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Accelerated Nervous System Development Contributes to Behavioral Efficiency in the Laboratory Mouse: A Behavioral Review and Theoretical Proposal

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ABSTRACT: *The emergence of the laboratory mouse as a favored species for genetic research has posed a number of problems for scientists interested in the reflection of genetic influences in mouse behavior. It is commonly thought that rat behavior, which has been studied more extensively than mouse behavior, could be easily generalized to mice. In this article, a number of categories of behavior displayed by the mouse (motor, spatial, defensive, social) are reviewed and contrasted with the same categories of behavior displayed by the rat. The comparison suggests that mouse behavior is simpler and more dependent upon elementary actions than the behavior of the rat. We suggest that the behavioral simplification in the mouse adapts it for a different ecological niche than that occupied by the rat. We propose that this simplification may be mediated by accelerated brain maturation during development. We further propose that this developmental acceleration in the mouse renders it less dependent upon complex social behavior and plastic nervous system changes associated with learning than the rat. This difference poses problems for the development of relevant methods of behavioral analysis and interpretation. Since the mouse's biological adaptations will be reflected in laboratory behavior, suggestions are made for behavioral approaches to the study and interpretation of mouse behavior.* © *2001 John Wiley & Sons, Inc.* Dev Psychobiol 39: 151–170, 2001

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INTRODUCTION

There are 1,814 species of muroid rodents (Nowak, 1999), and of these, the laboratory mouse (*Mus musculus*) and the laboratory rat (*Rattus norvegicus*) are the most widely used species for laboratory studies. Both belong to the same family, Muridae. The lineage that led to *Mus* diverged from *Rattus* about 10 million years ago (Bonhomme, Iskandar, Thaler, &

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Petter, 1985; Boursot, Auffray, Britton-Davidian, & Bonhomme, 1993; Shoshani, Goodman, Szelusniak, & Brauntzer, 1985). Among laboratory rodents, they are each other's closest relatives.

Both species are widespread, living in habitats from the subantarctic to deserts through forests through human commensalism (Nowak, 1999). While both species are catholic in their diet, the rat has a higher preference for animal matter and is more skilled at catching and killing animals, which includes small vertebrates. For example, rats may include mice in their diet (Nowak, 1999). The mouse is terrestrial and so occupies a narrower biological niche than the rat (Berry & Bronson, 1992), which is terrestrial, aquatic, and arboreal (Barnett, 1975).

There is general agreement that much more needs to be known about the social composition and territorial organization of both species in the wild. Commensal mouse populations normally consist of a mosaic of male-defended territories, each constituting a breeding subpopulation or deme of 4 to 12 individuals (Crowcroft & Rowe, 1963; Singleton, 1983). Home rage may vary form 2 to 400 m^2 (Quadagno, 1968). Typically, males defend a territory within which they will breed with resident or transient females (Hayashi, 1996; Hurst, 1986). Rats also live in groups, which may form part of an extended colony. Territories may range from 30 to 3,000 m^2. Individual animals may travel kilometers to obtain food, although in general, animals set up home bases close to food supplies (Barnett, 1975). Group breeding may take place in which a number of males pursue one or more females (Berdoy, 1994; Whishaw & Whishaw, 1996). Relative to mice, rats apparently possess a fluidity in social organization which permits the existence of high population densities with in a limited area when food is in abundance (Lore & Schultz, 1989), but mouse densities can be exceedingly high when breeding season ceases (Chambers, Singleton, & Krebs, 2000). Mice are also smaller and have a shorter life span. Both species are r-selected, that is, their life cycle and reproductive system are designed to maximize breeding effort (Wilson, 1975, discussed more later).

Because both species have been domesticated for laboratory research, comparative studies between the species, especially studies related to their biological specializations, would be expected to be especially useful (Whishaw, Haun, & Kolb, 1999; Whishaw, Sarna, & Pellis, 1998b). Surprisingly, there have been very few comparative studies until quite recently. It is commonly thought that rat behavior, which has been studied more extensively than mouse behavior, could be easily generalized to mice. Recent comparisons suggest that this does not appear to be the case (Whishaw, 1999). Based on comparisons of a variety of social and nonsocial behaviors, the mouse seems to exhibit a simpler behavioral repertoire and much less flexibility in dealing with novel situations. In this article, we first compare the two species across several behavioral systems and discuss the role of life history factors that may account for these differences. We then discuss the developmental processes that may have led to the adaptive differences between the mouse and the rat. Finally, the implications for using the behavior of the mouse for assessment of the genetic specification of the organization of nervous system in the newly developing field of genetic engineering (Jackson & Abbott, 2000) will be considered. In the following sections, our emphasis will be on behaviors that have been explicitly compared and which have yielded species differences. For investigators unfamiliar with phylogenetic approaches to behavior, our intent is not to cast one species as "good" and the other as "bad." Rather, we will argue that as we develop a better knowledge of the respective specializations of the two species, their use in laboratory investigations will be optimized.

Motor Behavior

Skilled movements, such as those of the mouth and paws, are important behavioral adaptations for grooming, nest building, and feeding in rodents. Skilled limb use in rodents is predominantly assessed by examining forelimb movements in food handling. Two types of tasks can be administered. In skilled-reaching tasks, animals reach through a slot or aperture for a food item. In an explicit comparison of mice and rats in skilled reaching, Whishaw (1996) reported that reaching movements are quite similar. Both species use olfaction, rather than vision, to locate a food object for which they will reach. Both species orient their body to initiate a reach, and an examination of 10 subcomponents of the reaching movement also indicated that the skilled movements in both species are quite similar. That is, the animals lift the paw, bring their digits to the midline of the body, and then adduct the elbow to the midline. They then open the digits as the limb advances and use the arpeggio movement in pronating the paw over the food.

Despite similarities in the movements used in reaching, measures of reaching acquisition and of reaching performance show a species difference. During training, rats display a progressive improvement in performance and at asymptote can reach high levels of accuracy in that they obtain food on 80 to 90% of reaches. Mice appear to acquire reaching

tasks quite quickly, but remain variable in their performance. After a similar length of training to that used with rats, the mice only achieve success levels of about 40 to 50%.

Spontaneous food-handling behavior in eating sunflower seeds has been compared in laboratory rats and mice, along with eight other rodent species (Whishaw et al., 1998b). Although all of the rodents used a similar basic pattern of identifying food by sniffing, picking up the food up by mouth, and holding and manipulating the food in the digits with an elbows-in posture as they sit back to eat, there are species differences. The manipulatory movements of the rats are comparatively complex and involve many asymmetric paw and limb adjustments in manipulating and opening the seeds. The mice appear to use much simpler movements in that they push the seeds into the mouth for biting with large symmetrical movements of the limbs.

In the mammalian order Carnivora, there is a strong correlation between dexterity and omnivorous diet (Iwaniuk, Pellis, & Whishaw, 1999, 2000). That is, species that eat a wide range of plant and animal material have the most sophisticated use of the forepaws. The wider range of food, especially animal prey that are actively caught and handled by rats (Nowak, 1999), may be reflected in the greater forepaw skills exhibited by rats when exposed to novel foods or test situations (Whishaw & Coles, 1996; Whishaw, DuBois, & Field, 1998a). Indeed, rats seem to be able to manipulate small prey more delicately than similar-sized mammals that are more dedicated predators (Ivanco, Pellis, & Whishaw, 1996).

