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RUNNING HEAD: Toxic Environment of War

Toxic Environment of War:

Maternal Prenatal Heavy Metal Load Predicts Infant Emotional Development

Abstract

Background: People in war zones are exposed to heavy metal contamination deriving from new-generation weapons, in addition to exposure to psychologically traumatizing war events. Pregnant women and their children-to-be are particularly vulnerable to both biological and psychological war effects. **Objective:** The aim of the current study was to analyse the impact of maternal prenatal heavy metal contamination on infant emotional development and to examine the potential moderating role of maternal symptoms of post-traumatic stress disorder (PTSD) in the association between heavy metal load and infant emotional development. **Methods:** The participants were 502 Palestinian mothers, pregnant in their first trimester during the 2014 War on Gaza. The mothers were recruited at their delivery (T1) and followed at the infants' age of 6-7 months (T2; $N = 392$). The load of five weapon-related heavy metals (chromium, mercury, vanadium, strontium, and uranium) was analysed by Inductively Coupled Plasma Mass Spectrometry (ICP/MS) from mothers' hair samples at childbirth (T1). Assessment of maternal PTSD symptoms was based on the Harvard Trauma Questionnaire (HTQ) and infant emotional development on the Infant Behavior Questionnaire (IBQ), both reported by mothers (T2). **Results:** Two of the analysed metals, chromium and uranium, adversely predicted children's early emotional development, indicated by decreased positive affectivity, increased negative emotionality, and problems in early orientation and regulation. Mother's PTSD did not moderate the impact of heavy metal contamination on children's emotional development. **Conclusions:** Adverse impact of war is not limited to those who experience it directly, but is passed on to future generations through multiple mechanisms. International organizations are obliged to protect parents and infants from the modern weaponry in wars.

Keywords: heavy metals, war trauma, PTSD, child development, emotional development

Introduction

Families living in war zones are exposed to contamination from new-generation weapons, in addition to experiencing losses, destruction and other traumatic war events. New-generation weapons include heavy metals with known and unknown potentially toxic, teratogen and carcinogen effects on human health (Skaik et al., 2010). Pregnant women and their children-to-be are particularly vulnerable to toxic effects of war, due to intensive development of the fetus and its sensitivity to environmental influences during the prenatal period (Andersen, 2003; Dollander & de Tychney, 2002). Studies show increased rate of birth defects and deformed babies in war areas heavily exposed to contamination of residuals of new-generation weapons (Alaani, Savabieasfahani, Tafash, & Manduca, 2011; Naim, Minutolo, Signoriello, & Manduca, 2013). However, research on the potential impact of maternal prenatal exposure to heavy metals on later infant development is lacking. Infants learn to express and regulate their emotions with the help of their caregivers, and optimal emotion development forms a crucial foundation for later social-emotional development and mental health (Calkins & Hill, 2007). Therefore, this study aims to examine, whether and how maternal prenatal weapon-related heavy metal load predicts infant emotional development, consisting of emotion expression and regulation.

War events, such as human and material losses, life threat and atrocities negatively influence mothers' mental health (Punamäki, Isosävi, Qouta, Kuittinen, & Diab, 2017). Maternal pre- and postnatal mental health problems have in turn found to form a severe risk for infant well-being and development, both in general (Field, 2011; Guyon-Harris, Huth-Bocks, Lauterbach, & Janisse, 2016; Kingston, Tough, & Whitfield, 2012) and in conditions of war and terrorism (Isosävi et al., 2017; Yehuda et al., 2005). We therefore analyse the role of maternal mental health problems, here symptoms of post-traumatic stress disorder (PTSD), in the association between maternal exposure to heavy metal load and infant emotional development.

Heavy Metal Toxicity in War Conditions

Metals with relatively high density or atomic weight are generally defined as *heavy metals.* Those are found naturally in the earth, but become concentrated through human made activities, such as agriculture, pollution or industrial disasters. Heavy metals can enter human tissues via inhalation, diet, or manual handling, and they can disturb vital bodily functions and organs, such as kidneys, lungs, liver, and brain, even in small quantities (Duruibe, Ogwuegbu, & Egwurugwu, 2007; Järup, 2003). Importantly, heavy metals can be classified into *toxicants* (with ability to cause acute poisoning and leading to serious organ damage or death), *neurotoxicants* (being particularly harmful to brain and other nervous system), *carcinogens* (inducing different forms of cancer), and *teratogens* (being particularly harmful to fetal development and inducing spontaneous abortions or birth defects). Finally, some heavy metals are *microelements,* being necessary for most living organisms in small quantities, but harmful in over-dose.

