

Effects of abuse pattern of gestational toluene exposure on metabolism, feeding and body composition [☆]

Patricia A. Jarosz ^{a,*}, Ellen Fata ^{b,d}, Scott E. Bowen ^{c,d},
K-L. Catherine Jen ^{b,d}, Donald V. Coscina ^{c,d}

^a College of Nursing, Wayne State University, Detroit, MI 48202, USA

^b Department of Nutrition and Food Science, Wayne State University, Detroit, MI 48202, USA

^c Department of Psychology, Wayne State University, Detroit, MI 48202, USA

^d College of Liberal Arts and Sciences, Wayne State University, Detroit, MI 48202, USA

Received 24 July 2007; received in revised form 13 November 2007; accepted 19 December 2007

Abstract

Aims: Inhalant abuse during pregnancy lowers birth weight and impedes early development. These studies explored the effects of brief, repeated, prenatal toluene exposures in pregnant female rats on body weight, metabolic rate, body composition, and food intake in their offspring.

Method: Rats were exposed to 0, 8000, 12,000, or 16,000 ppm of toluene twice daily for 15 min from gestational days 8 to 20. The effects of such exposures on post-weaning litter weights, oxygen consumption, carbon dioxide output, and body fat content were determined in 2 cohorts ($n=23$, $n=24$) of offspring. Food intakes and weight changes in response to 3 different diets (regular chow, purified diet, purified high fat diet) were examined in another cohort ($n=24$) from postnatal days 72 to 116.

Results: Litter weights showed a significant linear decrease as a function of toluene dose. Offspring exposed to the 16,000 ppm toluene dose displayed statistically lower energy expenditures than control rats. Male rats exposed to 8000 or 16,000 ppm toluene had significantly greater percentage of body fat as well as total body fat than the other groups. Toluene also significantly suppressed weight gain over the time chow was consumed compared to the 0 ppm control group. Finally there were trends for a main effect of toluene dose on food intake during chow and during high fat diet consumption, with rats in the 12,000 ppm group consuming more than the 0 ppm group on both diets.

Discussion: These data suggest that, in addition to other previously documented abnormalities in neurological development and behavior, the physiological regulation of metabolism and body composition in males as well as food intake and weight gain in both sexes may be altered by prenatal exposure to toluene.

© 2008 Elsevier Inc. All rights reserved.

Keywords: Toluene abuse; Inhalants; Volatile solvents; Energy expenditure; Respiratory quotient; Body composition; Food intake; Body weight; Pregnancy

1. Introduction

Inhalant abuse is the intentional breathing of the vapors from volatile substances for the purpose of becoming intoxicated. Toluene, which is found in glues, cleaning fluids, lacquers, paints

and many other common household products, is among the most common of abused inhaled substances. A troubling recent finding is that over 1.6 million women of childbearing age (18–25 years old) in the United States reported inhalant use in 2004 [1]. This is a 15% increase over the number of women in this same age group reporting inhalant abuse in 2000 [2]. Toluene can readily cross the placenta and contaminate fetal tissues and amniotic fluid [3,4]. Animal studies that simulate human patterns of toluene abuse during pregnancy suggest that prenatal exposure is associated with an increased risk of spontaneous abortions as well as a number of neurodevelopmental abnormalities in the offspring. The latter

[☆] This work was supported in part by NIDA R01 DA015951.

* Corresponding author. College of Nursing, Wayne State University, 5557 Cass Avenue, Detroit, MI, 48202, USA. Tel.: +1 313 577 1798; fax: +1 313 577 4188.

E-mail address: pjarosz@wayne.edu (P.A. Jarosz).

include low birth weight, growth retardation, minor craniofacial and limb malformations, microencephaly, and behavioral impairments [5–11], symptoms of which have been termed the “fetal solvent syndrome” [12,13]. Therefore, the increased rate of toluene abuse among females of childbearing age is a cause for alarm due to its potential negative effects on a developing fetus.

Bowen et al. [5] have reported the effects of brief, repeated, prenatal toluene exposure on the postnatal development and behavior of rats. Pregnant females were exposed to 0, 8000, or 12,000 parts per million (ppm) of airborne toluene twice daily for 15 min from gestational days (GD) 8 through 20. Offspring exposed to toluene in utero displayed the highest rates of growth restriction, physical malformations such as oral cysts and missing tails, as well as behavioral impairments such as altered negative geotaxis and decreased grip strength when compared to the sham exposure group. The 12,000 ppm-exposed pups also weighed significantly less than those in the 0 and 8000 ppm groups during the first 16 days of life. The incidence of low birth weights in other offspring of toluene-exposed pregnant females also has been reported in previous animal [6–11] as well as human studies [12–14].

