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Early child stimulation and attention-related executive functions at 11 years: 2004 Pelotas birth cohort study

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Abstract

The study aimed to explore associations between socioeconomic position (SEP) indicators, early child stimulation (ECS) and attention-related executive functions (EF) at age 11. Children born in Pelotas, Brazil, in 2004, were recruited to a birth cohort (n=4231, non-response rate at recruitment <1%) and followed from birth to age 11. SEP variables were family income and maternal schooling. At the 24 and 48-month followups, five markers of cognitive stimulation and social interaction were recorded and positive answers were summed to a score ranging from 0-5. At age 11, attentional-switching and control, and selective attention were assessed using the adapted Test-of-Everyday-Attention-for-Children (TEA-Ch). We used multivariable logistic regression models and mediation analysis to investigate potential mediator role of ECS in the association between SEP and EF. 3106 children were included in the analyses. Less than 7% of the more stimulated individuals showed low performance in attention-related EFs at age 11 compared with almost 20% in the bottom groups of stimulation. Higher child stimulation scores were associated with fewer impairments in attentional-control (ORadj 0.84; CI 95% 0.72-0.98) and attentional-switching (ORadj 0.85; CI 95% 0.73-0.99). Mediation analysis suggested that for attentional-switching, ECS mediated almost 20% of the total protective effect of maternal schooling for impaired EF. Assuming causal relationships, if maximum stimulation was provided to all children, the advantageous effect of maternal schooling on EF would be reduced by 47%. ECS may represent a protective factor for cognitive impairments in childhood and can be easily implemented at relatively low cost.

Keywords: Cohort, cognitive impairments, stimulation, early adolescence, mediation analysis

Introduction

Executive functions (EFs; also called executive control or cognitive control) are cognitive skills necessary to deliberately control and regulate our thoughts, emotions and actions in the face of conflicts or distractions. There is general agreement that there are three core EFs which, although distinct, are interconnected: inhibitory control, working memory and cognitive flexibility[16]. Inhibitory control makes it possible to control one's attention, behaviour, thoughts and/or emotions; is the ability to resist against doing something tempting to privilege what's more appropriate or needed. Working memory allows to hold and store information temporarily, in order to sustain the processes of human thought and providing a link between perception, long-term memory and action. Cognitive flexibility builds on the other two and allows changing perspective when thinking and acting and considering different angles in the decision-making process.

EFs are important to every aspect of people's lives throughout the life cycle. People with better EFs enjoy a better quality of life, have better health and achieve better academic performance than counterparts with poor executive functioning [8, 43]. Previous studies have linked poor EFs to social problems such as crime and violence, obesity, overeating, substance abuse, poor productivity, difficulty finding and keeping a job and marital problems [1, 20, 21, 29, 46, 57].

The first years of children's lives are both a time of great opportunity and vulnerability for the development of EFs[24]. Investigations showed that EFs begin to develop shortly after birth, with ages 3 to 5 a window of opportunity for great growth in these skills[49, 58]. By age 7, some of the capabilities and brain circuits underlying executive function abilities are similar to those found in adults [9]. EFs continue to strengthen significantly during childhood, adolescence and early adulthood, declining with advanced age. Regional differences in the course of neural development may be responsible for different developmental trajectories of inhibitory control, working memory and cognitive flexibility. [5, 31]

Developmental trajectories of EFs over time do not depend only on the integrity of the prefrontal cortex. Brain regions and circuits associated with executive functioning have interconnections with deeper brain structures that control responses to threat and stress [18]. Besides, the stimuli that the brain receives are essential to the development of EF. Thus, maturing executive functioning both influences and is affected by children's experiences, environmental factors and stimuli. Several studies showed that the development of executive function skills may be hampered by exposure to disadvantage environments, trauma and chronic stress resulting from neglect, abuse and/or exposure to violence[15, 35, 44]. In addition, poverty and socioeconomic deprivation have been proved to detrimentally affect child EFs, but these evidences were mainly based on high-income countries samples [27]. Findings from low- and middle-income countries are scarce, although children from these regions comprise a significant proportion of world's population and are exposed to more adverse contexts [27].

