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Research report

A comparison of wild-caught wood mice and bank voles in the Intellicage: assessing exploration, daily activity patterns and place learning paradigms

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Abstract

Our previous work has revealed very high baseline neurogenesis in the dentate gyrus of wood mice as compared particularly to bank voles; a difference which may be related to learning capacity. This study explored whether the newly-developed Intellicage system could be used to compare these species in simple spatial learning paradigms. The Intellicage is essentially a group-housing cage that also allows continuous automatic recording of each individual's behaviour. Seven wild-caught bank voles (*Clethrionomys glareolus*) were compared with seven wild-caught long-tailed wood mice (*Apodemus sylvaticus*) in the Intellicage system over 9 days. During the first 90 min after entering the cage, the wood mice were substantially more exploratory than the bank voles ($P = 0.003$). Over subsequent days, both species showed nocturnal activity increases with voles being 3.7 times more active overall. In the spatial learning paradigms, there were significant species-by-time interactions with wood mice outperforming bank voles on both place learning ($P = 0.027$) and subsequent reversal ($P = 0.006$). Conclusions are firstly that the wood mice show superior learning abilities in this paradigm, and secondly that the Intellicage serves as a valuable cognitive testing arena for small wild rodents, or for circumstances where cognition must be compared independent of different responses to handling or novel environments.

Keywords: Wood mice; Voles; Intellicage; Learning; Activity; Exploration; Comparative

1. Introduction

Previous work from our lab and collaborators has focused on neuroanatomical differences between laboratory mouse strains or between small rodent species, and the association of these differences with learning capacities [24,32,34]. In particular, with wild-caught small rodents, we have explored differences in intra/infrapyramidal mossy fibre projections (IIP-MF) and differences in neurogenesis in the dentate gyrus [1,32]. Neurogenesis is of particular interest because within species, increased neurogenesis has been shown to correlate positively with performance in hippocampal-dependent tasks [11,15,35]. Yet, results of interspecific comparisons of learning abilities in animals with notably high and low baseline neurogenesis have not been published.

In this study, we aimed to compare the exploratory tendencies, activity and learning of two sympatric wild-living species which show very divergent neurogenesis levels in the dentate gyrus. These species are the long-tailed wood mouse (*Apodemus sylvaticus*, family Muridae), which show a very high neurogenesis rate, and the bank vole (*Clethrionomys glareolus*, family Arvicolidae), which show a much lower

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rate [1]. The two species are found co-existing throughout Europe (including Great Britain, but not including north Scandinavia), with the bank voles showing a preference for the more northerly climes and higher altitudes. Male wood mice show territory sizes up to 0.43 ha, compared to a maximum of 0.38 ha in male bank voles [20]. However, radio-tracked male Apodemus have been seen to explore areas as large as 10 km^2 [6]. In reproductive periods the wood mice form overlapping territories, in non-reproductive periods they form mixed or single-sex groups [28]. Bank voles live socially in age-specific hierarchies [28,29]. While there are some positive indications for good learning rates by both species [13,23,32,33], the two have never been compared in the same arena. Furthermore, our own work has indicated that these two species are awkward to test in standard cognitive tasks for different reasons. While the Apodemus species are very reactive to handling and very capable of escape, the bank voles are easier to pick up, but very often freeze for long periods when placed in land-based learning tasks such as the puzzle box (Galsworthy, unpublished data) or radial maze (Kuptsov, unpublished data).

In order to avoid these problems, which may be particularly marked for wild-caught animals, outdoor semi-naturalistic cognitive tasks had been devised. Animals live freely within large enclosures and their visits to feeder boxes are recorded by means of transponders injected under their skin [7]. Not only does this provide initial exploratory and activity-pattern data, but successful automated temporal and spatial cognitive tests have been administered by controlling motorized doors on the feeder boxes [8,36]. However, such work clearly has seasonal and space limitations. Therefore, an effort was made to bring the transponder-based technology and no-handling approach into the laboratory.

