire on general and socioeconomic characteristics. Mothers filled out the Beck Depression Inventory (BDI; Beck et al., 1988) to assess depression levels during the postpartum period.

Lab assessment during the second year of life

At 16m, infants and their parents were invited to the Developmental Neuropsychology Lab to assess attention competence and cognitive development. Infants underwent an adaptation (Geva et al., 2016) of the paradigm developed by Ruff and her colleagues (Ruff & Capozzoli, 2003). Infants were seated on parents' laps in front of a table. An experimenter placed target toys on the table within the infants' reach, and parents were instructed to allow their children to explore freely. For the complete description of the experimental set-up at 16m, refer Figure 2. The procedure was videotaped for subsequent behavioral coding.

Global cognitive development was assessed by the Mental Development Index (MDI) of the Bayley Scales of Infant and Toddler Development–II (BSID-II);

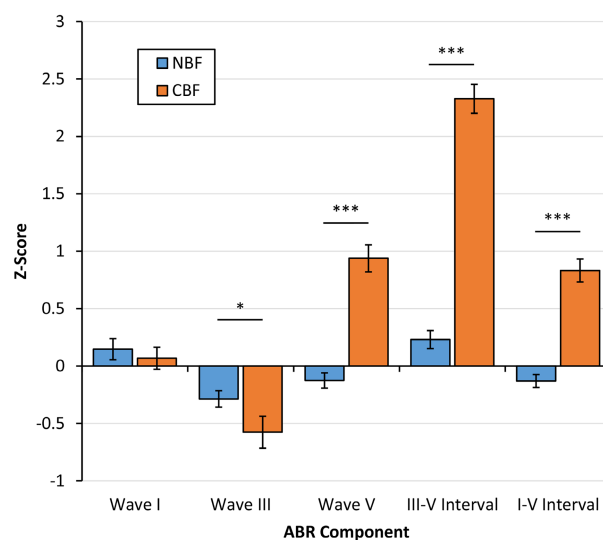


FIGURE 1 Differences in the primary ABR components between the NBF and CBF groups. Scores are based on gestational age-adjusted z-scores. ABR, auditory brainstem evoked response; CBF, compromised brainstem function; NBF, normal brainstem function. Results are expressed as mean \pm 1 standard error. $N=169$. * $p < .05$; *** $p < .001$.

Bayley, 1993). Language development was assessed using the Reynell Developmental Language Scales (RDLS; Reynell & Gruber, 1990). The RDLS includes two scales: the Verbal Comprehension Scale, measuring receptive language abilities; and the Expressive Language Scale, measuring spoken language abilities. The BSID-II and RDLS were administered by two trained clinicians.

Assessment at late adolescence

Originally, assessments in late adolescence were planned to take place in our lab. However, due to the COVID-19 pandemic restrictions, they were restructured and conducted through online platforms. Parents filled out an electronic questionnaire on social, familial, medical, and general characteristics. Assessments with adolescents were conducted in the participant's home environment via Zoom (Zoom Video Communications, San Jose, USA).

We developed a novel task named *The Cutlery Test* to evaluate FA ability among adolescents. The test was designed to assess exploratory behavior during free play in a setting with minimal performance-related demands. The purpose was to enable (but not necessitate) the use of complex spatial reasoning and visuomotor coordination skills, such as constructing intricately balanced three-dimensional models. We used objects not typically associated with play to facilitate creativity and mental effort suitable for adolescents and adults. Following preliminary pilot tests, we opted for a cutlery set comprising silver forks, knives, and spoons (6 each). The task entails a 5-min free-play session with cutlery on a clear table (Figure 3a). Participants were instructed to use the cutlery as they wished to craft a model of their choice (*In the subsequent minutes, please use this cutlery set to build a model of your choice*). If participants completed their model before the allotted time, they were prompted to construct another (*There is still more time, please build another model, and I will let you know when time is up*). Along with behavioral coding of FA, we also coded whether participants tried to construct a complex, three-dimensional model that requires gentle balancing for a substantial period of the session (i.e., at least 25% of construction time) or not (Figure 3b,c); we considered this index to reflect more significant visuospatial effort (Hanline et al., 2001). We had to adapt the test for online administration, which resulted in the omission of FA data for participants who had already been scheduled. Consequently, we had a final set of 25 participants with available data from the Cutlery Test (no significant differences were found between the available and missing sub-samples, except for less severe NBRS scores in the sub-sample with 17y FA data compared to the entire sample; Tables S3 and S4). Before online administration, the experimenter ascertained that participants used typical silver cutlery, had a clear

working area without distractions in the environment and that the video camera was positioned at an accurate angle, encompassing both the working area and the participant's upper body and head.

Adolescents' perceived academic functioning was assessed via the Student Subjective Wellbeing Questionnaire (SSWQ; Renshaw, 2020), which includes four subscales for evaluating (1) academic efficacy, (2) joy of learning, (3) educational purpose, and (4) school connectedness. The SSWQ also provides a global index for school-related wellbeing. The current study utilized the academic efficacy index as a marker for academic functioning in late adolescence, as it is the prominent SSWQ index associated with school achievement (Arslan, 2016; Arslan & Coşkun, 2020). This index measures the degree to which one's academic behaviors effectively meet school demands. The SSWQ was translated into Hebrew using the forward-backward translation method (Brislin, 1970) by two researchers fluent in English and Hebrew. The internal consistency of subscales and global scale of the Hebrew version in the current sample was acceptable (Cronbach's α values between .767 and .857) and comparable to previous samples (Renshaw et al., 2015).