Children's healthy development allows them to reach their full potential and increase their chances of achieving positive results in adult life[11]. There is evidence that preventive interventions aimed at promoting the healthy development of young children and improving EFs are helpful with evidence that disadvantaged children and those most behind on EFs may benefit the most[32]. Moreover, cognitive

stimulation and environmental enrichment were reported as efficient targets to improve child EFs development. However, there is a research gap regarding sociocultural contexts and cross-nation differences on the protective role of such interventions [27]. The present study aimed to:(1) examine the association between early child stimulation and attention-related executive functions at age 11 years and (2) explore the relationship between socioeconomic position indicators, early child stimulation and EFs in a large, prospective population-based study, the 2004 Pelotas Birth Cohort study from Brazil.

Methods

Participants

Pelotas is city located in the south of Brazil, with a population of about 330,000 inhabitants and where more than 99% of all deliveries take place in hospitals. During the calendar year of 2004, a birth cohort study including all births to mothers residing in the urban area was carried out in the city. Births were identified by daily visits to the five maternity hospitals. Mothers were interviewed soon after delivery and their newborns were examined by specially trained nutritionists under the supervision of a paediatrician. Using a pre-tested structured questionnaire, detailed information was obtained about demographic, socioeconomic, behavioural and biological characteristics, reproductive history and health care utilization. Newborns were examined in the first 24 hours after birth to estimate gestational age by physical and neurological assessment using Dubowitz' method[19] by the same interviewers who applied the questionnaires. Dubowitz' method consists in 34 items grouped into six dimensions (tone, tone type, reflexes, movements, abnormal signs and behaviour) and identifies neurologic abnormalities in preterm and term infants [19]. The non-response rate at recruitment was below 1%. A detailed description of the methodology is given elsewhere [48, 49]. All live births (n=4231) were enrolled in the cohort study. Followup assessments were made at home at mean (SD) ages 3.0 (0.1), 11.9 (0.2), 23.9 (0.4) and 49.5 (1.7) months and at a research clinic built especially for the study at 6.8 (0.3) and 11.0 (0.4) years, with follow-up rates between 87% and 96%.

Measures

Main predictor

At the 24 and 48-month follow-ups, five markers of cognitive stimulation and social interaction were recorded (each item a binary variable; yes/no): in the last week someone read/told a story to the child; the child went to a park/playground; went to other people's houses; watched TV and the child had a story book at home. Positive answers were summed to form a score ranging from 0-5. The mean value of the score assessed at 24 and 48-month follow-ups was used as the main exposure.

Outcomes

At the 11-year follow-up adolescents were assessed using the Test-of-Everyday-Attention-for-Children (TEA-Ch), a neuropsychological test battery, designed to be a game-like test for evaluation of attentional capacity [40, 46]. The test uses a series cognitive tasks to measure three attention-related EFs: attentional-control or inhibition (maintaining focus and inhibiting pre-potent responses), cognitive flexibility or

attentional-switching (switching between information) and selective-attention (attending to target stimuli among distracters). In addition, two other related cognitive abilities were assessed: verbal- and motor processing-speed (speed at which the child can read out words or put pen to paper, respectively). The tests were administered individually by trained research assistants (all of them psychologists) using a standardized procedure in a private and quiet room. The total duration of testing was about one hour, with a brief opportunity to rest between tasks as the examiner set up the next test. The tests used are described in detail below.

Attentional-control: The child was shown a trail made up of the numbers 1 and 2 (with 24 numbers in total). In the 'Same World' task, he or she had to read the numbers out as quickly as possible (while the tester kept his or her finger next to each in the trail until the child had read it correctly). The inhibition aspect of the 'Opposite Worlds' task was used to assess attentional-control EF. This is a basic form of 'Stroop' task, where the child is required to give a verbal response that contradicts the visual information given. The child was presented with a trail of digits and instructed to read out 'one' when presented with a 2 and 'two' when presented with a 1. The mean time taken to complete the 'Same World' task (time taken to read the trail of numbers) was taken as the measure of verbal-processing speed. Then mean time taken to complete the 'Opposite Worlds' task was taken as the measure of attentional-control. Higher reaction times indicate more impaired ability (taking into account verbal processing speed).

Attentional-switching: The dual-attention task of 'Sky-Search' subtest was used. The child initially selected pairs of spaceships from a task sheet containing matching and non-matching spaceships. The task was repeated but with the addition of another task: the child was also requested to count the number of noises played during the task. The difference in speed and accuracy when completing the task with and without the addition of noises was taken as an indication of switching. A higher score indicates more impaired dual attention.