The Intellicage (www.newbehavior.com) is a newly-developed group-housing cage that doubles as a complete recording and testing apparatus. The Intellicage records visits of individuals to "corners" by means of antennae which recognise the transponders located under the skin of the resident rodents. Each transponder has a unique code. The "corners" are effectively small (one-animal-only) operant chambers with access to water controlled by motorized doors. As such, the Intellicage provides resources for a variety of cognitive paradigms whilst offering an attractive alternative to repeatedly transferring animals into an alien arena for testing. Rather, the system allows animal exploration, learning and memory to be studied on an individual basis; yet within home cages, alongside peers, and with ample time for any paradigm.

Therefore, the aim was to compare the learning abilities of these two species in the Intellicage, thus providing a fair comparison of cognitive abilities regardless of any divergent responses that they may show to handling or introduction to new arenas. The hypothesis was that the wood mice would show superior learning to the bank voles. It was also expected that the bank voles would show low exploration on introduction to the Intellicage.

2. Materials and methods

2.1. Subjects

Seven male bank voles and seven male long-tailed wood mice were tested. Animals were trapped in standard Sherman live traps baited with dark rye bread soaked in sunflower oil. Traps were checked every 4 h and catches were immediately transferred into single-housing cages with standard food chow and water ad libitum. From the variety of wild rodents caught, seven adult male bank voles and seven adult male wood mice were identified by experienced field ecologists and selected for testing in the Intellicage system. All the bank voles tested were trapped in the mixed deciduous and evergreen forest surroundings of Chisti Lec Biological Station (Director: V.V. Pazhetnov). This station is located in the Tvier Region 400 km west of Moscow and 400 km south of St. Petersburg. All the long-tailed wood mice tested were trapped in the deciduous woods of Zvenigorod Biological Station of the Moscow State University and transported to Chisti Lec field station for testing. The seven bank voles weighed between 19 and 25 g, five of the seven wood mice weighed between 16 and 20 g (initial weight data missing for two, but these were not notably different in terms of size). The bank voles were caught between 1 and 2 weeks before testing and the wood mice were caught between 2 and 3 weeks before testing.

2.2. Apparatus and recording

The Intellicage (see Fig. 1) is an apparatus designed to fit inside a large standard rat cage of 20.5 cm high × 40 cm × 58 cm at the top and × 55 cm × 37.5 cm at the base (Techniplast, model 2000). The apparatus itself provides four recording chambers that fit into the corners of the housing cage covering a right-angle triangular 15 cm × 15 cm × 21 cm area of floor space each. Access into the actual chambers is via an outer plastic ring (50 mm diameter) and then inner ring (30 mm diameter, 20 mm deep into outer ring). Such a width is designed to accommodate only one 10–40 g rodent. Furthermore these rings double as circular antennae designed to register visits to the corner. The rodent entering this chamber encounters a choice between two 13 mm holes (one on the left, one on the right) which give access to water-bottle nipples. The holes can be closed by small motorized doors, thus barring access to either or both water bottles in each corner. The Intellicage has in-built capabilities for other features not employed in this study, see www.newbehavior.com for details (Fig. 1).

In addition to the Intellicage frame, each cage contained a small shelter in the centre on which the animals could climb to reach the food (standard lab mouse chow, ad libitum). The houses were two short and one long metal box joined in parallel to make an L-shape. Looked at from the front, this 6 cm high construction had three compartments—two 6 cm wide

