WIREs Wiley Interdisciplinary Reviews

Article title:

Spatial Cognition in Mice and Rats: Similarities and Differences in Brain and Behaviour

Article type:

- ☐ OPINIONS provide a forum for thought-leaders, hand-picked by the editors, to provide a more individual perspective on the field in question. (Average extent = 2,000-4,000 words, < 5 figures/tables, ~5 pages)
- ☐ PRIMERS are meant to be understood by a very general audience, such as undergraduates just entering a given field. (Average extent = 3,000 words, 3 figures/tables, ~4 pages)
- ☐ OVERVIEWS provide a broad and relatively non-technical treatment of important topics at a level suitable for advanced students and for researchers without a strong background in the field. (Average extent = 4,000-8,000 words, 10-16 figures/tables, 10-14 pages)
- ☒ ADVANCED REVIEWS, aimed at researchers and advanced students with a strong background in the subject, review key areas of research in a citation-rich format similar to that of leading review journals. (Average extent = 4,000-6,000 words, < 10 figures/tables, ~10 pages)
- ☐ FOCUS ARTICLES describe specific real-world issues, examples, implementations, etc. These articles are usually technical in nature. (Average extent = 3,000-4,000 words, < 7 figures/tables, ~5 pages)
- ☐ SOFTWARE FOCUS articles describe specific software packages of high utility in a certain field, with an emphasis on their capabilities and implementations rather than methodology. (Average extent = 3,000 words, 3 figures/tables, ~4 pages)

Authors:

Full name and affiliation; email address if corresponding author; any conflicts of interest

First author
Vincent Hok*, (1) Laboratory of Cognitive Neuroscience, CNRS and Aix-Marseille University, Marseille, France, (2) Fédération 3C, CNRS and Aix-Marseille University, Marseille, France. vincent.hok@univ-amu.fr
Second author

Bruno Poucet*, (1) Laboratory of Cognitive Neuroscience, CNRS and Aix-Marseille University, Marseille, France, (2) Fédération 3C, CNRS and Aix-Marseille University, Marseille, France. bruno.poucet@univ-amu.fr

Third author
Éléonore Duvelle, (4) UCL Psychology and Language Sciences, Faculty of Brain Sciences, London, United Kingdom.

Fourth author
Étienne Save, (1) Laboratory of Cognitive Neuroscience, CNRS and Aix-Marseille University, Marseille, France, (2) Fédération 3C, CNRS and Aix-Marseille University, Marseille, France.

Last author
Francesca Sargolini, (1) Laboratory of Cognitive Neuroscience, CNRS and Aix-Marseille University, Marseille, France, (2) Fédération 3C, CNRS and Aix-Marseille University, Marseille, France, (3) Institut Universitaire de France, Paris, France.

Keywords

Spatial cognition, Hippocampus, Behaviour, Place cells, Mice, Rats.

Abstract

The increasing use of mice models in cognitive tasks that were originally designed for rats raises crucial questions about cross-species comparison in the study of spatial cognition. The present review focuses on the major neuroethological differences existing between mice and rats with a particular attention given to the neurophysiological basis of space coding. Whereas little difference is found in the basic properties of space representation in these two species, it appears that the stability of this representation changes more drastically over time in mice than in rats. We consider several hypotheses dealing with attentional, perceptual and genetic aspects and offer some directions for future research that might help in deciphering hippocampal function in learning and memory processes.

Introduction

As pointed out by Hans J. Hedrich[1], the Norway rat (*Rattus norvegicus*) was the first mammalian species to be domesticated for scientific purpose as early as the first half of the 19th century. With the advent of molecular techniques in the late '80s and the development of transgenic mouse models, mice account nowadays for three-quarters of the mammals used in biomedical research[2]. For this reason, the mouse was the second mammal to have its genome fully sequenced, right after the human genome[3].

Historically, the rat has been most commonly used by physiologists, with a special attention given to learning and memory[4,5], whereas the mouse became the model of choice for genetic studies. By allowing manipulation of specific genes thought to be involved in cognitive processes, the knockout approach increased drastically the use of mice in behavioural research[6–8]. This has led to the confounding situation in which mice have been used extensively in behavioural paradigms originally

designed for rats, with virtually no consideration of the differences between these two species, as if they were fully interchangeable (see on this specific matter Refs [4,9–11]).

Rodents' abilities in spatial navigation tasks have been widely investigated for decades. This has led to the production of a vast amount of experimental data on brain and behaviour available in both species. In order to evaluate putative cognitive differences between these two species, we will first present the primary concepts in spatial navigation and discuss the nature of the spatial representation in the rodent brain. We then examine throughout the last sections the interactions between behaviour and brain activity that might explain interspecies differences when tested in common spatial tasks.

SPACE PERCEPTION

As early as the beginning of the 20th century, scientists began to investigate in details the mechanisms supporting the ability of animals to find their way back to their nest (*e.g.* Ref [12]). It appeared quickly that the selection of appropriate navigational strategies was primarily determined by the perception of space, that is, by the nature of the cues that could be used for navigation[a].

Cues for navigation

Cues useful for navigation are of two sorts: External cues provided by the environment (*allothetic cues*) and self-motion related cues (*idiothetic cues*). Allothetic cues encompass visual, tactile, auditory and olfactory signals whereas idiothetic cues are provided mainly by vestibular and proprioceptive inputs[14,15]. Note that a given sensory modality organ can provide both types of information: for instance, vision can convey allothetic information about static environmental landmark as well as idiothetic cues through the optic flow generated during self-motion.

In laboratory conditions, allothetic cues can be easily manipulated in order to trigger changes in behaviour and brain activity in freely-moving animals (*e.g.* Refs [16,17]). Conversely, manipulation of idiothetic cues cannot be achieved without partially restraining the animals (*e.g.* head fixed preparation[18]). These cues are otherwise always available (even in complete darkness), and are sometimes sufficient for an animal to estimate distance and orientation parameters. For instance, Wallace and Whishaw[19] recorded trajectories from rats moving around a circular table-top in either light or complete darkness conditions. Although their speed was lower in the dark, rats managed to head to their departure point with the same precision in both conditions. In addition, rats demonstrated knowledge of the distance to the goal, as their speed significantly decreased at the midpoint of the homeward trip, regardless of the length of the trip[19,20]. In this case, both direction and distance controlled the trajectory, independently from the availability of allothetic information. The ability of animals to keep track of their position with respect to a departure point is termed path integration and can prove, to some extent, to be sufficient for an animal to achieve accurate navigation[19,21]. Indeed, the principal limitation of this navigation strategy comes from the iterative nature of the process leading to accumulation of errors with increasing distance traveled[22,23].

[a] Following Gallistel[13], navigation is defined as "the process of determining and maintaining a course or trajectory from one place to another."

Although rodents are able to use idiothetic signals to navigate, they usually rely heavily on allothetic cues when available. In general, the visual modality is the most used. Olfactory and tactile signals can also help localisation, particularly when visual cues are less salient (*e.g.* olfactory-based navigation in the dark[24]; cooperation of olfactory and vision[25]; auditory cues[26]). However, landmarks can be unstable and allothetic cues may sometimes not be sufficient to disambiguate two similar environments (such a situation is probably more likely to happen in laboratory conditions). In natural conditions, animals combine allothetic and idiothetic signals to navigate, depending on their reliability. We generally refer to this process as multisensory integration[15,18].

Multisensory integration

To assess the relative contribution of each type of information to self-localisation, a common paradigm consists in causing a conflict between different sensory sources. For instance, in the experiment by Etienne and collaborators[27], hamsters first learned to go from their nest to a feeder located in the middle of a 220 cm diameter circular arena by following a baited spoon directed by the experimenter. Once there, the hamsters filled in their cheek pouches with food and came back to the nest. During training, a light spot was presented at the opposite side of the nest. During the test, this visual cue was rotated by either 90° or 180°, thus creating a conflict between visual and idiothetic cues. If hamsters relied exclusively on idiothetic cues, they would directly return to their nest. If they relied on the visual cue, they would aim at the opposite direction of the spotlight. The authors found that animals did neither one nor the other, but chose a position that was intermediary between the one indicated by self-motion cues and the one deduced from the visual cue. Interestingly, the deviation from the actual nest position depended upon the degree of conflict between self-motion cues and the visual cue. When the spotlight was rotated 90° (small conflict), the final position was far away from the nest position, as if the animals used preferentially the visual cue over idiothetic cues. On the contrary, when the spotlight was rotated 180° (large conflict), the final position was closer to the nest, thus suggesting that the idiothetic cues were given a larger weight than the visual cue. Overall, these results suggest that navigation relies on a weighted multisensory integration process[28]. In this context, the contribution of each sensory modality depends on the degree of confidence that can be attributed to them. There are several other examples suggesting that mammals navigate by combining allothetic and idiothetic cues[15,22,26,29]. In certain conditions, rats can show a hierarchy in the use made of different sensory modalities to guide navigation, vision being predominant over olfactory or self-motion cues[30]. However, the relative importance given to certain sensory sources over others greatly depends on their reliability within a reference frame[31,32].

To summarize, rodents can navigate using a combination of allothetic and idiothetic information, in a flexible and opportunistic manner, allowing switches between various strategies continuously in the course of navigation.

NAVIGATION STRATEGIES

"No wild animal roams at random over the country; each has a home-region, even if it has not an actual home."[33] *Home range*[b] concept (or *home-region* as previously defined by Ernest T. Seton) has been widely used in order to define the "area traversed by the individual in its normal activities of food gathering, mating, and caring for young."[34] In the wild, mice and rats show territorial behaviour like many other mammals[35,36], and show *home base* behaviour in laboratory settings[37]. In this context, home base refers to the location in which the animal spends a disproportionate period of time and from which it performs excursions[38]. During this home base behaviour, it appears that exploratory behaviour is organized[39] and that specific locomotor patterns can be identified[40].