To assess attention functioning in late adolescence, the Conners 3rd Edition short form (self-report) was administered, and the standardized scores of the Inattention and Hyperactivity scales were computed based on the age-adjusted norms (Conners, 2008). Cronbach's α values in our sample indicated acceptable internal consistency of the Inattention scale ($\alpha = .895$), and poor internal consistency of the Hyperactivity scale ($\alpha = .525$) possibly due to the low number of items (Tavakol & Dennick, 2011) for this scale in the short form ($k = 5$).

Behavioral FA indices at 16 months and 17 years

In toddlers, FA was coded when the child was engaged in a deliberate examination, including intent gaze and facial expression, active manipulation, minimization in extraneous bodily activity, a posture that encloses the stimulus and brings it closer to the eyes, and either no talking or soft talking clearly directed to the self (Ruff & Capozzoli, 2003). We modified the original coding scheme to suit FA behavior in adolescents (Table 2 provides a complete description of the scheme). We also coded the frequency of looking at the toy as an index of the orienting network. To account for the variability in observation length (i.e., the mean observation length was 7.90 min [$SD=0.52$] in toddlers and 4.38 min [$SD=0.92$] in adolescents), we considered the ratios of FA and looking at the toy to the total observation time as the dependent measures. Furthermore, we computed the ratio of FA from looking time for the structural equation modeling (SEM) analyses to avoid including two highly overlapping variables.

Two trained experimenters executed behavioral coding. Coding was conducted on a frame-by-frame

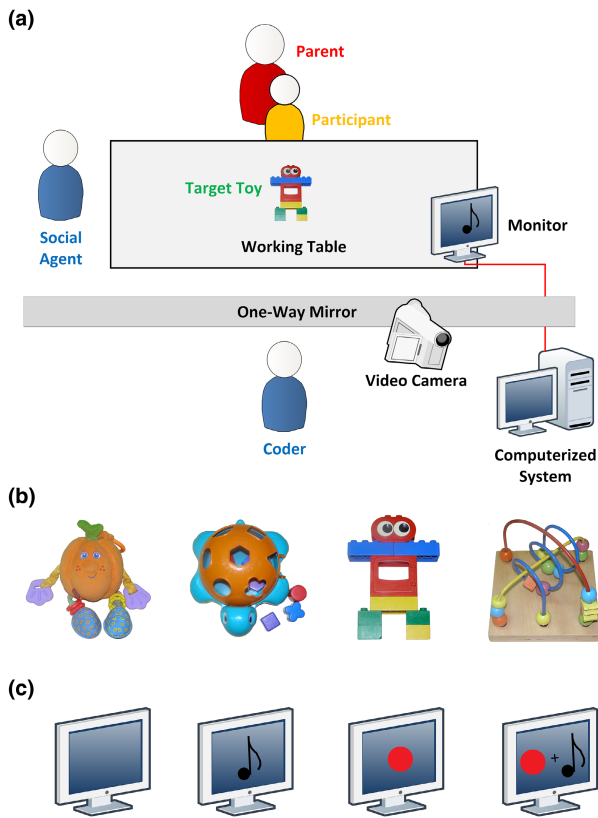


FIGURE 2 Graphical depiction of the attention evaluation set-up at the 16m lab assessment. (a) Infants were seated on parents' laps in front of the working table, with a monitor and an audio speaker positioned 45° to the left. An experimenter (i.e., social agent), positioned 90° to the right of the infants, placed target toys on the table within the infant's reach. Distractors were presented on the monitor, and the audio speaker from a computer system was placed in the control room. The procedure included four trials (2 min each) with four distinct toys. Throughout the task, distractors were presented in 7- to 11-s intervals. The distraction conditions were: (1) no distractor; (2) auditory distractor; (3) visual distractor; and (4) bimodal/auditory–visual distractor. The order of toys and distractors presentation was randomly assigned between trials and counterbalanced between participants. The procedure was videotaped for post hoc behavioral coding. (b) Target stimuli used in the experiment. (c) Distractors used in the experiment. Distractors will be described from left to right—no distraction; a low-saliency auditory distractor (a soft guitar tune, 40 dB hearing level); a low-saliency visual distractor (a looming ball); and a high-saliency bimodal distractor (a bouncing ball coupled with a bouncing noise, 40 dB hearing level).

timescale using the Behavioral Observation Research Interactive Software (BORIS; Friard & Gamba, 2016). Interrater reliability was assessed based on 25% of the observations randomly selected and coded by both experimenters. Intra-class correlation coefficients (ICCs) were computed by single-rating, absolute-agreement, 2-way random-effects models (Koo & Li, 2016). The analysis indicated good to excellent interrater agreement for both the ratio of FA (Toddlers: ICC = .884; 95% CI [.783, .940]; Adolescents: ICC = .927; 95% CI [.663, .987]) and orienting (Toddlers: ICC = .934; 95% CI [.872, .967]; Adolescents: ICC = .952; 95% CI [.516, .993]).