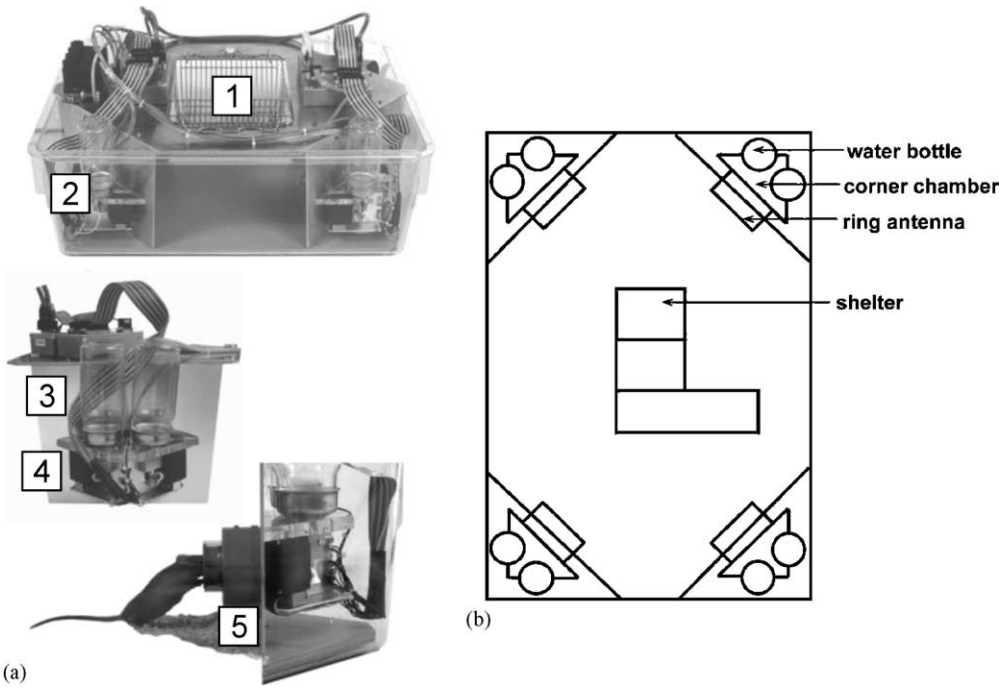

Fig. 1. An overview of the Intellicage. (a) The top picture shows the whole cage, the middle picture shows an individual removable corner from the outside, and the bottom picture shows a mouse entering a corner. Key: (1) food hopper; (2) Intellicage "corner"; (3) water bottles; (4) motorized doors controlling access to water bottle nipples; (5) the chamber entrance is a cylindrical antenna. (b) The overhead schematic shows the four triangular corners with ring antennae giving access to inner chambers, each holding two water bottles. Also shown is the metal housing shelter in the middle (which sits beneath the food hopper).

and ending 8 cm deep, and the third 5 cm wide, 16.6 cm long and open at the other end (see Fig 1b).

2.3. Procedure

Four to six hours before the animals were introduced into the Intellicages, they were anaesthetised by inhalation of methoxiflurane vapour and subcutaneously injected with glass-covered microtransponders (11.5 mm length, 2.2 mm diameter; UKID System, Collison & Co., Riverside International Park, Caterall, Preston, UK), weighed and returned to their cages. All animals recovered from the anaesthetic within minutes of exposure and all animals were later checked with a handheld scanner for retention of transponders before introduction to the Intellicages.

Introduction: Both groups of animals were introduced simultaneously to their respective Intellicages just before 20:00 on 4 July 2003. Habituation phase: The Intellicage system began recording from both cages 5 min later. All water access doors were open. Place learning: After 72 h, the water-access doors were closed in all corners but one. The corner chosen to retain access to water was selected as the corner least explored by the cage residents. In cage 1 (bank voles) this was corner 2. In cage 2 (wood mice), corners 1 and 2 were the least preferred and almost identical in value, so corner 2 was chosen to keep similarity with cage 1. Note also that over the first 3 days summed, corner 2 was the least visited in both cages. Reversal: Following another 72 h, the procedure was repeated, with the water-available (and now the most preferred) corner being closed and the new least-preferred corner being opened. In cage 1, the new corner opened was corner 1. In cage 2, the new corner opened was corner 3.

The experiment was run in the behaviour room of the animal house in Chisti Lec field station. One laptop ran and simultaneously recorded data from the two Intellicages. The cages were located next to each other, both approximately 1 m below and 1 m away from a south-east facing window. No other animals were housed or tested in this room during this time.

3. Results

A comparison of the two groups over the first 90 min shows the wood mice to be substantially more exploratory (Fig. 2). This difference, as measured cumulatively by the number of corners visited (i.e. maximum = 4 per mouse), was seen over the 90 min as a significant species-by-time interaction (F = 5.84, d.f. = 8, $P < 0.0001$). The cumulative difference first becomes significant at 30 min (Wilcoxon unpaired rank-sum test: $Z = 2.22$, $P = 0.03$). After 90 min this has increased further ($Z = 3.02$, $P = 0.003$) as the average wood mouse has visited three of the four corners, but most of the voles have yet to explore even one corner. Similarly, the time to initiate exploration (visit the first corner) was seen to be lower in the wood mice (median = 25 min) than the bank voles (median > 90 min: Wilcoxon unpaired rank-sum test: Z =