Military attacks are a source of heavy metal exposure among people living in war zones, as various heavy metals are used in new generation weapons. As an example, the waste of nuclear industry is re-used in depleted uranium weapons, which poses both radiological and chemical toxicity in humans (Hon, Österreicher, & Navrátil, 2015; Ifesinachi, 2014). In addition, weapons can be “enhanced" by the utilization of heavy metals as augmenters or as primary effective agents, and some new weapons are able to produce a 'molecular sieve' of toxic metal powder that can severely affect the human body (Apperson et al., 2007; Skaik et al., 2010). Analyses of wound tissues of war injuries provide evidence of civilian contamination to metals with toxicant, teratogen and carcinogen effects on human body (Skaik et al., 2010). Importantly, in addition to the risks posed by acute exposure, the persistence of heavy metals in post war environments can cause prolonged exposure, leading to accumulation of metals in compartments of the body (Järup, 2003; Manduca, Diab, Qouta, Albarqouni, & Punamäki, 2017).

Prenatal Heavy Metal Contamination and Infant Development

Prenatal development is sensitive to neurotoxicity due to intensive fetal neurological development and plasticity to environmental effects (Andersen, 2003; Dollander & de Tychey, 2002). According to the *developmental origin of health and disease* (DOHaD) hypothesis, exposure to environmental adversity during the pre- and perinatal period can negatively influence development and health throughout the life-span, through multiple mechanisms (Darney et al., 2011). First, heavy metals can produce their negative effects through inducing epigenetic modifications in the genome, thus affecting both the mother and the fetus (Cheng, Choudhuri, & Muldoon-Jacobs, 2012). Second, some heavy metals are able to cross the placental and blood-brain barriers and thereby induce neurotoxicity in the fetus (Grandjean & Landrigan 2006; Vahter 2009). Third, heavy metals can act as prenatal endocrine disruptors (Iavicoli, Fontana, & Bergamaschi, 2009) or they can negatively affect the transfer of nutrients to the foetus (Kippler et al. 2010). All these mechanisms have the potential to produce long-term negative effects on children's emotional development.

Yet, we could detect only one study that investigated the impact of prenatal exposure to heavy metals on children's early emotional development. Stroustrup and group (2016) analysed the impact of lead and mercury in maternal prenatal blood and bone on toddlers' (N = 500) emotion expression and regulation. Results showed that prenatal exposure to lead, but not to mercury, was associated with children's more intensive emotional reactions and difficulty in regulating them.

Instead, research is available on adverse effects of prenatal heavy metal exposure to children's later neurocognitive development and mental health. A study (N = 270) found that prenatal exposure to lead and cadmium (assessed in cord blood) predicted behavioral and emotional problems, such as aggressive and depressive symptoms, in 7–8 year old children (Sioen et al., 2013). Another study (N = 233) confirmed that high levels of mercury in umbilical cord and maternal blood delayed psychomotor development among one year olds (Jedrychowski et al., 2006). Yet another study (*N* = 917) found that prenatal methylmercury exposure (assessed in cord blood and maternal hair) predicted difficulties in attention, expressive language, and long-term memory in 7-year old children (Grandjean et al., 1997). In addition, prenatal heavy metal exposure has been identified as a risk factor of later ADHD (Froehlich et al., 2011) and autism spectrum disorders (Roberts et al., 2013).

Studies have typically focused on developmental impacts of single metals, although metals can accumulate in human body (Jaishankar et al., 2014). As an exception, an American study (*N* = 92) found a joint effect of seven heavy metals (cadmium, chromium, cobalt, lead, mercury, nickel and silver) on cognitive skills and health status among toddlers of mothers exposed in pregnancy (Lewis, Worobey, Ramsay, & McCormack, 1992). Children of exposed mother had more infections and other illnesses, and cognitive impairments in verbal, perceptual and motor abilities. Importantly, heavy metals deriving from new generation weapons are likely to co-occur as well. Wound tissues of war injuries have found to contain numerous heavy metals with toxicant, teratogenic and carcinogenic effects on human body, such as mercury, vanadium, chromium, strontium, and uranium (Skaik et al., 2010). Therefore, the current study focuses on these potentially weapon-related heavy metals in analysing prenatal heavy metal contamination and its impact on infant emotional development.

