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Lead, Attention, and Impulsive Behavior: Changes in a Fixed-Ratio Waiting-for-Reward Paradigm

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BROCKEL, B. J. AND D. A. CORY-SLECHTA. *Lead, attention, and impulsive behavior: Changes in a fixed-ratio waiting-for-reward paradigm.* PHARMACOL BIOCHEM BEHAV **60**(2) 545–552, 1998.—Similar to the effects observed in children diagnosed with attention deficit hyperactivity disorder (ADHD), experimental animals exposed to lead (Pb) exhibit behaviors attributed to "impulsivity" and "inability to inhibit inappropriate responding." Such behaviors have led some to suggest that Pb exposure is associated with attention deficit. Based on the hypothesis that attention deficits are related to an ineffectiveness of delayed reinforcement, this study examined the effects of chronic postweaning Pb exposure on an FR waiting-for-reward paradigm. Rats were exposed chronically from weaning to 0, 50, or 150 ppm Pb acetate in water and following 40 days of exposure, trained on a fixed-ratio (FR) wait behavioral baseline. A total of 50 lever press responses (FR 50) produced food delivery. After earning an FR pellet, "free" pellets could be obtained by waiting; emission of another lever press reinitiated the FR requirement. "Free" pellets were delivered at increasing intervals (2 s, 4 s, 6 s, etc.). Pb exposure increased response rates on the FR schedule and decreased the mean longest waiting time, but also resulted in a higher number of responses per reinforcer than exhibited by controls. These Pb-induced differences are consistent with an inability to manage delays of reinforcement. © 1998 Elsevier Science Inc.

Lead Fixed ratio Impulsivity Attention Delay of reinforcement

LEAD (Pb) exposure has remained a major environmental health issue worldwide. In the United States, the designated blood Pb (PbB) level of concern for pediatric populations has dropped from 40 μg/dl to 10 μg/dl over the past 15 years, due primarily to the clinical and experimental evidence that even current very low environmental Pb exposures can have adverse effects on humans (7). It is estimated that 1.7 million children between 1 to 5 years of age have PbB levels equal to or exceeding 10 μg/dl (6).

Of particular interest to this study are the reported learning deficits in children and experimental animals that have been exposed to low levels of Pb. Cognitive deficits in Pb-exposed children have been demonstrated by, among other measures, lower intelligence quotient (IQ) scores (3,15), indicative of a general cognitive impairment. But even subtests scores on intelligence tests are not specific enough to describe the precise nature of these deficits. According to teacher rating scales, increasing PbBs were associated with higher distractibility and impulsiveness scores (28). Observations of children in the classroom have indicated increases in time engaging in off-task behaviors that were dose dependently related to Pb levels (28). Pb-associated perseverative behaviors have been reported in children performing the California Verbal Learning Test for Children and the Wisconsin Card Sorting Test (40). Taken together, these data have led to the speculation that Pb-induced cognitive impairments could be related to attention deficits.

Considered collectively, however, the literature suggesting attention deficits as the basis for the cognitive impairments associated with Pb are seemingly contradictory. For example, while impulsivity and perseverative behavior have both been attributed to Pb exposure, they are distinctly dichotomous behaviors, and it would be difficult to understand how both could be simultaneously operative. Such examples underscore the difficulties inherent in 'attention' as a single behavioral construct when, in fact, it encompasses a wide range of re-

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sponse classes. It is evident that attention deficits may be caused by numerous different types of behavioral disruptions. For example, impulsiveness can be described as responding without consideration of alternatives and/or consequences (24), whereas perseverative behaviors seem to be associated with an inability to alter response patterns with changes in the environmental contingencies. Any attempt to define the role of attention deficits in Pb-induced learning impairments and understand their neurobiological basis, or to more precisely understand attention deficits and their central nervous system basis, must first operationally define these various behavioral disturbances comprising attention deficit and implement appropriate measures of them.

Similar to the effects observed in humans, behavioral disruptions have been reported in experimental animals exposed to low levels of Pb. Several studies using fixed interval (FI) operant schedules in primates (30,34) and in rats (12–14) have shown that Pb exposure increases rate of responding with response patterns sometimes atypical of FI responding. Rice (32) suggests that these data indicate that Pb-exposed animals exhibit an inability to inhibit inappropriate responding, because increases in response rates on this schedule do not increase reinforcement density. In further support of this interpretation, on a differential reinforcement of low rates (DRL) schedule, an operant schedule that requires subjects to refrain from responding for a set interval, primates with PbBs under 15 μg/dl took longer to learn the task (33), and primates with PbBs of 40 μg/dl had a higher number of inappropriate responses (31).