The low birth weight observed in offspring of toluene-exposed mothers supports the contention that a healthy maternal environment is critical for normal development. There is also growing evidence that an unfavorable fetal environment may alter hormonal and metabolic programming so as to maximize postnatal survival (i.e., developmental programming, see [15–17] for reviews). Furthermore, low birth weight may be a risk factor for obesity and other adult-onset disorders [18]. A fetus may become energy efficient during intrauterine development, then display excessive postnatal weight gain after consuming either normal or excessive amounts of food. Due to the rising incidence of toluene abuse, especially among young women of childbearing age, further characterization of the effects of prenatal toluene exposure on later postnatal life seems well worth investigating.

Previous methods of modeling toluene abuse commonly employed features such as lower solvent dosages, continuous exposure patterns, and/or gavage administration [6–11]. These studies modeled environmental or occupational exposure. Inhalant abusers typically inhale very rapidly and repeatedly. Bowen et al.’s [5] unique and more clinically relevant animal model of brief, repeated high-dose toluene exposure mirrors exposure levels, durations and patterns typically found with inhaled solvent abuse in humans. While the effects of some forms of gestational toluene exposure on food intake, birth weight and post-weaning body weight have been studied, there has been no research to date that has examined the consequences of brief, repeated toluene inhalation on such variables [5] and no research to our knowledge that has examined its effects on whole-body metabolic rate. Therefore, this research was conducted to undertake these investigations.

Using the Bowen et al. [5] method of toluene inhalation, it was hypothesized that the offspring would display the following effects as exposure doses increased: 1) have lower birth weights, 2) display lower energy expenditures (EEs) and higher respiratory quotients (RQs), 3) exhibit higher adult body weights and percentages of body fat, and 4) be more susceptible

to increasing their caloric intake, especially when fed a high fat diet as adults.

2. Methods and materials

2.1. Animals

Forty timed-pregnant female Sprague–Dawley rats were obtained from Charles River Laboratories (Portage, MI, USA) on GD 4 and individually housed in polypropylene cages with a 12-hour light/dark cycle (lights on 0600/lights off 1800). The temperature of the vivarium was maintained at 20–22 °C, with relative humidity levels averaging 55%. The dams had unlimited access to Rodent Lab Diet 5001 (PMI, Nutrition International Inc., Brentwood, MO) and water and were weighed every second day. All protocols had prior approval by the Wayne State University Institutional Animal Care and Use Committee.

2.2. Prenatal toluene exposure

All toluene exposure procedures were conducted in the behavioral pharmacology and toxicology laboratory, which was in the same building within which our lab is located. Following a four-day adjustment period, rats were assigned to one of four gestational treatment groups, based on equivalent average weights upon arrival. Dams were exposed to room air (0 ppm toluene) or 8000, 12,000, or 16,000 ppm toluene (#T324; Fisher Scientific, Fair Lawn, NJ) 15 min twice daily, 2 h apart, from GD 8 through GD 20 (see Bowen et al. [5] for a complete description of this procedure). Upon parturition in the behavioral pharmacology and toxicology lab, subsets of pups were assigned to us for use in the present research and group housed four per cage in the vivarium described above. One to two pups from each dam (one male and one female) were allocated to the studies. Offspring were weaned on postnatal day (PN) 21. Two experiments were conducted in the offspring: one examining metabolic rate and body composition shortly after weaning, the other examining weight gain in response to consumption of three different diets at an older age.

2.3. Metabolic study

At approximately 30 days of age, rats from all four prenatal exposure groups were placed in the absence of food and water into one of eight acrylic chambers of a metabolic apparatus (each 21 × 21 × 21 cm; total volume = 8.91) for 3 h during midday. The rates of oxygen (O₂) consumed and carbon dioxide (CO₂) produced were measured by an Oxyscan open circuit indirect calorimeter (Accuscan Instruments, Columbus, OH). The O₂ and CO₂ analyzers were first calibrated each test day with highly purified gas standards (Cryogenic Gases, Detroit, MI). Room air was drawn through each chamber at a rate of 1.5 L/min. The levels of O₂ and CO₂ were sequentially measured over the last 30 s of five-minute sampling periods, which generated difference scores between the data derived from each individual chamber vs. the room air. The concentrations of both gases were recorded in mL/kg of body weight/min.

Download English Version:

<https://daneshyari.com/en/article/2845568>

Download Persian Version:

<https://daneshyari.com/article/2845568>

[Daneshyari.com](https://daneshyari.com)