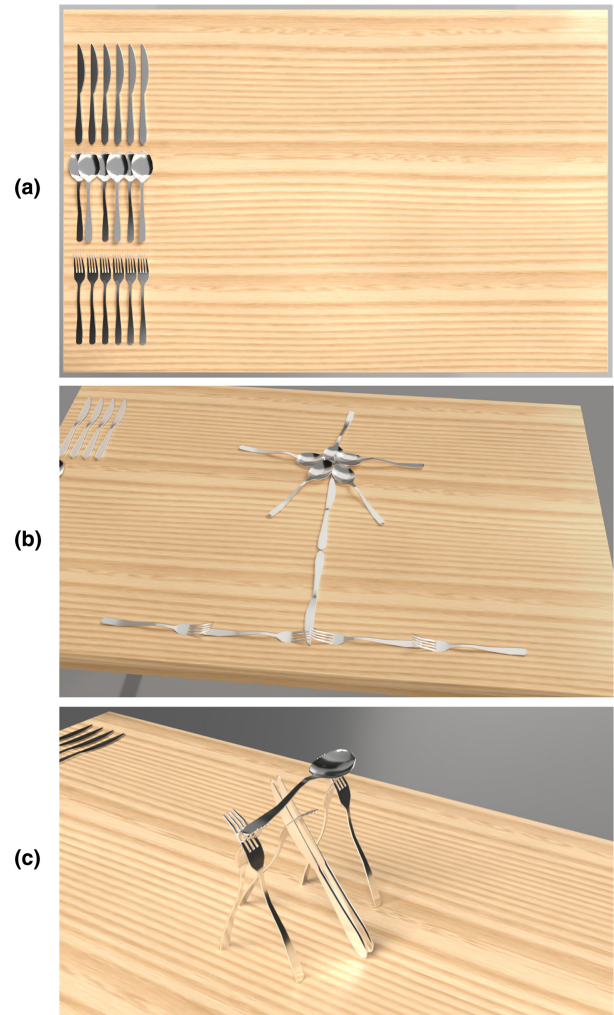


FIGURE 3 Graphical depiction of the Cutlery Test. (a) The initial setup with a cutlery set of 18 forks, knives, and spoons; (b) An illustrated example of a possible two-dimensional model; (c) An illustrated example of a possible three-dimensional model.

Analytic plan

Ascertainment of normality assumptions of the ABR, RDLS, MDI, SSWQ, and Conners 3 indices are based on normal distributions of standardized scores for the ABR (Karmel et al., 1988), RDLS (Reynell & Gruber, 1990), MDI (Bayley, 1993), and Conners 3 (Conners, 2008) and a validation study for the SSWQ (Renshaw et al., 2015). Analyses of behavioral attention indices indicated that data at both 16m and 17y were approximately normally distributed (Figures S1 and S2).

t-Tests were conducted to assess differences in outcomes between groups or within subjects. Pearson correlation coefficients between FA and ABR indices, language and cognitive outcomes in early childhood, and adolescents' self-report measures were computed to ascertain relations between FA and the other experimental measures and examine stability across ages between 16m and 17y. Differences in relations strengths were explored using Fisher's *z*-tests.

TABLE 2 Coding instructions for focused attention (FA).

Population	Criterion	Description
Toddlers	1	The child's gaze is oriented toward the target object (i.e., toy) or any part of the object (for toys with multiple pieces or parts)
	2	Active manipulation of the object, such that the child is deliberately rotating, fingering, opening, inserting, attaching, moving, lifting, or executing another deliberate motor action with the object; FA is not coded in stereotypic or repetitive activity with the object
	3	Concentrated look, such that the gaze is stable and oriented toward a specific part of the object. During active manipulations, the gaze is oriented toward the part of the object that is currently being manipulated
	4	Intent facial expression (e.g., furrowed brows)
	5	Minimization in extraneous body movement
	6	Either no talking/verbalization or soft talking/verbalization clearly directed to the self; FA is not coded when the child is talking with parents or examiners or laughs loudly
	7	A posture that encloses the object and brings it closer to the visual field of the child; may include subtle posture adjustments when the child reorganizes the toy to enable motor examination and keep the object at the center of the visual field while manipulating it
	8	Criterion 1 is mandatory. However, FA could also be coded when Criterion 2 is not followed (i.e., no active motor manipulation of the object), but only if the child is clearly examining the object visually and Criteria 3–7 are robustly evident
Adolescents	1	Participants' gaze is oriented toward the cutlery
	2	Active manipulation of the cutlery, such as rotating, connecting, placing, balancing, moving, lifting, or executing another deliberate motor action; FA is not coded in stereotypic or repetitive activity with the object or when merely arranging the work surface
	3	Concentrated look, such that the gaze is stable and oriented toward the part of the object that is related to the current crafting purpose of the participant
	4	Intent facial expression (e.g., furrowed brows; no yawing/wandering)
	5	Minimization in extraneous body movement (e.g., no fidgeting/itching)
	6	Either no talking or very subtle talking clearly directed to the self
	7	A posture that encloses the object and brings it closer to the visual field; may include subtle posture adjustments that scaffold the current manipulation
	8	Criterion 1 is mandatory. However, FA could also be coded when Criterion 2 is not followed (i.e., no active motor manipulation), but only when there is an ensuing active manipulation and if Criteria 3–7 are robustly evident

Note: Criterion 1 was the criterion for coding looking behavior.

