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Preterm Toddlers' Inhibitory Control Abilities Predict Attention Regulation and Academic Achievement at Age 8 Years

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Objective To determine if adverse effects of preterm birth on attention and academic abilities at age 8 years are mediated by children's inhibitory control abilities.

Study design Five hundred fifty-eight children born at 26-41 weeks gestation were studied as part of a prospective geographically defined longitudinal investigation in Germany. Toddlers' inhibitory control abilities were observed at age 20 months. At 8 years, attention and academic abilities were assessed.

Results Preterm birth negatively affected children's inhibitory control abilities (B = .25, 95% CI [.11, .39], $P < .001$) and directly predicted subsequent low attention regulation (B = .23, 95% CI [.07, .38], $P < .001$) and academic achievement (B = .10, 95% CI [.03, .17], $P < .001$), after adjusting for other factors. Higher ability to inhibit unwanted behaviors predicted better later attention regulation (B = .24, 95% CI [.07, .41], $P < .001$) and academic achievement (B = .10, 95% CI [.03, .17], $P < .001$).

Conclusions The lower a child's gestational age, the lower the inhibitory control and the more likely that the child had poor attention regulation and low academic achievement. Adverse effects of preterm birth on attention and academic outcomes are partially mediated by toddlers' inhibitory control abilities. These findings provide new information about the mechanisms linking preterm birth with long-term attention difficulties and academic underachievement. *(J Pediatr 2015;■:■-■).*

Preterm birth increases the risk of attention difficulties[1-4] as well as long-term academic underachievement.[3,5,6] Studies have suggested that early self-control abilities (eg, inhibitory or effortful control) may mediate effects of preterm birth on cognitive outcomes[7,8] and later achievement.[9,10] Inhibitory control predicts the development of the executive attention network[11] and is related to children's executive functions, high-level cognitive abilities that allow humans to show adaptive, goal-directed behavior in complex situations.[12] In an ever-changing and unpredictable environment, executive functions and self-control in particular, are not only vital to master real-life situations but also predictive of long-term academic achievement.[13-15]

One highly reliable indicator of early self-control is an individual's ability to inhibit undesirable behaviors (eg, wait for a treat instead of instantly grabbing it).[16] The inhibition of such behaviors that are driven by emotions has been coined "hot" effortful control. Children's performance in such emotionally valenced inhibitory task assessment has been shown to predict life-long academic attainment and achievement outcomes, even after controlling for cognitive ability and socioeconomic status (SES).[17-19]

Few studies on preterm children have specifically addressed potential links between low gestational age (GA) at birth, early self-control, and long-term outcomes.[20] A recent study suggested that inhibitory control might predict learning and attention regulation abilities at age 6 years in preterm children.[21] Other investigations have shown that very preterm children have problems with inhibitory control[8] and that these may be associated with delay of frustration, as well as attention and behavior problems in preadolescence.[22] Unknown is whether there is a dose-response effect of low GA at birth on inhibitory control in toddlers. If this is the case, inhibitory control abilities may be a functional indicator of the effects of preterm birth on the pathway to later attention and academic outcomes.

The aim of the current study was to test in a large sample of children born across the whole spectrum of gestation whether: (1) there are differences in early inhibitory control according to GA at birth; and (2) whether adverse effects of preterm birth on attention regulation and academic achievement at age 8 years are mediated by children's inhibitory control abilities using structural equation modeling (SEM). We hypothesized that: (1) GA at birth would directly and positively predict inhibitory control at corrected age 20 months and attention regulation and academic achievement abilities at age 8 years; (2) inhibitory

GA	Gestational age
SEM	Structural equation modeling
SES	Socioeconomic status

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control would also directly and positively predict attention regulation and academic achievement; and (3) the impact of GA at birth on later outcomes would be mediated by children's ability to inhibit undesirable behaviors, after statistically adjusting for potential confounders (ie, child sex, neonatal medical risk, and family SES at birth).