In a comparative analysis of grooming movements in six rodent species, Berridge (1990) reported differences between mice and rats in use of the limbs in grooming. Although both species display a similar sequence of movements during grooming, rats display four grooming phases whereas mice display only three phases. The first phase consists of a set of five to nine rapid, bilateral strokes forming elliptical trajectories over the nose. The second phase consists of a single, or series, of short strokes over the mystacial pads. The third phase consists of repeated, large-amplitude strokes across the face and over the ear whereas the fourth phases consists of tucking the head to lick the torso. As illustrated in the grooming patterns in Figure 1, rats display all four phases of grooming whereas mice seldom display Phase 2. Additionally, whereas the Phase 1 strokes in the rats are symmetrical, those of mice are asymmetrical. Phase 3 strokes across the head in the rat are asymmetric and complex whereas in mice these strokes are simple and bilaterally symmetrical. Other differences between the two species include fewer transitions from face washing to head shakes and forelimb flails to paw licks in the mice. Thus, in several respects, the grooming pattern of mice seems simpler than that of rats. Interestingly, of the six species examined by Berridge (1990), the rat displayed the most grooming traits.

Reflex tests are used to evaluate development or to monitor recovery after brain or spinal injuries. Reflex tests provide a favorite tool in the assessment of rodent behavior because the response is relatively reproducible and simple rating scales allow quantification of the strength of the response. Tactile stimulation of the skin or whiskers is predominantly used to trigger placing reactions of head, fore-, or hind-limbs (Crawley, 1999; Fox, 1969; Le Roy, Perez-Diaz, Cherfouh, & Roubertoux, 1999). Other common reflex tests include measurements of righting responses, either by placing the animal in an upside-down position on a flat surface or by dropping it from this position, and recording the animals' ability to land on all four limbs (Del Vecchio, & Rahwan, 1984; McAnulty et al., 1989; Pellis & Pellis, 1994; Pellis, Pellis, & Teitelbaum, 1991a). Although the performance and components of such reflexes appear to be similar in rats and mice, it must be noted that detailed comparisons of these behaviors have not been reported.

Measures of motor behavior in rats and mice have been achieved by scoring spontaneous behavior or by quantifying the degree of locomotor activity in open-field tests (Basso, Beattie, & Bresnahan, 1995; Bresnahan, Beattie, Todd, & Noyes, 1987). Footprints during normal overground walking (Clarke & Parker, 1986; De Medinaceli, Freed, & Wyatt 1982; Kunkel-Bagden, Dai, & Bregman, 1993) or in foot placement tasks (Kunkel-Bagden et al., 1993; Metz, Schwab, & Welzl, in press; Soblosky, Colgin, Chorney-Lane, Davidson, & Carey, 1997) also have been examined. In general, roughly similar results are obtained on such tests for rats and mice (see Crawley, 1999, for review). Nevertheless, for locomotor behavior, explicit comparisons between the species may be worth while using analytical tools such as those developed by Golani and colleagues (Drai, Benjamini, & Golani, 2000; Golani, Kafkafi, & Brai, 1999).

Spatial Behavior

Stimulated by the general question of how animals learn, and more specifically by a number of theories of spatial learning, many spatial tasks have been developed for laboratory spatial investigations.

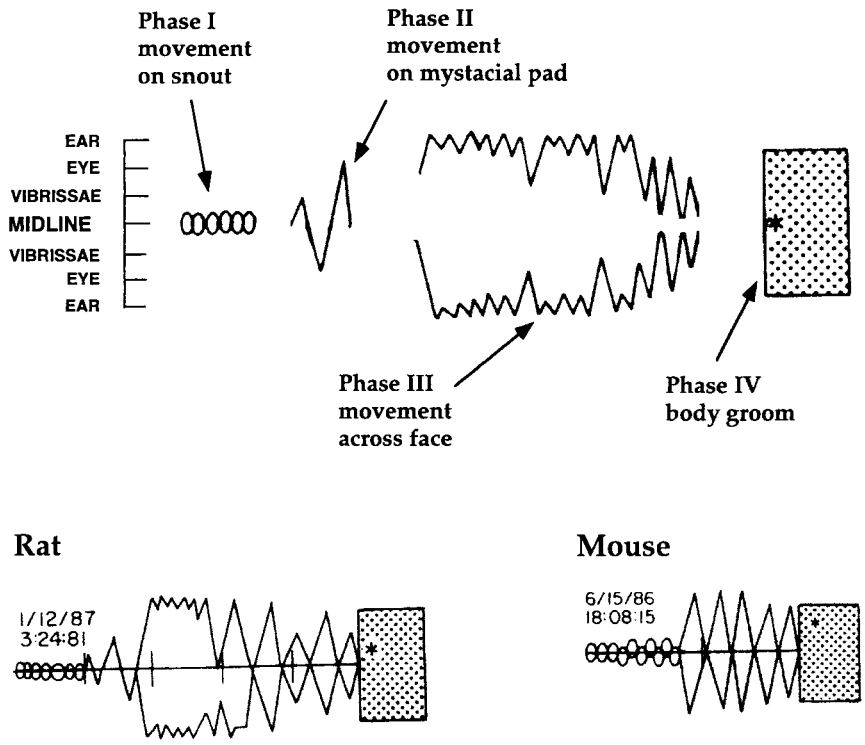

FIGURE 1 Comparison of the relatively fixed grooming sequence in rats and mice. The representation of grooming is indicated in the top panel of the figure. Circles indicate circular movements of the paws on snout, lines indicate movements of the paws across the mystacial pads and face, and the box indicates body grooming. There are four phases of grooming: Paw rubs around the snout, paw rubs around the mystacial pads, paw rubs across the face, and turning to lick the body. All four phases are displayed by the rat but Phase 2 seldom occurs in the mouse, and in the mouse, the rubs across the face are more stereotyped and symmetrical than those of the rat (bottom panel) (adapted from Berridge, 1990).

According to O'Keefe and Nadel's (1978) theory of spatial behavior, there are two primary forms of spatial behavior: locale navigation and taxon navigation. Taxon navigation is relatively simple, requiring only that an animal navigate to a visible, or otherwise clearly detectable, landmark. Locale navigation requires the conjoint use of a number of cues to locate a target that may not be visible or otherwise detectable. Locale navigation has been of particular interest to investigators of spatial behavior because the strategy of locating a place using the relationships between distal cues requires the integrated function of a number of forebrain regions, including the neocortex and limbic cortex.

A number of dry-land and swimming-pool tasks are used to study locale spatial navigation, but few tasks have specifically compared the performance of mice and rats in the same task. On dry-land tasks, such as the radial arm maze and t-maze, C57BL/6 mice were reported to perform as well as rats whereas their performance on a locale task in the swimming pool was reported as inferior (Whishaw & Tomie, 1996) as it is in similar dry-land tasks. For example, to get mice to escape from a table surface through a hole, a task a rat readily performs, Pompl, Mullan, Bjugstad, and Arendash (1999) required bright lights and fans.

In a more detailed comparison of mice and rats in swimming-pool navigation tasks, Long-Evans hooded rats and C57BL/6, CD1, and CD-1/C57BL6 mouse crosses were used (Whishaw, 1995). The animals were given two tasks. In the first task, they were required to swim from a number of locations from the wall of a circular swimming pool to find a platform located at a fixed point just beneath the surface of the water in one of the quadrants of the swimming pool. Because the platform was not visible, the animals had to learn to locate it in relation to some of the surrounding cues in the room, such as the room walls, windows, cupboards, doors, and so on. The mice were able to perform most of the requirements of the task. They swam well, they were able to reach the hidden platform, and their performance gradually improved

until they swam relatively directly to the platform. In comparison to rats, however, the acquisition of the task by mice was slower, and their performance at asymptote was less consistent.