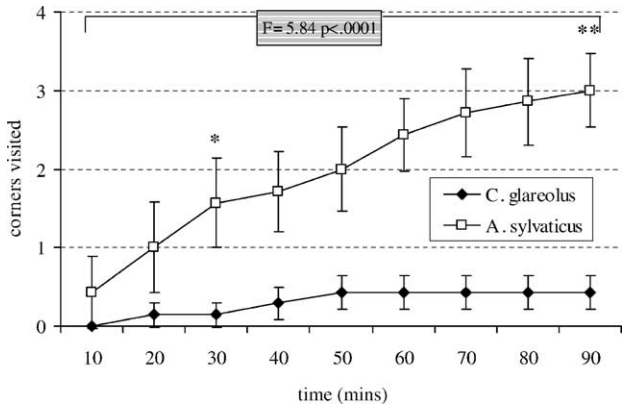

Fig. 2. Number of corners visited after introduction to the Intellicage (cumulative). Maximum = 4 corners visited. *F* and *P*-values indicate the significance of the species-by-time interaction in a repeated-measures ANOVA. Bars are standard error bars; (*) difference first becomes significant (Wilcoxon unpaired test: $Z = 2.22$, $P = 0.03$); (**) highly significant difference at 90 min ($Z = 3.02$, $P = 0.003$).

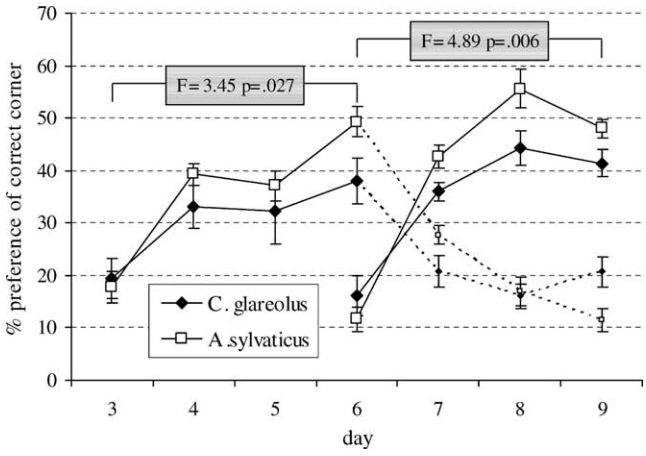

Fig. 4. Place learning and reversal for the two species. *F* and *P*-values indicate the significance of the species-by-day interaction in a repeated-measures ANOVA test for learning and relearning phases of the 'correct' (water-reinforced) corner. Dotted lines show the extinction for the first reinforced corner. Chance preference is 25%.

2.07, $P = 0.04$). We also employed an alternative method, namely time-to-event analysis, used often in survival analysis statistics. For this, a log-rank test for equality across cages in time to event revealed a chi-square of 5.65, $P = 0.018$) (Fig. 2).

Activity levels as measured by hourly total visits made to any corner over the first full day revealed that the wood mouse activity peaked 5 h after introduction and then declined, whereas the bank vole showed a similar but less notable peak over 6–9 h with only a hint of decline thereafter. The activity data over the next 8 days (2–9 inclusive) were employed as measures of habituated activity level and circadian pattern (see Fig. 3). Data indicate that the voles have a substantially higher activity level than the mice. The ratio of vole visits to mouse visits is 3.7 on average. Despite the greatest absolute difference being between 00:00 and 05:00 h, the greatest vole to mouse activity ratio was in the crepuscular period of 06:00–10:00 h. Both species show similar patterns of increased activity during night time, but the bank voles also exhibit smaller peaks of activity during dawn and midday. Note that these data are all based on group totals per hour, as the nature of the Intellicage output at that time did not summarise individual totals by the 216 hourly time-bins (Fig. 3).