Selective attention: The baseline condition of the 'Sky Search' task was used, how fast and accurately the child selected pairs of spaceships from the task sheet containing matching and non-matching spaceships (without the addition of the noises). In the test sheet, 20 (50%) of the spaceship pairs were identical. Reaction times in seconds to circle all of the spaceship pairs and number of correct pair circled were recorded. Motor-processing speed was taken as the time and accuracy to circle the spaceships in the 'practice' Sky Search' task sheet with only identical pairs. As recommended in the manual, motor processing reaction time was subtracted from the ability score to provide the final measure of selective attention. The higher the score, the more impaired the child's selective attention (taking into account motor ability).

Attention-related EFs variables were subjected to a Z-transformation and then dichotomized to define a low-performance group. This categorization was done using the cut-off point for the 10th percentile. Low

performance was defined as belonging to the worst 10th percentile (those children who took the most time to complete the task).

Potential confounding variables

An operational definition of confounding was used, that is, variables that were associated with both the outcomes and the predictor of interest, and not part of the causal chain [48].

Maternal variables included: family income in the month prior to delivery (collected as a continuous variable and categorized as quintiles); maternal schooling (complete years of formal education, categorized as 0-4, 5-8, 9-11 and \geq 12 years); age (<20, 20-34 and \geq 35 years); self-reported skin colour (categorized as white and black/other); parity (defined as the number of previous viable pregnancies and categorized as 0, 1 and \geq 2); smoking during pregnancy assessed retrospectively at birth by self-report (regular smokers were defined as those women who smoked at least one cigarette daily in any trimester of pregnancy); consumption of alcohol during pregnancy (any amount in any trimester of pregnancy) and maternal depression at the 12 month-follow up (assessed using the Edinburgh Postnatal Depression Scale, dichotomized at <13 and \geq 13 to produce a non-depressed/depressed classification).

Child variables included sex (male, female), preterm birth (gestational age less than 37 weeks) and number of siblings living in the same household at the 48-month follow-up (0, 1, and ≥ 2).

Statistical analyses

Prevalence rates of low performance in each attention-related EF were presented for every maternal and adolescent characteristic and chi-squares were calculated.

The association between early child stimulation score andlow performance in attention-related EFswas assessed through logistic regression. Variables were grouped and included in the adjusted analysis using a backward strategy selection. The difference in mean age of the adolescents at the 11-year followup was controlled for by the inclusion of age as a covariate in all analyses. Logistic regression models were conducted in the following order for each outcome: a) adjusting for age at time of testing (model 1), b) adjusting for maternal characteristics (model 2) and c) adjusting for model 2 variables plus child characteristics (model 3). If the significance level was below 0.20, the variable remained in the model as a potential confounder for the next level[40].

In addition, we used G-computation analysis[14] to evaluate if our main exposure (early child stimulation score) was a mediator in the association between maternal schooling or family income and EFs at 11 years. For that, we proposed a direct acyclic graph (DAG) in which sex, preterm birth, number of siblings, maternal age, smoking and alcohol use during pregnancy, and maternal depression were considered post confounders and maternal skin colour was considered a base confounder (Figure 2). When we analysed the effect of family income,maternal schooling was also considered a base confounder (Supplementary material Figure 1). We calculated the Natural Direct effect (NDE) and Natural Indirect effect (NDI) of the total effect of these socioeconomic position variables over the outcomes in order to estimate the percentage of the effect mediated by our early child stimulation score. In addition, we

calculated the controlled direct effect (CDE), from which we estimated the percentage of the effect that would still be present if we were able to keep our mediator constant, in other words if we were able to give all children the same stimulation, for our analysis we used the highest possible stimulation score of "5". For these analyses we dichotomize maternal schooling variable (0-4 years of schooling / 4 or more years) and use family income as a continue variable. We included in our models an interaction variable between exposure and mediator.

All analyses were performed with Stata software, version 14.1 (StataCorp LP, College Station, Texas).

Ethics

The study protocol of each follow-up was approved by the Medical Ethics Committee of the Federal University of Pelotas, affiliated with the Brazilian Federal Medical Council. Written informed consent was obtained from mothers (or caregivers) and adolescents who accepted to participate in the study.

Results

Attrition analysis

Of the 4231 participants constituting the original cohort, 98 died in the first eleven years of life and 3566 were interviewed at eleven years (68 refused to participate and 499 adolescents could not be found). Data on EFs and child stimulation score were available on 3176 adolescents. Multiple pregnancies were excluded for the analyses (n=70). Only adolescents from singleton pregnancies were included in the analyses (multiple pregnancies excluded; n=70). Children with severe mental impairment were excluded from the analyses (n=12). A final sample of 3106 adolescents was included in the present study (73.4% of the original cohort).

