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Lead Exposure Alters the Development of Agonistic Behavior in Golden Hamsters

ABSTRACT: *We tested the effects of exposure to different doses of lead acetate (either 0, 25, 100, or 400 ppm) on the development of aggressive behavior in male golden hamsters. Pups were tested for offensive responses across puberty, as they were maturing from play fighting to adult aggression. Our data show a dose-specific effect of lead exposure on the development of aggression during puberty at doses resulting in blood levels well below 20 μg/dl. Animals exposed to 25 ppm lead acetate were faster and performed more than twice as many attacks on intruders by late puberty. They were also twice as likely to initiate adult instead of play-fighting attacks around mid-puberty. These observations were independent of any effect on growth. Thus, exposure to low doses of lead enhanced aggression and accelerated its maturation. As such, our data support the association between exposure to low doses of lead and aggressive behavior in boys. © 2005 Wiley Periodicals, Inc.* Dev Psychobiol 47: 158–165, 2005.

Keywords: *aggression; puberty; play-fighting; impulsivity; toxicity; golden hamster*

INTRODUCTION

Lead exposure during development has been associated with enhanced violence. Early exposure to low doses of lead (leading to blood lead levels ranging from 10 to 30 μg/dl) has been correlated with disruptive and violent social behavior in children, especially boys (Bellinger, Leviton, Allred, & Rabinowitz, 1994; Dietrich et al., 2001; Needleman et al., 1996; Sciarillo, Alexander, & Farrell, 1992; Thomson et al., 1989; Wasserman et al., 1998). Seven and 11-year-old boys with elevated blood lead levels were more likely to engage in acts of bullying, vandalism, arson, shoplifting, and other delinquent behaviors (Needleman et al., 1996). Another study reported a significant link between prenatal lead exposures and self-reported juvenile delinquency through a long-term study tracking lead exposure in children's blood lead levels until mid-adolescence (Dietrich et al., 2001). However, these data need to be supported by experimental tests on the effects of early exposure to low doses of lead on aggressive behavior through animal studies.

In a laboratory setting, aggression can be described as offensive or defensive, each having separate characteristic behavioral sequences and neural circuitry (Adams, 1979; Blanchard & Blanchard, 1977; Blanchard, Wall, & Blanchard, 2003). Offensive responses are best observed in the presence of a smaller and younger intruder (Delville, David, Taravosh-Lahn, & Wommack, 2003; Miczek, 1979). Bigger residents are more likely to engage intruders and win fights. Hamsters are excellent subjects for laboratory studies on aggression. As adults, hamsters readily attack individuals placed in their home cage (Ferris et al., 1997). As juveniles, they engage in play-fighting with their littermates as soon as they develop motor coordination around postnatal day 20 (P-20) (Goldman & Swanson, 1975; Schoenfeld & Leonard, 1985). Their offensive responses toward smaller intruders change during puberty, as agonistic behavior matures from play-fighting to ''adult'' or ''serious'' aggression (Delville et al., 2003). The maturation of offensive responses is marked by a gradual shift of the body parts

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targeted during attacks. In early puberty (P-28 to P-40), play-fighting attacks are targeted at the cheeks and face of the intruders (Pellis & Pellis, 1988a,b; Wommack, Taravosh-Lahn, David, & Delville, 2003). Around mid-puberty (P-40 to P-50), attacks are focused on the flanks (Wommack et al., 2003). During late puberty and early adulthood (P-50 to P-70), attacks are targeted on the rump and/or lower belly, characteristic of adult aggression in hamsters (Pellis & Pellis, 1988a,b; Wommack et al., 2003).