Methods

Data were collected as part of the prospective Bavarian Longitudinal Study.[23] The Bavarian Longitudinal Study is a geographically defined, entire population sample of neonatal at-risk children born in Southern Bavaria, Germany, between January 1985 and March 1986 who required admission to a children's hospital within the first 10 days of life (N = 7505; 10.6% of all live births). In addition, 916 healthy term control infants (normal postnatal care) were identified at birth from the same hospitals in Bavaria during the same period. From the initial samples, 393 children born between 25 and 38 weeks of gestation (randomly drawn within the stratification factors sex, socioeconomic background, and degree of neonatal risk) and 165 healthy full-term (39-41 weeks GA) control children were assessed at corrected age 20 months and again at age 8 years. Full details of the sampling criteria and dropout rates are provided elsewhere.[23] Table I shows the descriptive characteristics of the final sample according to their GA group status (N = 558).

Participating parents were approached within 48 hours of the infant's hospital admission and were included in the study once they had given written consent for their child to participate. Toddlers' inhibitory control abilities were assessed at 20 months of age corrected for prematurity. At age 8 years, participating children and their mothers were assessed by an interdisciplinary study team for 1 entire day including neurologic assessments (conducted by pediatricians), parent interviews (conducted by psychologists), cognitive assessments, and behavior ratings (administered by psychological assistants and the whole team). All raters and assessors were blinded to preterm birth status of participating children. Ethical permission for the study was granted by the ethics committee of the University of Munich Children's Hospital and the Bavarian Health Council (Landesärztekammer Bayern).

GA at birth was determined from maternal reports of the last menstrual period and serial ultrasounds during pregnancy. Children were summarized into 5 GA groups (very preterm: <32 weeks GA; moderately preterm: 32-33 weeks GA; late preterm: 34-36 weeks GA; early term: 37-38 weeks GA; full-term 39-41 weeks GA) in order to make findings comparable with other studies.[24,25]

Infant postnatal complications were assessed using a comprehensive optimality index including 21 items (eg, intubation, severe anemia, cerebral hemorrhage).[26]

Family SES at birth information was collected through structured parental interviews and computed as a weighted composite score derived from the occupation of the self-identified head of each family (usually the father) together with the highest educational qualification held by either parent[27] into 3 predefined categories of low, medium, and high SES.

At corrected age 20 months, children's inhibitory control abilities were assessed with a standardized behavioral observation task. At the start of the raisin game, toddlers were presented with a raisin that was placed under an opaque cup within easy reach. After 3 training runs during which eating the raisin was allowed after short but increasing time intervals (instant eating, then 5 and 10 seconds waiting time) the

Table I. Descriptive sample characteristics according to GA groups

	<32 wk GA	32-33 wk GA	34-36 wk GA	37-38 wk GA	39-41 wk GA
	n = 104	n = 51	n = 126	n = 112	n = 165
GA at birth	29.74 (1.53)	32.49 (0.51)	35.07 (0.76)	37.56 (0.50)	40.07 (0.66)
Birth weight	1391 (353)	1649 (398)	2269 (566)	2796 (495)	3776 (447)
Child sex (male)	55.8%	39.2%	47.6%	44.6%	47.9%
Neonatal medical risk score	9.40 (2.57)	8.02 (2.67)	5.25 (2.79)	3.28 (2.74)	0.31 (0.56)
Cognitive abilities (20 mo)	101.65 (7.90)	104.84 (8.10)	105.65 (7.66)	106.88 (5.76)	107.55 (6.42)
Family SES					
Low	29.8%	27.5%	31.7%	33.0%	26.7%
Medium	41.3%	43.1%	26.2%	27.7%	44.8%
High	28.8%	29.4%	42.1%	39.3%	28.5%
Inhibitory control (waiting time in s) at age 20 mo					
Did not wait/waited ≤10 s	58.7%	41.2%	34.1%	34.8%	24.2%
Waited 11-59 s	30.8%	31.4%	36.5%	40.2%	48.5%
Waited 60 s	10.6%	27.5%	29.4%	25.0%	27.3%
Attention and achievement outcomes at age 8 y					
CBCL attention problems	2.78 (2.38)	2.24 (2.23)	1.76 (2.05)	2.18 (2.09)	2.01 (2.09)
Testers' attention rating	6.56 (1.23)	6.59 (1.18)	6.94 (1.08)	6.86 (1.17)	7.23 (1.05)
Mathematic test	−0.41 (0.69)	−0.31 (0.79)	−0.01 (0.67)	0.02 (0.67)	0.03 (0.66)
Reading test	−0.21 (1.38)	−0.36 (1.58)	0.24 (0.82)	0.07 (0.75)	0.14 (0.69)
Spelling/writing test	−0.39 (1.08)	−0.17 (1.05)	0.16 (0.96)	−0.07 (1.06)	0.06 (0.94)