Considering the clinical data, experimental models of different components of attention behavior would certainly be expected to be valuable in determining the behavioral mechanisms of Pb-associated cognitive deficits. Studies from other areas of research are beginning to devise some different behavioral procedures to study the various types of attention deficits and their underlying mechanisms. In an experiment to study the effects of benzodiazepines on "impulsivity" in rats, Bizot et al. (5) used a paradigm in which subjects could either respond on a fixed ratio (FR) schedule to obtain food pellets or refrain from responding to obtain "free" pellets (differential reinforcement of other behaviors, DRO), with the amount of time between free pellets increasing after each free pellet delivery. In a similar procedure, Long (23) reported that children who showed resistance to control by a multiple FR Extinction schedule were able to learn a multiple DRO FR without much difficulty. Children learned to refrain from responding more quickly when behaviors other than the designated response were reinforced, rather than waiting for the designated response to decline during extinction. The present study was designed to use a similar approach to begin to assess whether Pb exposure alters waiting behavior, the capacity to inhibit responding, and the response to delays in reinforcement.

METHOD

Subjects

Male Long–Evans rats (Harlan–Blue Spruce, Indianapolis, IN) were received at 21 days of age. On arrival, groups of 12 rats each of approximately equal weight were exposed to drinking water containing either 0, 50, or 150 ppm Pb acetate (Fisher Scientific, Pittsburgh, PA) dissolved in distilled deionized water. Pb exposure was sustained for the duration of the experiment. Rats were provided with Purina semipurified rat chow (Purina, St. Louis, MO) ad lib until body weights reached 300 g. Body weights were maintained at 300 g for the duration of the experiment. Typical standard rodent diets maintain excessively high levels of the essential metals Ca, Fe, and Zn that decrease oral absorption of Pb. The semipurified diet, which contains required rather than excess levels of these essential metals, thus permits the use of lower Pb acetate drinking water concentrations to achieve target PbB concentrations. Behavioral testing procedures were implemented at approximately 60 days of age. On the day prior to behavioral training, all but two animals had reached 300 g. These animals were placed on a food schedule that allowed a 3–5-g increase in body weight per day until body weights reached 300 g. Rats were individually housed in clear 45 × 24 × 21 cm plastic cages with wood chip bedding in a room that was maintained on a 12 L:12 D cycle and monitored for temperature and humidity. All procedures and animal care followed the National Institutes of Health and the University of Rochester Animal Care and Use Committee guidelines.

Apparatus

Behavioral testing was conducted in operant chambers (Coulbourn Instruments, Inc., Lehigh Valley, PA, Model E10-10) that were housed in light-attenuated enclosures equipped with fans for ventilation. Three response levers on the front wall of the operant chamber were 3.8 cm above a grid floor and were separated by 3.5 cm. Force of approximately 30 g was required to depress the lever microswitch. Food reinforcers (45 mg food pellets, P. J. Noyes Inc., Lancaster, NH) were delivered via a food trough that was located below the center lever. Extraneous sounds were masked with continuous white noise. A Digital Equipment Corporation (DEC PDP $^{11}/_{73}$) computer was programmed with the SKED-11 system (38) to control behavioral contingencies and data collection. Events during each session were stored sequentially with a resolution of 10 ms.

Procedure

Rats were trained to press one of three levers in an operant chamber via an overnight autoshaping program used routinely in this laboratory (9). All but eight animals learned to lever press after a single session. Seven rats were trained after an additional overnight training session, and one rat required three nonconsecutive training sessions. Across training sessions, the response requirement on the fixed ratio (FR) component was increased until 50 responses (FR 50) were required to earn a 45-mg food pellet. Once rats were responding on an FR 30 schedule, a wait component was added. The wait component allowed the rats to obtain "free" pellets after completing an FR until another lever response was emitted, which reinitiated the FR component. "Free" pellets were delivered at increasing intervals (i.e., 2 s, 4 s, 6 s, etc.). There was no upper limit for the waiting component; the FR component was reset only with a response on the operant lever. A reinforcement period of 3 s followed each pellet delivery during which lever responding had no programmed consequences. Time spent in the reinforcement period was not included in the measurement of the waiting length between pellet deliveries. This reinforcement period was used to separate pellet delivery and consumption from waiting behavior. Once all rats were responding on the FR 50 schedule, behavior was allowed to stabilize over 30 sessions. Behavioral sessions were conducted during the light cycle, 5 days a week, and were 15 min in duration.