Various studies have reported effects of exposure to low doses of lead on agonistic behavior in animal models (Delville, 1999; Holloway & Thor, 1987; Laughlin, Bushnell, & Bowman, 1991; Li et al., 2003; Sloman et al., 2003). For instance, exposure to low doses of lead enhances predatory aggression after cessation of treatment in cats (Li et al., 2003). In rainbow trout, exposure to low doses of lead was associated with a non-significant increase in successful attacks when compared with other trace metals (Sloman et al., 2003). In hamsters, exposure to low doses of lead during development is associated with enhanced aggression in early adulthood (Delville, 1999). However, it is unclear how and when these animals become more aggressive during development. Even though few studies have examined the effects of early lead exposure on play fighting in juveniles, the results have been contradictory. In rats, lead exposure is associated with enhanced play activity (Holloway & Thor, 1987). In contrast, lead exposure has been associated with decreased play activity in rhesus monkeys (Laughlin et al., 1991). However, the relationship between play and aggressive behavior was unclear in these studies. In rats, play and aggression are separate behaviors (Pellis, 2002). Hamsters may be helpful to resolve this issue. Contrary to rats, hamsters do not appear to have a developmental period dedicated to play during puberty (Delville, Newman, Wommack, Taravosh-Lahn, & Cervantes, 2005). Agonistic interactions during puberty are mostly restricted to offensive and defensive responses. Thus, using hamsters it is possible to test the effect of lead exposure on the maturation of offensive aggression, without the confounding effects of play. The current study was designed to test the effects of early exposure to different doses of lead on the development of agonistic behavior in male golden hamsters.

METHODS

Animals and Treatment

Adult male golden hamsters were raised in our laboratory colony originating from breeders purchased from Harlan Sprague Dawley (Indianapolis, IN). They were individually housed in Plexiglas cages ($32 \times 19 \times 12.5$ cm) containing sterilized wood shavings for bedding under a reversed light cycle (14L-10D, lights off at 10:00). The animals were randomly separated into four treatment groups according to the doses of lead acetate in their drinking water. The doses of lead acetate were prepared with filtered distilled water (E-pure, Barnstead/Thermolyne, Dubuque, IA) at the concentrations of 0, 25, 100, and 400 ppm. Previous studies in hamsters showed that exposure to 100 ppm lead acetate resulted in blood lead levels between 10 and 15 μg/dl (Delville, 1999). The goal of the present study was to test additional doses within this range. Water bottles were replaced regularly to prevent precipitation. Food (rodent diet in pellet form, Harlan Tekland, Madison, WI) and water were available ad libitum. The studies were approved by the IACUC of the University of Texas at Austin and the animals were kept in an AALAC-accredited facility.

Multiparous dams were exposed to lead water for at least 1 month prior mating. Both dams and pups were continually exposed to their respective lead treatment throughout the study. Food intake was recorded every other day for 2 weeks before and 2 weeks after parturition. Food pellets were placed inside the cages. Food intake was derived from the amount of food left inside the cages. This measurement was facilitated by the fact that hamsters have well-organized cages. Regardless of lead exposure, hamsters tended to hoard their food in one corner of their cages and nest in another (Cervantes, unpublished observations). Water intake (water drunk from drip-free bottles) was recorded every day for 2 weeks before and 2 weeks after parturition. Body weights were recorded once a week for the dams throughout pregnancy and for the pups throughout development. Based on the food intake data (i.e., no effect of lead on food intake), there was no necessity for pair-fed groups. The pups were weighed on a weekly basis to determine possible effects of lead on their growth and development. Each litter was culled on P-5 to six pups, including both males and females. Male offspring were weaned on P-25, individually housed, and kept at the same lead exposure as their respective dam.

Blood Lead Levels

Animals were sacrificed after another set of tests around P-70 and blood samples were collected to determine blood lead levels by anodic stripping voltammetry with a Lead Analyzer (Model 3910B, ESA, Chelmsford, MA), as previously explained (Salinas & Huff, 2003).

Behavioral Testing

All behavioral observations were recorded in the middle of the dark phase and consisted of the following.

Pre-Weaning Behavior. Pups will engage in agonistic interactions (i.e., play-fighting) as soon as they are capable of coordinated movements (Goldman & Swanson, 1975; Schoenfeld & Leonard, 1985). The litters ($n = 14$, per lead dose group) were observed before weaning on P-19, P-20, and P-21 in the absence of the dams for 10 min. Each litter contained six pups and no attempt was made to identify individuals. Observed behaviors related to the entire litter. Behavioral recordings were mostly

limited to Pins (defined by an animal pushing and keeping another down on the cage bottom). These observations were performed to confirm any effect of lead on the developmental onset of play-fighting.