Exploring space

Most mammalian species show increased exploratory activity when confronted with novelty and rodents are no exception[41,42]. This behaviour consists in moving towards unknown places or objects and gathering different types of information from several sensory modalities. Exploratory behaviour diminishes with habituation, albeit in different ways across species[43] and strains[44]. Interestingly, this diminution seems to depend on the integrity of the hippocampus (*e.g.* Refs [45–48], but see Ref [49] for contrasting results), a structure known for its major implication in spatial navigation[50]. Exploration is a central concept in spatial cognition, as this specific behaviour allows the animal to gain spatial knowledge and build representations of its environment[50,51]. It is a form of latent learning[52], which refers to the acquisition of knowledge occurring in the absence of explicit reward[53].

Organisation of exploration

Exploration behaviour can be triggered by a wide set of stimulus (*e.g.* a new environment[54], a new object in a familiar environment[47], a new spatial arrangement of objects[47,55], or even a change in the environment topology[56]). Novelty detection often interferes with the ongoing behavioural activities that animals have to perform, as if acting on the current goal of the animal, prioritising the gathering of new knowledge over feeding[41,42,57] or other behaviours[58]. However, despite its instinctive component and seemingly random structure, behavioural studies demonstrate that novelty exploration is actually quite organised[59,60] while still enabling the expression of inter-individual differences[61].

Basically, when exploring a new environment for the first time, a rodent will make excursions from its departure point to unexplored parts of its environment, most often following the borders, and regularly returning to a place termed 'home base'[39,62,63]. Specific behaviours such as rearing or grooming are more likely to occur at the home base[39]. The home base is usually the place where the animal was first released in the environment[64], but it has to provide sufficient shelter to be effective[38]. Regarding this latter observation, Whishaw and colleagues suggested that exploration would mainly serve to optimise safety. Exploration has similar patterns in the absence of visual cues: in the dark, rats placed in a new environment will still organise their displacements around a chosen home base. Their displacements show invariant characteristics, *e.g.* a dissociation between the

[b] *Home range* is not to be confused with the *territoriality* concept, the latter being the protected part of the home range. However, these two concepts largely overlap in some instance (*i.e.* territory can include the entire home range or only the nest; see Ref [34] for further discussion on this matter).

outward trajectory (*i.e.* away from the home base) and the return trajectory (towards the home base)[65].

More recently, a thorough characterization of mice exploratory behaviour was performed by Fonio and collaborators[60]. The authors demonstrated that exploration of a new and large circular arena could be decomposed in several behavioural patterns, the order of which was highly reproducible among individuals. These behavioural patterns progressively take place within the three-dimensional space: mice first make short back and forth trips from their home base following the wall (one-dimensional motion). Once they complete a full turn, they begin making small incursions inside the environment (two-dimensional) that progressively become independent from the home base. They end up performing jumping movements (three-dimensional). The authors highlighted the fact that in their experiment, exploration was free: the departure point of exploration trips was the mouse home cage, where *ad libitum* water and food were provided, and the time left for exploration was exceptionally long (45h in total). In common rodent experiments, exploration is forced and constrained in time and space, which might explain why the full pattern of exploratory behaviour is usually not observed. The importance of environmental limits (and probably geometrical information) is evidenced by the necessity for the mice to first entirely explore the borders before performing incursions towards the centre of the environment. In addition to providing shelter, borders[21] and geometrical layout[66] probably serve as anchor points necessary to build a spatial map of an environment[50,67].

Object exploration

The spontaneous exploration of objects is usually seen as good indication that mammals memorise and manipulate representations of space and objects in space (*e.g.* Ref [68] in hamsters; Ref [69] in rats). Indeed, the selective exploration of new objects in a known environment can only be possible if one has previously stored the arrangement of objects in this environment and is able to compare the current layout with the memorised representation. Many studies rely on spontaneous exploration to assess the memory for the nature or the position of objects, which relates to the 'what' or 'where' aspects of episodic-like memory[70,71]. In rodents, the hippocampus appears to be selectively involved in processing memory for object locations[47].

Exploration and task performance

Interestingly, Olton and collaborators showed the importance of exploration (also termed 'shaping' in that context) prior to testing. Rats that were not given the opportunity to explore a radial arm maze before testing, did not perform better than chance in the task[72]. Therefore, exploration (or simple pre-exposure to an environment), even in the absence of food, seems necessary for subsequent performance in navigation tasks[72–75]. As an example, Chai and White tested rats in their ability to discriminate neighbouring locations in a radial arm maze[75]. In this task, rats were confined to a specific arm of the maze, where they could either find food or not. When later tested with a free choice between adjacent arms that include the food-paired arm, rats demonstrated preference for this arm only if previously exposed to the entire maze[75,76]. If not pre-exposed to the maze, the knowledge acquired when restrained in an arm was not sufficient to build a representation of the environment and of the spatial configurations of the maze arms. In that regard, it is interesting to note that in complex environments rats spend more time exploring the topologically relevant parts

of a maze (*i.e.* the intersections), probably reflecting encoding of information on the connectivity layout of the environment[56,77].

Evidence reviewed above shows the crucial role of exploration in building a representation of space, and, by extension, in developing accurate navigation strategies. A navigation strategy can be defined by a set of rules to follow in order to reach a spatial goal when one is placed in a particular situation. Spatial information processing can endow the animal with navigation strategies allowing different degrees of behavioural flexibility and complexity. For example, turning left at the green sign is a response strategy whereas going to a specific place defined by its relationships with surrounding cues is a place strategy. Although there are different ways to categorize strategies, they are sharing common features[13,50,78].

Guidance

In certain navigation situations, the goal is either directly visible or cued. In that case, the best strategy, or at least the less cognitive demanding, is to orient towards the goal and approach it. This type of strategy is termed target approaching (when the goal itself is visible) or beacon approaching (if a cue is located at the goal position), or more generally cue, guidance or taxon strategy. It only requires learning of a single stimulus-response association.

Contrary to most functions described here, it is generally accepted that the hippocampus is not involved in guidance strategy, or at least that hippocampal lesions do not impair performance in cue-guided tasks[79–82]. The ability for rats with hippocampal lesions to perform a guidance strategy is often used as a control for non-spatial aspects of behaviour (*e.g.* sensory or motor abilities).

Response strategy

In some instances, the goal is neither visible nor directly cued but can be reached by means of associations between elements of the environment and actions (each association being independent from the others). This response (or stimulus-triggered response) strategy, also termed egocentric strategy[83], has been first studied by Edward C. Tolman in his search to identify the nature of the information used by animals to solve a spatial task[84,85]. A commonly used place/response task is the cross-maze task, in which rats are trained to retrieve food from one arm using either a place or a response strategy. During training, access to the north arm is blocked. Animals are then placed on the starting point of the south arm, and allowed to consume the food pellet located at the end of the east arm. In this phase, turning right (action) when facing the intersection (stimulus) will be sufficient to reach the goal. During the probe trial, access to the south arm is blocked. Animals are released from the north arm, and allowed to choose either the east arm (place learning) or the west arm (response learning). Similarly to the cue strategy, hippocampal lesions do not impair performance when the response strategy can be used to navigate towards a goal[86]. Conversely, the striatum is likely to be one of the key structures involved in this strategy[87]. Overall, it seems that in the intact animal, these two structures acquire different types of information simultaneously and in parallel[88], at least during the early phases of acquisition of the spatial task[89].

Routes

When specific actions can be associated to specific states as in the response strategy, but the knowledge of the state is not sufficient to select the action, one can use a route strategy. The route strategy has also been termed sequential egocentric strategy or sequence-based navigation[90]. It relies on a sequence of stimulus-response actions and it can also be used in a modified version of the Morris water maze in which neither proximal nor distal cues are present[90]. In this task, the animal has to cross three identical intersections before reaching its goal but the action to be performed at each of these intersections is different. Therefore, a sequence of stimulus – response associations must be learned and each choice must be selected according to its position in the sequence. We note that a route strategy is more complex than a succession of cue and response strategies, because the order of the stimuli in the sequence is important. Many structures are likely to be involved in this strategy, which holds a sequential (and possibly a timing) component. The CA1 field of the hippocampus would be one of the structures involved, along with other cortical and subcortical structures[90].

Place navigation

The strategy which probably requires the highest level of spatial information processing is the place (or map-based) strategy. It consists in localising the goal and oneself using the spatial relationships between elements of the environment. Contrary to the response strategy, it enables flexible behaviour, *i.e.* adaptability in the face of environmental changes. It was postulated to rely on a 'cognitive map', as defined by Edward C. Tolman[52].

Tolman[52] suggested that animals can manipulate representations of their environment and that they were not simply stimulus-response machines, in contradiction with the behaviourist approach, largely dominant at that time. Namely, Tolman proposed that rats could rely on a cognitive map to navigate, or, in other words, a neural representation of places and of the relationships between these places, independent of the current position of the subject. Tolman advanced several arguments to support this view. First, the rats are able to find shortcuts and to perform detours. Second, the rats show vicarious-trial-and-error behaviour (*i.e.* rats would occasionally pause and look back and forth at an intersection in a maze) when facing a choice. Third, the rats display several forms of latent learning. For example, that exploration improves further performance in a task[91] is evidence that the animal acquires information in the absence of an explicit reward. Another instance of such latent learning is provided by the observation that rats can incidentally learn what type of reward is available even when not currently motivated for this reward[92,93]. Fourth, the rats express hypothesis-based (or strategy-based) behaviour. This behaviour corresponds to a form of learning that shows a sudden shift from a near-random to near-perfect performance, contrary to what is observed with trial-and-error learning. Such a change in behaviour would underlie a non-incremental neural process, *i.e.* a sudden change of hypothesis about the world (see Ref [53] for a review of these arguments).