There are a number of potential reasons for the inferior performance of the mice. First, they are smaller, and thus it is possible that the large size of the pool in relation to their body size made the task more difficult. When the performances of the mice were compared to that of 24-days-old rat pups that were of comparable size, the mice were still inferior. Even when the swimming pool was filled to a higher level so that room cues would be more visible over the edge of the pool wall, the mice remained inferior. Of course, there are many other reasons that mice might be inferior. Rats are ecologically adapted to a habitat adjacent to rivers and lakes in which they swim to forage for food (Barnett, 1975) whereas mice are not. Thus, their learning differences may be related to ecological factors. The visual acuity of mice also is about one half that of rats: 0.5 cycles in most C57BU6 mice versus 1.0 cycles per degree in Long-Evans rats (Prusky, West, & Douglas, 2000). Thus, an inability of the mice to resolve cues as effectively as the rat also may contribute to poor mouse performance, but that acuity plays a crucial role in place learning is by no means clear (Prusky, Reidel, & Douglas, 2001).

In the second water-based spatial navigation task, animals were presented with matching-to-place problems (Whishaw, 1985). Animals were given two swimming trials each day, and on each day the platform was moved to a new location. Rats quickly learned to search for the platform at the location that it had been on the previous day. Upon not finding it, they then searched the pool until they found it at its new location. On their second trial, with the platform at the new location, they swam relatively directly toward it. Their improved latencies between the first and second trials indicated that they could learn the platform's new location in a single trial. Mice did not display similar one-trial matching-to-place learning. Their performance on the second trial was almost the same as that of the first trial. This result is not easily accounted for by reference to ecological factors and visual acuity because the mice had all acquired an initial place response and thus were able to swim well and to use visual cues to guide their swims to the hidden platform.

Potentially, anatomical differences might account for the relatively poor performance in relation to rats (McNamara, Namgung, & Routtenberg, 1996). A number of lines of evidence suggest that differences in the size of the hippocampus may be related to spatial performance (Krebs, Sherry, Healy, Perry, & Vaccarino, 1989). Consequently, we examined hippocampal size in rats and mice. We cut every section (at 50 μm) through the brain of 8 rats (4 male, 4 female) and 8 mice (4 male, 4 female) and tabulated the volume of the hippocampus (CA1 fields and dentate gyrus) relative to the rest of the brain, excluding the olfactory bulbs. There were no sex or species differences in hippocampal volume (Figure 2). Thus, although some structural or biochemical differences in the hippocampus may exist between mice and rats, a simple difference in hippocampal size cannot account for the poorer performance of mice as has been reported for other closely related species (Krebs et al., 1989).

Although the results of these swimming pool studies indicate that there is a difference in the spatial performance of mice and rats, they provide no insights in the behavioral origins of the difference. We have reexamined the swimming-pool spatial learning abilities in mice and rats to determine under what conditions equivalent spatial performance might be obtained. We first manipulated task variables to equate learning rates for the mice and rats. This was accomplished by changing the size of the swimming pool and reducing the number of trials given each day. Because mice are smaller and cool more quickly than rats, a reduction in the number of consecutive swimming trials prevents body temperature loss. The rats were tested in a swimming pool with a diameter of 153 cm whereas the mice were tested in a

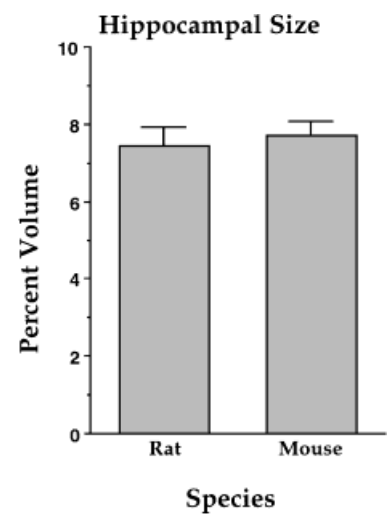

FIGURE 2 Hippocampal size (volume mean and SEs) as a percent of brain size (excluding olfactory bulbs). Each section of the brain was cut, photographed, and stored digitally. The volume of the hippocampus (hippocampus proper and dentate gyrus) was digitized in order to calculate hippocampal volume. The measurements show that there is no difference in hippocampal size between mice and rats.

swimming pool of 113 cm in diameter. The mouse swimming pool consisted of an insert placed in the middle of the rat swimming pool. Consequently, the spatial view for the rats and the mice was nearly identical. Training was limited to two trials each day with a 5-min intertrial interval. CD-1/ C57BL6 mouse crosses ($n = 9$ female) and Long-Evans rats ($n = 9$ female) were compared over 10 days of training.

Acquisition latencies for the rats and the mice are shown in Figure 3. There were no statistical differences in acquisition latencies between the mice and the rats. This finding demonstrates that when the task was simplified for the mice, equivalent acquisition performance could be obtained. Furthermore, when the animals were given a 60-s probe trial at the end of testing in which the platform was removed, there were no differences in search behavior. Both rats and mice spent significantly more time in the correct quadrant of the pool (the location in which the platform was previously present) than in other quadrants (Figure 3, insert).

To determine whether the spatial strategies used by rats and mice were similar, the search behavior of the animals during the probe trials was analyzed. The swimming patterns of the mice appeared more stereotyped than those of the rats. Notably, whereas the mice and rats swam across the platform's previous location equally often, the search patterns of the mice appeared more restricted to one or two routes. The mice swam to the platform's location and then looped around the pool to swim back on approximately the same path that had been taken on the previous swim.

To visualize this strategy difference, each linear swim trajectory that was directed toward the platform was drawn on a map of the pool. The result of this summary for each rat and each mouse is shown in Figure 4. It can be seen that the rats made very few long, direct swims toward the platform. In general, they appeared to take many curved paths in which they swam over the platform location and then circled around, crossing it a second or a third time. In contrast, the mice frequently swam to the platform in a straight line, and upon not encountering the platform, circled and then retraced almost the same direct path as that previously taken. This pattern of swimming on the part of the mice suggested that they may have acquired the place response using a more limited view of the room cues than was used by the

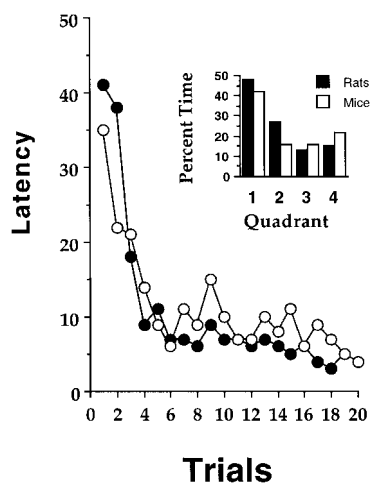

FIGURE 3 Acquisition latencies of rats and mice trained to swim to a hidden platform in the swimming pool in different-sized swimming pools. The rats were tested in a pool with a 153 cm diameter, and the mice were tested in a pool with a 113 cm diameter. The insert displays search performance on a probe trial. The platform had been located in Quadrant 1, and both the rats and mice preferentially searched this quadrant for the platform. The experiment demonstrates that by making the spatial task easier for the mice with a smaller pool, their performance can be made comparable to that of rats.

