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# The association between environmental lead exposure with aggressive behavior, and dimensionality of direct and indirect aggression during mid-adolescence: Birth to Twenty Plus cohort



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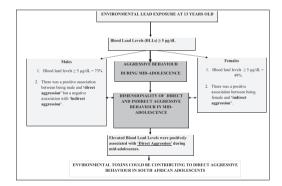
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## HIGHLIGHTS

# GRAPHICAL ABSTRACT

- Higher blood lead levels are associated with direct aggression in midadolescence.
- Males have higher blood lead levels than females during mid-adolescence.
- Adolescent males are positively associated with direct aggressive behavior.
- Adolescent females are positively associated with indirect aggressive behavior.
- Sociodemographic factors at birth influence dimensions of aggression later in life.



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# ABSTRACT

Chronic lead exposure is associated with neurological ill-health including anti-social behavior such as aggressive behavior. The main aim of this study was to examine the association between lead exposure at 13 years old and dimensions of aggressive behavior during mid-adolescence.

The study sample included 508 males and 578 females in mid-adolescence (age 14 to 15 years) from the Birth to Twenty Plus cohort in Johannesburg, South Africa. Blood samples collected at age 13 years were used to measure blood lead levels. Seventeen items characterizing aggression from the Youth Self Report questionnaire were used to examine aggressive behavior. Principal Component Analysis was used to derive composite variables from the original data for aggressive behavior; and data were examined for an association between blood lead levels and dimensionality of direct and indirect aggression and disobedience during mid-adolescence. We also examined the dimensions of aggression during mid-adolescence in relation to gender and socio-demographic factors.

Blood lead levels ranged from 1 to 28.1  $\mu$ g/dL. Seventy two percent of males and 47.7% of females in the study had blood lead levels  $\geq$  5  $\mu$ g/dL. There was a positive association between elevated blood lead levels and direct aggression (p < 0.05). Being male was positively associated with direct aggression (p < 0.001) but, negatively associated with indirect aggression (p < 0.001). Maternal education and age at birth were negatively associated with direct aggression during mid-adolescence.

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The significant association between elevated blood lead levels and direct aggressive behavior observed in this study may shed light on a possible environmental toxicological contribution to aggressive behavior in South African youth; and most importantly the type of aggressive behavior associated to lead exposure.

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## 1. Introduction

The World Health Organization (WHO) estimates that lead exposure accounts for 0.6% of the global burden of disease (World Health Organization, 2009). Lead is also considered an important environmental health hazard contributing to the environmental disease burden in Africa (Nweke and Sanders, 2009; Centers for Disease Control and Prevention, 2012b). A known cumulative toxicant, lead affects the "neurological, haematological, gastrointestinal, cardiovascular and renal systems" (World Health Organization, 2010b). Epidemiologic studies have shown evidence of lead-related adverse health outcomes, most notably acting on the central nervous system (CNS) (Needleman and Gatsonis, 1990; Hernberg, 2000; Lanphear et al., 2005; Schwartz et al., 2007; Shih et al., 2007; Yuan et al., 2006; Cecil et al., 2008; Cecil et al., 2011). The effects of lead exposure on the CNS in children are associated with reduced cognitive function, aggressive, violent, delinquent and criminal behavior, among others (Needleman et al., 1979; Needleman and Gatsonis, 1990; Needleman et al., 2002; Bellinger et al., 1992; Canfield et al., 2003; Lanphear et al., 2005; Mazumdar et al., 2011; Wright et al., 2008). The indirect costs of childhood lead exposure speak to the economic burden it places on the general public (World Health Organization, 2010a). Its adverse effects on the intellectual function of young people (Lanphear et al., 2000; Lanphear et al., 2005) may in turn affect the level of education they attain and employment opportunities available to them in the future. Additionally, there is a link between reduced educational attainment and the probability of being arrested (Lochner and Moretti, 2004). As such, environmental lead exposure contributes to great "lost opportunity costs" (World Health Organization, 2010a) and robs young people of their full potential in life.

