Although A and B cells in the monkey differ morphologically from α cells and β cells in the cat, the relative differences between monkey A and B cells in their central projections, somal size, dendritic field size, and axon caliber are, for the most part, qualitatively similar to the corresponding differences between cat α and β cells. Thus, in cats and monkeys, just as there are parallels between different ganglion cell types in their functional properties, there seem to be parallels in their structural properties and central projections. As in the cat and other mammals, visual function in primates seems to be mediated by a variety of different classes of retinal ganglion cells that have distinctive patterns of central projection.

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23. More complete descriptions of the procedures used for the preparation, electrophysiological recording, electrophoretic injection, injection site reconstruction, and histochemistry are given elsewhere (*16*).
24. This study differs from previous ones in that retinal ganglion cells were stained with HRP, whereas others have studied ganglion cell morphology in Golgi material. It is possible that some fine detail evident in Golgi-stained material may not be equally visible in our material. Nevertheless, the cell bodies of the HRP-filled cells in our sample from the cat appear similar in size to those of cells impregnated with the Golgi-rapid technique and somewhat larger than cells impregnated with Golgi-Cox (*15*). The diameters of dendritic fields of cells in our cat material are similar to those obtained by Boycott and Wässle (*15*) with the Golgi-Cox technique. In relative terms, our measurements of axon gauge in cat are also consistent with Boycott and Wässle's description, although they did not attempt to quantify axon diameter. Thus, it is unlikely that the most completely stained cells we have observed appear significantly different from the Golgi-stained cells observed by others.
25. The cell bodies and dendritic fields of filled cells were measured under the microscope through the use of a calibrated eyepiece graticule and a ×50 or ×100 oil immersion objective (*16*).
26. Axons were measured under the microscope, through the use of a calibrated eyepiece graticule and a ×100 oil immersion objective. Measurements were made distal to the axon hillock at a point past the axon's initial taper. In order to estimate the accuracy of our measurements, a sample of axons was measured independently by each of us and any discrepancies noted. Differences were rarely > 0.2 μm.
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Behavioral Effects of Lead and *Toxocara canis* in Mice

Abstract. *Adult mice were administered the common parasite* Toxocara canis *or lead or both. The parasite clearly altered mouse performance on tests of exploration, activity, learning, and motor coordination; behavioral effects in mice receiving lead alone were less general. Consequences of* Toxocara *administration appeared attenuated in animals receiving both agents. Parasite larvae were found in the central nervous system in all infected mice.*

Although an estimated 500 million to 1 billion people are infected with parasites, the behavioral consequences of such infection are virtually unknown. One common parasite is *Toxocara canis*, the dog roundworm; its eggs are passed by the dog's feces and may remain viable in the environment for years. This parasite is carried by perhaps two thirds of all domestic dogs and is the primary agent of visceral larva migrans (VLM) in the United States (*1, 2*). In VLM, the ingestion of embryonated parasite eggs by abnormal hosts such as humans or mice results in second-stage larvae migrating through the visceral organs, where they can remain viable for years (*3*). The difficulty of diagnosing and treating VLM in humans emphasizes the need for additional information concerning its behavioral consequences.

Ingestion of lead, another environmental hazard, may result in profound toxic manifestations as well as more sub-