Path analysis was then conducted to assess whether the associations between ABR integrity and language development (in early life) could be explained by an indirect effect of FA rather than mere orienting while controlling for neonatal medical risk using the NBRS. An additional SEM was conducted for the sub-sample who were also assessed in late adolescence to examine the possible indirect effect of neonatal ABR transmission time on academic efficacy (in late adolescence) via FA performance and language development in early childhood. In both SEMs, we utilized the standardized I–V interpeak interval latency as the neonatal ABR variable to include a continuous rather than a binary variable (Kline, 2023). We chose this component as it reflects the conduction efficiency along the brainstem tract traversing from the cochlear nerve to the lateral lemniscus and inferior colliculus (Parkkonen et al., 2009; Wilkinson & Jiang, 2006). Due to group differences in GA, Pearson correlations between GA and all dependent variables were assessed and found to be non-significant. Therefore, GA was not used as a covariate in the analyses. Due to gender differences between groups, gender effect on all dependent

variables was assessed. Only RLDS' verbal comprehension and expressive language differed between genders, with superior outcomes for girls (Table S5), as widely reported in previous studies in toddlers (Eriksson et al., 2012; Frank et al., 2021). Therefore, gender effects were controlled for in the first SEM.

Significance was assumed as $p < .05$. All analyses were conducted using RStudio v2023.09.01 (Posit team, 2024), with SEM analyses conducted using the *lavaan* package (Rosseel, 2012).

RESULTS

Neonatal ABR and FA

There was a significant difference in FA ratio at 16m between the NBF and CBF groups ($t_{(130)} = 3.15, p = .002$), suggesting that delayed response latencies of the brainstem's auditory centers during the neonatal period are associated with diminished FA ability in the second year of life

(Figure 4a). Regarding the specific ABR components related to the diminutions, the analysis indicated that delayed standardized latency scores of wave peak V and interpeak intervals III–V and I–V were the primary components associated with decreased FA durations. No similar associations were found for wave peaks I and III (Table 3).

An exploratory analysis of 17 y group differences in FA as a function of neonatal brainstem integrity revealed no significant difference between the NBF and CBF groups ($t_{(23)}=1.24$, $p=.227$; Figure 4b), but medium-size negative associations were found between the standardized latency scores of wave peaks III and V, and interpeak intervals III–V and I–V that were attained neonatally, and FA ratio at 17 y. Importantly, although, unlike the 16 m outcomes, these associations only revealed a trend toward significance (p range = .055 to .089; Table 3).

Fisher's z -tests indicated no significant difference between the correlation coefficients in 16 m and 17 y for each wave peak and interpeak interval with FA ratio, respectively, suggesting no decreases in the statistical power of these associations as a function of age. Taken together, these findings concerning the changes in the strength of the relations between neonatal brainstem efficacy and FA at 16 m compared to 17 y are not conclusive, as putatively, the reduced sample size at 17 y precludes drawing a more robust conclusion on that matter.

FA and cognitive and academic development

The mean ratio of FA to total session time was 0.237 (SD=0.11) in early childhood and a triplet ratio of 0.663

(SD=0.18) in late adolescence, based on the entire sample at each time point. When considering participants with observations at both times, a paired samples t -test indicated a significant increase ($t_{(23)}=-11.7$, $p<.001$) in FA from 16 m ($M=0.255$, $SD=0.10$) to 17 y ($M=0.658$, $SD=0.18$). The association between FA in the second year of life and FA 16 years later was $r=.379$ ($n=24$; Figure S3), reflecting a medium effect size (Cohen, 1988). However, this association was not statistically significant ($p=.068$), plausibly due to the relatively lower availability of observations in the 17 y FA assessment.

Notably, an increased FA ratio in early childhood was significantly associated with improved early cognitive development, as reflected in the MDI of the BSID–II and the verbal comprehension and expressive language indices in the RDLS. Regarding long-term outcomes, an increased FA ratio in the second year of life was associated with superior academic efficacy, joy of learning, global subjective academic wellbeing, and decreased inattention symptoms, based on adolescents' reports (Table 4).

FA in late adolescence was positively associated with concurrent perceived academic functioning reflected in the academic efficacy, school connectedness, and global subjective academic wellbeing indices in the SSWQ and decreased inattention and hyperactivity standardized scores in the Conners-3 (Table 4). Furthermore, adolescents who spent more time in FA also endeavored in more complex manipulations of the cutlery ($M=0.756$, $SD=0.11$) compared to adolescents who created two-dimensional models ($M=0.545$, $SD=0.18$), suggesting that FA ability was significantly associated with enhanced visuospatial effort and possibly with a greater

