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## The association between elevated blood lead levels and violent behavior during late adolescence: The South African Birth to Twenty Plus cohort

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### ABSTRACT

Epidemiological studies have shown the adverse neuro-behavioral health effects of lead exposure among children, in particular. However, there is lack evidence in this regard from developing countries. The main aim of this study was to assess the association between blood lead levels (BLLs) during early adolescence and violent behavior in late adolescence.

Our study sample from the Birth to Twenty Plus cohort in Soweto-Johannesburg, South Africa included 1332 study participants (684 females). BLLs were measured using blood samples collected at age 13 years. Violent behavior was evaluated using data collected at ages 15 to 16 years using the Youth Self Report questionnaire. First, bivariate analysis was used to examine data for an association between lead exposure in early adolescence and violent behavior items during late adolescence. Principal Component Analysis (PCA) was used for dimensionality reduction and six violent behavior components were derived. Data were further analyzed for an association between BLLs at age 13 years and violent behavior using PCA derived components; to determine the specific type(s) of violent behavior associated with lead exposure.

Median whole BLLs were 5.6 µg/dL ( $p < 0.001$ ). Seventy five percent of males and 50% of females had BLLs  $\geq 5$  µg/dL. BLLs ranging from 5 to 9.99 µg/dL were associated with physical violence ( $p = 0.03$ ) and BLLs  $\geq 10$  µg/dL were associated physical violence and fighting ( $p = 0.02$  and  $p = 0.01$ , respectively). When data were analyzed using continuous BLLs physical violence was associated with lead exposure ( $p < 0.0001$ ). Furthermore, males were more likely to be involved in violence using a weapon ( $p = 0.01$ ), physical violence ( $p < 0.0001$ ), and robbing others ( $p < 0.05$ ) compared to females.

The results from this study show the severe nature of violent behavior in late adolescence associated with childhood lead exposure. They highlight the urgent need for preventive measures against lead exposure among children in low or middle income countries such as South Africa.

### 1. Introduction

Lead is one of ten chemicals identified by the World Health Organization (WHO) as being of “major public health concern” and in need of action by Member States (World Health Organization, 2010). Approximately 600,000 new cases of children with intellectual disability are attributed to childhood lead exposure annually (Prüss-Ustün et al., 2011). In recent decades there has been a steady increase in

epidemiological studies showing a possible link between childhood lead exposure and lower socio-economic status (Morrens et al., 2012); altered pubertal development in girls and boys (Naicker et al., 2010a; Williams et al., 2010; Den Hond et al., 2011); and intellectual impairment and antisocial behavior (Needleman et al., 1979; Needleman and Gatsonis, 1990; Needleman et al., 2002; Bellinger et al., 1992; Dietrich et al., 2001; Canfield et al., 2003; Lanphear et al., 2005; Wright et al., 2008) among others.

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Contemporary research studies involving brain-imaging show possible neuro-anatomical bases underlying the neuro-behavioral changes associated with lead exposure. In a Cincinnati Lead study, analyses of childhood lead exposure and adult brain volume using magnetic resonance imaging (MRI) showed that elevated mean childhood blood lead levels were significantly associated with 1.2% reduction of the grey matter ( $p < 0.001$ ) (Cecil et al., 2008). The affected areas of the brain included prefrontal cortical areas such as the “medial and superior frontal gyri” with the “ventrolateral prefrontal cortex and anterior cingulate cortex”, and in the “postcentral gyri, the inferior parietal lobule”, and the cerebellar hemispheres. It is important to note that this grey matter loss was only significant among males (Cecil et al., 2008). Childhood lead exposure has also been reported to alter the integrity of white matter in adulthood (Brubaker et al., 2009). Other brain imaging studies have supported these findings (Stewart et al., 2006; Cecil et al., 2011; Caffo et al., 2008; Brubaker et al., 2010; Schwartz et al., 2010), suggesting that exposure to lead changes the structure and function of the brain, affecting executive functions and consequently resulting in neuro-behavioral changes such as violent behavior. Prefrontal cortex dysfunction is associated with aggressive and violent behavior (Brower and Price, 2001; Siever, 2008; Hawkins and Trobst, 2000; Grafman et al., 1996).