PbB Determinations

At 3 months of Pb exposure (during the 30 day stabilization period), a total of 100 μl of blood was obtained after the behavioral session for the purpose of determining PbB concentrations by nicking rats' tails following immersion in warm water. Whole blood was analyzed for Pb by anodic stripping voltammetry (Model 3010A Trace Metals Analyzer, Environmental Science Associates, Bedford, MA) according to the method of Morrell and Giridhar (26). The bottom limit of sensitivity of this technique is 5 μg/dl.

Data and Statistical Analysis

FR response rates were derived by taking the total number of responses divided by the total time spent in the FR component. Mean longest time to wait for a "free" pellet (MN long wait) was calculated as the mean longest time a rat would wait between "free" pellets before resetting the FR component (see Fig. 1). Responses per reinforcement, a measure of "efficiency," was equal to total number of responses divided by total number of reinforcers (both for the FR and Wait components). A ratio of MN long wait and mean time to complete an FR was calculated by taking the MN long wait and dividing it by the time to respond 50 times based on the overall FR response rate. Twenty sessions of baseline data after an initial stabilization period were analyzed in five blocks of four sessions each using RMANOVAs (repeated measures analysis of variance), with Pb concentration serving as the between factor and blocks of sessions as the within factor. Fisher's protected least-squares differences (PLSDs) were conducted to further characterize the differences indicated by a main effect of Pb, and post hoc simple effects ANOVAs were used to further describe interactions between blocks of sessions and Pb exposure. A criteria of $p < 0.05$ was used for both RMANOVA and post hoc analysis. All analysis were conducted using StatView 4.5 statistical software (Abacus Concepts, Inc).

RESULTS

PbB Levels

After 3 months of exposure to either 0, 50, or 150 ppm Pb acetate, group mean (±SE) PbB levels increased in a concentration-related fashion averaging <5, 10.8 ± 1.8 and 28.5 ± 4.3 μg/dl, respectively, $F(2, 21) = 28.8$, $p < 0.0001$. No overlap of Pb groups was observed as indicated by Fisher's PLSD (all *p-values* < 0.001).

FR Component Performance

Response rates increased across baseline sessions and ranged from approximately 85 to almost 200 responses per minute, $F(4, 132) = 6.5$, $p < 0.0001$. A main effect for Pb was found to be significant, $F(2, 33) = 4.6$, $p < 0.02$, with the 150 ppm group having higher response rates than both controls ($p < 0.01$), and the 50 ppm group ($p < 0.02$) (Fig. 2A). As seen in Fig. 2B, Pb exposure was also associated with a notably higher number of FR component resets, $F(2, 33) = 3.6$, $p < 0.04$, with controls averaging approximately four resets compared to almost 13 in the 150 ppm group ($p < 0.02$). The 50 ppm group did not differ significantly from either controls or the 150 ppm group.

Waiting Behavior

Pb produced a shorter MN long wait, $F(2, 33) = 6.7$, $p < 0.004$ (Fig. 3A) with controls averaging between 25–30 s, the 50 ppm group 15–20 s, while the 150 ppm group averaged approximately 10–15 s. Values of both the 150 ppm ($p < 0.001$) and 50 ppm group ($p < 0.04$) were significantly shorter than