Activity. Activity was recorded as a control for the possible effects of lead exposure on the frequency of attacks and bites. Hamsters were observed in a lat-maze for a period of 10 min on P-40. The lat-maze apparatus is commonly used for the assessment of activity (Griesbach & Amsel, 1998; Lipp et al., 1987). The letters lat in the lat-maze apparatus originate from a sacred stone cube used by Arabs in pre-Islamic times to worship a goddess called al-Lat. The lat-maze apparatus is an open square box ($63 \times 63 \times 21.5$ cm) with a smaller ($39 \times 39 \times 17.5$ cm) closed box set in the middle. The corridor space left between the boxes is marked with a line every 12 cm. The maze was placed in the animal room. The animals were placed at one corner of the maze and their behavior was observed. Number of lines crossed and corners turned were recorded as an index of activity. Escape attempts (animals trying to climb and jump out of the maze) were recorded as an index of stress.

Offensive Responses. Males were repeatedly tested for offensive responses after weaning on P-35, P-45, and P-56, corresponding respectively to early, mid- and late puberty in hamsters (Wommack, Salinas, Melloni, & Delville, 2004). During preliminary studies, repeated testing did not affect the maturation of offensive responses between P-35 and P-56. The animals were tested under a resident-intruder paradigm with a smaller (10%–20%) and younger (4–10 days) unknown intruder placed into the subject's home cage. A subset group of intruder animals experienced with defeat was kept for these behavioral tests. Each subject was exposed to different intruders across their development. Behavior was observed for 10 min and videotaped for later review with iMovie. The measures of offensive responses scored for the resident animals included frequencies and latencies of attacks and bites. An attack was defined as the combination of an approach immediately followed with an attempt to bite. Attack types were also recorded and were determined by the area targeted on the body of the intruder rather than the location of the bites, since the intruder may prevent or displace the attack. Attacks were targeting the following parts of the intruder: face and cheeks, flanks, or lower belly and rump. These attacks were labeled as Play-Fighting (face and cheeks), Side (flanks), or Adult (lower belly and rump) (Wommack et al., 2003). Attack types were compared as a percentage of all attacks combined. Frequencies and latencies of attacks and bites were used to assess the effect of lead on the intensity of agonistic responding across puberty. The differentiation of the types of attacks was used to assess effects of lead exposure on the maturation of agonistic behavior. Additional recordings included contact time and frequency of flank markings. Contact time was defined as the duration of time when the resident initiated contact and remained in close proximity to the intruder. Behaviors performed during contact time by the residents include olfactory investigations, attacks and bites. These behaviors are all elements of the aggression ethogram in hamsters (Grant & Mackintosh, 1963; Floody & Pfaff, 1977; Johnston, 1985; Siegel, 1985). Flank marking is a stereotypic scent marking behavior performed during agonistic encounters in golden hamsters (Johnston, 1975, 1985). The behavior is characterized by an arching of the back while the animal is rubbing its dorsolateral area against the cage walls (or other object in the environment) (Johnston, 1985).

Data Analysis

Food and water intake amounts were analyzed through two-way ANOVAs (F; independent variables: groups and repeated measures) followed by Fisher PLSD post-hoc tests. Lead levels determined from blood collected after sacrifice on P-70 were compared through a one-way ANOVA (F) followed by Fisher PLSD post-hoc tests. Body weights, percent of attack types, and latencies were analyzed in separate ANOVAs (F) followed by PLSD Fisher post-hoc tests for each test day and lead dose because of missing cells. Missing cells in latency and body weights were due to the fact that not all measurements were recorded. In addition, percentages of attack types could not be calculated for animals that did not fight on a particular day. Nonparametric data (frequency of behaviors) were analyzed through separate Kruskall–Wallis (H) tests followed by Mann–Whitney U-tests (two-tailed) for each test day and through separate Friedman (X^2) tests followed by Wilcoxon (Z) tests (two-tailed) for each group. The litter was used as the statistical unit for all data. Statistical values were considered significant if $p < 0.05$. Post-hoc tests were only performed when the main analyses were statistically significant.