Role of Maternal PTSD Symptoms

In addition to toxic exposure, people living in war zones are susceptible to other traumatic experiences, such as losses of loved ones, threats of life, and witnessing horrors. Ample evidence shows that these psychologically dreadful events increase the likelihood of mental health problems, such as symptoms of PTSD, depression, and dissociation (de Jong & Komproe, 2002). Yet, few studies have focused on pregnant women or mothers with infants in war conditions, although mothers may be especially vulnerable to trauma during the pregnancy and the postpartum (Kaitz, Levy, Ebstein, Faraone, & Mankuta, 2009) and their mental health in turn strongly influences infant well-being and development, including emotion regulation (Isosävi et al., 2017). Therefore, maternal PTSD, characterized by involuntary re-experiencing of traumatic events, avoiding reminders of traumatic events, hyperarousal for dangers, and dysfunctional cognitive-emotional processing (American Psychiatric Association, 2013) might accelerate the negative impacts of maternal prenatal contamination of heavy metals.

Research on victims of the 9/11 terrorist attacks showed a high increase of PTSD symptoms among pregnant mothers, which in turn negatively impacted fetal and infant development (Harville, Xiong, & Buekens, 2010). In particular, maternal prenatal exposure to the terrorist trauma predicted restricted fetal growth, low birthweight, and low newborn neurological status (Berkowitz et al., 2003). Further, the infants of mothers who suffered PTSD after the 9/11 trauma showed dysfunctional (low) cortisol levels (Yehuda et al., 2005) and high distress to novelty (Brand, Engel, Canfield, & Yehuda, 2006), both indicating infant's difficulties in stress and emotion regulation. To our knowledge, no prior study has analyzed the combined effects of maternal heavy metal load and mental health on infants' regulatory capacities in the context of war trauma, which is where the present study contributes.

Current Study

Research is available on the impact of single metals such as lead or manganese on child development and health, but there are no studies on the possible impact of maternal exposure to multiple heavy metals derived from new generation weapons. The present study was conducted in the aftermath of the 2014 war on Gaza (in the Israeli military terms the Protective Edge operation) that caused massive human and material destruction with about 100 000 displaced civilians seeking for safety in a small besieged area of Gaza (UN-Human Rights Council, 2014). Characteristic to the military operation was that the possible toxic war remnants of shelling and bombardments remained unremoved in ruins of houses for long periods of time due to the military siege and international boycott of Gaza Strip (OCHA, 2016).

This study aims to analyse the impacts of heavy metal load in delivering Palestinian women on infant emotional development, and the role of maternal PTSD symptoms in the association. We hypothesize that high maternal load of hair chromium (Cr), mercury (Hg), vanadium (V), strontium (Sr), and uranium (U), reflecting fetal long-term exposure to these metals, predicts decreased positive and increased negative emotion expression as well as difficulties in emotion regulation. Second, we investigate the potential moderating role of maternal postnatal PTSD in the association between maternal prenatal heavy metal load and infant emotion expression and regulation. We hypothesize that infants whose mothers were both exposed to high heavy metal contamination and suffer from postnatal PTSD symptoms, show especially high levels of negative emotional expressivity and difficulties in emotion regulation, and low level of positive emotional expressivity.

Method

Participants and Procedure

The participants were 502 Palestinian women recruited at their delivery in maternity units in four hospitals from the Gaza Strip (T1) and 392 of them were visited in their homes when their infants were 6-7 months old (T2). Three governmental and one private hospitals represented the four main Gaza Strip geographical areas: North (Al Awda Hospital, n = 100), Gaza City (Al Shifa Hospital, n = 202), Middle (Al Aqsa Hospital, n = 100), and South (Nasser Hospital, n = 100). The T1 assessment was conducted between January - March 2015. The inclusion criteria of the participating mothers were that they had been pregnant in their first trimester during the 54-days of intensive shelling and bombing of the Gaza Strip in year 2014, and that they accepted voluntary participation. One midwife in each hospital registered all deliveries during her work shift and obtained the participants' written informed consent. The midwife collected maternal hair samples.