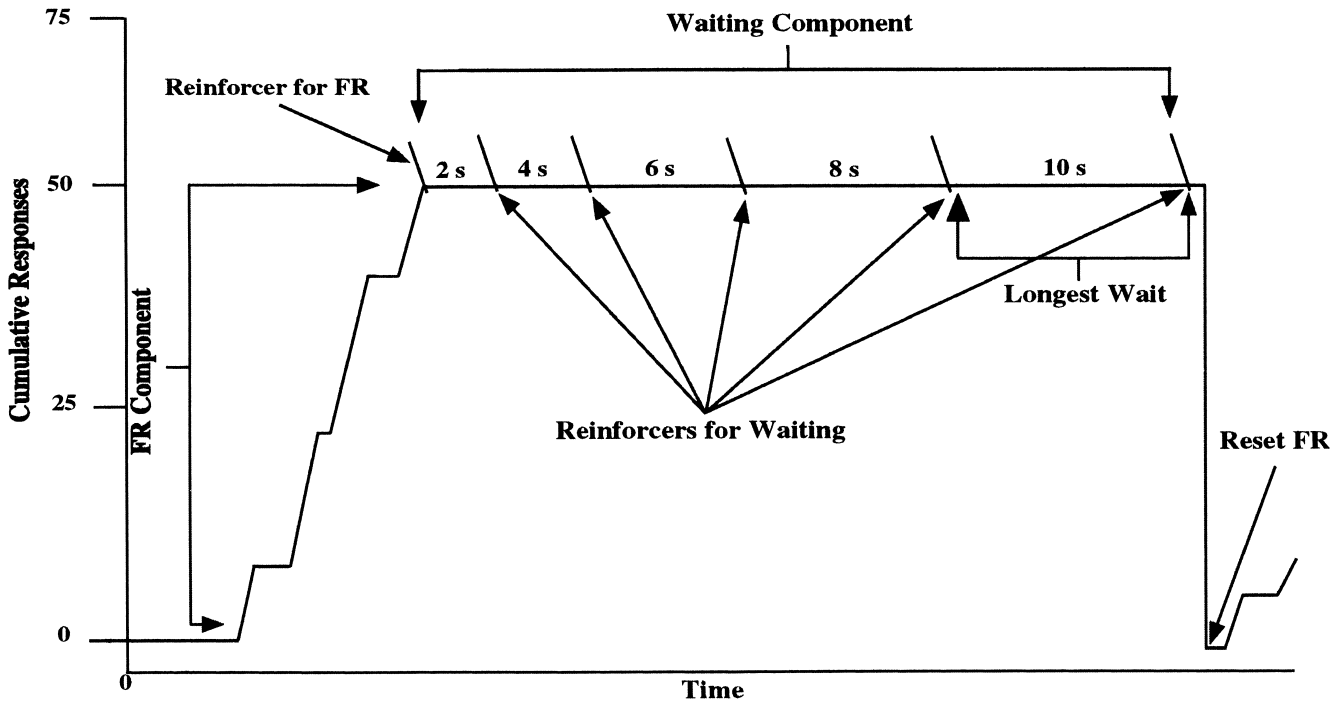

FIG. 1. Schematic of performance on the FR 50—Wait behavioral baseline.

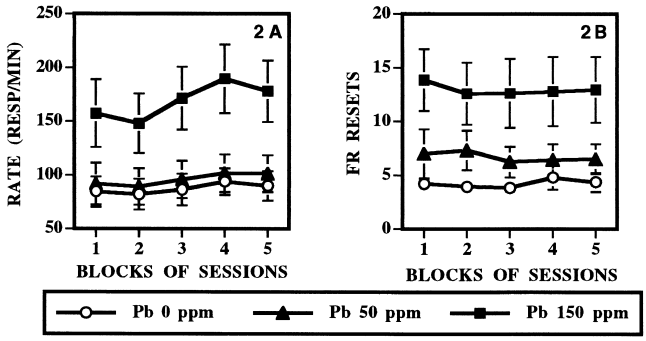

FIG. 2. The effects of Pb exposure (0 ppm, open circles; 50 ppm, filled triangles; 150 ppm, filled squares) across five blocks of 4 days each on response rate (A) and the number of FR resets (B). Each point represents a group mean, with each bar indicating ±1 SE (n = 12 per exposure group).

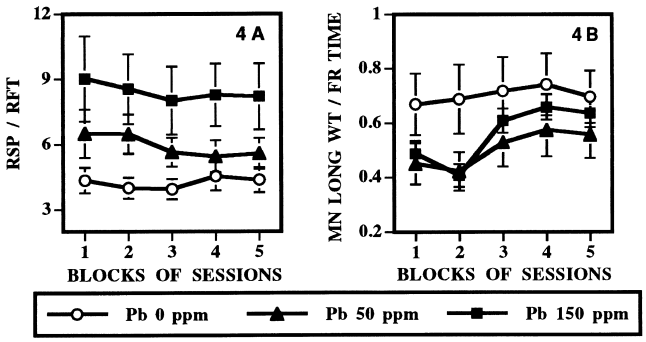

FIG. 4. The effects of Pb exposure across five blocks of 4 days each on responses per reinforcers (A) and ratio of MN long wait and mean time to complete an FR 50 (B). Each point represents a group mean, with each bar indicating ±1 SE (n = 12 per exposure group).

corresponding control group values. Because of their higher FR response rates and decreased waiting time, rats in the 150 ppm group actually received more "free" reinforcers, $F(2, 33) = 5.2$, $p < 0.02$, than did their counterparts in either the 0 ppm ($p < 0.004$) or the 50 ppm groups ($p < 0.03$) (Fig. 3B). Specifically, controls averaged approximately 40 wait reinforcers per session, while the 150 ppm group earned between 50–55 reinforcers.

Response Patterns

Although the 150 ppm Pb exposure was associated with an increased number of reinforcers, it also resulted in a higher response to reinforcement ratio, $F(2, 33) = 3.9$, $p < 0.04$ (Fig. 4A), with controls averaging about 4.5 responses per reinforcement or about half of the value of the 150 ppm group who averaged almost nine responses per reinforcer. These data indicate that rats exposed to 150 ppm Pb respond in a less efficient manner than controls ($p < 0.01$), with a similar though nonsignificant trend in the 50 ppm group.