In the place learning and reversal paradigms, animals in the two cages showed similar baseline preferences for the corners to be reinforced, followed by marked increases in preference as learning and re-learning took place (Fig. 4). A repeated-measures ANOVA (days as the repeated measure) confirmed that there was highly significant overall place learning ($F = 54.43$, d.f. = 3, $P < 0.0001$) and relearning ($F = 111.83$, d.f. = 3, $P < 0.0001$), but with significant species-by-day interactions for place learning ($F = 3.45$, d.f. = 3, $P = 0.027$)

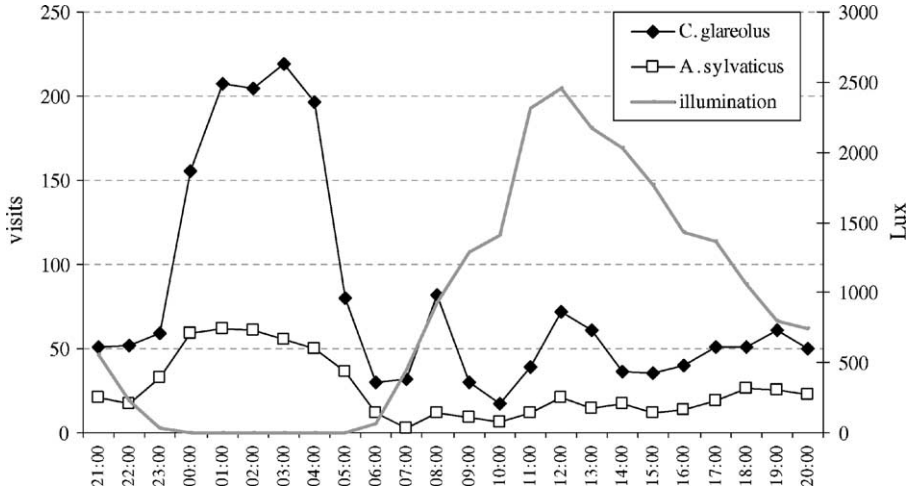

Fig. 3. Daily activity cycle for both species. Hourly activity of the two species during days 2–9 collapsed onto a single 08:00 p.m. to 08:00 a.m. scale and compared with mean hourly illumination recorded by both cages over the same time period.

and relearning ($F = 4.89$, d.f. = 3, $P < 0.006$), both nominating the wood mice as better learners, or, at least, as being less inclined to make non-rewarded visits.

Both species also showed marked extinction for the previous location in which water had been available ($F = 92.21$, d.f. = 3, $P < 0.0001$). Although a repeated-measures ANOVA from days 6 to 9 would indicate that the extinction was greater in the wood mice ($F = 11.27$, d.f. = 3, $P < 0.0001$), we urge caution for the following reasons: the two species start from significantly different baselines ($t = 2.21$, $P < 0.05$), and the voles are quicker to return to "chance" level (whether taken as 25%, or [100% − reinforced corner]/3). The extinction curves are therefore more complex and in this instance, perhaps less suitable for comparison between the species.

4. Discussion

Although this small study can by no means assert a causal link between neurogenesis and cognition across species, it nevertheless evidences the Intellicage as a powerful new tool to explore this relationship. This methodological development is the most important aspect of the presented work. The data acquired in this study demonstrate the usefulness of automated in-cage learning systems for species comparisons. Significant behavioral differences emerged rapidly with minimal experimenter requirement and despite modest sample sizes. The directions of all of the findings fit well with prior expectations from both wild and laboratory observation. The finding that the wood mice outperformed the bank voles in learning and re-learning place preferences provides support for the tentative hypothesis that neurogenesis in the dentate gyrus may be associated with increased cognitive flexibility in small rodent species. However, it is clear that more species would need to be similarly assessed in order to derive a correlation, let alone attribute causation.

Probably the most conspicuous behavioural difference observed between the two species was the initial exploration, echoing the observation that bank voles often freeze when placed in novel arenas. Most voles had still not visited even one corner after 90 min, whereas all mice had visited at least one corner after 55 min. This lack of exploration by the bank voles corroborates expectations based upon our unpublished efforts to test them in land cognitive tasks, and open field data showing bank voles to be the least exploratory out of several mouse and vole species [9].