RESULTS

Food and Water Intake

Daily averages of food intake both before and after parturition were not statistically different amongst the treatment groups. Food intake increased equally between groups during pregnancy, rising from about 20 g before to about 50 g after parturition. Daily averages of water intake did not differ significantly between groups. Daily water intake also increased during pregnancy rising from about 20 ml early in pregnancy to just over 30 ml after parturition. Consequently, daily lead acetate intake before parturition averaged 0.53 mg (25 ppm), 2.9 mg (100 ppm), and 9.87 mg (400 ppm). After parturition, these daily intake doses of lead acetate increased to 0.75 mg (25 ppm), 3.21 mg (100 ppm), and 10.45 mg (400 ppm).

Body Weights

Body weights were compared between treatment groups throughout development (Fig. 1). The pre-weaning weights were not significantly different between groups. Body weights at the ages of P-35, P-45, and P-56 re-

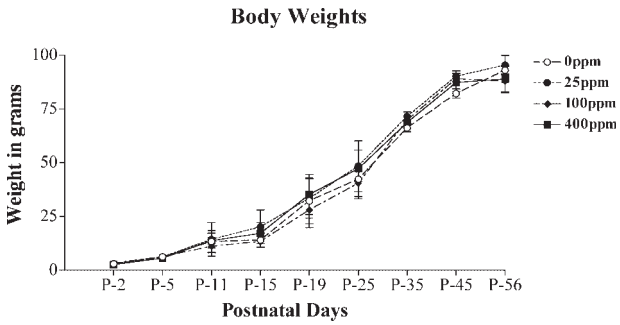

FIGURE 1 Comparison of body weights (mean ± SEM) between animals exposed to various doses of lead acetate (either 0, 25, 100, or 400 ppm) through their drinking water throughout development.

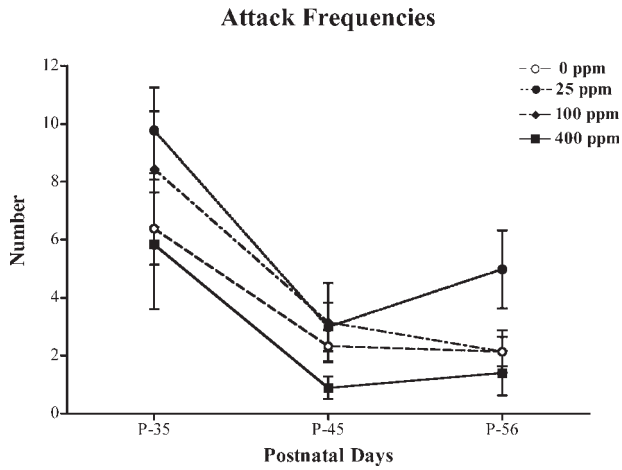

FIGURE 2 Comparison of attack frequencies (mean ± SEM) between animals exposed to various doses of lead acetate (either 0, 25, 100, or 400 ppm) through their drinking water throughout development. The animals were observed for offensive responses during a 10-min test in the presence of unknown intruders on postnatal day 35, 45, and 56 (P-35, P-45, and P-56).

mained comparable between groups. Pre-weaning and Post-weaning growth in all groups were unaffected by lead exposure.

Blood Lead Levels

Blood lead levels were sampled around P-70. The different lead conditions yielded statistically significant differences in blood lead levels [$F\ (3,22) = 394$, $p < 0.0001$]. The resulting group average lead concentrations were as follows: 0 ppm: 3.1 ± 1.0 μg/dl; 25 ppm: 5.5 ± 0.7 μg/dl; 100 ppm: 12.4 ± 2.0 μg/dl; and 400 ppm: 24.8 ± 1.2 μg/dl.

Behavior

Pre-Weaning Play-Fighting. Litters were observed for play-fighting in their home cage in the absence of the dams on P-19, P-20, and P-21. Number of pins ranged between 8 and 24 per 10 min, depending on observation days and groups. However, there was no statistically significant difference in frequency of pins amongst the different groups on these days.