Differences in response rates as a contribution to the effect on MN long wait can be accounted for by dividing MN long wait by time to complete an FR. A ratio of 1 would indicate that prior to resetting the FR component, time between "free" pellets was equivalent to the time it would take to complete an FR 50. Ratios less than 1 indicate that the time to complete an FR is longer than the MN long wait, i.e., early reset. Rats in the 150 ppm group did not earn reinforcement sooner for resetting the FR than could be obtained by waiting (ratio <1). In fact, Pb groups did not differ from controls on this measure, as indicated by a nonsignificant main effect of Pb, $F(2, 33) = 1.4$, $p > 0.05$ (Fig. 4B). This ratio increased across blocks of sessions, $F(4, 132) = 10.8$, $p < 0.0001$, in a manner that was dependent on Pb exposure; however, $F(8, 132) = 2.1$, $p < 0.04$. As indicated by simple effects ANOVA, this ratio remained unchanged across blocks in the control group, $F(4, 44) = 0.9$, $p > 0.05$, but increased in both the 50 ppm group, $F(4, 44) = 4.6$, $p < 0.004$, and the 150 ppm group, $F(4, 44) = 13.5$, $p < 0.0001$.

In Fig. 5, cumulative records from individual animals in the control and 150 ppm Pb groups on the last day of baseline illustrate the differences in overall response patterns. These individual records demonstrate the high response output and reduced waiting behavior in the 150 ppm Pb group.

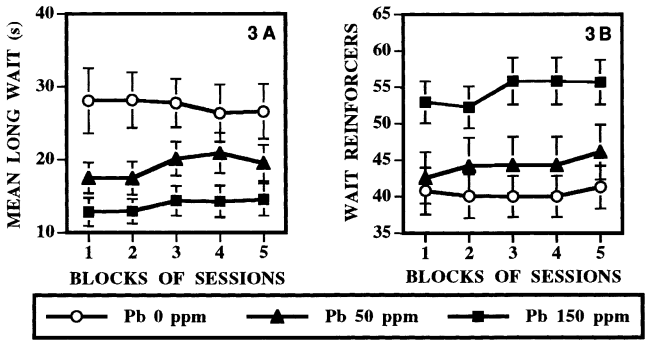

FIG. 3. The effects of Pb exposure across five blocks of 4 days each on MN long wait (A) and the number of wait reinforcers (B). Each point represents a group mean, with each bar indicating ±1 SE (n = 12 per exposure group).

DISCUSSION

This study demonstrated notable Pb-related differences in the pattern of responding on a multiple FR waiting-for-reward schedule of reinforcement utilized to address issues of reinforcement delay, impulsivity, and inability to inhibit responding as potential behavioral mechanisms of Pb-induced learning impairments. As exemplified by the cumulative records depicted in Fig. 5, Pb exposure, particularly the 150 ppm exposure concentration, resulted in accelerated FR response rates and more frequent reinitiation of the FR component, and thus a significantly shorter waiting time. This pattern of responding ultimately resulted in a greater number of reinforcers being earned by the 150 ppm group, because the resets occurred during the shorter interval wait durations between free pellets. Although this may appear to be a more optimal strategy of responding, given the greater number of total reinforcement deliveries it produced, the price associated with it was a virtual doubling of the number of responses emitted per each reinforcer obtained, making it actually a highly inefficient response pattern. Given the excessive effort required by this pattern, it is interesting to speculate about what its consequences would be over an extended time frame in humans.