In the late '70s, the concept of cognitive map was amended following discoveries on its putative neural bases (namely, the hippocampus[50]). This updated theory, supported by neural data, led to a large amount of research centred on the role of the hippocampus and related brain areas in spatial cognition. To date, although few criticisms (*e.g.* Refs [94–96]) and reformulations have been addressed (*e.g.* Refs [97–99]), the cognitive map concept offers one of the most fruitful experimental paradigm in cognitive neuroscience.

BRAIN SUBSTRATES OF NAVIGATION IN MICE AND RATS

Given the extensive behavioural evidence of a flexible use of the different cues (see section Space Perception), it is fair to assume that space representation at the neural level shows a great dependence on multisensory integration. Indeed, such integration is present at the neural level in the hippocampus[18,100], where place cells have been first described in the rat[101] and later on also in the mouse[102,103]. We shall review in the following sections the principal differences between these two species in terms of hippocampal place cell activity with a careful look to their basic properties and experience dependent dynamics.

Sidebar title: Hippocampal place cells and the representation of space

Since its discovery in the early '70s by John O'Keefe, hippocampal place cells have been extensively studied in numerous spatial memory paradigms. These pyramidal cells are selectively active in restricted portions of space and change their firing activity (*i.e.* both firing rate and location) according to the nature of the environment being tested. Therefore, these place cells, along with other spatially tuned types of neurons (*e.g.* grid cells[104], head direction cells[105]), are thought to provide the rat brain with a unique spatial signature characterizing a specific environment, and thereby a memory trace of the subject's place. Originally discovered in the rat[101], place cells have been found since then in other mammalian species, including mouse[102,103], big brown bat[106], non-human primates[107] and human[108]. Although there is little doubt on the role played by place cells across these various species in spatial processing, few constitutive differences remain, especially in the primate literature. For instance, it appears that hippocampal cells in the non-human primate brain are sensitive to whole-body motion[109] and spatial view[110] during passive translocation, while such factors have somewhat limited impact on rodent place cell activity (*e.g.* see Ref [111] on the "local view" issue). However, it is possible that these discrepancies arise from the experimental design *per se* (passive translocation *versus* active exploration) rather than in any interspecies differences[112].

Basic properties of hippocampal pyramidal cells

As mentioned in the Introduction, the growing number of mice used in behavioural studies focusing on learning and memory raises the question of interoperability of the various behavioural tests used in this field of research. To this end, Routh and collaborators[113] asked whether basic properties of hippocampal CA1 pyramidal cells share common features between rats (Sprague-Dawley) and mice (C57BL/6). In line with others[114–116], the authors found larger hippocampi in rats than in mice, this difference being partly due to a smaller width of the dentate gyrus in mice[113]. However, the total number of neurons might be similar in the two species, as the CA1 pyramidal neurons appeared to be more densely packed in mice[113,117].

Routh and colleagues found little difference between rats and C57BL/6 mice regarding the cellular morphologies and passive membrane properties of CA1 pyramidal neurons, except for a more hyperpolarized resting membrane potential, and a lower resonance frequency[c] in mice neurons. Since resonance frequency is thought to be directly related to the magnitude of the

[c] The membrane potential resonance property describes the ability of neurons to respond selectively to inputs at preferred frequencies[118].

hyperpolarization-activated cation current (I_h)[113,119], mice would have less I_h active at rest compared to rats. Furthermore, I_h has been shown to regulate dendritic integration of distal synaptic inputs to CA1 pyramidal cells[120–122]. Deletion of one of the two channels isoforms (HCN1) responsible of I_h enhances behavioural performance in a hippocampal-dependent task, increases the power of theta oscillations and synaptic plasticity at the entorhinal inputs to CA1 neurons[122]. This last result is of particular importance given the central role of synaptic plasticity and long-term potentiation in stabilizing the activity of hippocampal place cells[123]. As discussed below, differences in molecular composition of HCN channels might be a key component of place field instability generally observed in mice.

Basic spatial properties of place cells

Cross-species comparison of the functional properties of place cells appears critical in understanding the general principles underlying hippocampal function[124]. However, there is relatively little comparative information even for the basic spatial properties of place cells (*e.g.* firing rate, spatial coherence, spatial information content and place field size). Several non-exclusive factors might explain this lack of systematic comparison. First, over the 40 years of research on hippocampal place cells, rat has been the dominant model. It is only from the mid '90s that mice models have been used in learning and memory research with emphasis on the molecular and genetic aspects, but not on the fundamental spatial properties of hippocampal place cells. Second, the wide variety of strains in both species (*e.g.* inbred *versus* outbred) and genetic backgrounds used for transgenic research reduces drastically our ability to draw systematic comparisons. Third, no single methodology has been laid down to analyse the various parameters of the spatial discharge of hippocampal neurons. For instance, there exists at least six different ways if only to mathematically define a place field (*i.e.* the portion of space where the place cell is active) all species combined[125–130].

Despite all these limitations, it is possible to get a rough idea on the degree of similarity of basic spatial properties of hippocampal place cells recorded in both mice (C57BL/6) and rats (Long-Evans) using nearly identical criteria[131,103,132–138]. It appears from this selected sample (see Table 1) that average firing activity is similar in both species. The internal organization of the place field (*i.e.* spatial coherence; a measure of the extent to which the firing rate in a pixel is predicted by the rates of its neighbours[139]) is nearly identical as well. It seems that the main difference concerns the spatial information content, which is a measure of the extent to which a cell's firing can be used to predict the position of the animal[140]. This index is nearly twofold in rats. **However, inferring any particular behavioural alteration from variations of this measure can prove cumbersome given its dependency to other variables such as the place field size. Indeed, numerous experimental studies reporting a loss of spatial information content report also an increased size of hippocampal place fields (*e.g.* Ref [141–143]). However, it is unknown whether hippocampal place fields in mice are broader than those observed in rats. In addition, works performed by Markus and colleagues[144] suggest that place field reliability is more important for spatial navigation than the size of the place field *per se*. This issue will be developed in the following section.**

Table 1: Comparison of main properties of place cells in mice and rats

	Mice (range [Refs.])	Rats (range [Refs.])
Average firing (Hz)	1.1—2.27 [103,133,136–138]	0.79—1.73 [131,132,135]
Spatial coherence	0.51—0.71 [103,133,137,138]	0.64—0.67 [131,134,135]
Information (bits per spike)	0.7—0.85 [136–138]	1.43—2.11 [131,132,134,135]
Stability	0.3—0.45 [145,146]	0.5—0.7 [147,148]

Place cell activity over time

A great deal of studies that initially explored the relationship between place cell activity and behaviour involved lesioning or inactivating specific brain areas (see Ref [149] for a review on this specific matter). Most of these studies were performed in the rat and showed that performance deteriorated when place cell activity was altered[150–152]. Studies conducted in transgenic mice reached a similar conclusion[137,138,153–156].

Aging studies provided further support for the idea that place cell activity was tightly linked to behavioural performance in rodents[141,157–159]. More precisely, major differences are observed between young and aged animals when comparing place field stability across days[d]. For instance, hippocampal place cells in young rats show strong place field stability over time[160] while aged animals show spontaneous rearrangements of place field locations (*i.e.* place cells remap) from time to time[161]. At this point, it is important to note that the same aging effect has been reported for mice place cells[162]. **However, a major interspecies difference is found when comparing place field stability (see Table 1)**; hippocampal place cell representation in mice does show a marked instability in normal conditions[103,133,145,146].

Place field relative instability has been reported straight from the beginning of electrophysiological recordings in freely-moving mice[103,133], but has been specifically investigated by Kentros and collaborators a few years later[145]. Since then, this particular aspect of place cells in mice has been reported in other electrophysiological[146] and calcium imaging[163,164] studies. In the forthcoming sections we will review the different hypotheses that tried to explain interspecies differences regarding the place cells dynamics.

Attentional hypothesis

Kentros and collaborators[145] showed that mice place fields are unstable when the behavioural task did not require any particular attention (*i.e.* the animal was left free to explore an open environment). Conversely, when the animal had to perform a pellet chasing task or, to a greater extent, when it had to solve a spatial navigation task (*i.e.* the animal had to reach an unmarked zone in the environment to receive a reward), place cells showed highly reproducible patterns of activity between sessions. This work also showed that a positive correlation exists between the level of behavioural performance and the degree of place cells stability: the best performing animals had the

[d] A place cell that fires at the same location in a familiar environment across multiple sessions is said to show a stable place field.

more stable place fields. The authors assumed therefore that attentional processes were responsible for the increase of place field stability.

Such attentional effect is also observed in the rat but in very particular conditions. Zinyuk and collaborators[165] trained rats to perform either a simple pellet chasing task or a navigation task on a rotating arena. The continuous rotation of the arena in a cue-rich room allowed to dissociate the stationary room-based from the rotating arena-based reference frame. The animals that were trained in the simple pellet chasing task showed less stable place fields than the animals that were trained in the navigation task when tested on the rotating arena (*i.e.* firing was more organized in the task-relevant frame). In the same line, Fenton and Muller[166] showed that in a simple pellet-chasing task, place cell firing was not nearly as reliable in the time domain as in the positional domain (*i.e.* place cell discharge during different passes through the firing field is extremely variable, a phenomenon called overdispersion). Fenton and collaborators[147] showed that attention could constraint this temporal variability of place cell firing.