CBCL, Child Behavior Checklist.
Descriptive sample characteristics according to GA groups.
Data is presented as mean (SD) for continuous variables and percentages (%) for categorical variables.

actual test run started. Toddlers were asked to wait for 60 seconds before they could touch and eat the raisin. Waiting time until toddlers touched the raisins was measured with a stopwatch and coded into 3 categories of inhibitory control abilities: 1 = did not wait or waited up to 10 seconds (37%), 2 = waited between 11 and 59 seconds (39%), and 3 = waited for 60 seconds (24%). This categorization was chosen for 2 reasons: first, because participants were more or less equally distributed across the 3 groups, and second, because the cutoffs marked a meaningful differentiation of inhibitory behavior (ie, considering normative reaction times at age 20 months, waiting ≤10 seconds was classified as not waiting, whereas waiting for the entire task interval of 60 seconds indicated excellent inhibitory control, and toddlers who waited between 11 and 59 seconds were classified as intermediate).

Child behavior during a challenging cognitive assessment lasting 1 hour 20 minutes was evaluated by psychologists with the Tester's Rating of Child Behavior Task Orientation index scale (Cronbach α = .85; subscale interrater reliabilities intraclass correlation coefficient = .63-.97).[3] Second, child attention across the whole assessment day was evaluated as a consensus rating by the whole research team (team rating of attention regulation of psychologist, assistant psychologist, and pediatrician, α = .98).[3] These 2 attention ratings correlated highly with each other (r = .62, P < .01) and were, thus, z-scored and combined into a single scale of attention regulation. Third, mothers rated their children's attention problems as part of the Child Behavior Checklist.[28]

Achievement was assessed with standardized tests. Numerical representations and reasoning were measured with a comprehensive mathematics test.[29,30] Test tasks were presented to children in book form with 79 items assessing numerical estimations, calculation, reasoning, and mental rotation abilities. Item responses were scored for accuracy, and subscale scores were summed into a total mathematics test score. Children's reading abilities were measured with the Zürich reading test[31] and a pseudo-word reading test.[32,33] Total scores (based on number of errors) correlated highly with each other (r = .74, P < .001) and were, thus, combined to create a single, composite reading test score. Spelling and writing were assessed with a standard diagnostic test (Diagnostic Spelling Test).[34] Test scores were z-standardized according to the healthy full-term control children's scores within the sample.[35]

Statistical Analyses

Data were analyzed with SPSS v 22 (IBM Corporation, Armonk, New York) and Mplus 7 (Muthén and Muthén, Los Angeles, California). Structural equation modelling (SEM) was used to test the direct and indirect effects of the categorical variables GA group and inhibitory control on the latent variables attention regulation (combined Tester's Rating of Child Behavior and team rating of attention regulation) and mother rating of attention problems (Child Behavior Checklist, reverse coded to be entered into the SEM model) and academic achievement (math, reading, and writing/spelling tests) abilities at age 8 years. In addition, sex of the child, neonatal medical risk, and family SES were included as potential confounding variables (Figure). Subsequently, we explored whether the effects of early inhibitory control on childhood outcomes were explained by toddlers' cognitive abilities, assessed with the Griffiths Mental Development Scales[36] at 20 months' corrected age.