Data collection at T2 was conducted in June - October 2015, when the children were about 6-7 months old (M = 6.2 SD = 0.4). Ten fieldworkers with BA degrees in a relevant field and with former experience in research work collected the data, after attending a comprehensive training on the research tasks and procedures. The interviews took place in the participants' homes and partially in the governmental Primary Health Care Centres (PHCC) in each area. The average duration of the interview was 90 minutes. The participants received small presents for their participation in the study. Two members of the research team from Gaza supervised the fieldwork through regular supervisory meetings with the fieldworkers. The study was approved by Palestinian Health Research Council and the Helsinki Committee for Ethical Approval. The Research Board in the Islamic University of Gaza, Palestine, reviewed and approved the research tools and procedures.

The number of dropout between T1 and T2 was 110 participants (21.9%). The main reasons for dropping out from the study were death of the baby (n = 12, 2.4%), withdrawal for family reasons, and incorrect or changed home address after displacement resulted from the war. Importantly, the families that dropped out did not differ from those who remained in terms of child's gender or birthweight, or the age and education of the mother and the father. Instead, length of gestation ($t = 2.50$, $p = .01$) and newborn health ($t = 57.65$, $p < .01$) differed between participants and drop-outs; the participating mothers had longer gestations and they assessed their baby's health status at birth to be better, compared to those who withdrew from the study later on.

Measures

Family demographic and obstetric information (T1). Standard European and US birth register information was gathered at birth, including child's birthweight, length of gestation, mode of delivery, and need of intensive care unit (NICU). Mothers were also interviewed to gather family's background information, such as parental age, occupation, and health history.

Maternal heavy metal load at birth (T1). Altogether, load of 23 heavy metals was analysed from maternal hair samples, collected as mothers entered the delivery. The hair sample was four centimeters long, taken from scalp at the nape of the neck, to reflect environmental exposure during the last 4-5 months of pregnancy and the eventual release of metals previously accumulated in the body. The heavy metal loads were analyzed by *Inductively Coupled Plasma*

Mass Spectrometry (ICP/MS), as recommended by the International Atomic Energy Agency (1994) and described previously by Manduca, Naim, & Signoriello, 2014).

The current study focuses on five of the analyzed metals (chromium, mercury, vanadium, strontium, and uranium) that fulfilled three criteria: First, they were shown by earlier studies to be weapon-related (Manduca et al., 2017; Skaik et al. 2010). More specifically, these metals were detected in human wound tissue of war injuries in Gaza in at least two-fold amount higher compared to reference tissue from healthy individuals (Skaik et al., 2010). Except for chromium, all the selected metals were detected in ten-fold amounts in at least some wound types, categorized by Skaik and colleagues (2010). Uranium was consistently found in all types of wounds. Second, the selected metals were shown by an earlier study on the current sample to correlate statistically significantly with heavy metal loads in the newborn babies (Manduca et al., 2017). Third, these five metals in our data displayed variation that enabled us to analyze them with standard statistical analyses methods. To be more specific, two metals (cesium and nickel) that otherwise fulfilled the criteria were excluded from the analyses, due to majority of the samples displaying extremely low concentrations, undetectable by the ICP/MS analysis, and thus leading to a lack of variability between participants.

Infant emotional development (T2). Infant emotion expression and regulation were measured with the Very short form of Infant Behavioral Questionnaire-Revised (IBQ-R; Putnam, Helbig, Gartstein, Rothbart, & Leerkes, 2014). The measure includes 37 descriptions of the infant's positive and negative affectivity, behavior and orientation during daily situations, such as eating, bathing and separation. Mothers were asked to estimate on a 5-point scale (1 = never; 5 = always) about how often during the past week did the infant behave in the described way. The scale had to be modified for the present study, as factor analyses of the original measure (three separate factors) revealed that several of the items had very low or non-significant loadings. Consequently, we retained the three factors that were identified by earlier research (Leerkes et al., 2017; Putnam et al., 2014), but used only the highest loading items within each of the alleged dimensions. The sumscores that we used included five items for *positive affectivity* (α = .66), three items for *negative emotionality (social fear;* α = .83*)*, and seven items for *orienting/regulatory capacity* (α = .61).

Maternal PTSD (T2). Maternal PTSD symptoms were assessed by the Harvard Trauma Questionnaire (HTQ; Mollica et al., 1992). The 26-item questionnaire assesses intrusive, avoidance and hypervigilance symptoms according to the DSM-III with 16 items. The mothers reported to which extent they had experienced the symptoms in the last month on a 4-point scale (0 = not at all; 3 = severely). We constructed a mean score of the 16 DSM-III items to assess PTSD symptoms (α = 0.82) as well as a dichotomic variable indicating clinically significant PTSD (mean scores of 2.5 or higher, Mollica et al., 1992). The HTQ scale has shown its reliability within Arab populations, including Palestinians (Qouta, Punamäki, & El Sarraj, 2008; Salo, Qouta, & Punamäki, 2005).