Overall, Kentros and colleagues[145] explain the natural instability of place fields in mice by arguing that these animals pay less attention to distal environmental cues compared to rats. This idea is supported by the work of Eichenbaum and colleagues[167] showing that place cells in the mice are more easily controlled by local rather than distal cues. In this task, mice were allowed to explore a plus-maze that contained a large set of controlled stimuli, including local cues consisting of a distinctive surface on each maze arm. Additionally, distal cues, composed of distinct three-dimensional objects, were fixed on a curtain surrounding the maze. On the test phase, local and distal cues were rotated 90° in opposite directions. During this test phase, in control mice, place cells appeared to follow local rather than distal cues. However, these results could be also interpreted based on a hierarchical organization of sensory inputs, since the local cues were tactile and the distal cues were relying on the visual modality.

Hierarchical organization of sensory inputs

Although attention positively modulates place field stability in mice, it should be noted that this degree of stability remains relatively low when compared to recordings obtained in similar conditions in rats (see Table 1). Las and Ulanovsky[124] speculate that these discrepancies can be attributed to a differential use of sensory inputs in rats and mice. According to the authors, olfactory cues might play a much more important role in place field formation in mice than in rats. Indeed, theoretical[168] and experimental work[169] suggest that olfactory cues might control place field activity to a greater extent than what has been previously thought[170]. In addition, experimental data from several behavioural experiments (reviewed in Ref [171]) show that olfactory cues affect a wide set of behaviours in mice, perhaps more strongly than in rats (but see subsection Genetic Differences below). Added to the fact that visual acuity is poorer in mice[172], Las and Ulanovsky[124] suggest that rats would tend to develop more visually-based maps whereas mice would develop olfactory-based map. The relative importance of the various sensory information in shaping the place cell activity in mice remains however to be tested more thoroughly.

Another argument presented by Kentros and colleagues[145] in favour of genuine cognitive differences between mice and rats relies on results showing poorer performance in the Morris water maze task in mice[9–11]. This task is thought to rely heavily on a distal cues triangulation process[173], although rats could use preferentially directional responding over true place navigation on occasions[174,175].

Accordingly, rats use complex spatial strategies to find the hidden platform in the maze[4,176]. On the contrary, swimming patterns of the mice appeared more stereotyped, reflecting a preferential use of sequence-based navigation[177]. This last observation has to be considered along with further results obtained in rats by Hamilton and colleagues[178] showing that lesions of the dorsal tegmental nuclei (a brain structure known to contain head-direction cells) disrupt landmark-based navigation in this task. Given the predominant influence of the head-direction system on place cell activity[179], one can formulate the hypothesis that place field instability observed in mice might be closely linked to an instability in the head-direction signals. Indeed, when comparing head-direction cells characteristics between these two species, it appears that these cells are less reliably anchored to salient environmental cues in mice[180]. Nonetheless, particular caution should be taken in interpreting mice behavioural data obtained in the water maze task, as the nature of the behavioural strategy used during training could impact the way results are obtained in the probe trials[181–183]. For instance, adopting a spiralling search strategy during training can prove to be quite effective to locate the platform but mice showing such behaviour will score poorly in the final probe trial. Overall, it seems that mice use less robust and flexible strategies to solve spatial tasks than rats do[184] but show nonetheless a certain capability to switch strategies when given the opportunity[90].

Behavioural factors underlying stable place field activity

Exploratory behaviour (see section Exploring Space) is a complex response to novelty that results from a compromise between the motivation to gather information about the surroundings and the need to avoid predators[185,186]. As tracking technology improves, it is now feasible to analyse carefully the fine locomotor elements of exploratory behaviour in rodents[40]. Several studies by Golani and colleagues identified the moment-to-moment developmental sequence of forced[187,37] and free exploration[60] in rodents. Forced exploration refers to the procedure where the animal is placed directly into the test box at the start of the session, whereas in the free exploration procedure the animal has access to both the test box and its home cage[188].

In forced exploration, Long-Evans rats and BALB/cJtau mice show a gradual increase of excursion length when placed in the arena. For both species, path length increases across individuals both within and across multiple sessions, reflecting some habituation process. In contrast, in the same conditions, C57BL/6Jtau mice show a complete reversed profile across the session (*i.e.* when introduced in the arena, C57BL/6Jtau mice start with full circle excursions and only then proceed with smaller radial movements). This behaviour is likely to reflect greater risk taking of C57BL/6 mice compared to BALB/c[189]. In free exploration, these strain differences are much less pronounced, as C57BL/6 and BALB/c mice share common exploratory patterns[60].

To sum up, in classic studies of place cells in freely-moving rodents, the exploratory behaviour of C57BL/6 mice appears rather different from that of rats and might contribute to some extent to the differences observed in terms of place field stability. It is also important to note that a food pellet chasing task will likely interfere with the proper completion of exploratory behaviour[54,190]. Therefore, systematic comparisons of place cells recordings in different mice strains showing behavioural differences in forced but not in free exploration (*e.g.* C57BL/6 *versus* BALB/c) would shed light on the contribution of specific locomotor patterns to stabilize place cell activity.

Genetic differences

Although belonging to the same subfamily Murinae, rats and mice share only 30% of their DNA sequences[5]. Most of the genetic differences observed between these two species concern olfactory receptors, which are nearly 40% more numerous in rat's genome. Other major differences involve multiple biological processes such as pheromones detection, detoxification and proteolysis. Apart from the qualitative differences in genome sequences, rats and mice might differ also in channel subunit composition. For instance, as previously suggested by Routh and colleagues[113], a particular subunit composition of h channels (composed of HCN1 and HCN2 isoforms) in mouse would explain the lower hyperpolarization-activated cation current (I_h) at the entorhinal—CA1 synapse (see subsection Basic properties of hippocampal pyramidal cells above). Interestingly, Kandel and colleagues[191] performed hippocampal place cells recordings in HCN1 knockout mice in various behavioural tasks. They found that CA1 hippocampal place fields in these mice were larger and more stable than the controls. These electrophysiological data complement nicely the behavioural results showing improved performance of the HCN1 knockout mice in a hippocampal-dependent task[122]. Additionally, a recent study performed by Bittner and colleagues[192] showed that active dendritic integration in pyramidal neurons at the entorhinal—CA1 synapse is instrumental in forming new place fields and that similar mechanisms might be involved in stabilizing place cell activity.

To summarize, although sharing common basic neural features, rats and mice do show significant differences when comparing brain representations of space. The relative instability of representations in mice might lead to cognitive differences that are expressed not so much as differences in behavioural performance as differences in navigation strategy selection. Molecular variants of certain channels expressed in the mouse hippocampus might be directly related to this phenomenon but constitute undoubtedly only a small fraction of the pertinent genetic factors that are at play in space representation.

Conclusion

Much of our review focused on the major neuroethological differences existing between mice and rats in spatial cognition. Although sharing many behavioural characteristics in simple exploration tasks[10,37], the neural representation of space differs largely between these two species in terms of stability[133,145,146,163,164]. This last observation correlates to some extent with interspecies differences in navigational strategies used to solve spatial tasks[4,177,184]. Additionally, it appears that a simple modification in behavioural paradigms (*e.g.* free *versus* forced exploration) can induce important behavioural changes within one single strain[37,60]. On the other hand, growing evidence converge towards molecular explanation for the origin of place field instability in mice[113,122,191]. More importantly, these constitutive differences appear unrelated to the positive attentional effect observed on place field stability[145,146] as forebrain deletion of HCN1 does not involve changes in anxiety or attention[122].

Additionally, we let deliberately aside the strain issues in our review. All the behavioural and physiological data discussed in the previous section dealt with the C57BL/6 mouse genetic background unless otherwise stated. However, numerous reports stressed out the importance of the strain being used in spatial tasks, these between-strain differences leading sometimes to contrasting results[193–195,9,60,113,37]. Added to the fact that laboratory environment is likely influencing behavioural results[196] and that interindividual variability in genetically identical mice emerges with time[197], all

these considerations strongly support the need of a greater behavioural and physiological characterization of animal models used in learning and memory research[44].

Notes

[Please add any notes here]

References

1. Hedrich, H. J. Chapter 1 - History, Strains and Models. in Krinke, G. J. ed. The laboratory rat. Academic Press, London; 2000 pp.3–16.
2. Pankevich, D. E., Wizemann, T. M., Mazza, A.-M. & Altevogt, B. M. *International Animal Research Regulations: Impact on Neuroscience Research: Workshop Summary*. (National Academies Press, 2012).
3. Chinwalla, A. T. *et al.* Initial sequencing and comparative analysis of the mouse genome. *Nature* **420,** 520–562 (2002).
4. Frick, K. M., Stillner, E. T. & Berger-Sweeney, J. Mice are not little rats: species differences in a one-day water maze task. *Neuroreport* **11,** 3461–3465 (2000).
5. Gibbs, R. A. *et al.* Genome sequence of the Brown Norway rat yields insights into mammalian evolution. *Nature* **428,** 493–521 (2004).
6. Silva, A. J., Stevens, C. F., Tonegawa, S. & Wang, Y. Deficient hippocampal long-term potentiation in alpha-calcium-calmodulin kinase II mutant mice. *Science* **257,** 201–206 (1992).
7. Silva, A. J., Paylor, R., Wehner, J. M. & Tonegawa, S. Impaired spatial learning in alpha-calcium-calmodulin kinase II mutant mice. *Science* **257,** 206–211 (1992).
8. Bach, M. E., Hawkins, R. D., Osman, M., Kandel, E. R. & Mayford, M. Impairment of spatial but not contextual memory in CaMKII mutant mice with a selective loss of hippocampal LTP in the range of the θ frequency. *Cell* **81,** 905–915 (1995).