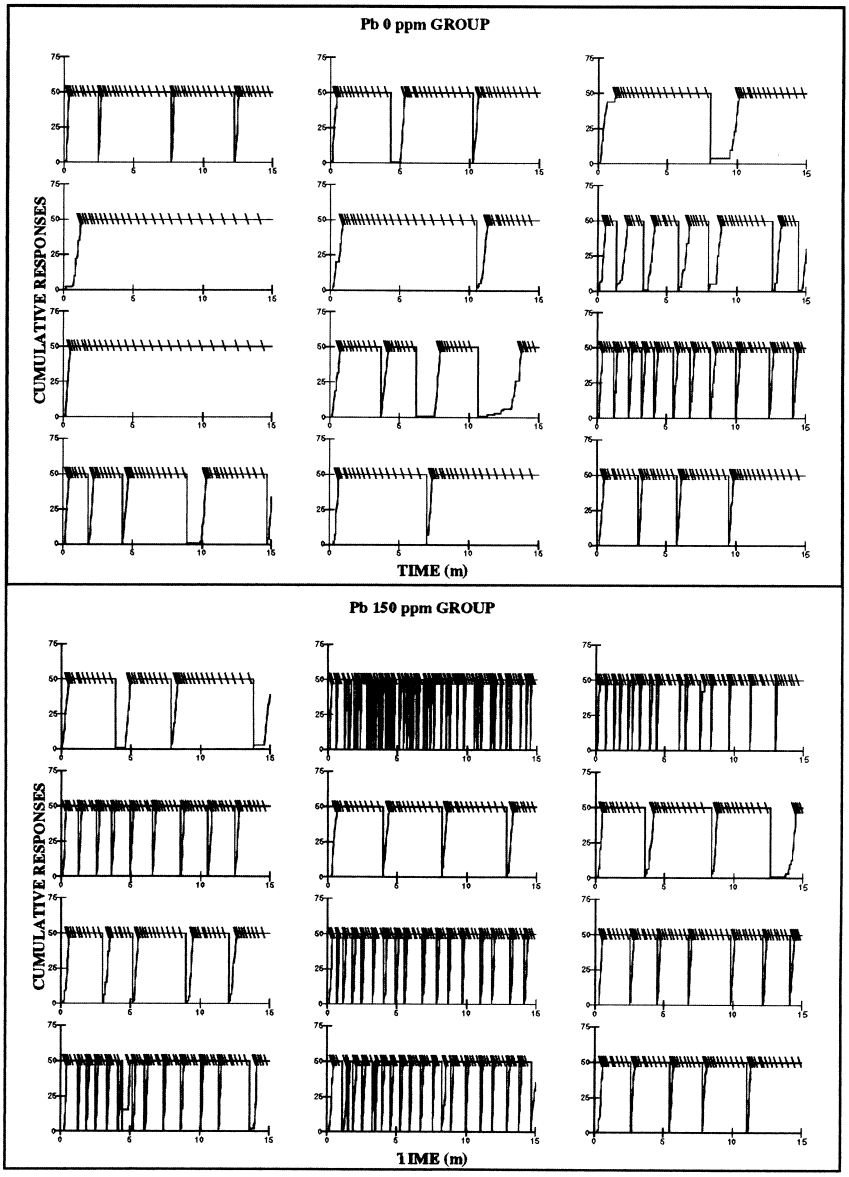

FIG. 5. Cumulative records for each rat in the 0 and 150 ppm exposure groups on the last day of baseline. Backslashes indicate reinforcers.

Such inefficient responding could result in an eventual dissipation of effort or lack of motivation. It should also be pointed out that these changes occurred in some cases at PbBs as low as 11 μg/dl (a 30% decrease in waiting behavior) in a species known for its resistance to Pb toxicity (36,42) and in the absence of any exposure-related effects on food or fluid consumption or any other signs of toxicity.

Despite the differences cited above, the ratio of the MN long wait by mean FR time, a ratio designed to determine efficiency of performance by calculating the extent to which the waiting duration compared to the time taken to complete the ratio, did not differ between control and 150 ppm groups. One possible explanation for the absence of a difference in this measure would be that waiting time decreased in response to the increased FR response rates observed in the 150 ppm group. Specifically, as the time to complete the ratio decreased (rates increased), the waiting time would decrease as well, because waiting times longer than the duration required to complete the ratio would actually decrease the total number of possible reinforcements. However, data over the stabilization period prior to the collection of the baseline data do not support this interpretation. As shown in Fig. 6, waiting behavior in the 150 ppm group showed no obvious changes as response rates increased, indicating a dissociation of these effects. Similarly, MN long wait of controls increased over this period even though response rates remained stable. These effects resulted in a separation between the controls and the 150 ppm group on both components of the task.

As previously noted, rats exposed to 150 ppm reset the FR more frequently, and in conjunction with their higher response rates actually received significantly more reinforcers than did controls. There are several hypotheses that might be