Missing information was more common among adolescents born to mothers less educated, younger, multiparous and smokers. Adolescents included in the analyses had lower frequencies of preterm birth than those excluded (Table 1).

Sample description

A description of the adolescents under study and their mothers is given in Table 2. About 15% of the mothers had ≤ 4 years of education and 10% had completed 11 years of education. Most of the mothers were white (74%), primiparae (40%), aged between 20 and 34 years old (67%) and did not smoke (74%) or drink alcohol during pregnancy (96.9%). Prevalence of maternal depression at the 12-month follow-up was almost 14%. There was a slight predominance of boys(52 vs 49%) in the study group. Approximately 39% were only children and 13% of all adolescents were born preterm.

Effects of maternal and child characteristics on low performance in attention-related EFs

Adolescents belonging to the poorest families, those of mothers with the lowest schooling and those who had three or more siblings living in the household showed the highest frequencies of low performance in attention-related EFs at age 11. Adolescents of multiparous mothers, and those of women self-classified as black/other were more likely to have higher frequency of low performance in attentional-control and selective attention than those born to women with two or more previous live births or self-classified as white. Male adolescents, those born preterm and adolescents of mothers that smoked during pregnancy were more likely to have low performance in selective attention. Maternal age, alcohol consumption during pregnancy and maternal depression were not associated with any of the outcomes.

Early child stimulation score

At the 24 and 48-month follow-ups, in the week prior to the interview, 54% and 67% of children had someone who read or told them a story; 42% and 69% went to a park/playground; 90% and 89% went to other people's houses; 84% and 97% watched TV and 57% and 78% of children had a story book at home, respectively. Outdoor activities (going to a park/playground and to other people's houses) did not differ according to the month of data collection.

Early child stimulation score was approximately normally distributed. The overall mean was 3.56 with standard deviation (SD) 0.88. Median value was 3.50.

Less than 1% (23 children) had a score ≤ 1 (Table 3). The scores with the highest frequencies were between 3 and 4.5, including approximately 74% of the children, whereas 8% had a score of 5. The most common activities for children with scores below 3 were going to someone else's house and watching TV. The least common activity for children with scores between 3 and 4 was going to a park or playground (Table 3).

Early child stimulation score and maternal and child's characteristics

Children with the highest stimulation score were those from the wealthiest families, born to mothers with 12 or more years of education, primiparae, self-identified as white, women that did not smoke during pregnancy and did not suffer depression at the 12-month follow-up. Only children and those born at term had higher stimulation scores than those with siblings and those born preterm. Mean stimulation score was similar among boys and girls (Table 4).

Early child stimulation score and low performance in attention-related EFs

Children less stimulated had greater frequencies of low performance in attention-related EFs than those with higher stimulation scores (Figure 1). Less than 7% of the more stimulated individuals at early age presented low performance at age 11 compared with almost 20% in the bottom groups of stimulation. Low performance in attention-related EFs was strongly associated with early child stimulation score in the crude analyses. A reduction in the magnitude of this association was observed after adjusting for maternal and child characteristics (Table 5). Nevertheless, in the final model, nearly 15% decrease of low performance in attentional-control and attentional-switching was observed for a one-unit increase in the early child development score.

Analyses of mediation

Early child stimulation score did not mediate the effect of maternal schooling or family income over attentional-control or selective- attention EFs (Supplemental data file Table 1). However, for attentional-switching, early child stimulation score mediated 17.5% of the total effect of maternal schooling, and if we were able to give full stimulation to all children (score=5), the effect of maternal schooling on attentional switching would be reduced in 46.5% (Figure 2a). In the case of family income, stimulation "naturally" mediate 3.3% of the effect over attentional-switching, however, if we were able to give full stimulation the percentage of effect that would still be present would be equal to zero (Figure 2b).

Discussion

Early child stimulation score was negatively associated with low performance in attention-related EF at age 11 in the crude analyses. Even though the magnitude of this effect decreased after adjustment, there is some evidence that child stimulation performed in the early years of life was associated with reduced risk of impaired scores of attention-related executive functions, mainly attentional-control and attentional-switching, at age 11.