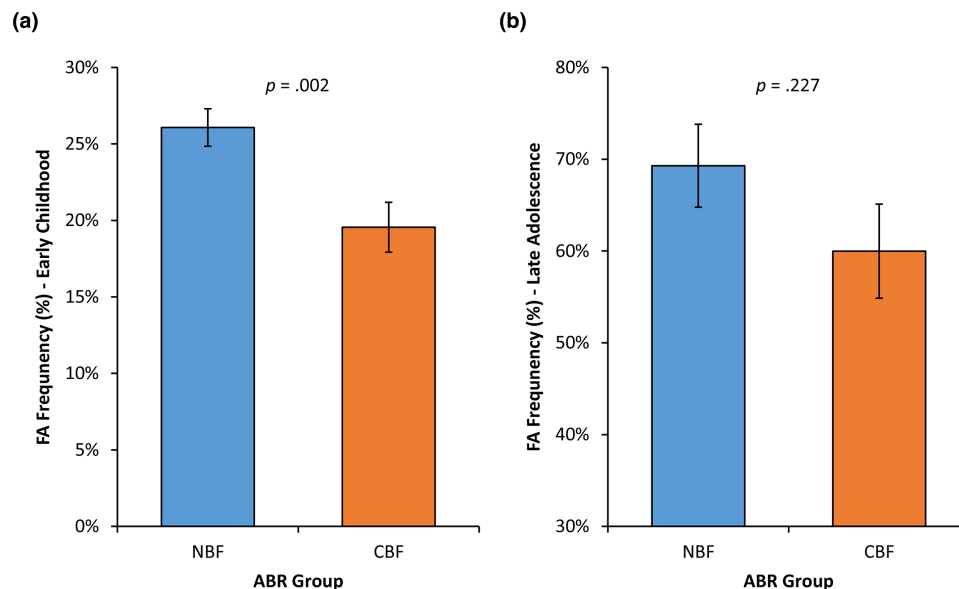


FIGURE 4 Differences in FA between the NBF and CBF groups. ABR, auditory brainstem evoked response; CBF, compromised brainstem function; FA, focused attention; NBF, normal brainstem function. (a) At 16 m, the CBF group ($n=45$) demonstrated a significantly decreased frequency of FA compared to the NBF group ($n=87$). (b) No similar difference was found between the NBF ($n=17$) and CBF ($n=8$) groups at 17 y. Results are expressed as mean \pm 1 standard error.

TABLE 3 Association between ABR components and focused attention.

ABR component	Wave I	Wave III	Wave V	Interpeak interval III–V	Interpeak interval I–V
Focused attention (16m)	.012 <i>n</i> = 130	−.061 <i>n</i> = 131	−.274** <i>n</i> = 130	−.231** <i>n</i> = 130	−.264** <i>n</i> = 130
Focused attention (17y)	−.286 <i>n</i> = 24	−.388# <i>n</i> = 25	−.347 <i>n</i> = 25	−.351 <i>n</i> = 25	−.355 <i>n</i> = 24

Note: ABR values reflect the standardized scores.

Abbreviation: ABR, auditory brainstem evoked response.

#*p* < .06;

***p* < .01.

TABLE 4 Association between focused attention performance and cognitive/academic-related outcomes in early childhood and late adolescence.

Variable	Early childhood			Late adolescence						
	MDI	Verbal comprehension	Expressive language	Conners 3: Inattention	Conners 3: Hyperactivity	SSWQ: Academic efficacy	SSWQ: Joy of learning	SSWQ: School connectedness	SSWQ: Educational purpose	SSWQ: Global score
Focused Attention (16m)	.301** <i>n</i> = 96	.199* <i>n</i> = 129	.174* <i>n</i> = 131	−.307* <i>n</i> = 44	−.124 <i>n</i> = 44	.464** <i>n</i> = 43	.340* <i>n</i> = 43	.187 <i>n</i> = 43	.254 <i>n</i> = 43	.437** <i>n</i> = 43
Focused attention (17y)	−.112 <i>n</i> = 20	.174 <i>n</i> = 24	.297 <i>n</i> = 24	−.535** <i>n</i> = 25	−.396* <i>n</i> = 25	.498* <i>n</i> = 25	.233 <i>n</i> = 25	.448* <i>n</i> = 25	.386# <i>n</i> = 25	.565** <i>n</i> = 25

Note: The Verbal Comprehension and Expressive Language indices are based on the Reynell Developmental Language Scales, and the MDI is based on the Bayley Scales of Infant and Toddlers Development; The inattention and hyperactivity indices are based on the standardized scores of the Conners-3 (self-report). The academic-related indices in late adolescence are based on the Student Subjective Wellbeing Questionnaire (SSWQ).

Abbreviation: MDI, Mental Development Index.

#*p* < .06;

p* < .05; *p* < .01.

ability to entertain novel options and execute them creatively ($t_{(23)} = 3.65, p = .001$).

SEM: From brainstem to learning through FA

Early language acquisition as a function of brainstem efficacy and FA

The first SEM was conducted to assess the indirect effect of neonatal brainstem transmission times on language acquisition at 16m via FA and looking behavior while controlling for medical risk in the NICU and gender effect on language outcomes. Fit indices revealed poor fit to the data ($\chi^2_{(11)} = 29.7, p = .002$; normed fit index [NFI] = .76, comparative fit index [CFI] = .82, Tucker-Lewis index [TLI] = .67, root mean square error of approximation [RMSEA] = .12, standardized root mean squared residual [SRMR] = .09). As gender effects were not the main theoretical focus of this study, a competing model excluding gender was explored. Fit indices of this model revealed a good fit to the data ($\chi^2_{(7)} = 10.5, p = .162$; NFI = .90, CFI = .96, TLI = .01, RMSEA = .06, SRMR = .05), that was superior to the initial SEM ($\chi^2\Delta = 8.74, df\Delta = 5, p = .120$). An examination of the paths revealed that the indirect path from neonatal ABR latencies of interpeak interval

I–V to receptive and expressive language ability via FA was significant, yet, the indirect path via looking was not (Figure 5a). We also assessed whether the NBRS was associated with the I–V interpeak interval latencies. Since it was not related, NBRS was removed from the long-term academic functioning model, which required condensing the parameters due to the decreased sample size.