Results

Descriptive results showed that children of lower GA groups had, on average, lower inhibitory control at corrected age 20 months and lower attention regulation and academic achievement abilities at age 8 years (Table I). Supporting our first hypothesis, preterm birth negatively affected children's inhibitory control abilities (B = .25, 95% CI [.11, .39]) and directly predicted low attention regulation (B = .23, 95% CI [.07, .38]) and academic achievement (B = .10, 95% CI [.03, .17]) after adjusting for other factors (Table II and Figure; available at www.jpeds.com). Our second hypothesis was also supported as a higher ability to inhibit unwanted behaviors predicted better attention regulation (B = .24, 95% CI [.07, .41]) and academic achievement (B = .10, 95% CI [.03, .17]). In other words, 1 unit of change in inhibitory control (eg, from "waited between 11 and 59 seconds" to "waited for 60 seconds") predicted a 0.25 SD change in the attention latent factor scores and a 0.19 SD change in academic achievement scores. Moreover, adverse effects of preterm birth on later outcomes were partly mediated by children's early inhibitory control abilities (indirect effects: B = .06, 95% CI [.01, .11] and B = .03, 95% CI [.00, .05], respectively), thus, supporting our third hypothesis. In addition to these main effects, being born female predicted better inhibitory control and attention regulation abilities.

Children of high vs medium/low SES had better inhibitory control, attention regulation, and academic scores (Table II). Neonatal medical risk had no statistically significant effect on toddlers' inhibitory control abilities and was dropped from the final SEM model in order to increase model fit. Overall, the model explained 32% of the variance in children's attention regulation, 20% of the variance in academic achievement, and 10% of the variance in early inhibitory control abilities, respectively. Fit values indicated good statistical model fit (χ^2/df = 33.85/42; P = .013; Comparative Fit Index = .979; Root Mean Square Error of Approximation = .040).

Finally, we explored whether the effects of early inhibitory control on childhood outcomes were explained by toddlers' cognitive abilities. Although such was not the case, including cognition in the model did not significantly increase the percentage of explained variance or improve model fit, and, thus, for reasons of statistical sparseness as well as clarity we dropped cognition from the model.

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Table II. Regression weights* using SEM

	Unstandardized				Standardized		
	B	SE	LB	UB	β	P value	R^2
Direct effects							
Attention							0.32
Inhibitory control	0.24	0.07	0.07	0.41	0.25	<.001	
GA group†	0.23	0.06	0.07	0.38	0.22	<.001	
SES – low‡	0.11	0.13	−0.21	0.44	0.05	.374	
SES – high‡	0.61	0.14	0.25	0.97	0.28	<.001	
Sex (female)	0.55	0.12	0.23	0.86	0.26	<.001	
Academic Achievement							0.20
Inhibitory control	0.10	0.03	0.03	0.17	0.19	<.001	
GA group†	0.10	0.03	0.03	0.17	0.19	<.001	
SES – low‡	−0.02	0.06	−0.18	0.13	−0.02	.663	
SES – high‡	0.34	0.06	0.19	0.49	0.29	<.001	
Sex (female)	0.06	0.05	−0.06	0.19	0.06	.191	
Inhibitory control							0.10
GA group†	0.25	0.05	0.11	0.39	0.24	<.001	
SES – low‡	0.05	0.12	−0.26	0.36	0.02	.680	
SES – high‡	0.29	0.12	−0.01	0.59	0.13	.012	
Sex (female)	0.35	0.10	0.10	0.60	0.17	<.001	
GA group†							0.003
SES – low‡	−0.08	0.11	−0.37	0.20	−0.04	.446	
SES – high‡	−0.06	0.11	−0.34	0.15	−0.03	.567	
Sex (female)	0.08	0.09	−0.15	0.26	0.04	.361	
Indirect effects							
Attention via inhibitory control							
From GA group†	0.06	0.02	0.01	0.11	0.06	.003	
Academic achievement via inhibitory control							
From GA group†	0.03	0.01	0.002	0.05	0.05	.005	

LB, lower boundary; *UB*, upper boundary.
LB and UB of 95% CI around the regression coefficient B.
The full model for SEM is shown in **Figure**.
*Linear regression results (when outcome is continuous such as attention and academic achievement) prohibit regression results (when outcome is categorical such as inhibitory control and GA group).
†GA groups were very preterm (<32 wk GA), moderately preterm (32-33 wk GA), late preterm (34-36 wk GA), early term (37-38 wk GA), and full-term (39-41 wk GA).
‡Medium SES was the reference category.