Research has indicated that sensitive periods are present in many domains of human cognition, and the development of EFs is not an exception. A sensitive period represents a time window of rapid individual change (i.e. brain structure and function) where an environmental stimulation has a stronger effect on development and subsequent disease risk than it would at other times.[4] During early childhood there is high brain plasticity and a complex interaction of genetic and experiential factors that contribute to shape the emerging brain.[34]Several authors within applied cognitive neuroscience have highlighted the importance of early detection and timely intervention strategies.[28, 52] The current paper demonstrated that early stimulation is important. However, in the present paper we did not compare time periods of stimulation and it could be possible that later stimulation may also be just as important as early stimulation for the EFs investigated and is an important future direction.

Even though research has suggested that EFs are trainable and can be improved with practice in children, adolescents and adults,[17, 33] some authors suggest that the earlier the training is applied, the more effective the intervention or program could be.[9, 56] A review of diverse EF interventions with children and adolescents reported a number of activities that have been shown to improve EFs, such as computerized training, non-computerized games, aerobics exercise and martial arts, mindfulness practices and add-ons to school curricula.[17] EF training appears to transfer, but the transfer to more than one objective measure of EFs on which the individual had not been trained, in most cases is narrow. There is controversy which type of training most efficiently supports the occurrence of transfer effects and the duration of these benefits.[23]

Parental cognitive stimulation, conceptualized as parents' didactic efforts to improve cognitive and language development by engaging their children in activities and providing rich and stimulant environments, is a strong predictor of cognitive abilities among children. [13, 39] Cognitive stimulation has been of interest for researchers aiming to understand the potentially modifiable environmental processes underlying socioeconomic disparities in children's cognitive outcomes.[53] The early child stimulation score applied in the present study was composed of five simple questions, intended to be markers of cognitive stimulation, parent-child interaction and more general interpersonal interactions. In previous research of the 2004 Pelotas cohort study, this score was shown to be strongly and independently associated with child development at the age of 24 months, showing much stronger effect among children from mothers with a low level of schooling.[3] A strength of this analysis is that we have extended such findings to objective and child completed tasks at age 11 years. Even though these markers cannot be directly translated into intervention strategies, they suggest that relatively simple stimulation strategies could have an important effect on attention-related EFs some years later. There is a growing body of evidence showing examples of successful cognitive stimulation interventions targeting disadvantaged families and their children from developing countries. [2]A randomized intervention conducted in 1986–1987 that gave psychosocial stimulation to growth-stunted Jamaican toddlers showed that a simple psychosocial stimulation intervention in early childhood for disadvantaged children had a substantial effect on labour market outcomes and compensated for developmental delays.[25]Specifically in Brazil, a studied conducted in the Northeast region showed that a very simple strategy such as lessons for mothers about how to interact with their infants can improve their mental and psychomotor development. [2] That said, it remains a

possibility that more cognitively able children may evoke more stimulation from caregivers they may respond better and ask for such activities. Thus, some level of bidirectionality in the associations is likely.

Both animal and human studies indicate that excess stress in early life is an important environmental condition that may influence brain development with the potential to adversely affect shortand long-term neurodevelopment outcomes. [22, 37, 38, 45] Exposure to early life adversity has been associated with deficits in the development of children's working memory, attention and inhibitory control skills, [36, 42] above and beyond the effects of early deprivation on global IQ. [30] In line with previous investigations, in our study, socioeconomic position (SEP) indicators were negatively associated with low performance in attention-related EFs. Higher SEP has been associated with better executive function performance across different measures of SEP and across different dimensions of executive function.[6, 26]. SEP affects families and child development in terms of both family stress processes and family investments in children. The family investment theory postulates a positive association between family income and child development. Low income would reduce the quantity and quality of investments in children (i.e. purchase of goods and services by parents), which in turn would affect their development and well-being. However, low SEP can also be related to higher levels of stress and greater irritability, depression and anxiety in the parents, which in turn could impair interactions between parents and children (family stress theory).[12]Recently, a growing body of work has found associations between SEP and both function and structure of brain areas that underlie executive function capabilities.[7, 54]

Much progress has been made in Brazil in the last decades to ensure universal access to primary education and to improve the quality of schools around the country.[55] However, data from the 2004 Pelotas cohort study indicated that almost one in 10 mothers did not complete primary education. Our study found that for attentional-switching, early child stimulation mediated almost 20% of the total effect of maternal schooling, and in the hypothetical situation where maximum stimulation is provided to all children, the advantageous effect of maternal schooling on this EF would be reduced in 47%. This result is important due to the possibility of reducing inequalities in development without acting on the more distal determinants and also more difficult to be modified, but directly on the children, giving them adequate stimulation in the first years of life. This could be provided either by parents at home or by the local community.