Statistical Analyses

To investigate the study aims, we used linear regression analysis with a combination of stepwise and hierarchical (forced) entry methods. The stepwise method is particularly useful in finding the best predictors among a set of variables (i.e., among the five metals and among the five interaction terms) without prior knowledge on the relative importance of each variable. In practice, stepwise regression analysis enters statistically significant predictors into the model in the order of the unique variance each of them explains (forward selection). In addition, the analysis drops predictors out if they have become redundant (backward selection).

We added the predictors into the model in blocks: in the first block, the covariates; in the second block, maternal PTSD symptoms; third, the five heavy metals (chromium, mercury, strontium, uranium and vanadium); and finally fourth, the five interaction terms between heavy metals and maternal PTSD symptoms. In the first and the second block, we used forced entry; in the third and the fourth block, we used the stepwise entry method. The dependent variables were infants' IBQ-emotional development (positive affectivity, negative emotionality, and orienting/regulatory capacity). The criteria of using background data as covariates were their associations with both the independent and dependent variables and theoretical meaningfulness.

Results

Descriptive Results

The average age of mother was 26 years (*SD* = 6 years) and age of father 31 years (*SD* = 6 years) at T1. Majority of the mothers worked at home (89%) and the rest were workers, nurses, teachers and students (11%). Nearly a half of the fathers were manual workers (41%), a quarter worked as security professionals (25%), a fifth were unemployed (21%), and the rest were civil servants, entrepreneurs, or students (13%).

Concerning obstetric data, the average length of gestation was 39 weeks (*SD* = 1.8 weeks), child's birthweight 3400gr (*SD* = 527gr), and 49.6% (*n* = 249) of the children were boys. The prevalence of preterm delivery was 1.5%, prevalence of low birth weight (< 2.500gr) 2.3%, and prevalence of a birth defect 4.5%. All babies were born alive, although one died in few minutes after birth. At T2, mean age of the infant was 6.19 ±0.41 (months), and 83% of the children were assessed as healthy by the mother.

Table 1 presents the means, standard deviations and observed ranges of the five analysed metals, three IBQ subscales, maternal PTSD symptoms, as well as child's age at T2. Observed ranges of the five metals were highly variable, with two metals (mercury and strontium) showing extremely high variation (> 1000 units). Concerning the means of IBQ at T2, mothers' reports indicate higher levels of positive dimensions, i.e., infant orienting/regulatory behaviors and positive affectivity, compared to infant negative emotionality. A fifth (20.1%; *n* = 78) of the mothers reported clinically significant PTSD.

Correlations between the study variables are also presented in Table 1. It is noteworthy that some of the analysed metals showed high correlations with each other, particularly vanadium and chromium. The subscales of infant emotional development were significantly correlated. Chromium and uranium were negatively correlated with child positive affectivity, and uranium was also negatively correlated with child orienting/regulation and positively correlated with child negative emotionality. Infant age (months) at T2 was the only background variable that correlated with both dependent (chromium and vanadium) and independent variables (IBQ positive affectivity), and was thus included as a covariate in this analysis.

Heavy Metal Load Predicting Infant Emotional Development

Results of regression analyses in Table 2 showed that our hypothesis of high maternal heavy metal load predicting decreased positive and increased negative emotions and difficulties in emotion regulation was substantiated for two of the potential five metals. Concerning child *positive affectivity,* $F(3,374) = 10.52$, $p < .01$, chromium entered the model first and remained as the sole predictor among the metals, decreasing the likelihood of children's positive affectivity. As seen in Table 1, uranium showed similar correlation with positive affectivity as chromium, thereby not adding to the association after chromium was already included in the model. Child's age was a significant covariate, indicating that older infants displayed more positive affect than younger infants. We also conducted the analysis without child's age as a covariate, and the results remained the same. Concerning child *negative emotionality,* $F(2,378) = 4.01$, $p = .02$, and *orienting/regulatory capacity,* $F(2,381) = 7.28$, $p < .01$, uranium was the best predictor for both of them, increasing the likelihood of infant's negative emotionality and less than optimal orienting and regulatory behaviors. Also chromium correlated negatively with orienting/regulatory behaviors (Table 1), but not above uranium. Altogether, chromium and uranium explained 2–4 % additional variance in child emotional development after the covariates.