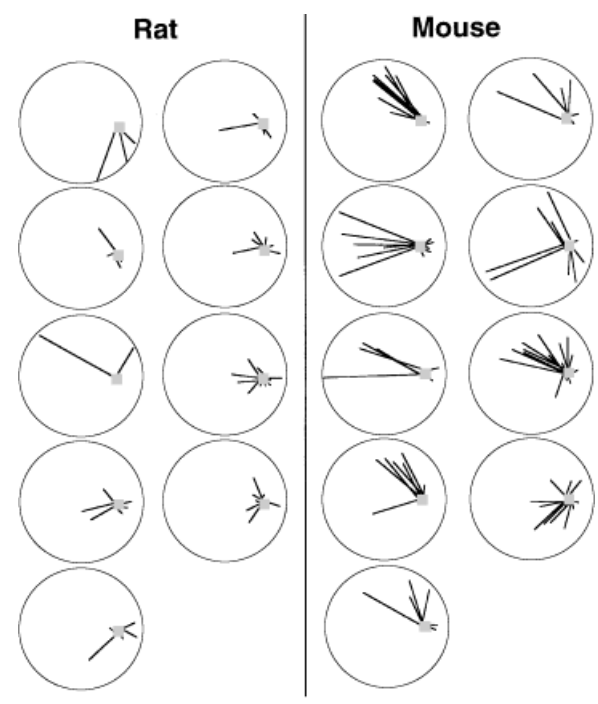

FIGURE 4 Swim patterns displayed by individual rats and mice on a probe trial. Each direct swim toward the platform made by an animal as it searched was drawn onto the representation of the pool. Note that the rats make few long, direct swims to the platform whereas the mice make many such swims. Trajectories of many individual mice appear to be made along the same route to the platform. The results of the experiment suggest that mice use a simpler route-related swim strategy, perhaps using a snapshot room view or landmark and vector strategy to learn the place task.

rats. That is, they may have used a strategy of swimming from a certain location along a certain route toward the platform. Such a strategy is sometimes explained as using a snapshot view of the room using a cue and vector strategy or using dead-reckoning (Giurfa & Capaldi, 1999). Thus, the mice may have been using fewer room cues or using room cues in a simpler way. Thus, place learning by mice may be simpler and more route dominated while place learning by the rat may be more complex and flexible.

The final spatial test presented to the rats and mice was a matching-to-place task (Whishaw, 1995). The task also was modified to make it simpler for the mice. The rats were given two trials each day for days, with the platform located at a new pool location each day. The mice also were given two trials each day, but the platform location was changed every 2nd day. Thus, the rats were allowed two trials to learn each new location of the platform whereas the mice were allowed four trials. Comparisons were made by summing the performance of the groups across four platform locations for each group. The results are shown in Figure 5. These results confirmed that the rats could learn each new place response in two trials, and further showed that the mice also could learn the task, but required four trials. Thus, again the rat's spatial strategy appeared more complex and flexible than that of the mice to allow for more rapid place learning.

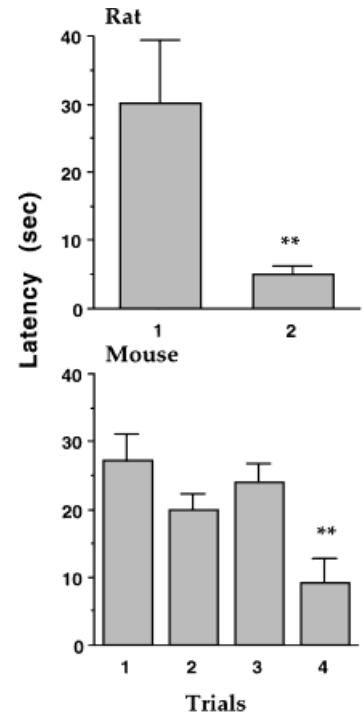

FIGURE 5 Matching-to-place performance in a rat and a mouse (means and SEs). The platform was moved to a new location of the swimming pool four times, and performance is summed across two daily trials per location for the rats and four trials given over 2 days per location for the mice. The experiment illustrates that rats display significant improvement by their second trial, whereas mice require four trials to match rat performance.

Social Play

Rats and mice have social systems that are both territorial and colonial. A dominant male will maintain a territory surrounding a den containing one or more reproductive females. These territories also may include one or more subordinate males. Non-territorial bands of younger males and females occupy less favored land surrounding such territories (Nowak, 1999). Both species have a rich repertoire of behavior patterns used for social investigation, affiliation, sex and aggression (Grant & MacIntosh, 1963). Although there are marked similarities in the social organization and behavior of mice and rats, there also are striking differences. The behavioral content of play among the juveniles of these two species is particularly illuminating.

Both species exhibit locomotor play, characterized by sudden jumps, turns, and runs (Pellis & Pellis, 1983; van Oortmerssen, 1971). Furthermore, both species may incorporate locomotor play into a social context in which animals approach and withdraw from one another, or chase each other (Pellis & Pellis, 1983; Terranova, Laviola, & Alleva, 1993). Rats also engage in play fighting. Play fights in rats involve attack and defense of the nape of the neck, which if contacted is gently nuzzled with the snout (Pellis, 1988; Siviy & Panksepp, 1987). The most common response to nape contact in juvenile rats is to rotate to supine (Pellis Pellis, 1987); this leads to a wrestle involving ventro–ventral contact (Panksepp, 1981). The defender also may launch counterattacks which may further prolong the play fight as well as lead to frequent role reversals (Pellis, 1988). Mice do not have such complex play fighting involving wrestling (Poole & Fish, 1975).

Mice achieve their peak frequency of play at a younger age than do rats, and this peak lasts for fewer days. However these differences in timing and duration do not account for the species differences in the complexity of play fighting. At no age observed—preweaning, postweaning, or early adulthood—did mice ever engage in playful wrestling (Pellis & Pasztor, 1999; Terranova et al., 1993; Terranova,

Laviola, de Acestis, & Alleva 1998), nor does the difference appear to arise from opportunity. Mice reared with rat litters also fail to engage in such play, even though the rat pseudosiblings solicit them to do so (Poole Fish, 1975). The difference in body size between mice and rats also cannot account for this behavioral difference. Other mouse-sized rodents engage in ratlike playful wrestling (Pellis, Pasztor, Pellis, & Dewsbury, 2000; Pellis, Pellis, & Dewsbury, 1989). It also should be noted that the absence of such play in mice is not a by-product of domestication; it also is absent in wild mice (Wolff, 1981).

Mice do have some aspects of attack and defense in their social play, however. Mice will pounce on one another (Wolff, 1981). A mouse running towards a partner's neck will be evaded by the recipient dodging laterally away and then fleeing (Pellis & Pasztor, 1999). Evasive dodging occurs in about 25% of the attacks to the neck area in rats (Pellis et al., 1989), but is the sole form of defensive behavior seen in the social play of mice (Pellis & Pasztor, 1999). With regard to its complexity, then, the play fighting present in mice is similar to the simplest form of such play present in rats. In addition, while both species have high rates of locomotor play (Hole & Einon, 1984), rats have rates of play fighting that are 10 to 15 times higher over the same age period (Pellis & Pasztor, 1999; Pellis & Pellis, 1997).

Evolutionary Distribution of Play in Rodents

If it is assumed that a behavioral trait is homologous (i.e., it can be traced to a common ancestor) and it is likely that play in different species of rodents is homologous, it is possible to map the trait onto a known phylogeny. By mapping a trait onto a phylogeny, the most parsimonious explanation for the distribution of character states between the species can be determined (Iwaniuk & Whishaw, 2000). The method can provide useful insight into the location and direction of evolutionary changes in a trait and the state of ancestral, or unknown, species in the lineage. This method is commonly used in evolutionary biology as a means of assessing the degree of homology in a trait and whether a trait contains phylogenetic information (DeQueiroz & Wimberger, 1993). To date, such methods have been infrequently used in the neurosciences, but remain a powerful means of assessing the evolution of neural structures and the relationship between structure and function.

Using this method, an analysis of the evolutionary changes in the complexity of play fighting present in 16 species of murid rodents indicated that relative to the ancestral state, rats have increased the complexity of their play whereas mice have simplified theirs (Pellis & Iwaniuk, 1999). To measure these species differences, a complexity index was developed incorporating seven criteria. These included the relative frequency of launching playful attacks, the presence of playful defense, the proportion of defensive tactics that lead to the avoidance of bodily contact, the proportion of defensive tactics that foster the maintenance of physical contact, the relative proportion of counterattacks directed at playful rather than agonistic body targets, the target sites competed for during play fighting, and the degree of resemblance of the playful encounters to their adult counterparts. Both the criteria and how they were converted to a numerical score of play complexity are more fully described elsewhere (Pellis & Iwaniuk, 1999; Pellis & Pellis, 1998).

