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### NeuroToxicology

Full Length Article

# Prenatal smoking exposure, measured as maternal serum cotinine, and children's motor developmental milestones and motor function: A follow-up study

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#### ABSTRACT

*Background:* Cohort studies have indicated an association between prenatal smoking exposure and children's motor difficulties. However, results are inconsistent and exposure is most often self-reported. Studies indicate that measurement of serum cotinine can result in a more accurate status of smoking exposure in comparison with self-report.

*Objectives:* To investigate whether prenatal smoking exposure, measured as maternal serum cotinine, is associated with maternal interview based assessment of motor development in infancy (age at crawling, standing-up and walking) and motor skills at young school age (assessed by the Developmental Coordination Disorder Questionnaire 2007 (DCDQ'07)).

*Method:* In 2002–2004, 1,253 pregnant women from Greenland and Ukraine were included in the INUENDO birth cohort. The participating women filled in questionnaires and 1,177 provided blood samples, which were analyzed for serum cotinine. Smokers were defined as women with a serum cotinine concentration >10 ng/ml. At follow-up when the offspring were 6–9 years of age 1,026 of the parents from the cohort participated. They completed an interview-based questionnaire including questions about age at motor milestones of their children. In addition, child motor development was assessed using the questionnaire "DCDQ'07". Linear regression analyzes were performed and adjusted for covariates; age of the mother and child, parity, sex, maternal educational level, maternal pre-pregnancy alcohol consumption and duration of breastfeeding. Data were stratified by country.

*Results*: No statistically significant difference in age at motor milestones was found comparing children of smokers with children of non-smokers. Also, there was no statistically significant difference in motor score (Developmental Coordination Disorder Questionnaire Score, DCDQ-score) among five to sevenyear-old children. However, in Greenland children of smokers had a lower DCDQ-score than children of non-smokers at eight to nine years (-2.2 DCDQ points, 95% CI: -4.3;-0.1). Supplementary results for the same age group in Greenland showed that children of smokers had higher odds of being classified with motor difficulties in comparison with children of non-smokers (OR = 1.9, 95% CI: 1.1;3.3).

*Conclusion:* Maternal serum cotinine was not related to delayed motor development milestones or reduced motor function abilities in children up to 7 years of age. Reduced motor skills observed in 8–9 years old exposed children warrant further study.

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#### 1. Introduction

Cigarette smoke contains several harmful substances that might affect the child prenatally. There are more than thousand







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potentially harmful substances in tobacco smoke, such as nicotine, polycyclic aromatic hydrocarbons (PAH) and Carbon monoxide (CO). They are known to cross the placental tissue and enter the foetal bloodstream (Dempsey and Benowitz, 2001; Delpisheh et al., 2006). Nicotine reduces uterine blood flow, which affects the foetal development and may cause preterm delivery, growth restriction and impaired neurodevelopment (Dempsey and Benowitz, 2001: Delpisheh et al., 2006). Epidemiological studies indicate that smoking during pregnancy can affect the child's brain and influence the child's development, behaviour and cognitive function negatively in the long term (Murin et al., 2011; Martin et al., 2006; Shea and Steiner, 2008; Rantakallio, 1983). Rat experiments imply that especially the cerebellum seems to be the target organ (Trasti et al., 1999). The cerebellum is involved in the control of the body balance and motor coordination, which offers a possible explanation of the influence of smoking on motor development (Trasti et al., 1999).

Cohort studies have indicated increased risk of children's motor difficulties after prenatal smoking exposure (Trasti et al., 1999; Larsson and Montgomery, 2011; Cornelius et al., 2001; Slykerman et al., 2007) although with inconsistent results. Childhood motor difficulties may persist until adulthood and may be a predictor of poor psychosocial functioning later in life (Brixval et al., 2016; Østergaard, 2008; Losse et al., 1991; Rasmussen and Gillberg, 2000). In addition smoking during pregnancy is still prevalent (Centers of Disease Control and Preventtion, 2012; Al-Sahab et al., 2010; Charrier et al., 2010; Egebjerg Jensen et al., 2008).

A study found that children of mothers who smoked during pregnancy had increased risk of developmental delay in comparison with children of non-smokers, based on 22 questions about developmental milestones (Slykerman et al., 2007). Another study investigated the association between prenatal smoking and fine and gross motor function in children aged nine and 19 months, but these results indicated no relation (Richardson et al., 1995). Similar results were found in one-year-old children in another study (Trasti et al., 1999). However, that study found that five-year-old children who were exposed to prenatal smoking had a lower balance score. Two other studies found no association between prenatal smoking exposure and fine and gross motor function in three- and four-year-old children (Julyez et al., 2007; Fried and Watkinson, 1990). One of the studies also examined the effect of prenatal smoking in relation to eve-hand coordination, but found no association (Fried and Watkinson, 1990). Three other studies used the same measure for eye-hand coordination. One of these studies examined four-year-old children, and found no effect of smoking during pregnancy (Barr et al., 1990). In contrast, a study of ten-year-old children found a negative association between prenatal smoking and eye-hand coordination (Cornelius et al., 2001), while another study found that children of mothers who smoked during pregnancy had a better test result (Makin et al., 1991). However, the study population consisted of only 90 children, and the exposed children performed worse in a drawing test. In relation to fine motor function a study also found a negative association to prenatal smoking exposure in children at 11 years, but only with the non-dominant hand (Larsson and Montgomery, 2011). The inconsistent results presented above may partly be explained by the use of different outcome measures between studies and self-reported exposure. To avoid the uncertainty, by self-report of the exposure, it is relevant to use objective measures of smoking exposure. Cotinine is a metabolite of nicotine which can be measured in serum and reflect an exposure to nicotine within the past two to three days (Parna et al., 2005; Baltar et al., 2011). Studies indicate that measurement of serum cotinine can result in a more accurate status of smoking exposure in comparison with self-report (Parna et al., 2005; Perez-Stable et al., 1995; Klebanoff et al., 1998). Studies which examine the consistency between self-reported smoking status and smoking status determined by levels of cotinine concentrations, found (in

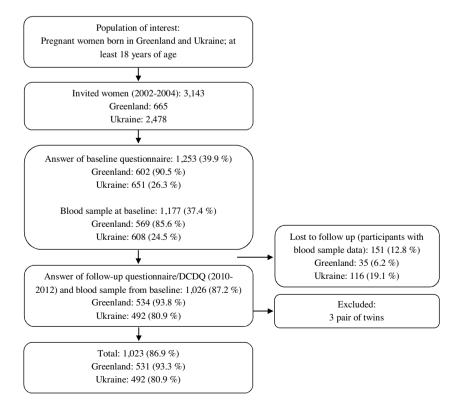


Fig. 1. Flow chart.

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