9. Whishaw, I. Q. A comparison of rats and mice in a swimming pool place task and matching to place task: Some surprising differences. *Physiol. Behav.* **58,** 687–693 (1995).

10. Whishaw, I. Q. & Tomie, J.-A. Of Mice and Mazes: Similarities Between Mice and Rats on Dry Land But Not Water Mazes. *Physiol. Behav.* **60,** 1191–1197 (1996).

11. Stranahan, A. M. Similarities and differences in spatial learning and object recognition between young male C57Bl/6J mice and Sprague-Dawley rats. *Behav. Neurosci.* **125,** 791–795 (2011).

12. Watson, J. B. & Lashley, K. S. Homing and related activities of birds. Carnegie Institution of Washington, Washington; 1915.

13. Gallistel, C. R. The organization of learning. MIT Press, Cambridge; 1990.

14. Save, E. & Poucet, B. Piloting. in Whishaw I. Q., Kolb B. eds. The behavior of the laboratory rat: a handbook with tests. Oxford University Press, New York; 2004 pp. 392–400.

15. Arleo, A. & Rondi-Reig, L. Multimodal sensory integration and concurrent navigation strategies for spatial cognition in real and artificial organisms. *J. Integr. Neurosci.* **6,** 327–366 (2007).

16. Save, E., Nerad, L. & Poucet, B. Contribution of multiple sensory information to place field stability in hippocampal place cells. *Hippocampus* **10,** 64–76 (2000).

17. Jeffery, K. J. Integration of the sensory inputs to place cells: What, where, why, and how? *Hippocampus* **17,** 775–785 (2007).

18. Ravassard, P. *et al.* Multisensory Control of Hippocampal Spatiotemporal Selectivity. *Science* **340,** 1342–1346 (2013).

19. Wallace, D. G. & Whishaw, I. Q. Dead reckoning. Whishaw I. Q., Kolb B. eds. The behavior of the laboratory rat: a handbook with tests. Oxford University Press, New York; 2004 pp. 401–409.

20. Wallace, D. G., Hines, D. J., Pellis, S. M. & Whishaw, I. Q. Vestibular Information Is Required for Dead Reckoning in the Rat. *J. Neurosci.* **22,** 10009–10017 (2002).

21. Zhang, S., Schönfeld, F., Wiskott, L. & Manahan-Vaughan, D. Spatial representations of place cells in darkness are supported by path integration and border information. *Front. Behav. Neurosci.* **8,** (2014).

22. Etienne, A. S. & Jeffery, K. J. Path integration in mammals. *Hippocampus* **14,** 180–192 (2004).

23. Poucet, B. *et al.* Is there a pilot in the brain? Contribution of the self-positioning system to spatial navigation. *Front. Behav. Neurosci.* **9,** 292 (2015).

24. Lavenex, P. & Schenk, F. Olfactory traces and spatial learning in rats. *Anim. Behav.* **56,** 1129–1136 (1998).

25. Rossier, J. & Schenk, F. Olfactory and/or visual cues for spatial navigation through ontogeny: olfactory cues enable the use of visual cues. *Behav. Neurosci.* **117,** 412–425 (2003).

26. Rossier, J., Haeberli, C. & Schenk, F. Auditory cues support place navigation in rats when associated with a visual cue. *Behav Brain Res* **117,** 209–14 (2000).

27. Etienne, A. S., Teroni, E., Hurni, C. & Portenier, V. The effect of a single light cue on homing behaviour of the golden hamster. *Anim. Behav.* **39,** 17–41 (1990).

28. Rotenberg, A. & Muller, R. U. Variable place-cell coupling to a continuously viewed stimulus: evidence that the hippocampus acts as a perceptual system. *Philos Trans R Soc Lond B Biol Sci* **352,** 1505–13 (1997).

29. Berthoz, A. & Viaud-Delmon, I. Multisensory integration in spatial orientation. *Curr. Opin. Neurobiol.* **9,** 708–712 (1999).

30. Maaswinkel, H. & Whishaw, I. Q. Homing with locale, taxon, and dead reckoning strategies by foraging rats: sensory hierarchy in spatial navigation. *Behav. Brain Res.* **99,** 143–152 (1999).

31. Biegler, R. & Morris, R. G. M. Landmark stability is a prerequisite for spatial but not discrimination learning. *Nature* **361,** 631–633 (1993).

32. Biegler, R. & Morris, R. G. Landmark stability: further studies pointing to a role in spatial learning. *Q. J. Exp. Psychol. B* **49,** 307–345 (1996).

33. Seton, E. T. Life-histories of northern animals : an account of the mammals of Manitoba. Scribner, New York City; 1909.

34. Burt, W. H. Territoriality and Home Range Concepts as Applied to Mammals. *J. Mammal.* **24,** 346–352 (1943).

35. Steiniger, F. Beiträge zur Soziologie und sonstigen Biologie der Wanderratte. *Z. Für Tierpsychol.* **7,** 356–379 (1950).

36. Hediger, H. Wild animals in captivity. Butterworth Scientific, London; 1950.

37. Drai, D., Kafkafi, N., Benjamini, Y., Elmer, G. & Golani, I. Rats and mice share common ethologically relevant parameters of exploratory behavior. *Behav. Brain Res.* **125,** 133–140 (2001).

38. Whishaw, I. Q., Gharbawie, O. A., Clark, B. J. & Lehmann, H. The exploratory behavior of rats in an open environment optimizes security. *Behav. Brain Res.* **171,** 230–239 (2006).

39. Eilam, D. & Golani, I. Home base behavior of rats (Rattus norvegicus) exploring a novel environment. *Behav. Brain Res.* **34,** 199–211 (1989).

40. Golani, I., Benjamini, Y., Dvorkin, A., Lipkind, D. & Kafkafi, N. Locomotor and exploratory behavior. in Whishaw I. Q., Kolb B. eds. The behavior of the laboratory rat: a handbook with tests. Oxford University Press, New York; 2004 pp. 392–400.

41. Chitty, D. & Shorten, M. Techniques for the Study of the Norway Rat (Rattus norvegicus). *J. Mammal.* **27,** 63–78 (1946).

42. Chance, M. R. A. & Mead, A. P. Competition between Feeding and Investigation in the Rat. *Behaviour* **8,** 174–182 (1955).

43. Poucet, B., Durup, M. & Thinus-Blanc, C. Short-term and long-term habituation of exploration in rats, hamsters and gerbils. *Behav. Processes* **16,** 203–211 (1988).

44. Wahlsten, D., Rustay, N. R., Metten, P. & Crabbe, J. C. In search of a better mouse test. *Trends Neurosci.* **26,** 132–136 (2003).

45. Roberts, W. W., Dember, W. N. & Brodwick, M. Alternation and exploration in rats with hippocampal lesions. *J. Comp. Physiol. Psychol.* **55,** 695–700 (1962).

46. Leaton, R. N. Exploratory behavior in rats with hippocampal lesions. *J. Comp. Physiol. Psychol.* **59,** 325–330 (1965).

47. Save, E., Poucet, B., Foreman, N. & Buhot, M.-C. Object exploration and reactions to spatial and nonspatial changes in hooded rats following damage to parietal cortex or hippocampal formation. *Behav Neurosci* **106,** 447–56 (1992).

48. Harley, C. W. & Martin, G. M. Open Field Motor Patterns and Object Marking, but Not Object Sniffing, Are Altered by Ibotenate Lesions of the Hippocampus. *Neurobiol. Learn. Mem.* **72,** 202–214 (1999).

49. Moses, S. N., Sutherland, R. J. & McDonald, R. J. Differential involvement of amygdala and hippocampus in responding to novel objects and contexts. *Brain Res. Bull.* **58,** 517–527 (2002).

50. O'Keefe, J. & Nadel, L. Hippocampus as a Cognitive Map. Clarendon, Oxford; 1978.

51. Poucet, B., Chapuis, N., Durup, M. & Thinus-Blanc, C. A study of exploratory behavior as an index of spatial knowledge in hamsters. *Anim Learn Behav* **14,** 93–100 (1986).

52. Tolman, E. C. Cognitive maps in rats and men. *Psychol. Rev.* **55,** 189–208 (1948).

53. Johnson, A. & Crowe, D. A. Revisiting Tolman, his theories and cognitive maps. *Cogn. Crit.* **1,** 43–72 (2009).

54. Lever, C., Burton, S. & O'Keefe, J. Rearing on hind legs, environmental novelty, and the hippocampal formation. *Rev Neurosci* **17,** 111–133 (2006).

55. Wilz, K. J. & Bolton, R. L. Exploratory behavior in response to the spatial rearrangement of familiar stimuli. *Psychon. Sci.* **24,** 117–118 (1971).

56. Alvernhe, A., Sargolini, F. & Poucet, B. Rats build and update topological representations through exploration. *Anim. Cogn.* **15,** 359–368 (2012).

57. Cowan, P. E. Systematic patrolling and orderly behaviour of rats during recovery from deprivation. *Anim. Behav.* **25, Part 1,** 171–184 (1977).

58. Bindra, D. Stimulus change, reactions to novelty, and response decrement. *Psychol. Rev.* **66,** 96–103 (1959).

59. Avni, R., Zadicario, P. & Eilam, D. Exploration in a dark open field: A shift from directional to positional progression and a proposed model of acquiring spatial information. *Behav. Brain Res.* **171,** 313–323 (2006).

60. Fonio, E., Benjamini, Y. & Golani, I. Freedom of movement and the stability of its unfolding in free exploration of mice. *Proc. Natl. Acad. Sci.* **106,** 21335–21340 (2009).