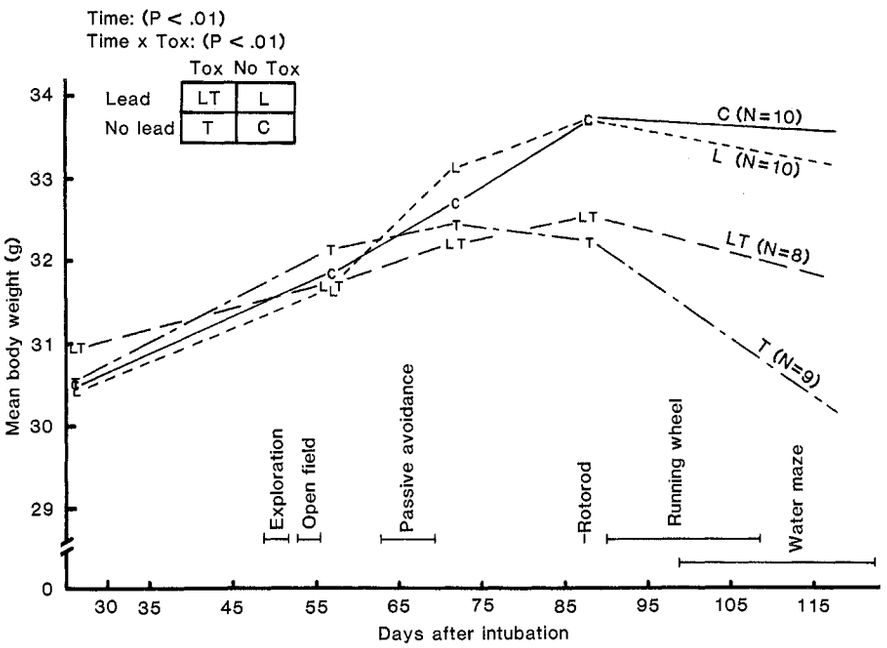

Fig. 1. Time line of body weight and behavioral measures. The four groups are represented by a 2 × 2 factorial design (inset). Results of analyses of variance with time as a repeated measure are presented in the upper left corner. All groups started with ten animals; *N* values give the number of animals surviving at the end of the experiment. *C*, control; *L*, lead; *T*, *Toxocara*; and LT, lead and *Toxocara*.

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tle behavioral changes. The likelihood of lead poisoning is greatest in children who engage in pica, that is, who regularly ingest nonfood substances such as paint, soil, plaster, and crayons. Pica occurs in about 25 percent of children 1 to 6 years of age, and often more than one type of substance is ingested (*4*). Children who eat soil are also at greater risk of toxocariasis. Since both lead and *Toxocara* are prevalent in the environment, it is important to investigate the behavioral consequences resulting when one is eaten or when both are ingested simultaneously.

We used adult male Binghamton heterogeneous mice (*5*) that were approximately 75 days old at the beginning of the experiment. They were housed individually in a vivarium at 21°C, with white lights on between 8:00 a.m. and 8:00 p.m. Mice from nine litters were randomly assigned to either the control group, whose members were intubated with 0.1 ml of saline and given distilled water to drink; the *Toxocara* group (T), which received distilled water and a single intubation of 1000 eggs suspended in 0.1 ml of saline; the lead group (L), which was given drinking water containing 0.5 percent lead acetate beginning 1 day after intubation with saline (0.1 ml); or the lead plus *Toxocara* group (LT), which received a single intubation of 1000 eggs and drinking water containing 0.5 percent lead acetate. In mice intubated with *Toxocara* eggs, larvae reach the brain by 2 days after infection and remain viable there for at least 4.5 months (*6*).

We monitored body weight throughout the experiment (Fig. 1). Weights of all groups were approximately the same from about 27 to 75 days after the treatments began. By 88 days after intubation the animals burdened with the parasite had lost weight. The weight of LT mice was less severely affected than that of T mice 119 days after intubation. Further, although postnatal administration of 0.5 percent lead acetate may severely retard the growth of mouse pups (*7*), our data (Fig. 1) suggest that in the adult this effect is small or nonexistent.

To examine behavioral changes in the mice, we administered a test battery that has been used before in our laboratory and is sensitive to neurological insult. Different tests were given at different periods after intubation (Fig. 1). The first test (some 50 days after intubation) examined exploratory behavior as a function of change in a familiar environment (Fig. 2). We removed the lid to the cage and replaced it with a plexiglass second tier. A chain allowed access to the second level. Although there were no between-group differences in the number of times mice crossed their cages, the number of times T mice changed levels was significantly reduced. Further, mean latency to first ascent was considerably