Role of Maternal PTSD in Impacts of Heavy Metal Contamination

Against to our hypothesis, maternal PTSD symptoms did not moderate the association between maternal heavy metal load and infant emotional regulation. In other words, infants of mothers exposed to high prenatal heavy metal contamination and suffering high PTSD symptoms did not show especially high levels of negative emotionality or difficulties in emotion regulation or low levels of positive emotionality. Also infants of mothers with clinically significant PTSD were not more vulnerable to negative impacts of maternal heavy metal contamination on their emotional development.

Discussion

Heavy metal contamination through military attacks composes a severe health hazard and human right violation among civilians living in war zones, and expecting mothers and fetuses may be particularly vulnerable. The current study analysed the impact of maternal prenatal toxic heavy metal exposure on infant emotional expression and regulation, as both are important developmental tasks during the first year of life. The participants of the current study were Palestinian mother-infant dyads in the context of the 2014 offensive war on Gaza. The mothers and children continued to live in a contaminated environment also after the war, due to the Israeli siege and international boycott of Gaza Strip (OCHA, 2016). Results revealed that two of the analysed metals, chromium and uranium, adversely predicted children's early emotional development, indicated by decreased positive affectivity, increased negative emotionality, and problems in orientation and regulation at the age of 6-7 months. In contrast, the results did not support the hypotheses that maternal PTSD symptoms would accelerate the negative impacts of heavy metals on infant emotion expression and regulation.

Risks of Prenatal Chromium and Uranium Exposure on Infants

To our knowledge, this was the first study to analyse the impact of war-related prenatal heavy metal exposure on infant development. The concentrations of five weapon-related heavy metals, chromium, mercury, vanadium, strontium and uranium, were detected from maternal hair samples at childbirth. Compared to blood, urine, or amniotic fluid samples, hair samples are better able to detect long-term heavy metal contamination (Menezes-Filho et al., 2011), in our study, maternal cumulative exposure to toxic metals during the pregnancy. Our finding that chromium and uranium predicted alterations in early emotional development suggests that fetal in utero contamination can have long-term negative impact on child development.

Chromium and uranium have well-documented detrimental effects on human body. Chromium is a steely-grey, lustrous, hard and brittle metal with a high melting point. It is a naturally occurring element in the earth's crust, with several oxidational forms (Cefalu, & Hu, 2004; Duruibe et al., 2007). Although the *trivalent* form of chromium (Cr-III) is an essential nutrient for most living organisms, the industrially produced, *hexavalent* chromium (Cr-VI) is toxic. In war areas people are exposed to it via contaminated air, food and water, due to the modern weaponry and absorption in the soil. The hexavalent chromium can cause various health effects, ranging from rashes, allergic reactions and respiratory problems to immune system impairments, organ damages and cancers (Pellerin & Booker, 2000; Sharma et al., 2012).

Our results on the association between in utero exposure and problematic infant emotional development contributes to the understanding of the detrimental effects of hexavalent chromium. In particular, increased maternal hair chromium at delivery decreased 6-month-old infant's positive affectivity and expressions of pleasure, i.e. smiling, laughter, and attempts to approach new objects and people. The findings thus add to earlier research that found postnatal chromium contamination to form a risk for autism spectrum disorders in school age (Yorbik, Kurt, Hasimi, & Oztürk, 2010) and physical development in preschool age (Xu et al., 2015). The finding is worrying, as positive emotional valence and effective regulation would be salient for infant wellbeing, contributing to children's later mental and physiological health and socio-emotional development.

In regard to uranium, it is a silvery-white, radioactive heavy metal that is in low concentrations found naturally from the earth's crust. Based on its nuclear properties, industrially produced *enriched uranium* is exploited in power plants and nuclear weapons (Bjørklund, Christophersen, Chirumbolo, Selinus, & Aaseth, 2017). *Depleted uranium*, which arises as a by-product of the industrial production of enriched uranium is somewhat less radioactive, but has a very high density, making it widely utilized in military operations with new generation weapons (Hon et al., 2015). All forms of uranium are both radiologiocally and chemically toxic, affecting the normal functioning of kidney, liver, heart, brain, and many other organs (Bjørklund et al., 2017).