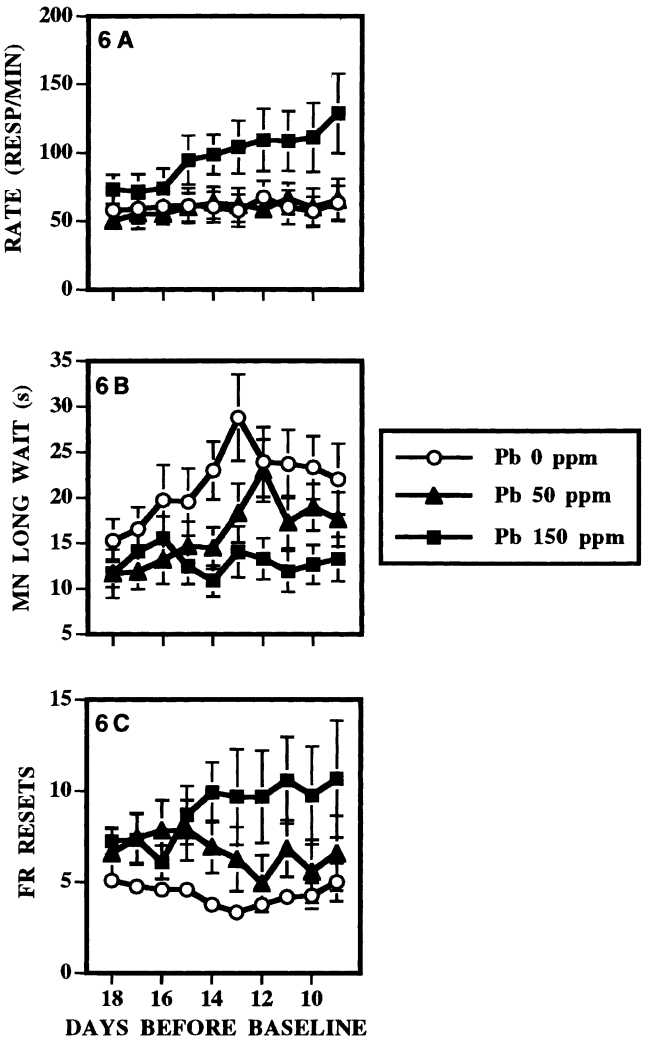

FIG. 6. The effects of Pb exposure across 10 days that occurred 9 to 18 days prior to the first baseline day on response rate (A), MN long wait (B), and number of FR resets (C). Each point represents a group mean, with each bar indicating ±1 SE (n = 12 per exposure group).

invoked to explain this pattern of effects. It has been stated that Pb exposure is associated with an inability to inhibit responding (31). Such an inability may have been manifest on this baseline, as suggested by the more frequent resets of the FR component of the schedule. Alber and Strupp (1) suggested a similar interpretation as the basis of a Pb-related increase in the number of errors in a delayed spatial alternation paradigm used to assess aspects of cognitive dysfunction including attention deficits. The authors attributed this deficit to "impatience" caused by the variable nature of the delays in this task. Although the term was not explicitly defined by the authors, they later refer to an inability to inhibit prepotent responding. In their study, however, increased errors were evidenced by Pb-exposed groups across all delay values, including the 0-s delay. If Pb exposure acted to increase "impatience" or the "inability to inhibit prepotent responding," it might be expected that the reduction in accuracy should increase with delay value in such a procedure. In the current study, an explanation based on inability to inhibit responding fails to explain why Pb-treated rats exhibited any waiting behavior.

An alternative explanation for the current findings is the possibility that the pattern of responding observed in the current study was maintained by the higher density of reinforcement it produced, as is apparent in Fig. 5. This higher density of reinforcement was a result of a higher rate of responding on the FR (and thus shorter time to reinforcement) as well as a shorter duration of waiting. In support of such a possibility, Fig. 6 shows that for the 150 ppm group, the increase in response rate and total number of FR reinforcers occurred in parallel. The current findings, however, are also consistent with the interpretation that Pb exposure is associated with an inability to manage delays of reinforcement, a hypothesis that has been likewise proposed to explain some of the behavioral disturbances associated with attention deficit disorder (4,37). Specifically, increasing delays of reward may have been aversive, and this aversive stimulation would be terminated by a response that reinitiated the FR component. These various possibilities remain to be examined.

Defining the nature of Pb-induced deficits in cognitive function based on attention deficits remains problematic, given that attention deficit remains a global construct composed of numerous different response classes, both overlapping (e.g., perseveration and inability to inhibit responding) and nonoverlapping (enhanced distractibility and perseveration, or distractibility and inability to inhibit responding). The diagnostic criteria for attention deficit disorder outlined by the American Psychiatric Association (2) includes descriptions of such behaviors as "easily distracted by extraneous stimuli," "difficulty in sustaining attention in tasks," "shifts from one uncompleted activity to another," which are quite distinct from the patterns of perseverative behavior often reported in experimental animal studies (8,20,29,35) and human epidemiological studies of Pb [e.g., (40)]. These patterns of disruption might be more appropriately described by other American Psychiatric Association diagnostic phrases for attention deficit disorder, such as "not easily distracted," "extended attention to a particular task," and "failure to shift from one activity to another." It is interesting to note that attention deficits have not been uniformly observed in human studies though [e.g., (25,43,44)].