Total activity levels throughout the next 8 days were consistently and markedly higher in the bank voles. Both species revealed nocturnal increases in activity, but the bank voles also showed secondary peaks during dawn and midday. This finding is consistent with the described polyphasic activity pattern of Microtinae [17]. However, it has been known since the 1930s that although voles in cages are usually more active at night [5], they are also more readily trapped during the day [18]. As summarized by Halle [17], literature has accumulated to explain this phenomenon by species interaction. Bank voles are subordinate in inter-specific competition and tend to follow a more diurnal pattern when sharing the field [2,16] or experimental [7] environment with wood mice. As can be seen from the results obtained here, this appears to be due to more direct interaction than mere proximity. However, we cannot rule out that the proximity of wood mice may have some other influences on the voles' behaviour.

The "higher activity" reported in this study was based on number of visits to the corners, but in voles this higher rate of visits to the corners could reflect a need for higher (or more regular) water consumption due to only dry food being available in Intellicage. Whereas wood mice naturally eat seeds, bank voles prefer leaves, mushrooms and fruits [4]. It is also noted that bank voles urinate much more than wood mice, as can be seen when cleaning cages. Higher water consumption should be confirmed by volume measurements in future experiments. However, a higher total level of visits for water does not explain why the bank voles were slower to learn the location of the water, and why they persisted in making so many visits to the incorrect corners. Yet "errors" in any learning paradigm may have multiple sources of causation. It may be that Intellicage paradigms need to be designed to punish errors so that they do not reflect, in part, superfluous activity.

Place learning is generally considered to be a hippocampal-dependent task and it is noted that wood mice show more effective place learning not only in the initial phase but also in the relearning. Adult generated, immature neurons are thought to be involved or even necessary for the acquisition of new hippocampal-dependent memories [35]. However, it is difficult to conclusively draw a link between adult neurogenesis and cognitive abilities [19]. In rats, there are results showing better performance in hippocampal-dependent tasks in animals with enhanced neurogenesis [11,30], yet other data show no correlation between spatial memory performance and amount of new cells generated in the dentate gyrus [27]. Birds allowed to store and retrieve food show an increased cell proliferation [31], whereas wild-living grey squirrels, which also scatter-hoard, show no enhanced neurogenesis during seasonally increased demands for spatial memory processing [22]. Wood mice and bank voles are scatter-hoarding species, too—but there have been no explorations of how this behaviour varies with neurogenesis over time or manipulation within each species. In terms of interspecific comparisons, the total number of adult generated neurons in the dentate gyrus per se appears to give no obvious prediction for hippocampal-dependent learning capability; the net daily production of new cells in the dentate gyrus in rats lies in between wood mice and voles [1,3] but comparison of spatial learning in rat and wood mouse reveals better performance in rat than wood mouse [33]. Even if an overall correlation does emerge, a direct relationship should not be claimed without considering additional potentially related characteristics, like differences in the total number of granule cells and distribution of IIP-MF in the hippocampus.

There is another caution regarding the data—and that is one of interactions within cages. Although there appeared to be a degree of "arguing" (vocalizations) amongst the bank voles during the first 1–2 days, neither bank voles nor wood mice showed any sign of harmful aggression during the whole experimental period. Nevertheless, it may well be the case that the animals within each cage influence each other's behaviour in less overt ways, and this exacerbates differences seen in exploration, activity or learning. Therefore, these data should be validated by replication and by single-animal tests where possible. At least in laboratory mice, it was found that the Intellicage system discriminated rapidly between animals with various degree of hippocampal damage housed together with controls [25], indicating that social interactions were of minor importance.

Beyond extending the study and exploring the relationship between neurogenesis and learning processes, the use of the Intellicage may be relevant to ecotoxicological research, where small native rodents are often used. Both species reported here have been used to explore effects of the intake of highly toxic substances due to pollution [10,12] and the effectiveness of repellants [21]. Yet it is anticipated that the major use of Intellicage will be for cognitive assessment of experimental manipulations in laboratory mice, particularly when emotionality confounds need to be avoided. As such, the cognitive data derived from Intellicage schedules should be validated in terms of known laboratory tests and influences. This would mean assessment by strain differences, lesions, or correlations with other standard cognitive tasks on an individual differences basis [14,26]. Such exploration with varying species and paradigms whilst making direct comparisons with other tasks should reveal optimal schedules for cross-species or within-manipulation comparisons, and we anticipate the development of new levels of complexity in learning assessment. The Intellicage clearly has the potential to become a powerful system for the remote studying of complex cognitive behaviour, both in small wild rodents and in laboratory counterparts.