Long-term academic functioning as a function of brainstem efficacy and FA

The second SEM was conducted to assess whether neonatal brainstem transmission times are associated with academic efficacy in late adolescence through an indirect effect on language acquisition at 16m via FA. Fit indices indicated a good fit to the data ($\chi^2_{(5)} = 4.96, p = .421$; NFI = .89, CFI = 1.00, TLI = 1.00, RMSEA = .00, SRMR = .06). An examination of the paths revealed that the indirect path from neonatal ABR latencies of the I–V interpeak interval to language acquisition via FA remained significant once removing looking ratio, and that academic efficacy in adolescence was significantly associated with language acquisition at 16m (Figure 5b). As expected, the second model is weaker as the sample size for the long-term follow-up was limited, producing

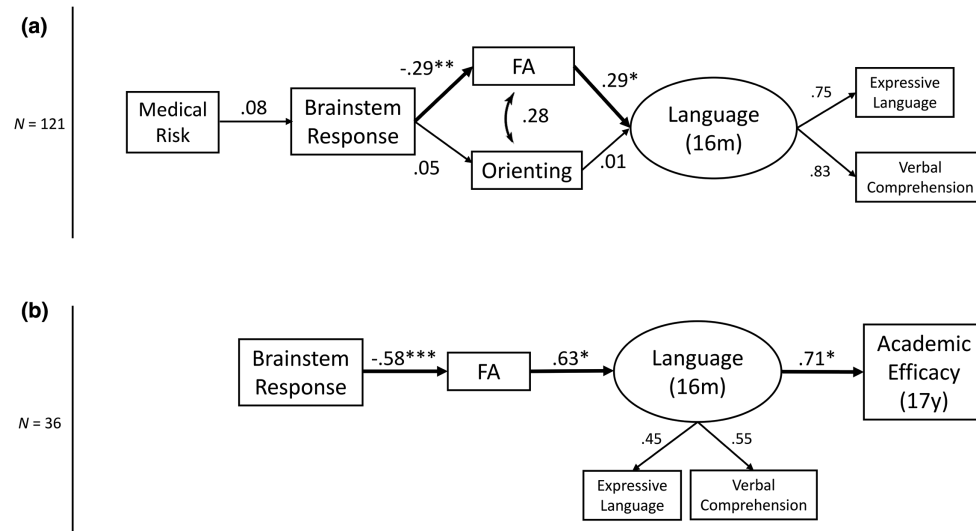


FIGURE 5 SEM models of auditory brainstem evoked response (ABR) effect on (a) language outcomes at 16m via focused attention (FA) and orienting; and an extension of the significant path to (b) academic efficacy at 17y. Brainstem response represents ABR I–V interpeak interval latencies. * $p < .05$; ** $p < .01$; *** $p < .001$.

only four subjects per parameter. Therefore, the findings from this model should be interpreted with caution and as a call for developing this notion in future research.

Summary of findings

The study explored the association between FA and language and academic development from early childhood to adolescence as a function of neonatal brainstem function integrity. Early childhood FA was associated with improved global cognitive development, verbal comprehension and expressive language skills in the second year of life, as well as long-term academic outcomes, including academic efficacy, joy of learning, and overall academic wellbeing at 17y. These longitudinal trajectories support the link between early FA competence and learning efficacy.

The findings also point to a promising methodological advent. We devised a novel paradigm to assess FA in adolescents, the Cutlery Test that elicited preliminary findings, including a positive association between FA ability at 17y and concurrent academic efficacy, improved task performance, and decreased inattention and hyperactivity symptoms, thus accentuating the nexus between FA and academic and attention functioning in late adolescence.

From a neuropsychological standpoint, the findings evinced that FA was associated with language and academic development and was distinct from more basic orienting behavior, suggesting that FA serves a distinct role in learning. Finally, taking a developmental neurobiological perspective, the study supported the postulated connection between neonatal brainstem integrity and the development of early FA capacity, evident as a direct effect in the first 2 years of life. Path analyses

revealed that brainstem response latencies in the neonatal period are associated with early language acquisition and long-term academic efficacy through an association with FA, thus accentuating the role of FA in learning and pinpointing a possible neural mechanism implicated in the establishment of FA.

DISCUSSION

The present study instigated a comprehensive pioneering journey to explore the interrelations between neonatal brainstem functioning, FA development, and their consequential links to learning outcomes at 16 months and 17 years by using a longitudinal prospective design. FA ability emerged as a significant factor in early life, affecting language acquisition in infancy and academic outcomes in adolescence. Furthermore, pilot data on FA in 17-year-old adolescents who were followed up from birth, explored here via a novel paradigm, were also strongly associated with concurrent academic functioning, more complex exploratory behavior, and lower levels of inattention and hyperactivity symptoms. Data attained from participants born preterm supports the notion concerning involvement of neonatal brainstem integrity in affecting the child's ability to vitalize attention for learning purposes, thus impacting language and academic development throughout childhood.

FA as a pillar for language and academic development

Our study highlights the importance of FA as a weighty factor associated with both immediate and long-term

cognitive, language, and academic outcomes. The observed positive associations of FA at 16 months with global cognitive development (i.e., MDI) and receptive and expressive language indices reflect the connection between FA and early cognitive and linguistic functioning. Importantly, FA ratios in early life and late adolescence were also associated with one's perceived academic efficacy at 17 years, thus underscoring the broad involvement of FA in learning.