How, then, are such apparently contrasting attention deficits for Pb-induced learning impairments to be ultimately reconciled, because all such response classes seem appropriately described as "attention deficits" in that they involve behavior inappropriate to the ongoing stimulus conditions. In the case of distractibility, presumably, alternative or inappropriate behavior occurs in the presence of defined stimulus conditions, whereas in the case of perseveration, the appropriate change of behavior fails to occur in the presence of stimuli, indicating reinforcement availability contingent upon a change in behavior. To refer to both patterns of behavior simply as "attention deficits," however, is not useful, in that it blurs the obvious distinctions between these two. An apparent reconciliation of these two patterns of behavior is also suggested by jointly defining these impairments as "an inability to inhibit inappropriate responding" or "inability to inhibit prepotent responding." It is not clear, however, that the use of such putative explanations offer anything other than a restatement of the observed behavioral deficits.

It is certainly possible that several, even disparate, types of attention deficits contribute to Pb-induced learning impairments, and/or that these various deficits are observed under different types of environmental conditions and contexts.

What seems critical at the current time are more explicit hypotheses based on the current information and the development of specific behavioral methodologies to address them. This will require operational definitions of these different response classes [e.g., what constitutes impulsivity? see (22)], as well as research into the controlling variables for each of these defined response classes (under what environmental conditions does impulsivity occur?). Such strategies should then provide the direction for studies aimed at understanding the underlying neurobiological substrates.

Although several authors have already posited prefrontal cortex as the basis of the cognitive deficits attributed to Pb based on similarities of its effects to those of prefrontal cortical lesions [e.g., (1,21,32)], similar profiles of effects are seen in response to lesions of other regions as well, including nucleus accumbens, hippocampus, and amygdala (18,19,27,39, 41). Moreover, Pb exposure exerts effects on a wide variety of neurotransmitter systems, many of which interact and modulate each other's function, resulting in a high degree of complexity [e.g., (10)]. Finally, if prefrontal cortex serves as the site of Pb's behavioral manifestations, it is difficult to explain why Pb exposure does not generally produce deficits in such functions as memory (1,11,17). Thus, it seems more likely that Pb exposure may directly or indirectly impact a number of regions/systems and/or that different behavioral deficits produced by this neurotoxicant are controlled by different neurobiological alterations. Such facts further stress the need to more precisely define the associated behavioral impairments and suggest that explicit statements about the specific basis of these dysfunctions at the current time are premature.

The experiments described here show that "waiting" behavior is quite sensitive to Pb exposure, with decreases in MN long wait time observed in this study even at the lower exposure level, which was associated with PbBs of only 11 μg/dl. Fully examining the impact of Pb exposure on waiting per se and elaboration of the underlying behavioral processes may be achieved by additional modifications of this procedure. For example, one way to further determine the importance of reinforcement density vs. delay of reinforcement in the effects of Pb on this paradigm would be to associate longer wait periods with a higher magnitude of reinforcement or make the delay constant but short in duration. To control for possible differences based on differences in response rates, the FR component of this procedure could be replaced with a variable interval (VI) schedule of reinforcement. This schedule generates a steady rate of responding with few pauses (16) and exposure-related alterations in response rate would, under the contingencies of this schedule, be independent of the time to reinforcement. In this experiment the 150 ppm group earned more reinforcers than controls. This issue could be addressed by limiting the number of reinforcers available during the behavioral session.

Finally, it should be pointed out that the higher Pb exposure concentration in this study resulted in significant increases in FR response rates. This contrasts with our previous observation (9) in which Pb exposure at concentrations that resulted in PbBs comparable to those of the current 150 ppm group had no sustained effect on FR responding. This difference could reflect the differences in the reinforcement contingencies in the two studies. In the current study, a choice of either reinitiating the FR or inhibiting responding (waiting) and thus subsequently obtaining free reinforcer deliveries was available, whereas Cory-Slechta (9) utilized standard FR contingencies with no opportunities for free reinforcement deliveries. The FR wait schedule used here appeared to engender lower response rates than those associated with the standard FR schedule of Cory-Slechta (9). In fact, response rates of the 0 ppm group from that study are similar to the means of the 150 ppm group in the current investigation. These findings may indicate that the waiting contingencies of this paradigm decrease FR rates, an effect attenuated by Pb exposure. Further, they raise the interesting possibility that the absence of Pb effects observed on typical FR schedules (9,30), as opposed to the more reliable changes in fixed interval (FI) schedule-controlled behavior, could be the result of a ceiling effect on response rate rather than to any schedule specificity.

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