Activity. Individual animals were tested for activity in a lat-maze on P-40 for 10-min periods. The number of lines crossed by the different groups ranged from 333 to 383. The number of corners turned ranged from 61 to 68 between the groups. The frequency of escape attempts ranged from 14 to 20 between the groups. These data did not yield any statistically significant difference between groups.

Offensive Responses. Animals were tested for offensive responses on P-35, P-45, and P-56. As shown before (Goldman & Swanson, 1975; Wommack et al., 2003; Taravosh-Lahn & Delville, 2004), attack frequencies were highest on P-35 (Fig. 2) and decreased over time in most groups. The decrease was statistically significant for animal exposed to 0, 25 and 100 ppm lead acetate, but was only a trend in animals exposed to 400 ppm [0 ppm: $X^2\ (2) = 11.4$, $p < 0.01$; 25 ppm: $X^2\ (2) = 12.2$, $p < 0.01$; 100 ppm: $X^2\ (2) = 8.3$, $p < 0.05$; 400 ppm: $X^2\ (2) = 4.9$, $p < 0.1$]. By P-45, animals exposed to 0, 25, and 100 ppm lead acetate performed significantly fewer attacks than on P-35 (0 ppm: $Z = 2.5, p < 0.05$; 25 ppm: $Z = 3.0, p < 0.01$; 100 ppm: $Z = 2.5$, $p < 0.05$). Frequency of attacks remained low on P-56 and did not differ significantly between P-45 and P-56 for any of the groups. Changes in bite frequency over time were also analyzed, but the differences were not statistically significant [0 ppm: $X^2\ (2) = 1.54$, $p > 0.1$; 25 ppm: $X^2\ (2) = 5.54$, $p > 0.05$; 100 ppm: $X^2\ (2) = 0.81, p > 0.1$; 400 ppm: $X^2\ (2) = 3.65$, $p > 0.1$].

There was no statistically significant difference in frequencies and latencies of attacks and bites nor contact times between groups on P-35 and P-45. Nevertheless, statistically significant differences were observed between treatment groups on P-56 (Fig. 3). Lead exposure had statistically significant effects on attack frequency [$H(3) = 10.5, p < 0.05$] and attack latency [$F\ (3,38) = 4.2$, $p < 0.05$]. Animals exposed to 25 ppm lead acetate performed twice as many attacks as compared to animals exposed to 0 ppm ($p < 0.05$) and 400 ppm ($p < 0.01$) lead acetate. In addition, animals exposed to 25 ppm lead acetate had shorter attack latencies compared to 0 ppm ($p < 0.01$), 100 ppm ($p < 0.05$), and 400 ppm ($p < 0.01$) lead acetate. Lead exposure also led to statistically