The Matthew Effect implies that preliminary resources become more salient over time, such that advantages or disadvantages accumulate (Walberg & Tsai, 1983); *For unto every one that hath shall be given, and he shall have abundance* (Matthew XXV:29). The current findings can be interpreted accordingly, such that efficient FA ability in early childhood can lead to a sequence of positive feedback loops of learning and academic performance. Conversely, nascent deficits can exacerbate and impinge higher functions as time progresses. We posit that children who manifest FA proficiency early on might be better positioned to benefit from learning opportunities, thus accumulating language skills and knowledge faster than their counterparts who operate with weaker FA foundations. Gradually, these advantages (or disadvantages) can accrue into conspicuous gains (or shortfalls) in academic and cognitive outcomes that persist throughout childhood and adolescence and, putatively, also into adulthood (Bilgin et al., 2018; Eves et al., 2021).

Importantly, we detected a medium, although not statistically significant effect size for the association between FA in early childhood and late adolescence. Previous studies found significant medium effect sizes for FA consistency in early childhood (Gaertner et al., 2008; Lawson & Ruff, 2004). We expected a protracted association lasting until adolescence, thus, only a partial support to our second hypothesis was obtained. A straightforward reasoning for this finding could point to the relatively small sample size of the FA follow-up at 17 years. However, a Matthew Effect alternative interpretation is that solid FA foundations in early childhood promote the establishment of fundamental apparatuses (e.g., language proficiency) that continually scaffold cognitive and academic development even if FA gaps are bridged until adolescence.

The findings also advocate the unique role of FA in shaping inter-linked neurocognitive domains. The SEM suggests that FA ability—conceived to be contingent on operations of all three attentional networks via the navigation of the executive one—is intricately involved in language development. In contrast, basic orienting (i.e., an orienting network's faculty) per se had no significant contribution in the model. Congruently, Schroer and Yu (2023) had recently found that only when toddlers looked at an object while actively exploring it with their hands were they more likely to benefit from parents' verbalizations to learn new words; merely looking at the object was insufficient. Increased FA in adolescence was

also associated with more complex visuomotor performance in the Cutlery Test and with diminished attention deficit hyperactivity disorder (ADHD)-related symptomatology. These observations collectively raise the notion that FA is a pivotal attention skill that reflects more global executive attention functioning and fosters proficiency in learning (Ruff & Rothbart, 2001).

From neonatal brainstem integrity to efficient learning through FA

To the best of our knowledge, this study is the first attempt to seek the neural mechanism serving FA in childhood. The early development of the brainstem is especially relevant, as it may affect protracted trajectories of broad attention networks (Forte et al., 2017; Geva et al., 2017). We conceptualized the integrity of brainstem functions as a major candidate, as it is directly involved in regulating arousal and sensorimotor operations that enable FA (Cheng et al., 2019; Vestergaard-Poulsen et al., 2009) and explored it prospectively by launching a very long-term experimental design.

Our path analyses from birth to 17 years of age portray the complex interplay by which neonatal brainstem functioning might affect language acquisition in toddlerhood and academic outcomes in late adolescence via its impact on FA. Previous studies have pinpointed the negative consequences of delayed neonatal ABR responsivity on social development (Geva et al., 2014; Miron et al., 2016, 2021) and behavioral inhibition (Geva et al., 2014). Delayed ABR latencies at 6 months were also associated with decreased MDI scores in 2-year-old preterm toddlers (Wang et al., 2020). Further, children (Claesdotter-Hybbinette et al., 2015; Talge et al., 2022) and adults (Juselius Baghdassarian et al., 2018) diagnosed with ADHD show atypical ABR patterns, and 8-year-old preterm children classified with neonatal CBF in the ABR test showed blunted bottom-up activation needed to alert social attention (Geva et al., 2017). To our knowledge, this is the first study to demonstrate that brainstem integrity, identified near birth, can be a precursor of FA efficacy in childhood.

These relations may carry clinical implications. FA impairment was particularly associated with delayed latencies in wave peak V and interpeak intervals III–V and I–V. This can be deciphered through the functional roles and neuroanatomical bases of these distinct ABR components. While wave peaks I and III mostly signify peripheral auditory responses and initial stages of brainstem processing, wave peak V is instrumental in higher-order auditory processing, associated with activation of the lateral lemniscus and inferior colliculus (Parkkonen et al., 2009; Wilkinson & Jiang, 2006). Moreover, interpeak intervals III–V and I–V reflect the conduction efficiency of the neural pathway and integration of auditory information (Wilkinson & Jiang, 2006). Accordingly, a

meta-analysis of 7 studies including 433 children demonstrated that ADHD diagnosis was associated with delayed latencies of wave peak V and interpeak interval I–V (Talge et al., 2022). These findings converge with the premise that a neonatal brainstem compromise can elicit cascading effects on attention development (Burstein & Geva, 2021; Geva & Feldman, 2008; Tucker et al., 2000). It is important to bear in mind that FA does not operate in isolation; it relies on the seamless integration of multisensory information, gaze shifting and maintenance, and arousal modulation. Early disruptions in higher-order brainstem centers (i.e., the wave V-related inferior colliculus and lateral lemniscus) involved in multisensory integration (Liu et al., 2022) via ascending projections from the cochlear nucleus and descending cortical inputs (Felmy, 2019) or the efficient transmission of auditory signals (i.e., interpeak intervals III–V and I–V) can, thus, directly obstruct the establishment of FA, which necessitates timely multisensory coordination by the later-evolving cortical hubs.