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References

[1] Amrein I, Slomianka L, Poletaeva I, Bologova N, Lipp HP. Marked species and age-dependent differences in cell proliferation and neurogenesis in the hippocampus of wild-living rodents, Hippocampus, published online 29 April 2004.
[2] Brown L. Field experiments on the activity of the small mammals, Apodemus, Clethrionomys and Microtus. Proc Zool Soc London 1956;126:549–64.
[3] Cameron HA, McKay RD. Adult neurogenesis produces a large pool of new granule cells in the dentate gyrus. J Comp Neurol 2001;435:406–17.
[4] Castien E, Gosalbez J. Diet of *Clethrionomys glareolus* in the Western Pyrenees (North Iberian Peninsula). Folia Zool 1996;45:137–44.
[5] Davis D. Rhythmic activity in the short-tailed voles, Microtus. J Anim Ecol 1933;2:232–8.
[6] Dell'Omo G, Shore RF. Behavioral effects of acute sublethal exposure to dimethoate on wood mice, *Apodemus sylvaticus*. II. Field studies on radio-tagged mice in a cereal ecosystem. Arch Environ Contam Toxicol 1996;31:538–42.
[7] Dell'Omo G, Shore RF, Lipp H-P. An automated system, based on microchips, for monitoring individual activity in wild small mammals. J Exp Zool 1998;280:97–9.
[8] Dell'Omo G, Ricceri L, Wolfer DP, Poletaeva II, Lipp H. Temporal spatial adaptation to food restriction in mice under naturalistic conditions. Behav Brain Res 2000;115:1–8.
[9] Dell'Omo G, Pleskacheva MG, Wolfer DP, Lipp HP, Shore RF. Comparative effects of exposure to an organophosphate pesticide on locomotor activity of laboratory mice and five species of wild rodents. Bull Environ Contam Toxicol 2003;70:138–45.
[10] Dmowski K, Kozakiewicz A, Kozakiewicz M. Small mammal populations and community under conditions of extremely high thallium contamination in the environment. Ecotoxicol Environ Safety 1998;41:2–7.
[11] Drapeau E, Mayo W, Aurousseau C, Le Moal M, Piazza PV, Abrous DN. Spatial memory performances of aged rats in the water maze predict levels of hippocampal neurogenesis. Proc Natl Acad Sci USA 2003;100:14385–90.
[12] Erry BV, Macnair MR, Meharg AA, Shore RF. Seasonal variation in dietary and body organ arsenic concentrations in wood mice *Apodemus sylvaticus* and bank voles *Clethrionomys glareolus*. Bull Environ Contam Toxicol 1999;63:567–74.
[13] Galea LA, Kavaliers M, Ossenkopp KP, Hampson E. Gonadal hormone levels and spatial learning performance in the Morris water maze in male and female meadow voles, *Microtus pennsylvanicus*. Horm Behav 1995;29:106–25.
[14] Galsworthy MJ, Paya-Cano JL, Monleon S, Plomin R. Evidence for general cognitive ability (g) in heterogeneous stock mice and an analysis of potential confounds. Genes Brain Behav 2002;1:88–95.
[15] Gould E, Beylin A, Tanapat P, Reeves A, Shors TJ. Learning enhances adult neurogenesis in the hippocampal formation. Nat Neurosci 1999;2:260–5.
[16] Greenwood P. Timing of the activity in the bank vole *Clethrionomys glareolus* and the wood mouse *Apodemus sylvaticus* in a deciduous woodland. Oikos 1978;31:123–7.
[17] Halle S. Voles-small graminivores with polyphasic patterns. In: Halle S, Stenseth NC, editors. Activity patterns in small mammals: an ecological approach. Heidelberg: Springer; 2000. p. 192–215.
[18] Hamilton W. Activity and home range of the field mouse, *Microtus pennsylvanicus pennsylvanicus* (Ord.). Ecology 1937;18:255–63.
[19] Kempermann G. Why new neurons? Possible functions for adult hippocampal neurogenesis. J Neurosci 2002;22:635–8.
[20] Kikkawa J. Movement activity and distribution of the small rodents *Clethrionomys glareolus* and *Apodemus sylvaticus* in woodland. J Anim Ecol 1964;33:259–99.
[21] Kleinkauf A, MacDonald DW, Tattersall FH. A bitter attempt to prevent non-target poisoning of small mammals. Mammal Rev 1999;29:201–4.
[22] Lavenex P, Steele MA, Jacobs LF. The seasonal pattern of cell proliferation and neuron number in the dentate gyrus of wild adult eastern grey squirrels. Eur J Neurosci 2000;12:643–8.
[23] Lejeune H, Huynen MC, Ferrara A. Temporal differentiation in two strains of small rodents: a wood mouse (*Apodemus sylvaticus*) and an albino mouse (*Mus musculus* OF1). Behav Process 2000;52:155–69.
[24] Lipp HP, Schwegler H, Crusio WE, Wolfer DP, Leisinger-Trigona MC, Heimrich B, et al. Using genetically-defined rodent strains for