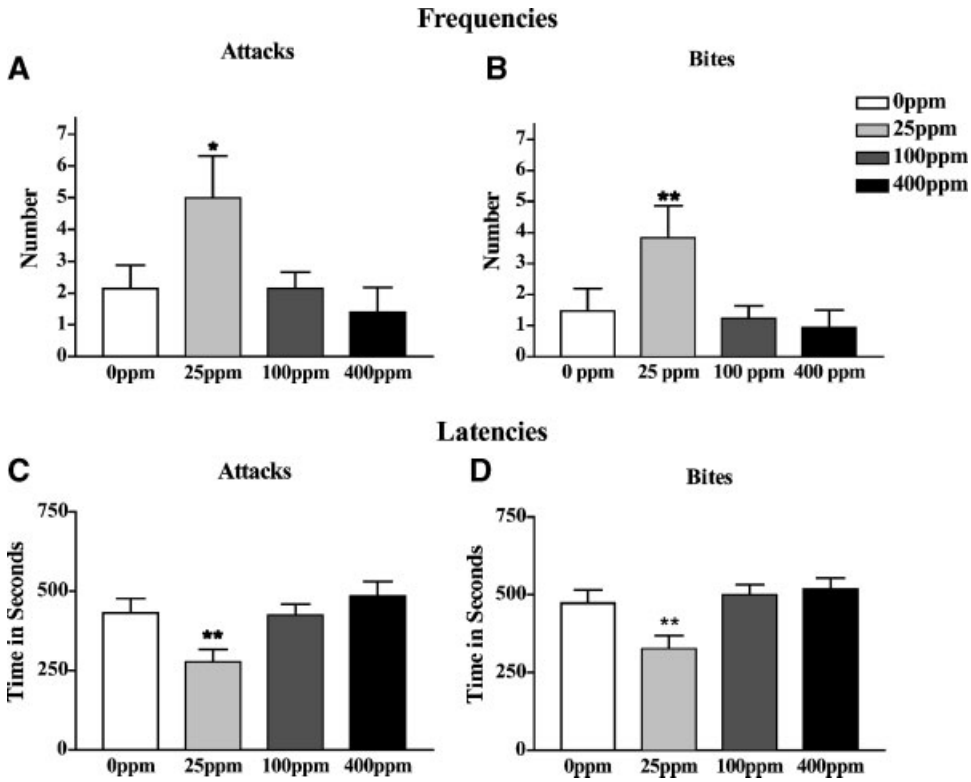

FIGURE 3 Comparison of attack (A) and bite (B) frequencies as well as attack (C) and bite (D) latencies (mean ± SEM) between animals exposed to various doses of lead acetate (either 0, 25, 100, or 400 ppm) through their drinking water throughout development. The animals were observed for offensive responses during a 10-min test in the presence of unknown intruders on postnatal day 56 (P-56). * $p < 0.05$, comparison between 25 ppm and controls. ** $p < 0.01$ comparison between 25 ppm and controls.

significant effects on bite frequency [$H(3) = 13.3$, $p < 0.01$] and bite latency [F (3,38) = 4.5, $p < 0.01$]. Hamsters exposed to 25 ppm lead acetate performed twice as many bites as compared to animals exposed to 0 ppm ($p < 0.01$) and 400 ppm ($p < 0.01$) lead acetate. Also, animals exposed to 25 ppm lead acetate had shorter bite latencies compared to 0 ppm ($p < 0.01$), 100 ppm ($p < 0.01$), and 400 ppm ($p < 0.01$) lead acetate.

The quantification of types of attacks led to the following observations. On P-35, about 50% of attacks were targeted at the face and cheeks, about 40% of attacks at the flanks, and less than 10% at the back and rump. These differences did not differ between groups. As the animals matured, the proportion of Adult attacks increased and Play-Fighting attacks decreased. By P-56, about 80% of attacks were targeted at the back and rump. A significant difference between groups was apparent only on P-45, as the animals performed various combinations of all types of attacks (Fig. 4). On that day, statistically significant differences were observed for the proportion of Play Fighting and Adult attacks [respectively; F (3,32) = 2.95, $p < 0.05$; F (3,32) = 2.93, $p < 0.05$]. On P-45, the proportion of Adult attacks was twice as high in hamsters exposed to 25 ppm lead than in the other groups (0 ppm: $p < 0.05$; 100 ppm: $p < 0.05$; 400 ppm: $p < 0.05$). This observation was accompanied by a lower proportion of Play-Fighting attacks in animals exposed to 25 ppm lead acetate (0 ppm: $p < 0.05$; 100 ppm: $p < 0.05$; 400 ppm: $p < 0.05$). Finally, the proportion of Side attacks did not differ between treatment groups [F (3,32) = 0.437, $p > 0.1$].

Other measures of agonistic behavior included contact time and flank markings. A similar pattern of differences between groups was observed with higher frequencies in animals exposed to 25 ppm lead acetate, but these differences were not statistically significant on any test day for contact time [P-35: $H(3) = 1.67$, $p > 0.1$; P-45: $H(3) = 4.98$, $p > 0.1$; P-55: $H(3) = 7.27$, $p > 0.05$] nor flank marking [P-35: $H(3) = 0.78$, $p > 0.1$; P-45: $H(3) = 3.16$, $p > 0.1$; P-55: $H(3) = 1.96$, $p > 0.1$].

