



## The association between pre-pregnancy overweight/obesity and offspring's behavioral problems and executive functioning

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### ABSTRACT

The prevalence of obesity among women of childbearing age has been rising dramatically over the last decades. Pre-pregnancy obesity may have negative neurodevelopmental consequences for the offspring. The present study examined the association of maternal pre-pregnancy overweight and obesity with child behavior problems and executive functioning at age 5 years. Data of 4094 mother-child pairs of the Amsterdam Born Children and their Development birth cohort study was used. Child behavioral problems were assessed with the maternal and teacher version of the Strengths and Difficulties Questionnaire. Two executive functioning constructs, inhibitory control and cognitive flexibility, were measured with the Response Organization Objects task of the Amsterdam Neuropsychological Tasks test battery. Increased maternal pre-pregnancy BMI was associated with an increase in children's behavioral problems (OR total behavioral problems reported by mothers pre-pregnancy obesity versus normal weight: 1.78 [95% CI 1.17 to 2.69] and reported by teachers for pre-pregnancy overweight versus normal weight: 1.32 [1.00 to 1.74]). Maternal pre-pregnancy obesity was associated with an increase in peer relationship problems reported by teachers (OR: 1.77 [1.18 to 2.64]). It was also associated with a small decrease in cognitive flexibility (increased Reaction Time in ms:  $B = 67.59$  [5.88 to 129.30] and Within Subject Standard Deviation in ms:  $B = 76.46$  [32.00 to 120.92]), but not with inhibitory control. Cognitive flexibility did not mediate the association between maternal pre-pregnancy BMI and children's behavioral problems.

### 1. Introduction

Obesity is a major public health problem. Among women of reproductive age, the prevalence of obesity was 30% in the United States and the prevalence ranged from 7 to 25% in Western European countries in 2016 [1]. Obesity before and during pregnancy increases the risk of pregnancy complications such as gestational diabetes and pre-eclampsia [2]. Moreover, based on the 'Developmental Origins of Health and Disease' hypothesis stating that prenatal factors impact fetal development and thereby can induce long lasting consequences for offspring's physical and mental health, it may also be expected that maternal obesity has long term effects for the health of the child [3].

Several studies have shown that children of mothers who were obese before and during pregnancy seem to more often have internalizing and externalizing problems than children of mothers with a normal weight; this difference can already be observed at preschool age

[4–6]. Children of obese mothers had a 40% higher odds of having emotional or behavioral problems compared to children of normal weight mothers [7]. Additionally, children of obese mothers seem to more often have developmental disorders: the odds of having an attention deficit hyperactivity disorder (ADHD) or autism spectrum disorder (ASD) is increased by 62 and 36% respectively [4,7,8]. However, not all studies find consistent associations of maternal pre-pregnancy overweight or obesity with child behavioral problems within their study [9,10]. Also, some studies, although not all [11] have failed to find an association of maternal pre-pregnancy weight and child behavior using more advanced data analysis techniques such as sibling analyses and paternal BMI analyses [12,13], rendering it questionable whether maternal pre-pregnancy weight is causal to offspring behavioral problems.

Most studies did not examine the interaction of child's sex with maternal BMI before and during pregnancy on child's behavior,

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although boys may be at higher risk for behavioral problems after exposure to maternal obesity than girls [14,15]. Also, most studies on this topic rely on parental report to measure child behavior [7], but it could be better to incorporate data of child behavior from more than one informant, preferably both parent and teacher report [16,17]. One reason for this is that child behavior varies across home and school situations [17]. Also, some behavioral problems are more difficult to observe and rate for parents than teachers; teachers have the opportunity to see children interact with many other children in the classroom [16,17]. A study that used both parental and teacher reports showed a positive association of maternal pre-pregnancy BMI with child behavioral problems reported by teachers but not reported by mothers [18].

Maternal obesity before and during pregnancy has not only been associated with behavioral problems but also seems to have a negative impact on children's neurocognitive development [19], such as children's executive functioning (EF) performance [20–22]. Moreover, EF has been shown to mediate the association between maternal obesity before pregnancy and children's ADHD symptoms [22]. Although the association between EF and mental health disorders is rather complex [23], there are clear indications that EF plays a role in the development of children's behavioral problems in the general population [23–25]. For example, the EF skills flexibility and inhibition may be important skills in predicting child behavior, including both externalizing and internalizing behavior [24]. To date, it has not been tested whether similar mediation patterns apply in children of obese mothers with respect to other behavioral problems than ADHD symptoms.

The aim of this study was to replicate and extend previous findings linking maternal pre-pregnancy overweight and obesity with children's behavioral problems (by using both maternal and teacher reports) and EF. Also, the potential mediating role of children's EF was examined.