The results of this analysis is illustrated in Figure 6, suggesting that the social play repertoire of the mouse has diminished over evolutionary time. However, this

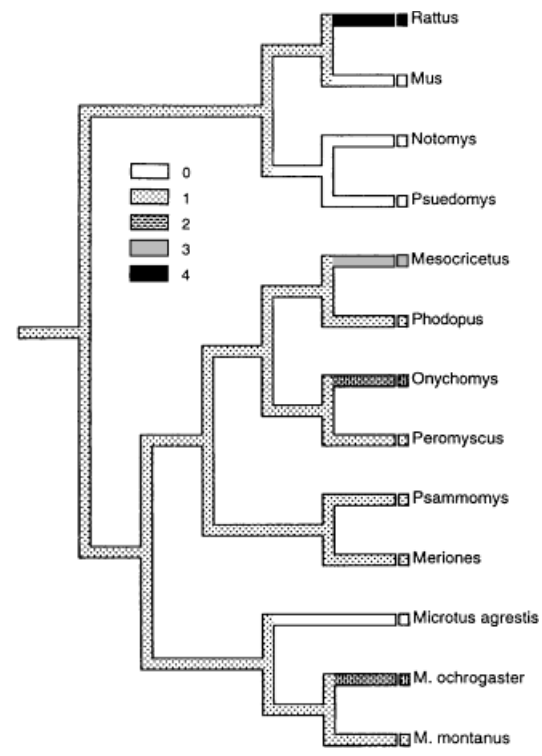

FIGURE 6 Play behavior mapped onto the phylogeny of murid rodents. The complexity of play fighting present in 16 species of murid rodents indicated that relative to the ancestral state, rats have increased the complexity of their play whereas mice have simplified theirs. The insert represents play complexity with the score of 0 indicating little or no play and a score of 4 indicating very complex play (adapted from Pellis & Iwaniuk, 2000).

does not mean that the existing behavioral elements that mice use in play are not highly labile. Indeed, the performance of the various locomotor patterns present in the solitary and social play of mice is influenced by the number and sex of siblings present and by prior social experience (Laviola & Alleva, 1995). Although there is this flexibility in the expression of playful behavior, the range of the behavioral repertoire available to mice for play is much reduced compared to that of rats (Pellis & Pellis, 1998).

Food Defense

Further support for this hypothesis of behavior simplification in mice is provided by the differences in the occurrence of the lateral dodge in mice and rats. As already noted, both species use the dodge in play, appearing in response to playful attacks to the neck by the 2nd week of postnatal life (Pellis & Pasztor, 1999; Pellis & Pellis, 1997). This defensive tactic continues to occur in the sexual and agonistic encounters of the adults (Pellis & Pellis, 1987; Pellis, Pellis, Manning, & Dewsbury, 1991b, 1992a; Whishaw & Kolb, 1985). In rats (Whishaw & Tomie, 1987), but not so much in mice (Whishaw et al., 1998a), the dodge also is used to protect a small food item held in the mouth. The use of dodging to protect food emerges in rats following weaning, in the 3rd week of postnatal life (Bolles & Woods, 1964). Whereas the behavior pattern appears to be fully matured by about 30 days, the ability to coordinate the movements of the dodge to maintain a rump-to-head orientation towards the robber does not fully develop until following puberty (at around 60 days). In the absence of social experience in the juvenile phase, the orientational component of the dodge does not develop into the adult form (Pellis, Field, & Whishaw, 1999).

Two conclusions may be drawn from this developmental pattern. First, applying dodging to food protection occurs later in development than its use in play. Second, the effective use of dodging for food protection appears to require experiential feedback. These findings suggest that both mice and rats have a more hard-wired use of dodging for social defense, but only rats have effectively co-opted this tactic for food defense. Lesion studies support this conclusion. Decorticate rats can use the dodging tactic during play fighting both as juveniles and as young adults (Pellis et al., 1992a) whereas decorticate adults fail to dodge in response to a food-robbing partner (Whishaw & Tomie, 1988). That is, the simpler use of the dodge is organized subcortically, but its transference to food protection requires cortical control and possibly experience.

Sexual Behavior

Sexual and aggressive interactions also suggest that while both species share many of the same behavior patterns (Grant & MacIntosh, 1963), the behavioral repertoire of the mouse is simpler and involves less sophisticated control mechanisms than that of the rat.

In standard tests involving small enclosures, both female mice and rats tend to remain passive, and the males of both species engage in little preliminary contact prior to mounting. In larger enclosures, reflecting more naturalistic situations, both female mice (Hurst, 1986) and female rats (McClintock & Adler, 1978; Whishaw & Whishaw, 1996) play a more active role, moving toward and away from the male, thus setting the timing and pace of copulations. When the female is ready to mate, she entices the male to follow, but unlike the mouse, the female rat has a rich repertoire of behavior patterns, such as ear wiggling and jerky jumps in front of the male (Beach, 1976), that seem to facilitate her ability to attract the male's attention.

Similarly, whereas the males of both species sniff the partner's nose and the anogenital area, as is true for most other murid rodents (Eisenberg & Kleiman, 1977), the contact on other body areas is more complex in the rat. Male mice contact the nape area as they mount the female (Pellis et al., 1991b) whereas male rats contact and nuzzle the nape in contacts that do not lead to mounting as well as those that do. That is, nuzzling the nape seems to be an important component of courtship for rats in some situations (Calhoun, 1962; Pellis, personal observation). Therefore, both the male and female precopulatory behavior of the mouse is simpler than that in the rat.

Conspecific Aggression

The reduced sophistication of behavior in mice also is reflected in male–male agonistic encounters. Both rats and mice, as appears typical for most murid rodents (Pellis, 1997), deliver offensive bites to the lower dorsum and flanks and defensive bites to the face. Introducing an unfamiliar male into the territory of a resident male is a simple way of polarizing offense and defense, as the resident launches most of the offensive bites and the intruder delivers most of the defensive bites (Blanchard & Blanchard, 1994).

When bitten on the rump, one of the defensive tactics available to both rats and mice is to roll over onto supine and thus withdraw the bitten area from the attacker (Pellis, 1997). The sequelae following this maneuver, however, differ between the species. The defending rat may remain motionless in the supine

position. Given the important role of motion as a stimulus for attack (Thor, Wainwright, & Holloway, 1981), this behavior may lessen the likelihood of attack. Alternatively, the supine rat makes slow tracking movements that align its teeth with the opponent's face, thus actively inhibiting further attacks (Blanchard & Blanchard, 1977).

In contrast, although about 20% of bites to the rump are defended by rotating to supine, mice do not remain in the supine position once extricated from the attacker's teeth (Pellis et al., 1991b). The reason for the mouse's failure to remain in the supine position appears to reside in the greater likelihood of an attacking mouse delivering a bite to the abdomen of the supine opponent (Blanchard, O'Connell, & Blanchard, 1979). Such a bite is potentially fatal, as the teeth can damage the abdominal organs, as compared to ripping muscle tissue in bites to the rump.

One interpretation of this species difference is that while both species have the taxon-specific offensive target, the behavior of the mouse is more stimulus-bound so that as the target is withdrawn, the attacker bites at the largest exposed area of the opponent. In contrast, the rat will engage in a variety of maneuvers to gain access to the hidden rump area (Blanchard, Blanchard, & Takahashi, 1977). Again, this suggests that the mouse is more stimulus-bound in its behavior and not able to produce novel combinations of movements to attain a goal. That is, in attempting to make a nape attack, a rat must withhold simple reflexive biting and modify its movements until it is able to attack a preferred target. Thus, it behaves as if it has a schema as opposed to biting reflexively. Other social contexts further illustrate the reduced complexity of aggressive behavior in mice.