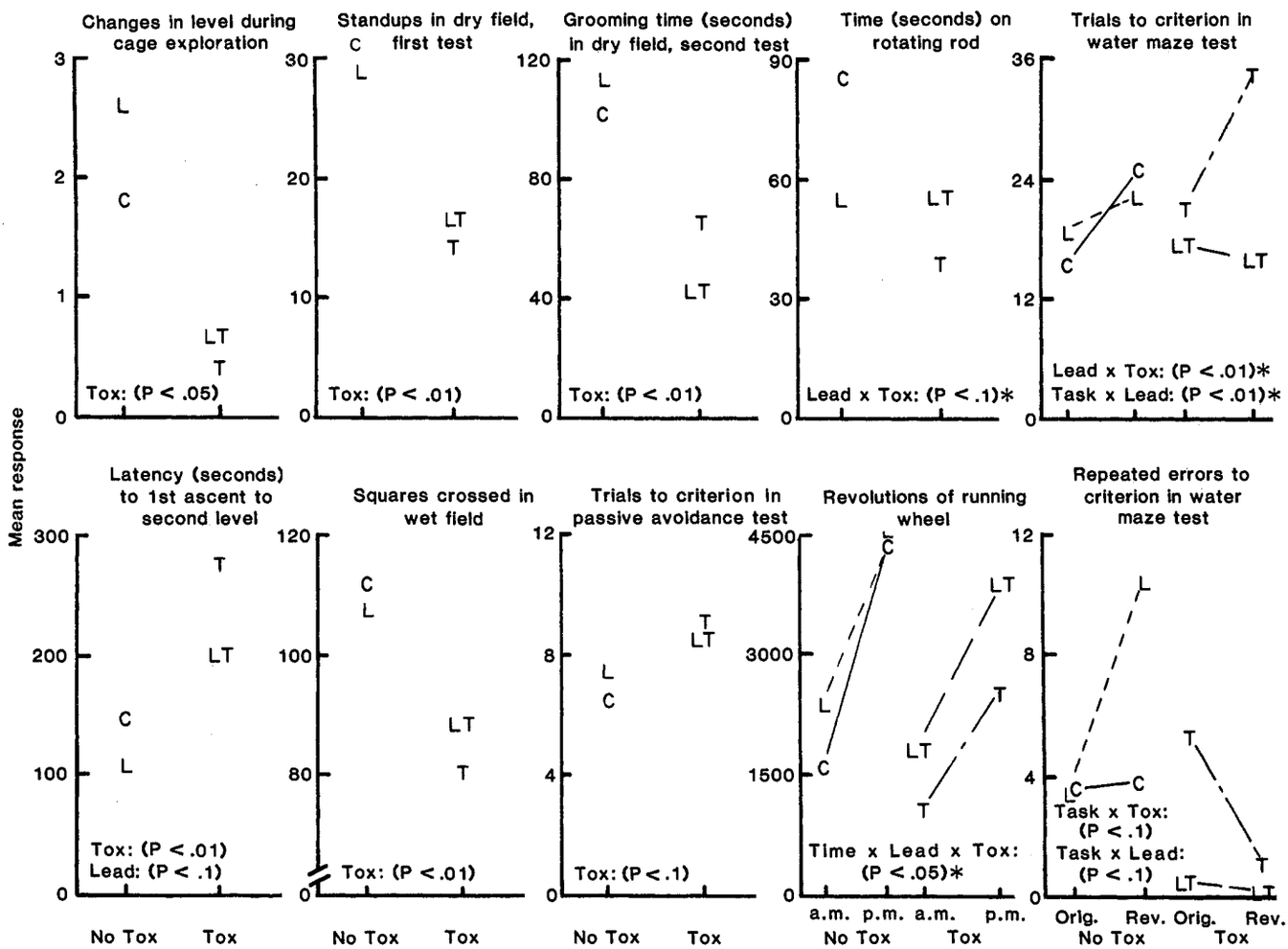

Fig. 2. Mean behavioral responses for each of the four groups on the various tests administered at the times specified in Fig. 1. Appropriate univariate analyses of variance were conducted on each dependent variable [for the running wheel test both a.m. and p.m. (repeated) evaluations were made, and for the water maze task observations of each animal were made during both original and reversal learning]. Significant sources of variance and associated *P* values are given at the bottom of each panel. Only the highest-order interaction sources are reported in the case of several significant interactions. Asterisks indicate that the sources involved in an interaction were also present in significant lower-order interactions or main effects; *Tox*, *Toxocara*.

longer in T mice than in the other three groups.

When the mice were approximately 125 days of age (52 to 55 days after intubation), we observed their behavior in an open field (Fig. 2). Mice were placed in a dry open field (*8*) for 5 minutes, and the number of squares they crossed and the number of times they stood up were counted. Next, we observed for 1 minute the number of squares over which mice swam in a sink (*9*) filled with 17°C water. Sixteen minutes after being removed from the water, the mice were retested in the same dry open field. All groups crossed approximately 180 squares during the original dry open field test. However, the T and LT mice stood up only about half as frequently during this period as the control and L groups. In the wet open field the control and L groups swam over approximately 110 squares while the T and LT groups swam over 80 to 90 squares. This difference was primarily due to the parasite-burdened groups crossing fewer peripheral squares. All the groups crossed fewer squares in the second dry open field test than in the first. However, the decrease was smaller in *Toxocara*-infected mice and was associated with less time spent grooming. In particular, the infected mice did not stand up to groom, whereas the other mice did so regularly.