DISCUSSION

The results of this study show a dose-specific effect of lead exposure on the development of aggression during

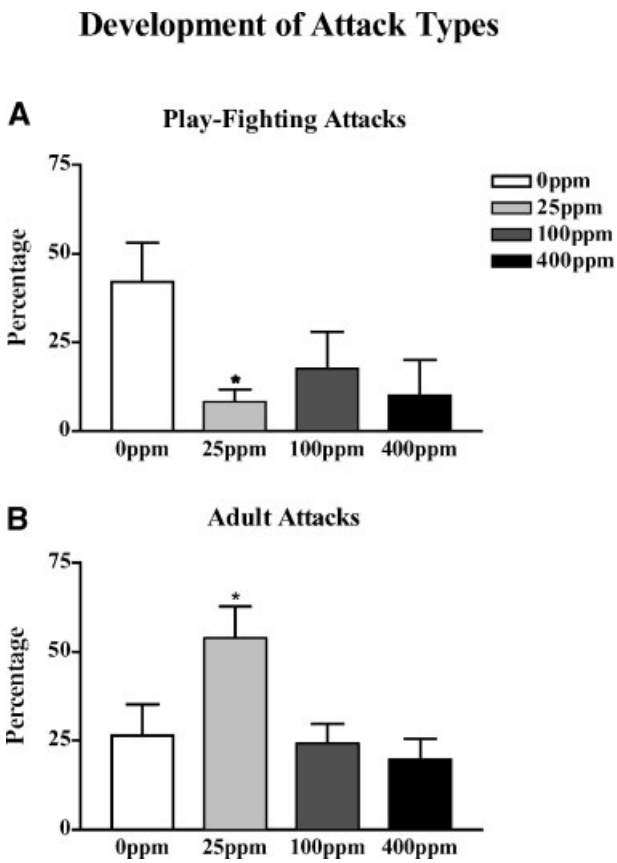

FIGURE 4 Comparison of the percentages (mean ± SEM) of Play-Fighting attacks (A) and Adult attacks (B) made between animals exposed to various doses of lead acetate (either 0, 25, 100, or 400 ppm) through their drinking water throughout development. The animals were observed for offensive responses during a 10-min test in the presence of unknown intruders on postnatal day 45 (P-45). $^{*}p < 0.05$, comparison between 25 ppm and controls

puberty. Exposure to 25 ppm lead acetate accelerates the maturation of offensive responses from play fighting to adult aggression. In addition, the same level of lead exposure enhances aggression by late puberty. Interestingly, exposure to higher concentrations of lead acetate had no statistically significant effect on the development of aggressive behavior. More importantly, it is the lowest dose leading to blood lead levels well below 20 μg/dl that enhanced aggression. This observation confirms the concern that exposure to low doses of lead can affect aggression in children (Center for Disease Control, 1991).

During the present study, animals exposed to 25 ppm lead acetate became more aggressive than their controls. Although these animals were always at the high end of the variability between groups during the study, the differences between groups only became statistically significant by P-56. On that day, hamsters exposed to 25 ppm lead acetate performed twice as many attacks and bites towards their intruder than their controls. Our data show that exposure to lead acetate can enhance aggression in late puberty. Lead exposure increased the intensity of adult aggressive behavior. However, exposure to higher doses of lead had no effect on aggression, or possibly reversed the effects of exposure to 25 ppm lead acetate. This finding is surprising and does not fit typical dose-dependent effects. However, it is important to note that offensive responses observed in a resident-intruder model can be affected by a variety of factors, such as social memory, emotional responsiveness, or motivation (Delville et al., 2003). It could be argued that the factors affecting the performance of offensive aggression are differentially affected by increasing doses of lead. Thus, as lead doses increased, different behavioral outcomes could be observed. During pilot studies, animals that were exposed to 1,000 ppm lead acetate (which resulted in blood lead levels well above 30 μg/dl) were found to be particularly fearful of their intruders. Although this dose was not used in this study, it is possible that the higher lead doses were associated with a partial reversal of the effects of exposure to 25 ppm lead acetate. It must also be noted that animals exposed to 400 ppm lead acetate, although not statistically different, were always at the lower end of the variability between groups.