Full-blown attack and defense of the rump area can occur between members of a colony and between strangers that meet in a neutral area (Blanchard & Blanchard, 1990; Brain, 1981, 1989; Calhoun, 1963). In both of these situations the options available to mice are limited to two—fight or flee. Rats have a third option: Subordinate males in a colony may use a rougher version of the play fighting typical of juveniles to interact forcefully with the dominant male. Whereas these interactions appear rougher than comparable play fights in the juvenile phase, they still involve attack and defense of the nape, which is nuzzled if contacted, and so are unlike real fights which involve bites directed at the rump (Pellis & Pellis, 1987). The rough play appears to function as a means of testing the dominance-holding capacity of the dominant-male (Pellis, Pellis, & McKenna, 1993).

When unfamiliar adult male rats are introduced in a neutral arena, they again typically engage in a rough form of play fighting, and only if this seems to fail in establishing a dominance relationship will they escalate to serious fighting (Smith, Fantella, & Pellis, 1999). Therefore, this evidence suggests that rats, unlike mice, have a quasi-aggressive form of interaction that can be used to assess and manipulate another rat while avoiding unrestrained combat. This permits rats a wider range of options in their social interactions and suggests a greater degree of sophistication in the neurobehavioral control mechanisms involved in producing aggressive behavior. Again, some of the subtle uses of play fighting in older rats depends on the experiences gained as juveniles (Byrd & Briner, 1999); the acquisition of such experience-based flexibility in behavior appears to be dependent on the function of cortical mechanisms (Pellis, Pellis, & Whishaw, 1992b). Of course, not all strains of mice have been evaluated with regard to aggressive behavior. Nonetheless, given that the studies described earlier were based on outbred strains, it is highly likely that the results are representative of house mice generally.

Barbering

A curious difference in conspecific aggression is the barbering behavior displayed by many strains of laboratory mice (Silvan, 1966), a behavior that has not been reported in rats. During barbering, a conspecific, presumably a subordinate conspecific, sits passively while a pair mate grasps a single whisker and plucks it out (Sarna, Dyck, & Whishaw, 2000). By repeating this operation, a barber frequently leaves the recipient clean shaved. The operation seems obviously painful, as the recipient winces, but does not attempt to escape. Strozik and Festing (1981) report that the barber is usually dominant, and since barbering is more commonly found in certain mouse strains, it may have a genetic component (Hanchska, 1952). Cross-fostering experiments suggest that both inheritance and learning contribute to barbering (Carruthers, Halkin, & King, 1998).

A potential reason for passive acceptance of barbering by mice is an absence of more complex social behavior for parrying the advances of the plucker. Of course, we admit that this hypothesis is speculative, and it could be equally argued that the ability to pluck a single whisker is a demonstration of behavioral complexity. Alternately, the behavior may be aberrant as not all strains of mice barber equally. Nevertheless, even if barbering were pathological, the pathology may emerge in mice as a result of an absence of more complex social behavior to parry plucking.

Predatory Defense

Defensive behavior of both wild and domesticated rats and mice has been compared by Blanchard and colleagues (Blanchard & Blanchard, 1989; Blanchard, et al., 1998). Although the dangers that have been most influential in shaping mammalian defense patterns include attacks by both conspecifics and predators, the paradigm that has received most analysis involves defense against predation.

The task involves avoiding a cat by escaping into a visible burrow system. The apparatus is a large, open surface area with tunnels and chambers that is maintained under a 12:12 hr light:dark cycle, under constant red light to which the animals are insensitive, opening onto the large surface area. Groups of Swiss-Webster mice or second-generation wild rats were studied. A live domestic cat or a toy cat was Placed into the open area, and the response of the animals was recorded for a 16-hr period.

The pattern of defensive behavior in rats and mice is similar, but there are several differences. On the initial presentation of the predator, mice retreat from the open surface and then return to engage in risk assessment. This behavior consists of returning to the surface area and peeping through the opening in order to see the cat. If an obstacle obscures the view of the cat, the mice change their vantage point. After a period of about 5 to 10 min of risk assessment, the mice retreat to the depths of the burrows and remain there for some hours. In contrast, the rats immediately retreat to the depths of the burrows and engage in prolonged freezing behavior.

The reason that the rats do not engage in initial risk assessment appears to be related to their use of vocal communication. The first rat to observe the cat emits an alarm call that alerts other members of the colony to danger so that all members of the colony do not have to view the predator to avoid it. Thus, the greater complexity of social organization of rats seems to have resulted in their use of different defensive strategy than that used by mice. This apparent use of vocal communication in rats may suggest the use of a more complex behavior than simple predatory inspection, as vocal communication is widely thought to involve relatively complex signaling (Marler, Evans, & Hauser, 1992).

A Caveat: The Contribution of Domestication

Most of the research summarized in the present review has been conducted with domesticated animals. Could the differences described here be an artifact of domestication?

As the two species have tended to be used for different laboratory purposes, subtle differences in selection regimes could have yielded big differences in neurobehavioral systems. Therefore, the various behavioral differences discussed previously may be typical of domesticated, but not wild, animals. For example, with regard to defensive behavior, it has been shown that laboratory mice and rats are more dissimilar to each other than are wild-caught mice and rats (Blanchard & Blanchard, in press). Furthermore, studies of domestication have revealed that selection for one trait can involve the unexpected co-selection of other suites of traits (Budiansky, 1999). Our conclusions about the relative differences between mice and rats then may be different if we had data comparing wild-caught members of the two species across all the behavioral tasks discussed. Alternatively, it may simply be that domestication may enhance our ability to detect and evaluate species differences.

As animals are domesticated, they become tamer and this easier to handle. One way of achieving such taming is to reduce the range of stimuli capable of producing a strong defensive reaction. In this regard, it may not be surprising that wild rats and mice are more similar to each with respect to defensive behavior than are their domesticated counterparts: A domesticated rat or mouse making a mistake is less likely to end up as someone's meal. Thus, the degree of information processing about the potential danger of a situation is likely to be limited in wild animals, as they are more likely to engage in reflexive responses that have been proven successful over evolutionary time due to the effects of natural selection (Ellis, 1982). With domestication, and hence, the loosening up of these reflexive relationships, it could be argued that species differences in being able to engage in more complex information processing are likely to be revealed.

The possibility that complexity increases with domestication appears unlikely, however. If domestication were the primary cause of all of the differences between rats and mice, it would be predicted that comparisons of non-life threatening behavior would be as similar in wild as in domesticated rats and mice. Indeed, this appears not to be the case. For example, the greater complexity of courtship behavior in rats compared to mice has been found in both wild and domesticated rats and mice (McClintock & Adler, 1978; Hurst, 1986). Furthermore, play behavior is as different in feral animals as it is in domestic animals. Therefore, the species differences in behavioral flexibility and complexity may not be by-products of domestication, but rather, fundamental differences in the way that the two species have evolved to solve the

problems of survival and reproduction. Consideration of the differences in the two species niches and life histories support this possibility.

DISCUSSION

In comparison with the rat, we suggest that the mouse has a seemingly simplified behavioral repertoire for both non-social and social purposes. That is, the range of behavioral options available to mice is curtailed, and the actions that are available appear to be under simpler, more reflexive, control. For example, the difference is illustrated in the use of simpler pattern of limb use for grooming, use of a simpler constellation of visual cues in spatial navigation, switching to ventral bites when confronted by supine defending conspecifics, and less reliance on vocal communication. Its visual acuity is also less, but the sensitivity of other sensory systems has not been studied. We propose that the differences between rats and mice occur because the mouse is adapted for a different ecological niche than the rat, perhaps even as a result of frank competition. We also suggest that simplification in the mouse is mediated by accelerated brain maturation during development, which renders the mouse less dependent upon complex social behavior. Finally, we suggest that having a more rapidly maturing nervous system renders the mouse less plastic and less likely to change and adapt to conventional learning tasks.