According to expert reports, children in war zones are at particularly high risk of health hazards due to depleted uranium (WHO, 2001). The findings of the current study emphasize that prenatal exposure to uranium can also be dangerous on children's psychological development. The results showed that high maternal uranium hair concentrations at delivery interfered with the optimal early emotional development, by increasing negative affectivity of social fear and decreasing regulatory capacity such as the ability to sustain orientation or sooth among 6-7 month-olds.

Interestingly, studies of *animal* models also show a link between uranium contamination and emotion expression, suggesting that uranium exposure during the gestation and lactation potentially leads to passive, depressive-like behaviors in rodent offspring, indicated by freezing and immobility (Legrand, Elie et al., 2016). Further, exposure during *postnatal* development has been found to impair rodent brain development, leading to anxiety- and depressive-like behaviors as well as problems in object recognition and memory functions (Lestaevel, Dhieux, Delissen, Benderitter, & Aigueperse, 2015). Thus, the evidence of developmental effects of pre- and postnatal uranium exposure is rather well-documented in animal models, and possibly supports our findings on prenatal human exposure.

Impact of Maternal PTSD

We expected that maternal PTSD symptoms would accelerate the negative impact of heavy metal contamination on infants' emotional development. Research has shown maternal mental health problems to impair early child development through at least two mechanisms, the first related to pregnancy and the other to postpartum period. Maternal stress and anxiety during the pregnancy has found to program fetal hypotalamic-pituitary-adrenal (HPA) axis towards greater reactivity, making the infant physiologically more easily stressed and thus prone to negative emotionality (Davis et al., 2007; Glover, O'Connor, & O'Donnell, 2010). In the postpartum period, optimal infant emotion regulation is highly dependent on dyadic interaction, in which the mother is active in responding to infant physiological and emotional needs (Calkins & Hill, 2007). Mother's PTSD symptoms, especially intrusive and hypervigilant, can interfere with her ability to sensitively read infant's cues of distress and successfully sooth the baby (Boscuet Enlow et al., 2011; Van Ee, Kleber, & Mooren, 2012), which in turn may increase likelihood of child negative emotionality and regulatory difficulties.

Contrary to our expectations, maternal PTSD symptoms did not moderate the association between heavy metal load and infant emotion expression and regulation. Surprisingly, maternal PTSD was also directly unrelated to infants' emotional development. Available research in war conditions reveals that parents employ all their psychosocial resources to protect their children. For instance, a study showed that maternal posttraumatic growth and positive posttraumatic cognitions could protect both maternal mental health and infant development from the negative effects of war trauma (Diab, Isosävi, Qouta, Kuittinen, & Punamäki, 2018). We may thus speculate that mothers consciously cherish and buffer the wellbeing of their infants from their mental health problems in conditions of war, but toxic contamination of modern weaponry is beyond their power.

Limitations

Despite the heavy metal concentrations measured from a relatively large sample and longitudinal design, this study has several limitations. First, in assessing infant emotional development and maternal PTSD, we relied solely on maternal reports, inducing same-source bias. Records of observations, parental interviews of infant behavior in various emotion-elicit situations, and physiological stress regulatory markers would have provided independent and therefore more reliable assessment. Concerning maternal PTSD, clinical interviews would have guaranteed more objective detection of mental health problems (Pawlby, Sharp, Hay, & O'Keane, 2008). In addition, the assessment tool of infant emotional expressivity and regulation (Infant Behavior Questionnaire, Very short form, Putnam et al., 2014) fitted the data relatively poorly, which forced us to omit items with non-significant and very low factor loadings. Our shortened version of the IBQ may be considered narrow in terms of different qualitative aspects of infant behavior in various situations.

Second, we assessed maternal hair heavy metal contamination only at birth, when mother-infant contaminations were positively correlated (Manduca et al., 2017). In the aftermath of 2014 war on Gaza, the participating mother-infant dyads were deprived from international protection. The military siege was not lifted, and many of the contaminated areas and buildings could not be cleaned (Manduca et al., 2017). Therefore, instead of mere prenatal contamination, more chronic exposure from pre- to postnatal period might have affected the infant development. Further analyses are necessary to disentangle the prenatal and accumulating postnatal impact of toxic war-remnants on child development.