61. Kabbaj, M., Devine, D. P., Savage, V. R. & Akil, H. Neurobiological Correlates of Individual Differences in Novelty-Seeking Behavior in the Rat: Differential Expression of Stress-Related Molecules. *J. Neurosci.* **20,** 6983–6988 (2000).

62. Golani, I., Benjamini, Y. & Eilam, D. Stopping behavior: constraints on exploration in rats (Rattus norvegicus). *Behav. Brain Res.* **53,** 21–33 (1993).

63. Drai, D., Benjamini, Y. & Golani, I. Statistical discrimination of natural modes of motion in rat exploratory behavior. *J. Neurosci. Methods* **96,** 119–131 (2000).

64. Nemati, F. & Whishaw, I. Q. The point of entry contributes to the organization of exploratory behavior of rats on an open field: An example of spontaneous episodic memory. *Behav. Brain Res.* **182,** 119–128 (2007).

65. Wallace, D. G., Hamilton, D. A. & Whishaw, I. Q. Movement characteristics support a role for dead reckoning in organizing exploratory behavior. *Anim. Cogn.* **9,** 219–228 (2006).

66. Cheng, K. A purely geometric module in the rat's spatial representation. *Cognition* **23,** 149–178 (1986).

67. Touretzky, D. S. & Redish, A. D. Theory of rodent navigation based on interacting representations of space. *Hippocampus* **6,** 247–270 (1996).

68. Thinus-Blanc, C. *et al.* A study of spatial parameters encoded during exploration in hamsters. *J. Exp. Psychol. Anim. Behav. Process.* **13,** 418–427 (1987).

69. Ennaceur, A. & Delacour, J. A new one-trial test for neurobiological studies of memory in rats. 1: Behavioral data. *Behav Brain Res* **31,** 47–59 (1988).

70. Dere, E., Huston, J. P. & De Souza Silva, M. A. Integrated memory for objects, places, and temporal order: Evidence for episodic-like memory in mice. *Neurobiol. Learn. Mem.* **84,** 214–221 (2005).

71. Eacott, M. J., Easton, A. & Zinkivskay, A. Recollection in an episodic-like memory task in the rat. *Learn Mem* **12,** 221–223 (2005).

72. Olton, D. S., Collison, C. & Werz, M. A. Spatial memory and radial arm maze performance of rats. *Learn. Motiv.* **8,** 289–314 (1977).

73. Ellen, P., Parko, E. M., Wages, C., Doherty, D. & Herrmann, T. Spatial problem solving by rats: Exploration and cognitive maps. *Learn. Motiv.* **13,** 81–94 (1982).

74. Sutherland, R. J., Chew, G. L., Baker, J. C. & Linggard, R. C. Some limitations on the use of distal cues in place navigation by rats. *Psychobiology* **15,** 48–57 (1987).

75. Chai, S.-C. & White, N. M. Effects of Fimbria-Fornix, Hippocampus, and Amygdala Lesions on Discrimination Between Proximal Locations. *Behav. Neurosci.* **118,** 770–784 (2004).

76. Gaskin, S., Chai, S.-C. & White, N. M. Inactivation of the dorsal hippocampus does not affect learning during exploration of a novel environment. *Hippocampus* **15,** 1085–1093 (2005).

77. Poucet, B. & Herrmann, T. Exploratory patterns of rats on a complex maze provide evidence for topological coding. *Behav Process.* **53,** 155–162 (2001).

78. Redish, A. D. Beyond the Cognitive Map. MIT Press, Cambridge; 1999.

79. Morris, R. G., Garrud, P., Rawlins, J. N. & O'Keefe, J. Place navigation impaired in rats with hippocampal lesions. *Nature* **297,** 681–683 (1982).

80. Jarrard, L. E., Okaichi, H., Steward, O. & Goldschmidt, R. B. On the role of hippocampal connections in the performance of place and cue tasks: Comparisons with damage to hippocampus. *Behav. Neurosci.* **98,** 946–954 (1984).

81. Rasmussen, M., Barnes, C. A. & McNaughton, B. L. A systematic test of cognitive mapping, working-memory, and temporal discontiguity theories of hippocampal function. *Psychobiology* **17,** 335–348 (2013).

82. Packard, M. G. & McGaugh, J. L. Double dissociation of fornix and caudate nucleus lesions on acquisition of two water maze tasks: Further evidence for multiple memory systems. *Behav. Neurosci.* **106,** 439–446 (1992).

83. Kesner, R. P., Farnsworth, G. & DiMattia, B. V. Double dissociation of egocentric and allocentric space following medial prefrontal and parietal cortex lesions in the rat. *Behav. Neurosci.* **103,** 956–961 (1989).

84. Tolman, E. C., Ritchie, B. F. & Kalish, D. Studies in spatial learning. II. Place learning versus response learning. *J. Exp. Psychol.* **36,** 221–229 (1946).

85. Tolman, E. C. & Gleitman, H. Studies in spatial learning: VII. Place and response learning under different degrees of motivation. *J. Exp. Psychol.* **39,** 653–659 (1949).

86. Packard, M. G. & McGaugh, J. L. Inactivation of Hippocampus or Caudate Nucleus with Lidocaine Differentially Affects Expression of Place and Response Learning. *Neurobiol. Learn. Mem.* **65,** 65–72 (1996).

87. McDonald, R. J. & White, N. M. A triple dissociation of memory systems: Hippocampus, amygdala, and dorsal striatum. *Behav. Neurosci.* **107,** 3–22 (1993).

88. McDonald, R. J. & White, N. M. Parallel information processing in the water maze: Evidence for independent memory systems involving dorsal striatum and hippocampus. *Behav. Neural Biol.* **61,** 260–270 (1994).

89. Jacobson, T. K., Gruenbaum, B. F. & Markus, E. J. Extensive training and hippocampus or striatum lesions: Effect on place and response strategies. *Physiol. Behav.* **105,** 645–652 (2012).

90. Rondi-Reig, L. *et al.* Impaired Sequential Egocentric and Allocentric Memories in Forebrain-Specific–NMDA Receptor Knock-Out Mice during a New Task Dissociating Strategies of Navigation. *J. Neurosci.* **26,** 4071–4081 (2006).

91. Kimble, D. P. & Greene, E. G. Absence of latent learning in rats with hippocampal lesions. *Psychon. Sci.* **11,** 99–100 (1968).

92. Spence, K. W. & Lippitt, R. An experimental test of the sign-gestalt theory of trial and error learning. *J. Exp. Psychol.* **36,** 491–502 (1946).

93. Bendig, A. W. Latent learning in a water maze. *J. Exp. Psychol.* **43,** 134–137 (1952).

94. Bennett, A. T. Do animals have cognitive maps? *J. Exp. Biol.* **199,** 219–224 (1996).

95. Gibson, B. M. Cognitive maps not used by humans (Homo sapiens) during a dynamic navigational task. *J. Comp. Psychol.* **115,** 397–402 (2001).

96. Bennett, M. R. & Hacker, P. M. S. History of cognitive neuroscience. Wiley-Blackwell, Chichester; 2008.

97. Poucet, B. Spatial cognitive maps in animals: new hypotheses on their structure and neural mechanisms. *Psychol Rev* **100,** 163–82 (1993).

98. Eichenbaum, H., Dudchenko, P., Wood, E., Shapiro, M. & Tanila, H. The Hippocampus, Memory, and Place Cells: Is It Spatial Memory or a Memory Space? *Neuron* **23,** 209–226 (1999).

99. Jacobs, L. F. & Schenk, F. Unpacking the cognitive map: The parallel map theory of hippocampal function. *Psychol. Rev.* **110,** 285–315 (2003).

100. Chen, G., King, J. A., Burgess, N. & O'Keefe, J. How vision and movement combine in the hippocampal place code. *Proc. Natl. Acad. Sci.* **110,** 378–383 (2013).

101. O'Keefe, J. & Dostrovsky, J. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Res.* **34,** 171–175 (1971).

102. McHugh, T. J., Blum, K. I., Tsien, J. Z., Tonegawa, S. & Wilson, M. A. Impaired hippocampal representation of space in CA1-specific NMDAR1 knockout mice. *Cell* **87,** 1339–1349 (1996).

103. Rotenberg, A., Mayford, M., Hawkins, R. D., Kandel, E. R. & Muller, R. U. Mice Expressing Activated CaMKII Lack Low Frequency LTP and Do Not Form Stable Place Cells in the CA1 Region of the Hippocampus. *Cell* **87,** 1351–1361 (1996).

104. Fyhn, M., Molden, S., Witter, M. P., Moser, E. I. & Moser, M.-B. Spatial representation in the entorhinal cortex. *Science* **305,** 1258–64 (2004).

105. Taube, J. S., Muller, R. U. & Ranck, J. B. Head-direction cells recorded from the postsubiculum in freely moving rats. I. Description and quantitative analysis. *J Neurosci* **10,** 420–35 (1990).

106. Ulanovsky, N. & Moss, C. F. Hippocampal cellular and network activity in freely moving echolocating bats. *Nat Neurosci* **10,** 224–233 (2007).

107. Matsumura, N. *et al.* Spatial- and task-dependent neuronal responses during real and virtual translocation in the monkey hippocampal formation. *J. Neurosci.* **19,** 2381–2393 (1999).

108. Ekstrom, A. D. *et al.* Cellular networks underlying human spatial navigation. *Nature* **425,** 184–8 (2003).

109. O'Mara, S. M., Rolls, E. T., Berthoz, A. & Kesner, R. P. Neurons responding to whole-body motion in the primate hippocampus. *J. Neurosci.* **14,** 6511–6523 (1994).