The One-to-One Fallacy

It is well known that with respect to learning, as well as other behaviors, animals display what is called biological preparedness. That is, animals are innately preprogrammed to see certain cues and responses as naturally fitting together so that they are readily learned. Gerlai and Clayton (1999) have seized upon this notion to decry laboratory-based tests of rodents, and particularly laboratory-based tests of mouse behavior. Instead, they argue, ''the challenge is to design appropriate behavioral tests that exploit the natural memory capabilities of the species in question and thereby make these tests sensitive enough to detect the genetic effects that we wish to study'' (p. 50). We can refer to this position as the one-to-one fallacy. That is rather than using appropriate phylogenetic methods (e.g., as illustrated in Fig. 6), extrapolations are made from a single species occupying a particular biological niche to a single behavioral test. Gerlai and Clayton, after first assuming that all learning and memory resides in the hippocampus—a position with which most neurobehaviorists would disavow—argue that if only mice were studied in their natural habitat, then neurobiologists would be instructed by the animal's natural behavior and accordingly design ethologically and ecologically appropriate tests for the hippocampus. These tests then would reveal the genetic basis of learning and memory and so would be valuable in the assessment of animals whose genes have been manipulated. Although we agree that animals display biological preparedness, we believe that there are a number of reasons to conclude that it is fallacious to dismiss laboratory-based behavioral analysis or their conclusions on these grounds and unwise to assume that salvation lies in ''ethological'' tests.

First, as Gerlai and Clayton (1999) cite, among the best demonstrations of biological preparedness are those made in the laboratory. Second, the apparent impoverishment of mouse behavior, relative to rat behavior, that we consider in the present article, is unlikely simply due to the fact that behaviorists have been very successful in devising ecologically relevant tests for rats and have been unsuccessful in doing so for mice. This is due, in part, to the fact that mice and rats are closely related species and are thus more, rather than less, likely to share similar biological tendencies. It also is due, in part, to the fact that both species have been examined on a wide enough array of behaviors, as we review here, to provide some reasonable estimates of their relative abilities. For example, if it is generally the case that the visual acuity of mice is less than that of rats, it is unlikely that mice will display equivalent visual problem solving on some hypothetical ecologically relevant task. Third, the arguments made with respect to rats and mice in the present article are not simply test-based, but are performance-based. We have considered a wide range of behaviors including grooming, play, aggression, motor skill, and sensory ability as well as they way that the two species perform in certain, more formal tests. Available evidence that we have reviewed suggests that the behaviors displayed by the respective species in the laboratory are very similar to the same behaviors that they display in their natural habitat. Finally, if anything, ecological considerations simply confirm the suggestion that mice are behaviorally impoverished relative to rats. An example may be useful.

It is well known that laboratory mice are excellent nest builders (Lynch & Hegmann, 1972; Wolfe & Barnett, 1977) (Figure 7). If given some pieces of paper they will, within a few days, build nests that are far superior to those built by rats. Nevertheless, if home-building ability of the two species is examined

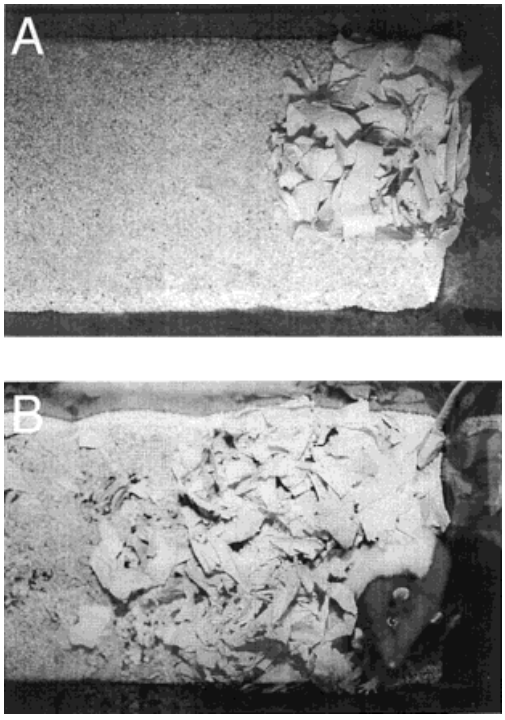

FIGURE 7 Nest at 4 days after building materials were supplied for (A), a mouse (which is in the nest) and (B), a rat. Note that the mouse nest appears more complete and complex than the nest of the rat although the rat has chewed up the paper towel building material than has the mouse (see text for discussion).

in the animals' natural habitats, it is found that both species can make more elaborate homes. Mice can build burrows with a number of chambers and runways (Lynch, Sulzbach, & Connolly, 1988). Rats build elaborate tunnel systems that are not only spatially complex but which also reflect the social composition of the group (Pisano & Storer, 1948). If rats are provided with similar opportunities in the laboratory they build similar complex, socially relevant, burrow systems (Flannelly & Lore, 1977). It could be argued that the ability to build spatially complex dwellings that reflect group composition may require more ability than that required to build a single nest. Nevertheless, as reviewed by Barnett (1975), under appropriate circumstances, rats do build complex nests as well.

Sources of Selective Pressure

It is commonly supposed that species with complex traits evolve from ''simpler'' ancestors; and therefore, if one species has complex behavior, closely related species should be similar. Phylogenetic analysis of behavior of animals in a number of orders suggest that complex traits are frequently lost (Iwaniuk & Whishaw, 2000; Sturmbauer, Levinton, & Christy, 1996). Some of the evidence, reviewed here suggests that mouse behavior may have undergone simplification over evolutionary time whereas the behavior of the rat may have increased in complexity in relation to ancestral species. For example, phylogenic reconstruction using comparative statistics (Figure 6) suggests play complexity is increased in rats, relative to ancestral state, but decreased in mice. Dodging is elaborated in social play, aggression, and in food protection in rats but plays only a rudimentary role in mice, and so on.

Both species are widely distributed, and in many places, their territories are likely to overlap. Competition for similar resources may have provided the pressure to differentiate, or at least to maintain differentiation. Thus, the mouse is small, uses less space, produces more offspring, has a shorter life span, occupies a narrower range of environments, is less social, and consumes a narrower range of food stuff. Consistent with the principle of competitive exclusion (Colinveaux, 1986), these differences minimize conflict of animals that may occupy overlapping niches. This form of differentiation is not unique to rats and mice, as parallels are seen in many other species whose niches overlap (e.g., North American coyotes and wolves).

A possible explanation for the difference in behavioral flexibility between mice and rats may stem from their reproductive strategies. Both species are r-selected, in that their life cycle is designed to maximize the number of offspring produced by giving birth to large numbers of offspring from an early age, as compared to k-selected species which specialize in producing fewer but higher quality young (Wilson, 1975). Even so, the r-to-k distinction is a relative one, so that comparison of any two species can reveal them as being more or less in a particular strategy (Daly & Wilson, 1983). The earlier onset of sexual maturity and of old age in mice relative to rats (Silvan, 1966) suggests that the mouse is more strongly r-selected than the rat. It also would appear to have more offspring, as revealed by litter size from our laboratory (mouse litter size $= 15.5 \pm 1.2$ vs. rat litter size $= 11.7 \pm 1.2$, $p < 0.05$). With a premium on attaining rapid sexual maturity, the mouse's overall development may be accelerated relative to the development of the rat.