Third, mothers who remained as participants from T1 to T2 had longer gestations and healthier newborns, compared to those who withdrew from the study. It is thus important to note that the analysed follow-up sample is biased towards obstetrically less risky infants. Research shows these risks to have negative impact on child emotional development (Cassiano, Gaspardo, & Linhares, 2016), which is important to consider when reviewing the results of this study.

Fourth, we were restricted by the regression analytic methods when investigating several metals simultaneously. In real life and under conditions of war, metals often occur together, as indicated by the correlations between metals. Importantly, chromium and vanadium, showing the highest correlation (r = .83) in our study, were both found as components of metal "augmented" weaponry used against the Palestinian population during the war on Gaza in 2008/09, as these metals were found to be embedded in wounds caused by Israeli weaponry (Skaik et al., 2010). Yet, in stepwise regression analysis, only one of the predictors that explain overlapping variance in the outcome was included in the model, based onField (2006). Concerning conclusions, however, our results on the detrimental effects of chromium and uranium were similar and consistent. In future studies, it would be important to better understand and model the joint, potentially interacted effects of various, co-occuring heavy metals.

Conclusions

The study reported associations between war-related toxic contamination in utero and infant development, which calls for serious concern of civilian safety and human rights. Whereas earlier research has shown detrimental effects of prenatal toxic exposure on gestation, birth and newborn health (Alaani et al., 2011; Naim et al., 2013), the results of this study indicated that the adverse impact of new weapon technology is not limited to children's physical health. In contrast, maternal exposure to war-related chromium and uranium during pregnancy was associated with impaired early emotional development of the child, with potential long-term impact on child behavior, personality and stress regulation. Thus, it appears that the impact of war is not limited to those who experience it directly, but is passed on to future generations through multiple mechanisms.

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Table 1. Descriptive information and Pearson's correlations of the analysed metals, children's temperamental regulation (IBQ), maternal PTSD symptoms, and children's age (covariate).

Variables	*M*	*SD*	Range	1	2	3	4	5	6	7	8	9	10
1 Chromium (Cr)	0.97	0.99	0.07–7.52	1									
2 Mercury (Hg)	6.81	112.45	0.01–2480.00	.06	1								
3 Vanadium (V)	0.54	0.46	0.01–3.92	.83**	.02	1							
4 Strontium (Sr)	61.49	75.34	3.20–1480.00	.46**	.01	.49**	1						
5 Uranium (U)	0.21	0.21	0.00-2.49	.38**	.04	.38**	.49**	1					
6 IBQ: Positive affectivity	3.86	0.82	1.00-5.00	-.16**	-.03	-.10	-.02	-.16**	1				
7 IBQ: Negative emotionality	2.30	1.19	1.00-5.00	.05	-.00	.01	.05	.14**	-.06	1			
8 IBQ: Orienting / regulation	4.33	0.54	1.71-5.00	-.13*	-.07	-.07	-.08	-.18**	.46**	-.14**	1		
9 Mother: PTSD symptoms	1.99	0.58	1.00-3.69	-.15**	-.02	-.03	-.09	-.09	.00	-.06	-.04		
10 Child's age at T2	6.19	0.41	5.00-9.00	-.14**	-.03	-.16**	.07	.08	.23**	.07	.01	-.01	1

* $p < .05$, ** $p < .01$, $N = 392$.

Table 2. Heavy metal load predicting children's temperamental regulation. *N* = 392.

Child temperamental regulation (IBQ) at T2														
	Positive affectivity				Negative emotionality					Orienting/regulatory capacity				
	β	R^2	ΔR^2	p		β	R^2	ΔR^2	p		β	R^2	ΔR^2	p
Model 1:		.05	.05		*Model 1:*		.00	.00		*Model 1:*		.00	.00	
Child's age	.23			< .001***	PTSD	-.04			.461	PTSD	-.04			.389
Model 2:		.06	.01		*Model 2:*		.02	.02		*Model 2:*		.04	.04	
Child's age	.24			< .001***	PTSD	-.02			.720	PTSD	-.07			.170
PTSD[a]	.10			.052	U	.15			.007**	U	-.19			< .001***
Model 3:		.08	.02											
Child's age	.22			< .001***										
PTSD	.08			.12										
Cr	-.13			.013*										

Note. IBQ = Infant Behavior Questionnaire-Revised (IBQ-R; Putnam et al., 2014), Very Short Form; PTSD = Maternal post-traumatic stress disorder, measured with Harvard Trauma Questionnaire (HTQ; Mollica et al., 1992); Cr = Chromium; U = Uranium.