the identification of hippocampal traits relevant for two-way avoidance behavior: a non-invasive approach. Experientia 1989;45:845–59.
[25] Lipp H-P, Vyssotski AL, BenAbdallah N, Galsworthy MJ, Dell'Omo G, Amrein I, et al. Hippocampal lesions in mice: behavioral effects in the watermaze, naturalistic environment and Intellicage. Abstract presented at FENS annual meeting, 2004.
[26] Matzel LD, Han YR, Grossman H, Karnik MS, Patel D, Scott N, et al. Individual differences in the expression of a "general" learning ability in mice. J Neurosci 2003;23:6423–33.
[27] Merrill DA, Karim R, Darraq M, Chiba AA, Tuszynski MH. Hippocampal cell genesis does not correlate with spatial learning ability in aged rats. J Comp Neurol 2003;459:201–7.
[28] Montgomery WI, Gurnell J. The behaviour of Apodemus. Symp Zool London 1985;55:89–115.
[29] Niethammer J, Krapp F. Handbuch der Säugetiere Europas. 1. Rodentia I, Wiesbaden: Akademische Verlagsgesellschaft; 1978. p. 107–46, 337–58.
[30] Nilsson M, Perfilieva E, Johansson U, Orwar O, Eriksson PS. Enriched environment increases neurogenesis in the adult rat dentate gyrus and improves spatial memory. J Neurobiol 1999;39:569–78.
[31] Patel SN, Clayton NS, Krebs JR. Spatial learning induces neurogenesis in the avian brain. Behav Brain Res 1997;89:115–28.
[32] Pleskacheva MG, Wolfer DP, Kupriyanova IF, Nikolenko DL, Scheffrahn H, Dell'Omo G, et al. Hippocampal mossy fibers and swimming navigation learning in two vole species occupying different habitats. Hippocampus 2000;10:17–30.
[33] Schenk F. Comparison of spatial learning in woodmice (*Apodemus sylvaticus*) and hooded rats (*Rattus norvegicus*). J Comp Psychol 1987;101:150–8.
[34] Schwegler H, Lipp HP. Variations in the morphology of the septo-hippocampal complex and maze learning in rodents: correlation between morphology and behaviour. In: Alleva E, Fasolo A, Lipp HP, Nadel L, Ricceri L, editors. Behavioural brain research in naturalistic and semi-naturalistic settings: possibilities and perspectives. Dordrecht: Kluwer Academic Publishers; 1995. p. 259–76.
[35] Shors TJ, Miesegaes G, Beylin A, Zhao M, Rydel T, Gould E. Neurogenesis in the adult is involved in the formation of trace memories. Nature 2001;410:372–6.
[36] Vyssotski AL, Dell'Omo G, Poletaeva II, Vyssotsk DL, Minichiello L, Klein R, et al. Long-term monitoring of hippocampus-dependent behavior in naturalistic settings: mutant mice lacking neurotrophin receptor TrkB in the forebrain show spatial learning but impaired behavioral flexibility. Hippocampus 2002;12:27–38.