A major strength of the present study was the method of data collection (prospective information obtained among a large unselected population) combined with the use of standardised measurements performed by trained fieldworkers, high follow-up rates and low missing data for most variables of the study. There are, however, a number of limitations to this study that must be considered. First, it is possible that different results would have been obtained if all children whose mothers originally enrolled in the 2004 cohort study were included in the analyses. However, children lost to follow-up were of poorer, younger and less educated women than those included, suggesting that the current associations could be underestimated, and in the event that they had been included we would have been able to see greater protective effects of child stimulation on executive functions at 11 years. Second, neither specific measure of parental EFs nor IQ was available in 2004 Pelotas cohort study, preventing us to explore the role of inheritance of poorer EFs and IQ on the associations studied. Third, as associations tended to be weakened

after adjustment, the possibility of residual confounding cannot be completely ruled out. Other studies comparing results among different settings are necessary to add evidence to the literature. Finally, our results were drawn for a single middle-sized city and may not represent the Brazilian population as a whole.

Conclusions

In our study child stimulation performed in the early years of life had a positive effect in attentional-control and attentional-switching EFs at age 11. Early child stimulation may represent an easy-modifiable protective factor for preventing cognitive impairments in childhood. Such impairments are linked with a myriad of negative long-term outcomes, such as poor academic success, social problems and mental and physical health disorders in later life. Given the large numbers of children in developing countries that are at heightened risk for poor development due to a multitude of risk factors (e.g., poverty, low maternal education, poor nutrition), easy-implementable, low-cost and effective interventions must be a priority in policy-makers agenda.

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Conflict of interest

The authors have no conflicts of interest to declare

Authors' contributions

Alicia Matijasevich, Rebecca M. Pearson, Chritian Loret de Mola and Aluísio J. D. Barros participated in the design of the study, undertook the analysis, interpreted the results and drafted the first version of the article. Jessica M. Maruyama, Carolina La Maison, Tiago N. Munhoz, Iná S. Santos and Fernando C. Barros collaborated in the interpretation of the findings and writing of the article. All authors approved the final version of the manuscript submitted.

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Variables	Included	Not included	p-value*
	(n=3106)	(n=1125)	
Family income (Real), mean (sd)	809.5 (1095.1)	795.7 (1149.5)	0.721**
Maternal schooling (years), mean (sd)	8.2 (3.4)	7.7 (3.7)	< 0.001**
Maternal age (years), mean (sd)	26.3 (6.9)	25.4 (6.6)	< 0.001**
Parity ≥2, %	32.9	39.2	0.002
Maternal skin colour, White, %	73.5	71.7	0.299
Smoking during pregnancy, %	26.5	30.3	0.046
Alcohol during pregnancy, %	3.1	4.0	0.130
Child's sex, male, %	51.5	52.8	0.609
Preterm birth, %	12.8	18.4	< 0.001
	12.0	10.7	NO.001

Table 1. Comparison of maternal and child characteristics between those included and not included in the present study