The accounts concerning the interrelationship between neonatal *auditory* brainstem deficits and subsequent impairment in FA may be elaborated by additional explanations. Early auditory processing deficits alone can affect global attention development and other modalities' processing and integration capabilities (Bailey, 2010; Dellapiazza et al., 2018), for example, when using audio cues to guide visual attention. Alternatively, prolonged ABR latencies may also reflect deficits in other modalities and functions whose pathways run adjacent to the auditory pathway, as probed here. Although the ABR test primarily gauges auditory processing, the regions implicated—especially wave V-germane regions like the inferior colliculus—are also related to visual and somatosensory processing, as well as eye movement and spatial orientation (Gruters & Groh, 2012). Lastly, abnormalities in ABR latencies might reflect a broader brainstem dysfunction (Munjal et al., 2010; Washnik et al., 2019) that also affects arousal regulation and behavioral control (Geva et al., 2014), which are imperative for FA.

Taken together, the findings outline the development of FA as it first buds through processes mitigated by brainstem pathways, supporting higher-order language and symbolic capacities that serve as the building blocks of learning and academic agency throughout childhood.

Limitations

Certain limitations in the current study warrant attention. The attrition rate at 17 y, although expected in such long-term longitudinal designs, could be a source of bias. The absence of significant differences in most medical and demographic characteristics between those who persisted in the study and those who dropped out partially

mitigates this concern (Nunan et al., 2018). One indication using the NBRIS suggests that children with lesser developmental concerns tended to stay in the study for a longer duration. Notably, the long-term SEM analysis, which included only four observations per parameter (based on only 36 participants with available FA observations at 16 m and academic efficacy self-report at 17 y), should be treated as exploratory, calling for additional corroboration with larger samples. This limited sample necessitates that these findings should be treated as promising although preliminary ones and should be further investigated in future research. The same limitation should be considered for the preliminary findings regarding FA in late adolescence, as measured in the Cutlery Test, which included data from only 25 participants. Still, given the promising direction documented here, we suggest this task could have significant merits, as it enables the evaluation of exploratory behavior in adolescents and adults using an ecologically valid setting. Data revealed robust associations between FA outcomes in this test and concurrent academic and attention functioning.

An additional limitation involves implementing subjective self-report measures to gauge academic efficacy and ADHD symptoms in adolescents. Self-report measures are a feasible evaluation method but often introduce biases (Althubaiti, 2016; Silberg et al., 2020). Specifically, in our study, social desirability bias is possible, suggesting that participants may have had a proclivity to portray a more positive picture of their school-related capabilities. However, this concern is moderated by the previous establishment of the concurrent validity of the academic efficacy index in the SSWQ with non-subjective school performance indices such as grade point average and standardized achievement tests (Arslan, 2016; Arslan & Coşkun, 2020).

This investigation considered the involvement of neonatal brainstem functioning in attention and learning development following preterm birth. The link between the brainstem and early maturation of executive attention in full-term children remains to be explored. Implementing ABR indices during the third trimester, when the brainstem paths undergo marked developmental spurts (Ghio et al., 2021), in full-term samples could be an intriguing future direction. This endeavor will require technological advances that enable tapping brainstem activity in utero during the decisive period of the brainstem's maturation spurts.

Future directions

Empirical data from decades of research have consistently linked preterm birth to persistent difficulties in attention and academic development (Anderson et al., 2021; McBryde et al., 2020; Twilhaar et al., 2018), including diminished FA ability during the first 2 years of

life (Burstein et al., 2021). In the current study, we probed possible underlying factors that shape such trajectories. We demonstrated that FA is significantly associated with preterm children's learning outcomes throughout childhood and that the integrity of the brainstem might affect the development of FA. The findings align with theoretical models suggesting that brainstem abnormalities—which are more prevalent following preterm delivery—might destabilize arousal-modulated executive attention faculties (i.e., FA) that facilitate learning (Galgani et al., 2023; Geva & Feldman, 2008; Johnston et al., 2014).

The inferred negative attention and learning sequelae of preterm birth call for attention. Theoretical frameworks suggest that the primary platform for learning in infancy is the child's relationship with primary caregivers (Bowlby, 1988; Stern, 1985; Welch, 2016). Clinical research has substantiated encouraging conduits for improving parental sensitivity, attunement, and mindfulness in ways that scaffold the cognitive and psychological development of children with attention, emotion, and psychophysiological regulation deficits (Burgdorf et al., 2019; Meppelink et al., 2016). Future studies should focus on exploring the specific mechanisms of change of such parental interventions and investigate their potential merits in diminishing deficits in brainstem-modulated attention abilities like FA.

CONCLUSIONS

The current study further supports the prominent role FA plays in guiding the cognitive and academic development of preterm children. By spotlighting the influence of early brainstem integrity on FA and learning trajectories, we offered a possible and insightful mechanism by which early integrity of brainstem functioning supports attention development in ways that can serve academic development. The findings align with theories emphasizing how cognitive development builds upon the integrity of earlier maturing pathways. This premise, therefore, advocates the potential merits of early interventions that specifically tackle skills imperative for learning, like regulating arousal and orienting to be able to effortfully focus our attention to learn.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose.



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DATA AVAILABILITY STATEMENT

The data necessary to reproduce the analyses presented here will be supplied by the corresponding author upon relevant requests by academic scholars. The analytic code necessary to reproduce the analyses presented in this paper is available from the first author. The materials necessary to attempt to replicate the findings presented here are accessible within this publication and [Supporting Information](#). The analyses presented here were not preregistered.

ORCID

Or Burstein  <https://orcid.org/0000-0003-2638-8018>
 Maya Sabag  <https://orcid.org/0009-0003-9242-634X>
 Ronny Geva  <https://orcid.org/0000-0002-5724-2153>

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