Discussion

This study found that preterm birth negatively affects toddlers' abilities to inhibit undesirable behaviors as well as later attention regulation and academic achievement. Better inhibitory control at age 20 months predicted better attention regulation and academic achievement at age 8 years. Most importantly, adverse effects of preterm birth on later outcomes were partly mediated by children's early inhibitory control abilities after statistically adjusting for child sex and family SES. Resistance to temptation (ie, inhibitory control) is a relatively stable individual characteristic that predicts neural activation in frontostriatal circuitries that integrate motivational and self-control processes.[37] Previous studies showed that preterm children have difficulties with inhibitory control[8] and that these predict later learning and attention problems.[21,22] Our results suggest a dose-response effect of low GA at birth on inhibitory control across the whole GA spectrum. This new finding of a link between GA, inhibitory control, and later outcomes may represent an important new piece in the process of life-course underachievement after preterm birth. First, an easy 5 minute raisin game task represents a promising new tool for follow-up assessments after preterm birth. Second, the results of this study suggest potential innovative avenue to intervention. Early childhood trainings enhancing self-control may help alleviate long-term achievement problems,[38] and research on normal population samples has shown that executive function abilities including self-control can be trained.[39] According to Rose's public health-oriented approach to preventive medicine, shifting the population distribution of a risk factor (ie, low self-control) prevents more overall burden of disease than targeting only individual people at high risk.[40] However, preterm children may not only have lower inhibitory control abilities than full-term children but also be more vulnerable to environmental influences further decreasing their abilities to inhibit undesirable responses.[41,42] As our findings apply to the whole GA spectrum of preterm and full-term children, it may, thus, be recommended to adopt a combination of both population and targeted approaches to interventions in order to achieve the highest benefits.[43]

It has previously been reported that the relationship between GA and academic outcomes is not linear but curvilinear with increasingly stronger effects below 33-36 weeks[25,35,44,45]; thus, we explored this possibility. Results, however, showed that effects of preterm birth on early inhibition and effects of inhibition on later outcomes were overall not stronger in the more preterm compared with the term groups.

Prior studies have not assessed the links between preterm birth, early inhibitory control, and later achievement

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longitudinally in a large sample of children across the whole GA range. In our study, children's abilities were assessed by independent raters who were blinded to GA groups. As a direct and standardized measure of early human self-control behavior, the raisin game is not only more reliable and objective than questionnaires,[16] but it also has higher ecological validity than many other experimental paradigms. Such tasks have, however, been criticized as longer waiting times may not always indicate that a child exerted higher self-control but also that he or she was simply less tempted by the treat (ie, raisin)[16] or too shy to reach for the cup. Individual children's preferences and situational affects may have influenced their inhibitory control abilities (ie, waiting times). We used only 1 task to measure inhibitory control, whereas the use of multiple behavioral tasks assessing different aspects of the underlying construct of inhibition could have improved the reliability of results. Furthermore, for research as well as clinical practice, one could initially offer a selection of different treats (eg, raisin, chocolate, marshmallow, nibbles) to children and let them choose one in order to overcome individual preferences. Our participants were 20 months old when the task was administered. This is a very young age to test inhibitory control, and toddlers were given 2 training runs to allow them to understand the concept of the "game" they were asked to participate; these training runs may have positively influenced our participants' inhibitory control abilities. An additional pitfall of the task was that although behavioral inhibition (ie, waiting time) was measured in seconds as a continuous variable, it was not normally distributed in our sample (ceiling effects as 24% of toddlers waited an entire minute to touch and eat the raisin). As a result, we used a trichotomized variable. One may suggest an operationalization that is more tailored to children's ages and abilities (ie, allow longer waiting times) in future studies.