* x^2 test; ** ANOVA test

		Low performance in		
Variables	n (%)	Attentional-	Attentional-	Selective
		control (p10)	switching (p10)	attention (p10)
		n (%)	n (%)	n (%)
Family income (quintiles)		p<0.001	p=0.021	p<0.001
1 st (poorest)	560 (18.0)	74 (13.2)	64 (11.4)	69 (12.3)
2^{nd}	632 (20.4)	78 (12.3)	68 (10.8)	81 (12.8)
3 rd	629 (20.3)	62 (9.9)	70 (11.1)	65 (10.3)
4 th	680 (21.9)	52 (7.7)	50 (7.4)	52 (7.7)
5 th (wealthiest)	605 (19.5)	27 (4.5)	46 (7.6)	26 (4.3)
Maternal education (v)		p<0.001	p<0.001	p<0.001
<=4	445 (14.5)	63 (14.2)	58 (13.0)	84 (18.9)
5-8	1252 (40.7)	150 (12.0)	142 (11.3)	137 (10.9)
9-11	1083 (35.2)	70 (6.5)	76 (7.0)	60 (5.5)
12+	298 (9.7)	10 (3.4)	21 (7.1)	12 (4.0)
Maternal age (v)		n=0.562	n = 0.259	n = 0.084
<-19	578 (18.8)	p=0.502 60 (10 4)	p=0.25	p=0.004 60 (10 4)
20-34	2066 (67.0)	187 (9.1)	192 (9.3)	202 (9.8)
35+	438(14.2)	44(101)	37(85)	202 (9.0)
55	430 (14.2)	44 (10.1)	57 (0.5)	2) (0.0)
Parity		<i>p</i> =0.024	<i>p</i> =0.073	p = 0.002
0	1232 (40.0)	103 (8.4)	121 (9.8)	99 (8.0)
1	836 (27.1)	72 (8.6)	64 (7.7)	70 (8.4)
2+	1015 (32.9)	117 (11.5)	109 (10.7)	123 (12.1)
Maternal skin colour		<i>p</i> <0.001	<i>p</i> =0.397	<i>p</i> <0.001
White	2284 (73.5)	181 (7.9)	213 (9.3)	167 (7.3)
Black/other	822 (26.5)	112 (13.6)	85 (10.3)	126 (15.3)
Smoking during pregnancy		n=0.356	n=0.990	n=0.021
No	2266 (73 5)	208(92)	216(95)	198(87)
Yes	817 (26.5)	84 (10.3)	78 (9.6)	94 (11.5)
Alcohol during pregnancy		n = 0.854	n = 0.454	n = 0.711
No	3011 (06.0)	p=0.034 270 (9.0)	p=0.434 201 (0 7)	p=0.711 283 (9.4)
NO	05(31)	270(9.0) 8 (8 4)	231(9.7) 7(7.4)	203(9.4) 10(105)
1 05	95 (5.1)	8 (8.4)	7 (7.4)	10 (10.3)
Maternal depression at 12m		<i>p</i> =0.241	<i>p</i> =0.764	<i>p</i> =0.390
No	2619 (86.1)	238 (9.1)	254 (9.7)	244 (9.3)
Yes	423 (13.9)	46 (10.9)	43 (10.2)	45 (10.6)
Child's sex		p=0.407	p=0.744	<i>p</i> =0.003
Male	1598 (51.5)	144 (9.0)	156 (9.8)	175 (11.0)
Female	1508 (48.6)	149 (9.9)	142 (9.4)	118 (7.8)
Preterm hirth		n-0.100	n - 0.112	n<0.001
No	2689 (87 3)	248(92)	247(92)	233(87)
Yes	393 (12.7)	44 (11.2)	46 (11.7)	59 (15.0)
		(/	- ()	()

Table 2. Maternal and child characteristics and low performance in attention-related executive functions at age 11

Number of siblings		<i>p<0.001</i>	<i>p<0.001</i>	<i>p<0.001</i>
0	1201 (38.7)	76 (6.3)	103 (8.6)	83 (6.9)
1	1110 (35.7)	96 (8.7)	105 (9.5)	103 (9.3)
2	480 (15.5)	52 (10.8)	38 (7.9)	55 (11.5)
3+	315 (10.1)	54 (17.1)	52 (16.5)	52 (16.5)
NT / 1	2, , 10	.1		

Note: p-value = x^2 test; p10 = worst percentile (those adolescents who took the most time to complete the task)

Early child	n	Percentage of children reporting each activity ^b				
stimulation score ^a		Visit	TV	Book	Story	Park
0	1	0	0	0	0	0
0.5	1	0	100	0	0	0
1	21	33.3	90.5	19.1	4.8	0
1.5	55	80.0	89.1	21.8	18.2	7.3
2	177	88.7	95.5	31.1	24.3	24.9
2.5	319	96.6	98.1	57.4	41.4	44.5
3	502	96.0	98.8	78.7	70.7	48.4
3.5	639	98.8	98.8	90.5	83.4	68.9
4	620	99.2	99.5	98.2	94.7	78.4
4.5	532	100	100	100	100	100
5	239	100	100	100	100	100

Table 3. Percentage of children reporting activities or having a book by child stimulation score

^a Mean value of the scores assessed at 24 and 48-month follow-ups

^b Visit, child went to someone else's place; TV, watched TV for any amount of time; Book, child owns a story book; Story, someone told or read a story to the child; Park, child was taken to park or playground. All activities refer to the week prior to the interview