Our data also indicate that lead exposure has little effect on attack frequency early in puberty. As such, our data differ from reports of lead affecting play in rats and monkeys (Holloway & Thor, 1987; Laughlin et al., 1991). However, it must be noted that our study focused exclusively on offensive responses rather than play. The significance of the effect of lead on adult rather than play-fighting offensive responses suggests a differential effect of lead on the mechanisms or neural structures underlying the behavior across puberty. It is interesting to note that post-weaning exposure to lead is sufficient to enhance impulsive responses in rats (Brockel & Cory-Slechta, 1998, 1999). Perhaps, the enhanced aggression observed in our animals in late puberty is related to enhanced impulsivity. In adult hamsters, attack frequency has been associated with impaired capacity to adapt to a delay in reward (David et al., 2004).

Our data include an unexpected finding. Lead exposure affects the peri-pubertal maturation of agonistic behavior from play-fighting to adult aggression. During puberty, offensive responses (attacks) shift from the face and cheeks (Play-Fighting attacks), to the flanks (Side attacks), and finally to the lower belly and rump (Adult attacks) (Wommack et al., 2003; Taravosh-Lahn & Delville, 2004). Our data show a dose-specific effect of lead exposure on this maturation. Animals exposed to 25 ppm lead acetate had an accelerated development of offensive responses. This effect was evident on P-45, which corresponds to mid-puberty in hamsters

(Wommack et al., 2004). Such a finding has never been reported in lead-exposed animals. Previous data have shown a delay in the onset of puberty in lead-exposed animals (Ronis et al., 1998). However, it is unlikely that our observations are related to a delayed maturation of the hypothalamo-pituitary gonadal axis. The peri-pubertal maturation of agonistic behavior in male rodents is controlled by adrenal and not testicular steroid hormones (Delville et al., 2005; Pellis, 2002; Romeo et al., 2003).

It must be noted that in the present study, blood samples were collected 2 weeks after the last test of offensive responses. It is possible that animals had higher blood lead levels during these tests. However, it is unlikely that animals exposed to 25 ppm lead acetate in their drinking water had blood lead levels above 20 μg/dl between P-35 and P-56.

The present study partially replicates previous findings in golden hamsters exposed to low doses of lead. In this previous study, lead-exposed hamsters also become more aggressive toward an intruder (Delville, 1999). The study consisted of a comparison between animals exposed to 100 ppm lead acetate during development and their controls. In the present study, animals exposed to 25 ppm lead acetate during development became more aggressive whereas animals exposed to 100 ppm lead acetate did not differ from the controls. Interestingly, exposure to 100 ppm lead acetate in both studies resulted in similar blood lead levels ranging from 10 to 15 μg/dl, regardless of differences in assay procedures (graphite furnace atomic absorption spectrometry vs. anodic stripping voltammetry). It could be argued that the behavioral differences between the experiments are related to the timing of exposure. In the present study, the dams were exposed to lead acetate at least 1 month before pregnancy. In the previous study, lead exposure started around mid-pregnancy (Delville, 1999). This difference could alter the behavior of the pups. Also, it could be argued that it takes a few weeks for blood lead levels to stabilize after the start of exposure. Thus, animals in the previous study could have been exposed to much higher lead levels during fetal development, which could have had detrimental effects early in life (i.e., decreased body weight and delayed behavioral development). This possibility was evidenced by body weight observations and behavioral tests performed around P-20. In the previous study, lead exposed animals were lighter than their controls after birth. In addition, these animals initiated play-fighting activity later than their controls at around P-20. In the present study, the females were mated after stabilization of blood lead levels and lead exposure had no effect on body weight at any time during development. In addition, all animals were actively play-fighting around P-20.

It is important to note that food and water intake did not differ significantly between treatment groups. These observations associated with a lack of differences in body weight and growth show that the inclusion of pair-fed groups was not necessary in the present study.

In conclusion, our data show that exposure to low doses of lead throughout development alters the maturation of aggressive behavior. First, lead exposure accelerates the peri-pubertal maturation of the behavior. Second, as lead exposed animals initiate adult aggression earlier they also become more aggressive in late puberty. These results may help explaining violent behavior in adolescents exposed to low doses of lead (Dietrich et al., 2001; Needleman et al., 1996).

NOTES

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