110. Rolls, E. T. & O'Mara, S. M. View-responsive neurons in the primate hippocampal complex. *Hippocampus* **5,** 409–424 (1995).

111. Muller, R. U., Bostock, E., Taube, J. S. & Kubie, J. L. On the directional firing properties of hippocampal place cells. *J Neurosci* **14,** 7235–51 (1994).

112. Gavrilov, V. V., Wiener, S. I. & Berthoz, A. Discharge correlates of hippocampal complex spike neurons in behaving rats passively displaced on a mobile robot. *Hippocampus* **8,** 475–490 (1998).

113. Routh, B. N., Johnston, D., Harris, K. & Chitwood, R. A. Anatomical and Electrophysiological Comparison of CA1 Pyramidal Neurons of the Rat and Mouse. *J. Neurophysiol.* **102,** 2288–2302 (2009).

114. Kalisch, R. *et al.* Anxiety and Hippocampus Volume in the Rat. *Neuropsychopharmacology* **31,** 925–932 (2005).

115. Kovačević, N. *et al.* A Three-dimensional MRI Atlas of the Mouse Brain with Estimates of the Average and Variability. *Cereb. Cortex* **15,** 639–645 (2005).

116. Ma, Y. *et al.* A three-dimensional digital atlas database of the adult C57BL/6J mouse brain by magnetic resonance microscopy. *Neuroscience* **135,** 1203–1215 (2005).

117. Buzsáki, G. *et al.* Hippocampal network patterns of activity in the mouse. *Neuroscience* **116,** 201–11 (2003).

118. Hutcheon, B. & Yarom, Y. Resonance, oscillation and the intrinsic frequency preferences of neurons. *Trends Neurosci.* **23,** 216–222 (2000).

119. Narayanan, R. & Johnston, D. Long-Term Potentiation in Rat Hippocampal Neurons Is Accompanied by Spatially Widespread Changes in Intrinsic Oscillatory Dynamics and Excitability. *Neuron* **56,** 1061–1075 (2007).

120. Magee, J. C. Dendritic Ih normalizes temporal summation in hippocampal CA1 neurons. *Nat. Neurosci.* **2,** 508–514 (1999).

121. Robinson, R. B. & Siegelbaum, S. A. Hyperpolarization-Activated Cation Currents: From Molecules to Physiological Function. *Annu. Rev. Physiol.* **65,** 453–480 (2003).

122. Nolan, M. F. *et al.* A Behavioral Role for Dendritic Integration: HCN1 Channels Constrain Spatial Memory and Plasticity at Inputs to Distal Dendrites of CA1 Pyramidal Neurons. *Cell* **119,** 719–732 (2004).

123. Dragoi, G., Harris, K. D. & Buzsáki, G. Place representation within hippocampal networks is modified by long-term potentiation. *Neuron* **39,** 843–53 (2003).

124. Las, L. & Ulanovsky, N. Hippocampal neurophysiology across species. in Derdikman, D. & Knierim, J. J. eds. Space, Time and Memory in the Hippocampal Formation. Springer, Vienna; 2014. pp. 431–461.

125. Muller, R. U., Kubie, J. L. & Ranck, J. B. Spatial firing patterns of hippocampal complex-spike cells in a fixed environment. *J Neurosci* **7,** 1935–50 (1987).

126. Mehta, M. R., Barnes, C. A. & McNaughton, B. L. Experience-dependent, asymmetric expansion of hippocampal place fields. *Proc. Natl. Acad. Sci.* **94,** 8918–8921 (1997).

127. Hollup, S. A., Molden, S., Donnett, J. G., Moser, M.-B. & Moser, E. I. Place fields of rat hippocampal pyramidal cells and spatial learning in the watermaze. *Eur J Neurosci* **13,** 1197–208 (2001).

128. Mankin, E. A. *et al.* Neuronal code for extended time in the hippocampus. *Proc. Natl. Acad. Sci.* **109,** 19462–19467 (2012).

129. Dragoi, G. & Tonegawa, S. Preplay of future place cell sequences by hippocampal cellular assemblies. *Nature* **469,** 397–401 (2011).

130. Tanila, H., Sipilä, P., Shapiro, M. & Eichenbaum, H. Brain aging: impaired coding of novel environmental cues. *J Neurosci* **17,** 5167–5174 (1997).

131. Poucet, B., Thinus-Blanc, C. & Muller, R. U. Place cells in the ventral hippocampus of rats. *Neuroreport* **5,** 2045–2048 (1994).

132. Save, E., Cressant, A., Thinus-Blanc, C. & Poucet, B. Spatial firing of hippocampal place cells in blind rats. *J Neurosci* **18,** 1818–26 (1998).

133. Rotenberg, A., Abel, T., Hawkins, R. D., Kandel, E. R. & Muller, R. U. Parallel instabilities of long-term potentiation, place cells, and learning caused by decreased protein kinase A activity. *J Neurosci* **20,** 8096–8102 (2000).

134. Save, E., Paz-Villagrán, V., Alexinsky, T. & Poucet, B. Functional interaction between the associative parietal cortex and hippocampal place cell firing in the rat. *Eur J Neurosci* **21,** 522–30 (2005).

135. Renaudineau, S., Poucet, B. & Save, E. Flexible use of proximal objects and distal cues by hippocampal place cells. *Hippocampus* **17,** 381–395 (2007).

136. Cacucci, F., Wills, T. J., Lever, C., Giese, K. P. & O'Keefe, J. Experience-dependent increase in CA1 place cell spatial information, but not spatial reproducibility, is

dependent on the autophosphorylation of alphaCaMKII. *J. Neurosci.* **27,** 7854–7859 (2007).

137. Renaudineau, S., Poucet, B., Laroche, S., Davis, S. & Save, E. Impaired long-term stability of CA1 place cell representation in mice lacking the transcription factor zif268/egr1. *Proc. Natl. Acad. Sci.* **106,** 11771–11775 (2009).
138. Rochefort, C. *et al.* Cerebellum Shapes Hippocampal Spatial Code. *Science* **334,** 385–389 (2011).
139. Muller, R. U. & Kubie, J. L. The firing of hippocampal place cells predicts the future position of freely moving rats. *J Neurosci* **9,** 4101–10 (1989).
140. Skaggs, W. E., McNaughton, B. L. & Gothard, K. M. An Information-Theoretic Approach to Deciphering the Hippocampal Code. in Hanson, S. J., Cowan, J. D. & Giles, C. L. eds. Morgan Kaufmann, San Mateo, CA; 1993. pp. 1030–1037.
141. Cacucci, F., Yi, M., Wills, T. J., Chapman, P. & O'Keefe, J. Place cell firing correlates with memory deficits and amyloid plaque burden in Tg2576 Alzheimer mouse model. *Proc Natl Acad Sci U A* **105,** 7863–7868 (2008).
142. Nakashiba, T., Young, J. Z., McHugh, T. J., Buhl, D. L. & Tonegawa, S. Transgenic inhibition of synaptic transmission reveals role of CA3 output in hippocampal learning. *Science* **319,** 1260–1264 (2008).
143. Russell, N. A., Horii, A., Smith, P. F., Darlington, C. L. & Bilkey, D. K. Long-Term Effects of Permanent Vestibular Lesions on Hippocampal Spatial Firing. *J. Neurosci.* **23,** 6490–6498 (2003).
144. Markus, E. J., Barnes, C. A., McNaughton, B. L., Gladden, V. L. & Skaggs, W. E. Spatial information content and reliability of hippocampal CA1 neurons: effects of visual input. *Hippocampus* **4,** 410–421 (1994).

145. Kentros, C. G., Agnihotri, N. T., Streater, S., Hawkins, R. D. & Kandel, E. R. Increased attention to spatial context increases both place field stability and spatial memory. *Neuron* **42,** 283–95 (2004).

146. Muzzio, I. A. *et al.* Attention Enhances the Retrieval and Stability of Visuospatial and Olfactory Representations in the Dorsal Hippocampus. *PLoS Biol* **7,** e1000140 (2009).

147. Fenton, A. A. *et al.* Attention-like modulation of hippocampus place cell discharge. *J Neurosci* **30,** 4613–4625 (2010).

148. Hok, V., Chah, E., Save, E. & Poucet, B. Prefrontal cortex focally modulates hippocampal place cell firing patterns. *J Neurosci* **33,** 3443–3451 (2013).

149. Muir, G. M. & Taube, J. S. The Neural Correlates of Navigation: Do Head Direction and Place Cells Guide Spatial Behavior? *Behav. Cogn. Neurosci. Rev.* **1,** 297–317 (2002).

150. Mizumori, S. J. Y., Miya, D. Y. & Ward, K. E. Reversible inactivation of the lateral dorsal thalamus disrupts hippocampal place representation and impairs spatial learning. *Brain Res.* **644,** 168–174 (1994).

151. Leutgeb, S. & Mizumori, S. J. Y. Excitotoxic Septal Lesions Result in Spatial Memory Deficits and Altered Flexibility of Hippocampal Single-Unit Representations. *J. Neurosci.* **19,** 6661–6672 (1999).

152. Cooper, B. G. & Mizumori, S. J. Y. Temporary Inactivation of the Retrosplenial Cortex Causes a Transient Reorganization of Spatial Coding in the Hippocampus. *J. Neurosci.* **21,** 3986–4001 (2001).

153. Nakazawa, K. *et al.* Requirement for hippocampal CA3 NMDA receptors in associative memory recall. *Science* **297,** 211–218 (2002).

154. Nakazawa, K. *et al.* Hippocampal CA3 NMDA Receptors Are Crucial for Memory Acquisition of One-Time Experience. *Neuron* **38,** 305–315 (2003).