## 2. Material and methods

### 2.1. Participants

This study was embedded in the Amsterdam Born Children and their Development (ABCD) study (<http://www.abcd-studie.nl>), a population-based prospective birth cohort study that examines the relationship between maternal lifestyle and psychosocial determinants during pregnancy to multiple aspects of development and health of the child. Details on the design, inclusion and data collection of the ABCD study have been described elsewhere [26]. Between January 2003 and March 2004, a total of 8266 pregnant women in Amsterdam filled out a questionnaire and were enrolled during their first prenatal care visit. In 2008 and 2009, 6161 mothers (75% of the original sample) were sent a follow-up questionnaire, approximately two weeks after their child's 5th birthday. Attrition was largely due to withdrawal, infant or maternal death and loss-to-follow-up as a result of an unknown address or emigration. The study population of the current study included only mother-child pairs of whom the pre-pregnancy Body Mass Index (ppBMI) was known and at least one of the relevant child outcomes was available. All singletons of mothers with a ppBMI  $\geq 18.5$  were included; singletons of mothers with underweight were excluded. This resulted in a final dataset of 4094 (50% of original sample) mother-child pairs. We applied no restrictions regarding maternal age, ethnicity and socio-economic status (SES). Approval of the study was obtained from the Central Committee on Research Involving Human Subjects in the Netherlands, the Medical Ethical Committees of the participating hospitals and from the Registration Committee of the Municipality of Amsterdam. Mothers gave written informed consent for themselves and their children.

### 2.2. Measures

#### 2.2.1. Pre-pregnancy body mass index

ppBMI was calculated based on retrospectively self-reported height and weight, which was assessed using a questionnaire filled out in the second trimester of pregnancy with the following questions: "How tall are you?" and "What was your last measured weight before pregnancy?". Missing data on these questions was completed with data from pregnancy files. ppBMI was categorized (normal: 18.5 till 25 kg/m<sup>2</sup>, overweight: 25 till 30 kg/m<sup>2</sup> or obese:  $\geq 30$  kg/m<sup>2</sup>).

#### 2.2.2. Child behavior

Children's behavior was reported by their mothers and the primary school teachers using the validated Dutch version of the Strengths and Difficulties Questionnaire (SDQ) for parents and teachers respectively when the child was 5 years old (range: 5 to 7 years) [27]. The SDQ is a short screening questionnaire for behavioral problems and has been shown to be reliable and valid in the Dutch population of 5 to 6 years old children [16]. The questionnaire consists of 25 questions with a 3 points Likert Scale (*very true, partly true, not true*). The 'total behavioral problems' scale as well as the subscales 'emotional problems', 'conduct problems', 'hyperactivity/inattentive problems' and 'peer relationship problems' (all consisting of five questions per subscale) were used. A higher scale score indicates more behavioral problems. The scores were dichotomized into normal and borderline/clinical score using the 90th percentile score (based on scores of Dutch children at age 5 to 6 years) as cut-off scores for the four subscales and the sum scale: respectively 12, 4, 3, 6 and 2 for the maternal reported SDQ and 11, 3, 2, 6 and 3 for the teacher reported SDQ [16]. Analyses were performed with maternal reported outcomes and teacher reported outcomes separately.

#### 2.2.3. Child executive functioning

Two executive functions, inhibitory control and cognitive flexibility, were measured with the Response Organization Objects (ROO) task of the Amsterdam Neuropsychological Tasks (ANT) test battery [28]. Children completed the ROO task on a laptop during the extensive examination at 5 years (range 5 to 7 years) [29]. Children were individually tested pre-dominantly in the morning or early afternoon during school days in a quiet room by trained investigators. The tasks were presented on a laptop and responses to task stimuli had to be made using the mouse. Before starting each task, the investigator gave a verbal task instruction while showing the child an example of the task on the computer screen. Thereafter, the child did a practice run to become familiar with the task stimuli and response mode. When the investigator felt sure that the child understood the task demands, the test trial started [29].

The ROO task consisted of three parts: A fixed congruent part (part 1): When a red ball appeared on the left side of a white fixation cross on the screen, children had to click the left mouse button with their left forefinger, and vice versa; a fixed incongruent part (part 2): When a white ball appeared on the left side of the fixation cross, children had to click the right mouse button with the right forefinger, and vice versa; and a random mix part of part 1 and 2 (part 3) [30]. There were 30 trials per part in which signal duration was variable until the child responded. Part 1 and 2 had a duration of 3 to 4 min each, and part 3 had a duration of 6 to 8 min. Children made a valid response when they clicked the correct mouse button 200 to 6000 ms after the stimulus appeared on the screen [29]. Inhibitory control was evaluated by contrasting part 2 and part 1 on the outcome measures speed (mean reaction time, MRT), fluctuation in speed (within subject standard deviation in mean reaction time, WSSD), and accuracy (percentage of errors, ER). Cognitive flexibility was evaluated by contrasting the congruent part of the random mixed part 3 with part 1 on the outcome measures speed (MRT), fluctuation in speed (WSSD) and accuracy (ER) [29,31]. The cognitive flexibility test was more complex than the inhibitory control test since cognitive flexibility required both the

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