An overall increase in the rate of development may have left the mouse less time and resources available for the development of a more complex and versatile behavioral repertoire. Indeed, a smaller proportion of

the mouse's postnatal life is composed of the juvenile phase (Silvan, 1966); that is, the time period between weaning and sexual maturity (Pagel & Harvey, 1993). Animals with less of their growth occurring postnatally are less likely to engage in complex social play (Pellis & Iwaniuk, 2000) and are likely to have a less complex repertoire of behavioral skills as adults (Joffe, 1997). As noted earlier, some of the skills present in adult rats are dependent on experiences accrued in the juvenile phase. Not only does the mouse appear to be equipped with simpler decision rules for action in various situations but the behavioral options appear to be more resistant to augmentation and modification with experience than is the case in rats (e.g., the acquisition of skilled reaching and matching-to-place learning).

The Effect of Accelerated Development on the Brain

Even though the behavior of the mouse is less complex in many behavioral domains compared to the rat, the mouse has a relatively larger brain (Eisenberg, 1981; Iwaniuk, Nelson, & Pellis, in press). This may be, in part, an artifact of its small size. Even so, a smaller relative brain size in the rat cannot be an impediment to developing behavioral versatility. For example, the wood rat has a relative brain size larger than both the Norway rat and mouse, yet the Norway rat is more versatile in its behavioral responses (Mann, Glickman, & Towe, 1988). Nevertheless, despite the mouse having a relatively larger brain than the rat, a greater proportion of its brain is developed prior to birth (Pellis & Iwaniuk, 2000). Developmental acceleration may leave the mouse less able to rely upon flexible learned behavior when dealing with conventional laboratory learning tasks. That is, accelerated brain development may result in a brain that is generally less plastic and less equipped to depend upon learning as an adaptive strategy. Thus, differences between the rat and mouse may be reflected in differences in the complexity of synaptic organization.

To estimate whether there is a neural basis for reduced behavioral flexibility, we have attempted to evaluate the potential for brain plasticity in the two species. There have been many attempts to compare the organization of the cerebrum of different species of mammals (for a review, see Rockel, Hiorns, & Powell, 1980). The general finding appears to be that cortical thickness increases with increasing brain size, but that, with the exception of visual cortex, the number of neurons in a column of cortical tissue is constant across mammalian phylogeny (Rockel et al., 1980). In addition, the relative proportion of pyramidal and nonpyramidal cells also is constant across species (Winfield, Gatter, & Powell, 1980). Thus, as the brain grows larger, there is an increase in the neuropil that accounts for the increase in cortical thickness. This increased neuropil can be presumed to reflect an increase in the number of synapses in the larger brains, which in turn presumably reflects an increase in cognitive capacity.

Given that there is roughly a fourfold difference in the weight of the rat and mouse brains (see Table 1), and that the mouse cortex is only about 60% as thick as the rat brain, it is reasonable to predict that the rat has more synapses per equivalent volume of cortical tissue. We have tested this prediction by measuring the length of dendritic fields of layer III pyramidal cells in the parietal cortex of rats and mice. Overall, mice have dendritic arborization that is about 70% of that of rats (B. Kolb & G. Gorny, unpublished, observations). Thus, rats would appear to have significantly more synaptic space than mice.

One assumption, however, is that synapse size is constant in rats and mice. We are unaware of any direct studies comparing synapse size in the same cortical regions of rats and mice, but comparison of studies looking at the visual cortex in rats versus the temporal cortex in mice (Kurt, Davies, Kidd, Dierssen, & Florez, 2000; Sirevaag & Greenough,

Table 1. Comparisons Between the Brains of Rats and Mice

	Species		
Measure	Rat	Mouse	Mouse/Rat
Brain weight (male)	2.17 g	0.5 g	.23
Cortical thickness	0.98 mm	.6 mm	.61
Dendritic length (apical)	1,226 μm	832 μm	.68
Dendritic length (basilar)	1,994 μm	1,440 μm	.72
Spine density (apical)	.67/μm	.83/μm	1.24
Spine density (basilar)	.76/μm	.91/μm	1.20
Synapse size	.4 μm	.19 μm	.48

1985) shows that mice have synapses that are about 50% the size of those in rats. If this difference is generally true in the cortices of the two species, then we would predict that synapses could be closer together in mice than in rats. Given that about 95% of the excitatory synapses on pyramidal cells are on spines, an estimate of spine density should show a difference between rats and mice and, in fact, it does (Table 1). Terminal tip spine density in layer III cells in the parietal cortex is about 20% higher in mice than in rats (Sakic et al., 1998; Teskey, Hutchinson, Gorny, & Kolb, 1999).

To estimate the total synapse number on pyramidal cells, we can multiply the dendritic, length by the spine density. For the apical dendrites this would be $1226 \times 0.67 = 821$ and $832 \times 0.83 = 690$, respectively. This yields a difference of about 15% in favor of rats, and a similar difference is found for the basilar fields as well. Thus, assuming that spine density is constant across the dendritic field in rats and mice, rats have about 15% more synapses per pyramidal neuron than mice. This is a large difference and, if true, would be consistent with the hypothesis that the rat cortex has a greater capacity for synaptic change than the mouse cortex. One difficulty with this measure, however, is that it assumes that the spine-density measure is actually a similar estimate of the number of spines in mice and rats. When spines are measured in Golgi-stained material, it is only those spines that are visibly protruding from the edges of the dendritic wall that can be measured. Spines that are protruding up toward the viewer or away from the viewer behind the dendrite cannot be seen. This is not problematic unless the diameter of the dendrite differs in the two species. Measuring dendritic diameter cannot be done accurately with light microscopy, as light microscopes are $\times 2000$ below that needed for an accurate measure of dendritic diameter. Given that the dendrites of rats are longer than those of mice, we would expect that the dendrites of rats might be a bit bigger than those of mice, at least close to the cell body or the primary apical dendrite. If this were true, then we have an underestimate of density in the rat. The simplest conclusion would be that rats do have more synapses, and the difference is at least 15%, but it may actually be greater. The larger number of total synapses in rats could be taken as evidence of greater cortical complexity in rats, but this is merely a hypothesis. One way to test the idea would be to compare the effect of experience, such as complex housing or the learning of a specific task, on dendritic length and spine density (e.g., Greenough & Chang, 1989). One would predict that there would be more change in the more complex system. We are unaware of any such studies.

CONCLUSIONS

Behaviorally, given its life history, the mouse appears to be a pared-down version of the rat. Moreover, compared to ancestral species, the rat appears to have undergone gains in complexity and the mouse losses in complexity with respect to their common ancestor. Consequently, the mouse can do many of the same things as the rat, but more simply and with less capacity for modifying the existing behavioral repertoire. Therefore, the mouse poses a problem for neurobehavioral research as it is a species functioning at a low level of complexity, relative to the rat, concentrating emphasis on just those behaviors directly needed for successful survival and reproduction. Manipulations of neural processes are thus limited in their ability to alter behavioral output. This need not be a drawback for the genetic analysis of behavior and may be an aid in identifying the genetic basis of basic behaviors. However, this may be a drawback for those neurobiologists who target plasticity and social behavior as a primary object of investigation. It also may be a drawback in comparing the results produced in different laboratories in which the focus of the analysis is on behaviors that might be a less pronounced part of an animal's ethogram. Crabbe, Wahlsten, and Dudek (1999) have remarked on the widely divergent results that can be obtained in the behavior of mice tested in different laboratories even when the same tests using the same apparatus are applied. That is, the possibility of making Type I errors in behavioral analysis increase as the statistical variability in behavior decreases. We suggest, therefore, that the genetic analysis of the mouse might be more usefully directed toward the more fundamental aspects of behavior as opposed to those aspects of behavior that involve social complexity and require extensive neural plasticity. At a minimum, more fundamental aspects of behavior require careful consideration when the primary focus of an investigation is on behavioral plasticity (Huerta, Scearce, Farris, Empson, & Prusky, 1996) or social behavior. Finally, given the close relationship between rats and mice, we do not envision the behavioral difference between rats and mice to have resulted from large numbers of genetic changes affecting each behavior, but rather from fewer genetic changes acting upon the rate of development.

NOTES

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