155. Davis, S. *et al.* The Formation and Stability of Recognition Memory: What Happens Upon Recall? *Front. Behav. Neurosci.* **4,** (2010).

156. Zhao, R., Fowler, S. W., Chiang, A. C. A., Ji, D. & Jankowsky, J. L. Impairments in experience-dependent scaling and stability of hippocampal place fields limit spatial learning in a mouse model of Alzheimer's disease. *Hippocampus* **24,** 963–978 (2014).

157. Mizumori, S. J., Lavoie, A. M. & Kalyani, A. Redistribution of spatial representation in the hippocampus of aged rats performing a spatial memory task. *Behav Neurosci* **110,** 1006–1016 (1996).

158. Wilson, I. A. *et al.* Place cell rigidity correlates with impaired spatial learning in aged rats. *Neurobiol Aging* **24,** 297–305 (2003).

159. Hok, V., Chah, E., Reilly, R. B. & O'Mara, S. M. Hippocampal dynamics predict interindividual cognitive differences in rats. *J Neurosci* **32,** 3540–3551 (2012).

160. Thompson, L. T. & Best, P. J. Long-term stability of the place-field activity of single units recorded from the dorsal hippocampus of freely behaving rats. *Brain Res.* **509,** 299–308 (1990).

161. Barnes, C. A., Suster, M. S., Shen, J. & McNaughton, B. L. Multistability of cognitive maps in the hippocampus of old rats. *Nature* **388,** 272–275 (1997).

162. Yan, J., Zhang, Y., Roder, J. & McDonald, R. J. Aging effects on spatial tuning of hippocampal place cells in mice. *Exp Brain Res* **150,** 184–193 (2003).

163. Ziv, Y. *et al.* Long-term dynamics of CA1 hippocampal place codes. *Nat. Neurosci.* **16,** 264–266 (2013).

164. Rubin, A., Geva, N., Sheintuch, L. & Ziv, Y. Hippocampal ensemble dynamics timestamp events in long-term memory. *eLife* **4,** (2015).

165. Zinyuk, L., v S Kubik, Kaminsky, Y., Fenton, A. A. & s, J. B. Understanding hippocampal activity by using purposeful behavior: place navigation induces place cell

discharge in both task-relevant and task-irrelevant spatial reference frames. *Proc Natl Acad Sci U A* **97,** 3771–6 (2000).

166. Fenton, A. A. & Muller, R. U. Place cell discharge is extremely variable during individual passes of the rat through the firing field. *Proc Natl Acad Sci U A* **95,** 3182–7 (1998).
167. Cho, Y. H., Giese, K. P., Tanila, H., Silva, A. J. & Eichenbaum, H. Abnormal hippocampal spatial representations in alphaCaMKIIT286A and CREBalphaDelta- mice. *Science* **279,** 867–869 (1998).
168. Kulvicius, T., Tamosiunaite, M., Ainge, J., Dudchenko, P. & Wörgötter, F. Odor supported place cell model and goal navigation in rodents. *J. Comput. Neurosci.* **25,** 481–500 (2008).
169. MacDonald, C. J., Carrow, S., Place, R. & Eichenbaum, H. Distinct Hippocampal Time Cell Sequences Represent Odor Memories in Immobilized Rats. *J. Neurosci.* **33,** 14607–14616 (2013).
170. Quirk, G. J., Muller, R. U. & Kubie, J. L. The firing of hippocampal place cells in the dark depends on the rat's recent experience. *J. Neurosci.* **10,** 2008–2017 (1990).
171. Schultz, E. F. & Tapp, J. T. Olfactory control of behavior in rodents. *Psychol. Bull.* **79,** 21–44 (1973).
172. Prusky, G. T., West, P. W. R. & Douglas, R. M. Behavioral assessment of visual acuity in mice and rats. *Vision Res.* **40,** 2201–2209 (2000).
173. Tanila, H. Wading pools, fading memories—place navigation in transgenic mouse models of Alzheimer's disease. *Front. Aging Neurosci.* **4,** 11 (2012).
174. Hamilton, D. A., Akers, K. G., Weisend, M. P. & Sutherland, R. J. How do room and apparatus cues control navigation in the Morris water task? Evidence for distinct

contributions to a movement vector. *J. Exp. Psychol. Anim. Behav. Process.* **33,** 100–114 (2007).

175. Hamilton, D. A. *et al.* The relative influence of place and direction in the Morris water task. *J. Exp. Psychol. Anim. Behav. Process.* **34,** 31–53 (2008).
176. Gallagher, M. & Pelleymounter, M. A. Spatial learning deficits in old rats: A model for memory decline in the aged. *Neurobiol. Aging* **9,** 549–556 (1988).
177. Whishaw, I. Q., Metz, G. A. S., Kolb, B. & Pellis, S. M. Accelerated nervous system development contributes to behavioral efficiency in the laboratory mouse: A behavioral review and theoretical proposal. *Dev. Psychobiol.* **39,** 151–170 (2001).
178. Clark, B. *et al.* Lesions of the dorsal tegmental nuclei disrupt control of navigation by distal landmarks in cued, directional, and place variants of the Morris water task. *Behav. Neurosci.* **127,** 566–581 (2013).
179. Calton, J. L. *et al.* Hippocampal place cell instability after lesions of the head direction cell network. *J. Neurosci. Off. J. Soc. Neurosci.* **23,** 9719–9731 (2003).
180. Yoder, R. M. & Taube, J. S. Head direction cell activity in mice: robust directional signal depends on intact otolith organs. *J. Neurosci. Off. J. Soc. Neurosci.* **29,** 1061–1076 (2009).
181. Schenk, F. Comparison of spatial learning in woodmice (Apodemus sylvaticus) and hooded rats (Rattus norvegicus). *J. Comp. Psychol.* **101,** 150–158 (1987).
182. Lipp, H.-P. & Wolfer, D. P. Genetically modified mice and cognition. *Curr. Opin. Neurobiol.* **8,** 272–280 (1998).
183. Wolfer, D. P. & Lipp, H.-P. Dissecting the Behaviour of Transgenic Mice: Is it the Mutation, the Genetic Background, or the Environment? *Exp. Physiol.* **85,** 627–634 (2000).

184. Cressant, A., Besson, M., Suarez, S., Cormier, A. & Granon, S. Spatial learning in Long-Evans Hooded rats and C57BL/6J mice: Different strategies for different performance. *Behav. Brain Res.* **177,** 22–29 (2007).

185. Suarez, S. D. & Gallup Jr., G. G. An ethological analysis of open-field behavior in rats and mice. *Learn. Motiv.* **12,** 342–363 (1981).

186. Crusio, W. E. & van Abeelen, J. H. The genetic architecture of behavioural responses to novelty in mice. *Heredity* **56 (Pt 1),** 55–63 (1986).

187. Tchernichovski, O., Benjamini, Y. & Golani, I. The dynamics of long-term exploration in the rat. Part I. A phase-plane analysis of the relationship between location and velocity. *Biol. Cybern.* **78,** 423–432 (1998).

188. Welker, W. I. 'free' versus 'forced' exploration of a novel situation by rats. *Psychol. Rep.* **3,** 95–108 (1957).

189. Augustsson, H. & Meyerson, B. J. Exploration and risk assessment: a comparative study of male house mice (Mus musculus musculus) and two laboratory strains. *Physiol. Behav.* **81,** 685–698 (2004).

190. Wells, C. E., Krikke, B., Saunders, J., Whittington, A. & Lever, C. Changes to open field surfaces typically used to elicit hippocampal remapping elicit graded exploratory responses. *Behav Brain Res* **197,** 234–238 (2009).

191. Hussaini, S. A., Kempadoo, K. A., Thuault, S. J., Siegelbaum, S. A. & Kandel, E. R. Increased Size and Stability of CA1 and CA3 Place Fields in HCN1 Knockout Mice. *Neuron* **72,** 643–653 (2011).

192. Bittner, K. C. *et al.* Conjunctive input processing drives feature selectivity in hippocampal CA1 neurons. *Nat. Neurosci.* **18,** 1133–1142 (2015).

193. Upchurch, M. & Wehner, J. M. Differences between inbred strains of mice in Morris water maze performance. *Behav. Genet.* **18,** 55–68 (1988).

194. Roullet, P. & Lassalle, J. M. Genetic variation, hippocampal mossy fibres distribution, novelty reactions and spatial representation in mice. *Behav. Brain Res.* **41,** 61–70 (1990).

195. Bertholet, J.-Y. & Crusio, W. E. Spatial and non-spatial spontaneous alternation and hippocampal mossy fibre distribution in nine inbred mouse strains. *Behav. Brain Res.* **43,** 197–202 (1991).

196. Crabbe, J. C., Wahlsten, D. & Dudek, B. C. Genetics of Mouse Behavior: Interactions with Laboratory Environment. *Science* **284,** 1670–1672 (1999).

197. Freund, J. *et al.* Emergence of Individuality in Genetically Identical Mice. *Science* **340,** 756–759 (2013).

Figure captions

[Please insert any figure captions here]

Tables

[Please insert any tables here]

Further Reading/Resources

[Please insert any further reading/resources here]

Related WIREs Articles

DOI	Article title
10.1002/wcs.1164	Hippocampus
10.1002/wcs.1171	Development of spatial cognition
10.1002/wcs.1198	Psychology of spatial cognition
10.1002/wcs.1272	Parallel and convergent processing in grid cell, head-direction cell, boundary cell, and place cell networks

Hippocampal place fields. Spatial navigation in rats and mice relies on the activity of hippocampal place cells. Place fields in the two species, however, differ in subtle ways that may reflect different navigation strategies. ┼

216x382mm (96 x 96 DPI)