In South Africa lead has been used in, among other items, petrol, paint, batteries, solder, electrical appliances, fishing weights and road markings (Mathee et al., 2009). Lead continues to be used in traditional medicines (Mathee et al., 2015), and leaded ammunition (Mathee, 2014; Mathee et al., 2017) among others. Given that South Africa has a long history of blood lead concentrations above the Centers for Disease and Control and Prevention (CDC)'s recommended reference level of 5  $\mu\text{g}/\text{dL}$  in children (von Schirnding et al., 1991; von Schirnding et al., 2003; Mathee et al., 2006; Naicker et al., 2010b; Mathee et al., 2013) and violent behavior characterized by physical violence, violence using a weapon, bullying, emotional violence and sexual violence during adolescence (Burton and Leoschut, 2012; Mncube and Harber, 2013), there is good reason to examine the association between childhood lead exposure and violent behavior among young people. In addition, in view of the fact that 98% of children exposed to lead live in low or middle income countries such as South Africa (World Health Organization, 2009), it is vital that more research is conducted in these communities to examine its deleterious health effects. Currently, most of the empirical data demonstrating the detrimental effects of lead exposure comes from the developed countries. More locally-generated empirical data are essential to inform decisions and policies related to prevention and control of lead exposure in South Africa and other low or middle income countries. To our knowledge, no study has been conducted in South Africa showing the relationship between lead exposure and violent behavior during adolescence. In this study we hypothesized that there is an association between lead exposure at 13 years old and violent behavior during late adolescence in South Africa. Principal Component Analysis (PCA) derived components were used to determine the type or types of violent behavior associated with lead exposure among South African adolescents.

## 2. Materials and methods

### 2.1. Study population

Study participants were selected from the Birth to Twenty Plus (BT20+) cohort in Johannesburg, South Africa. BT20+ is the largest and longest running birth cohort in Africa. It was initiated at the cusp of democracy in South Africa with the intention to address the foreseeable health problems as a result of heightened demand for access to health care services in urban areas due to increased urbanization. A total of 3273 study participants were enrolled in the birth cohort from 23 April to 8 June 1990. The cohort is representative of the South African racial demographics as defined by the “Apartheid” system<sup>1</sup>; comprised of 78%

Black Africans, 6% Whites, 12% Mixed Ancestral and 4% Indians. Initially the White population group was under-represented mainly because during the time of enrollment most White families used the private health practitioners and facilities. This imbalance was later rectified at age 10 years by enrolling a supplementary sample of 120 White children born during the cohort enrolment dates.

Even though the cohort has a very low attrition rates, White families have shown a higher attrition compared to others. The study is still in contact with > 70% of the original study participants. For more details regarding the cohort, see Richter et al. (2007) and Richter et al. (2004).

To be included in the current study, study participants needed to have blood lead measurements at 13 years old and violent behavior data collected at ages 15 to 16 years (late adolescence). With these criteria, a total of 1332 study participants (684 females) comprised of 87.2% Black African and 10.4% Mixed Ancestral adolescents were included in the study. White and Indian study participants were excluded due to low numbers, 1.54% and 0.88% respectively.

### 2.2. Blood lead measurement

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 Analyst 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 violent behavior in late adolescence and socio-demographic factors

Data on violent behavior were collected in the 15th year data collection wave using the Youth Self Report (YSR) questionnaire. Information for the YSR questionnaire for violent behavior was collected at two time points, 11/12 and 15/16 years old. Study participants were contacted by telephone at home, work, or through nominated contactable family members or friends to secure appointment dates for data collection. Study participants came to the BT20+ data collection site and were compensated a minimum of R50 for transport. The YSR questionnaires were administered by trained field workers - most of whom have been with the cohort since its inception and have a very long trusting relationship with the study participants (Richter et al., 2004).

The YSR is a self-report questionnaire comprising 112 items assessing behavioral competency and problems of children and adolescents aged 11 to 17. It assesses aggressive and oppositional behavior attention seeking problems, as well as psychotic, impulsive, social interaction, and conduct problems among others (Achenbach, 1991). Regarding the sensitivity and specificity of the YSR questionnaire, the Achenbach System of Empirically Based Assessment (ASEBA) scales for internalizing and externalizing for YSR are 0.90 for alpha, 0.85 for test-retest reliability and 0.56 for long term stability for the United States. In general psychometric results from different cultural backgrounds have approximated those from the United States (Achenbach et al., 2008). Furthermore, YSR was used in adolescents from different cultural

<sup>1</sup> The racial categories Black African, White, Mixed Ancestral and Indian/Asian were enforced through legislation in Apartheid South Africa. Even though they are no longer enforced, to a great extent they remain part of South African vocabulary.

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