Moreover, we controlled for a number of confounding variables and found that neonatal medical risk and treatment (including surgeries) were not related to toddlers' inhibitory control abilities in our sample. Preterm individuals often have general cognitive impairments,[35,44,46] and these are associated with their academic outcomes. Although the relationship between cognitive abilities and achievement was not the focus of this study, we explored whether the effects of early inhibitory control on childhood outcomes were explained by toddlers' cognitive abilities, assessed with the Griffiths Mental Development Scales[36] at 20 months of corrected age. This alternative model showed that the effects of inhibitory control on later attention and achievement were significant over and above the effects of cognitive abilities; for reasons of statistical sparseness as well as clarity we, thus, decided to drop cognition from the model.

In summary, adverse effects of preterm birth on later attention regulation and academic achievement are partially mediated by children's early inhibitory control abilities. These findings provide new information about the mechanisms linking preterm birth with long-term attention difficulties and academic underachievement. The raisin game is an easy and effective tool that has good face-validity assessing inhibitory control in young children, takes only 5 minutes, and can be used in clinical practice for routine follow-up assessments after preterm birth in order to identify children at risk of attention and learning problems. Executive function abilities can be trained[39]; thus, our findings provide potential avenues to interventions aimed at increasing preterm children's long-term achievement. ■

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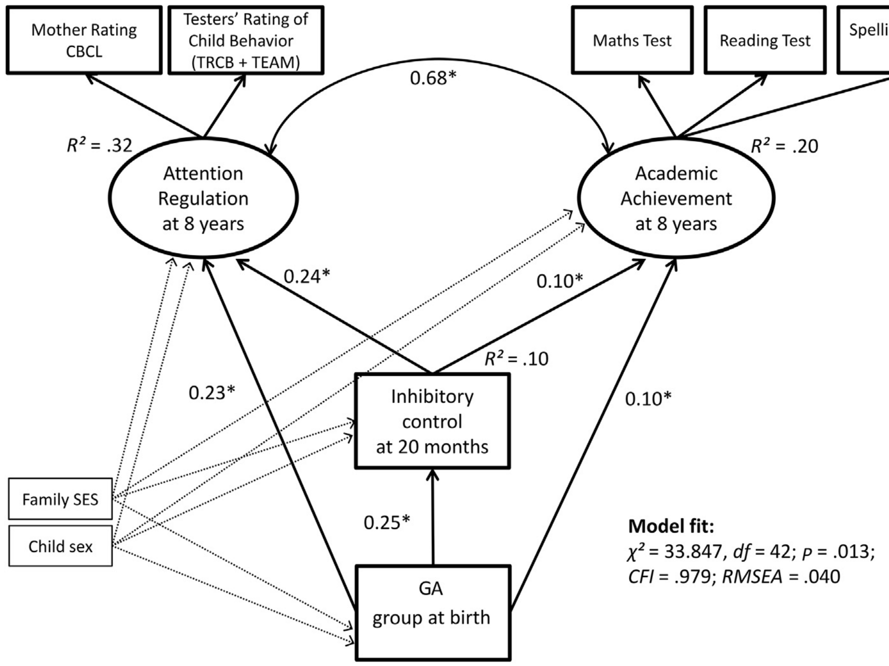

Figure. Structural equation model showing direct and indirect effects of preterm birth and early inhibitory control on attention regulation and academic achievement at age 8 years (N = 558). *Solid lines* represent hypothesized effects, *dotted lines* represent influences of control variables (standardized regression coefficients). R^2 variances indicated and other numbers are *B* coefficients. *P < .001. *CBCL*, Child Behavior Checklist; *TRCB*, Tester's Rating of Child Behavior; *TEAM*, team rating of attention regulation; *CFI*, Comparative Fit Index; *RMSEA*, Root Mean Square Error of Approximation.

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