On the 63rd day after intubation, each mouse was tested on a step-through passive avoidance task (*10*). A light on one side of the apparatus was turned on, and the mice fled to the darker side. This response was then paired with a 0.5-second, 0.3-mA shock. The criterion for learning was two consecutive trials (in a maximum of 15 trials) in which the mouse avoided shock. *Toxocara*-infected animals tended to take longer (9.0 trials) than control mice (6.5 trials) to reach criterion. The performance of LT mice appeared quite similar to that of T animals (Fig. 2).

On the 88th day after intubation, the mice were placed on a rotating rod for 3 minutes. For the first 30 seconds the rod turned at 1 rev/min; speed was then increased to 9 rev/min. All treated mice spent less time on the rod than the control mice (Fig. 2). The LT mice remained on the rod about as long as the L mice and longer than the T animals. Subsequently, the mice were placed in cages with running wheels for a 5-day test period. All groups showed diurnal patterns of activity from day 2 to day 5, but the mice administered *Toxocara* alone made markedly fewer wheel revolutions. The L mice were somewhat more active in the morning than the controls, and the performance of the LT mice was almost identical to that of the control group.

Finally, half of the mice in each group were randomly selected for a T-maze test in 17°C water to evaluate acquisition and reversal of a spatial discrimination task. Criterion for learning was nine successful trials out of ten. The T group took more trials to acquire and reverse the spatial discrimination than any of the other groups (Fig. 2). This effect of *Toxocara* was not seen in the LT group. Mice in the T group tended to show more repeated errors on original learning than on reversal learning. The opposite trend was observed in the L group, and repeated errors were not seen in the LT group. Finally, T and LT mice took longer to escape from the water maze on successful trials than mice that were not infected with *Toxocara*.

Mice were killed by cervical dislocation 130 days after intubation, and the brains were removed and sagittally bisected. One-half was fixed in 10 percent buffered Formalin solution. Saggittal, 5-μm sections were cut beginning at the medial surface and thereafter every 800 μm for a total of five sections. The sections were stained with hemotoxylin and eosin and examined for the distribution and nature of lesions. The other half of the brain was used to count larvae directly. A known weight of tissue was squashed between two slides and larvae were counted under a microscope at ×10 magnification. Blood lead concentrations also were determined by differential pulse anodic stripping voltametry (*11*).

Neither pathological changes nor parasites were observed in the control specimens. In the *Toxocara*-infected mice, lesions and parasites were observed in the cerebral and cerebellar cortices, thalamus, hypothalamus, tectum, pons, and medulla. Occasionally larvae were observed in the leptomeninges or lateral ventricles. Sections from the parasite-infected mice revealed a striking encephalitis that showed an affinity for white matter areas, including the internal and external capsules and cerebellar peduncles. The corpus callosum was most extensively injured, with major portions of the tract destroyed in some animals. Mean blood lead concentration in the control animals was 5.1 ± 1.2 μg/dl (N = 8), whereas in the L mice it was 23 ± 2.8 μg/dl (N = 7) and in the LT mice 23 ± 4.6 μg/dl (N = 6). Thus, administration of *Toxocara* did not affect terminal blood lead concentrations. Furthermore, lesions and foci of larvae were similarly distributed in both the T and LT mice.

Whereas continued lead administration to adult mice may affect selected behavior, a single intubation with *Toxocara* eggs severely alters a broad spectrum of behavior. Mice treated with both lead and *Toxocara* frequently appeared less severely impaired than those administered *Toxocara* alone. It is not known how lead interacts with the parasite to produce this effect. However, larvae viability and distribution in the central nervous system were similar in both the *Toxocara*-infected group and the group receiving the parasite plus lead (*12*).

This experiment showed the impact of one kind of parasite on the behavior of mice. In light of the tendency for lead administration to minimize the behavioral indices of infection, one could speculate that if a child were exposed to both parasite and lead, problems in diagnosing *Toxocara* infection could be compounded. Since human behavior may also be measurably altered by parasites transmitted from pets and common surroundings, which may be contaminated additionally by other toxic products, further investigation is warranted.

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8. The field, in a 28 by 28 by 20 cm opaque plexiglass box, had a grid of 25 squares 5.6 by 5.6 cm.
9. The sink measured 60 by 60 by 35 cm and its floor was divided into 36 7-cm squares.
10. Mice were placed in a shuttle box with a 60-W light bulb mounted 6 to 8 inches above the apparatus. Trials were 4 minutes long and were separated by 45-second intervals.
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