Variables	Mean (SD)	p-value*
Family income (quintiles)		p<0.001
1 st (poorest)	3.25 (0.95)	*
2 nd	3.29 (0.86)	
3 rd	3.46 (0.84)	
4 th	3.73 (0.80)	
5 th (wealthiest)	4.04 (0.72)	
Maternal education (y)		p<0.001
<=4	2.97 (0.85)	1
5-8	3.36 (0.85)	
9-11	3.84 (0.75)	
12+	4.23 (0.65)	
Maternal age (y)		p<0.001
<=19	3.44 (0.86)	1
20-34	3.61 (0.88)	
35+	3.51 (0.91)	
Parity		p<0.001
0	3.73 (0.83)	1
1	3.61 (0.87)	
2+	3.31 (0.90)	
Maternal skin colour		p<0.001
White	3.62 (0.87)	1
Black/other	3.40 (0.89)	
Smoking during pregnancy		p<0.001
No	3.65 (0.88)	1
Yes	3.33 (0.87)	
Alcohol consumption during pregnancy		p=0.052
No	3.57 (0.88)	*
Yes	3.39 (0.86)	
Maternal depression at 12m	· · ·	p<0.001
No	3.60 (0.88)	*
Yes	3.38 (0.92)	
Child's sex	· · ·	p=0.365
Male	3.55 (0.88)	*
Female	3.58 (0.88)	
Preterm birth	· · ·	p=0.003
No	3.58 (0.88)	*
Yes	3.44 (0.92)	
Number of siblings		p<0.001
0	3.77 (0.83)	•
1	3.58 (0.87)	
2	3.36 (0.88)	
3+	3.01 (0.86)	

Table 4. Early child stimulation score and maternal and child characteristics

Note: SD= standard deviation; * ANOVA test

Table 5. Crude and adjusted logistic regression models investigating the association between early child stimulation score and low performance in attentionrelated executive functions at age 11

	Attentional-control (p10)	Attentional- switching (p10)	Selective attention (p10)
	OR (CI 95%)	OR (CI 95%)	OR (CI 95%)
Model 1 = adjusted for age at time of testing	<i>p</i> <0.001	<i>p</i> <0.001	<i>p</i> <0.001
	0.62 (0.54; 0.71)	0.74 (0.65; 0.85)	0.67 (0.59; 0.77)
Model 2 = Model 1 + maternal characteristics	$p=0.014^a$	$p=0.011^{c}$	$p=0.053^{e}$
	0.82 (0.71; 0.96)	0.82 (0.71; 0.96)	0.86 (0.74; 1.00)
Model 3 = Model 2 + child's characteristics	$p=0.026^{b}$	$p=0.034^d$	$p=0.096^{f}$
	0.84 (0.72; 0.98)	0.85 (0.73; 0.99)	0.88 (0.75; 1.02)

Note: p10 = worst percentile (those adolescents who took the most time to complete the task)

^a Adjusted for Model 1 + maternal characteristics (family income, maternal education, parity and skin colour)

^b Adjusted for Model 2 + child's characteristics (preterm birth and number of siblings)

^c Adjusted for Model 1 + maternal characteristics (family income, maternal education and parity)

^d Adjusted for Model 2 + child's characteristics (preterm birth and number of siblings)

^e Adjusted for Model 1 + maternal characteristics (family income, maternal education, age, parity, skin colour and smoking during pregnancy)

^f Adjusted for Model 2 + child's characteristics (preterm birth and number of siblings)

		Attentional-control	1	Attentional-switching		Selectiveattention	
		B (SE)	%	B (SE)	%	B (SE)	%
Schooling	NDE	0.046 (0.024)	1	0.031 (0.017)	0.8246	0.083 (0.030)	1
	NIE	-0.011 (0.015)	0	0.007 (0.013)	0.1754	-0.007 (0.016)	0
	CDE	0.0986 (0.056)	1	0.020 (0.025)	0.5351	0.125 (0.053)	1
Income	NDE	-0.024 (0.014)	1	-0.020 (0.011)	0.9672	0.012 (0.011)	1
	NIE	0.005 (0.007)	0	-0.001 (0.007)	0.0328	-0.006 (0.007)	0
	CDE	-0.037 (0.019)	1	0.002 (0.012)	0	-0.017 (0.016)	0

Supplemental data file Table 1. G-computation analysis to evaluate if early child stimulation score was a mediator in the association between maternal schooling or family income and executive functions at 11 years.

NDE = natural direct effect;

NIE = natural indirect effect (effect that is mediated through the stimulation score);

CDE = control direct effect (effect that would still be present if the score stimulation was kept constant at a maximum level)