The Port Pirie Cohort was the first study to prospectively evaluate the association between lifetime blood lead exposure in children and "emotional and behavioral problems" (Burns et al., 1999). Children 11 to 13 years from a lead smelting neighbourhood in Port Pirie, Australia were included in the study. Using a cut-off score of 15  $\mu$ g/dL, in both sexes a correlation between higher cumulative blood lead levels and total behavior problems was found. In boys, the highest correlation was between elevated lifetime blood lead levels and "aggressive behavior", "delinquent behavior", and "attention problems"; and in girls with "aggressive behavior", "attention problems"; and in girls with "social problems", "anxious/depressed", and "withdrawn" (Burns et al., 1999).

South African children particularly from poor communities are exposed to environmental lead through various mediums such as use of lead based paint in children's toys (Mathee et al., 2007) and playground equipment for children in Johannesburg, Ekurhuleni, and Tshwane (Mathee et al., 2009); use of lead in subsistence fishing where waste lead for example from "wheel balancing and alignment centers" is collected, melted and recycled to make new craft sinkers (Mathee, 2014); and pregnant women who practice geophaphia thus increasing the risk of prenatal lead exposure (Mathee et al., 2014) among others.

Naicker et al. (2012) examined the relationship between lead exposure and socio-behavioral adjustment including aggressive behavior during early adolescence in the Birth to Twenty Plus (BT20 +) cohort in South Africa. With regards to aggressive behavior, blood lead levels at age 13 years were negatively associated with aggressive behavior item 'I argue a lot' 95% CI [-0.23 to -0.02] but positively associated with 'I attack other people' 95% CI [0.09-0.98] (Naicker et al., 2012). To further examine these findings at a later stage in adolescence and determine the specific type(s) of aggressive behavior related to

environmental lead exposure, we set out to determine the association between lead exposure in early adolescence and aggression items in midadolescence (at ages 14 to 15 years old). The use of Principal Components Analysis (PCA) in this study allowed for a more comprehensive integration of aggressive behavior. We examined lead exposure at age 13 years old and dimensions of aggression during mid-adolescence. These data are essential for public health and environmental health policymakers to address this important public health problem in the country.

## 2. Methods and materials

### 2.1. Study population

BT20 + is the largest and longest running longitudinal birth cohort in Africa. The cohort includes all singleton births at public health facilities during a seven-week period from April 23 to June 8, 1990 in Soweto/Johannesburg, South Africa. The birth cohort is representative of long-term urban residents. Over the years, the cohort has reported a very low attrition rate of <3% annually – with the highest rate reported in the first two years of the study; mostly due to movement away from the study area (Norris et al., 2007). The cohort is described in detail elsewhere (Richter et al., 2004; Richter et al., 2007).

For this study, Black African and Coloured (mixed race heritage) study participants with blood lead samples at age 13 years and who had completed the Youth Self Report(YSR) during mid-adolescence at ages 14 to 15 were included (n = 1086). White and Indian study participants were excluded due to very low numbers. In addition, to test if study participants exhibiting aggressive behavior during mid-adolescence have early predisposition to aggressive behavior, study participants with YSR data for year 11 were included in the study.

#### 2.2. Blood lead measurements

Venous samples of whole blood were collected at age 13 years into EDTA-containing tubes previously determined to be free of trace metals. Blood sampling was undertaken by professional health officials, using sterile equipment and aseptic techniques. Blood samples were vortexed and rolled on the coulter mixer for at least 10 min until properly mixed. They were diluted 10 times with 1,1% (v/v) Triton X-100 using automatic Hamilton Microlab 500 diluter into disposable 10 mL Sterilin plastic tubes covered with screw caps and mixed well using a vibration mixer. Blood lead levels were measured using Perkin Elmer 600 AAnalyst atomic absorption spectrometer with a THGA graphite furnace, Zeeman background correction and AS-800 Autosampler. Both blood samples and samples for quality control were prepared and measured in-house.

# 2.3. Measurement of aggressive behavior in mid-adolescence and potential confounders

Data were collected from the cohort at age 14 to 15 years using the YSR questionnaire. This questionnaire is a self-report measure used to examine social and behavioral problems in children and adolescents aged 11 to 17 years. These include aggressive behavior, substance abuse, breaking rules, social problems, thinking disorders, anxiety disorders, depression, mood disorders, impulsive behavior and others (Achenbach, 1991). Seventeen of the 112 questionnaire items examine aggressive behavior. Each item has four response options: not true, sometimes true, true and very true. The aggressive behavior response

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