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Progression and stop organization reveals conservation of movement organization during dark exploration across rats and mice

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ABSTRACT

Spatial orientation is a ubiquitous feature of animal behavior. Environmental and self-movement cues are sources of information used to maintain spatial orientation. The literature has typically focused on differences between mice and rats using environmental cues to guide movement. The current study uses the organization of exploratory behavior under dark conditions to investigate species differences in self-movement cue processing. Mouse and rat exploratory behavior was recorded under dark conditions on a circular table without walls. The resulting movements were segmented in progressions (movement ≥ 3 cm/s) and stops (movement < 3 cm/s). Mice exhibited longer travel distances, faster progression peak speeds, and weaker tendency to scale progression peak speeds to Euclidean distances relative to rats. In contrast, similar levels of performance were observed on measures (progression path circuity, change in heading, stability of stopping behavior) sensitive to vestibular pathology. These results are consistent with species differences in a variety of performance variables; however, self-movement cue based spatial orientation did not differentiate between mice and rats. This work establishes a translational foundation for future work investigating the neurobiology of self-movement cue processing using species-unique neuroscience techniques.

1. Introduction

Most species rely on both environmental (i.e., visual, olfactory, auditory) and self-movement (i.e., vestibular, proprioceptive, optic flow) cues for navigation. Nevertheless, navigational performance on analogous tasks sometimes differs between species, even though these species evolved to thrive in similar environments. For example, both rats and mice are able to navigate accurately within visual and non-visual environments; however, in the Morris Water Task (MWT) rats acquire place responding faster than mice (Stackman et al., 2012; Frick et al., 2000). One explanation is that performance deficits in mice resulted from their impaired visual acuity, relative to that of rats (Prusky et al., 2000), although these species appear to perform similarly on land-based tasks (Whishaw and Tomie, 1996), suggesting other mechanisms may underlie species differences in navigational performance. A second possibility is differences in self-movement cue processing between species, given that navigation and the underlying neural signals typically depend on both environmental and self-movement cues (Biegler and Morris, 1996, Stackman et al., 2012; Harvey et al., 2018; Yoder and Taube, 2009; Yoder et al., 2015; for reviews, see Yoder et al., 2011; Yoder and Taube, 2014). Therefore, additional work is necessary to examine whether mice and rats differ in self-movement cue processing and if so, how this difference contributes to the organization of exploratory behavior.

In both visual and non-visual environments, rats and mice organize their exploratory movements into a sequence of progressions and stops (Wallace et al., 2006b; Blankenship et al., 2017; Donaldson et al., 2018, for review, see Thompson et al., 2018). Progressions are relatively fast (≥3.0 cm/s) non-circuitous trajectories of varying length, whereas stops are relatively slow (< 3.0 cm/s) segments of the path that are commonly associated with large changes in heading. Rodent species also appear to establish a "home base" relatively early during exploration, which may serve to reset their sense of location or orientation during extended exploration trials (Eilam and Golani, 1989; Tchernichovski and Golani, 1995; Zadicario et al., 2005; Avni et al., 2006). When environmental cues are available, they can assist in anchoring home base position (Hines and Whishaw, 2005); however, recent studies suggest that in the absence of environmental cues, self-

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movement cues are sufficient for home base establishment, although any impairment to this system (e.g., vestibular dysfunction) can disrupt exploratory behavior. For example, mice with dysfunctional otolith organs, a system associated with self-movement cue processing, exhibited more circuitous progressions, larger changes in heading during stops, and less stable home base positions in darkness, relative to control mice (Blankenship et al., 2017). Similar disruptions in exploratory movement organization have also been observed in a mouse model of Usher syndrome, a disease marked by impaired vestibular function (Donaldson et al., 2018). These observations demonstrate that self-movement cues facilitate accurate home base establishment and movement organization during exploration, even in the absence of salient environmental cues.

An understanding of the neural mechanisms underlying spatial cognition is based on numerous studies involving mice and rats. Many studies in mice rely on genetic models, whereas many studies in rats have used brain lesions and electrophysiology, to investigate the brain mechanisms and sensory signals involved in spatial orientation. As such, it is often assumed that both species have similar abilities in self-movement cue processing and overall cognitive abilities; however, no study has directly compared the organization and kinematics of mouse and rat exploratory movements under dark conditions (i.e., no access to salient visual cues). To this end, the current study applies sequential path and stop cluster analyses to mouse and rat movements under dark conditions. These results may provide a foundation to explain the species differences observed in navigational tasks.

2. Methods

2.1. Subjects

Female C57BL/6 J (n = 7; age 3–6 mo. at the start of the study) were obtained from the breeding colony established at Indiana University-Purdue University Fort Wayne (IPFW). Mice were pair housed in standard shoebox cages with a 12-hour light/dark cycle. Behavioral testing occurred during the light phase. Mice were provided ad libitum access to food and water prior to and during the experiment. The Purdue Animal Care and Use Committee approved all procedures.

Female (n = 6) Long Evans rats approximately 90 days of age were obtained from the breeding colony established at Northern Illinois University (NIU). Rats were pair housed in standard shoebox cages with 12 h dark/light cycles, and all testing was conducted during the light phase. Rats had ad libitum access to food and water prior to and during the experiment. The Institutional Animal Care and Use Committee at Northern Illinois University approved all procedures.

Several factors influenced the selection of female rodents to utilize as subjects in the current study. First, studies on the neurobiology of spatial orientation typically include male rodents, and this study will establish a foundation to future sex difference studies. Next, previous work has failed to observe sex differences in self-movement cue processing using the food hoarding paradigm (Köppen et al., 2015).

2.2. Apparatus

The exploration apparatus was similar for both species of rodents, with the exception that mouse exploration was conducted on the campus of IPFW and rat exploration was conducted on the campus of NIU. The possibility that the site of testing may have influenced performance in one or both species cannot be ignored; however, there is no evidence of any systematic effects of either location, and other studies (in either species) suggest no systematic differences between labs. Exploratory arenas were circular (112 cm diameter) wooden tables painted white and positioned 34.5 cm above the floor. Attached to the edge of the table was a clear plastic tab (20 cm wide and 15 cm high). The position of the tab, relative to the room, varied systematically across mice and rats. The table was located in a lightproof room with infrared emitters to illuminate the room under completely dark conditions. Attached to the ceiling was a color/infrared camera that recorded behavior at 30 frames per second. The resulting videos were saved for offline analysis.

2.3. Procedures

Mice and rats were individually transported to the testing room in an opaque container. Prior to entering the testing room, rodents were carried in a random circuitous paths, thereby attenuating the ability to continuously update their current position relative to the colony room. Upon entering the testing room, the researcher gently placed the rodent on the center of the table. The mouse or rat explored the table for 40 min. At the end of the session, the researcher removed the rodent from the table and engaged in a similarly circuitous path as they transported to it to the animal colony. Prior to running the next rodent, the surface of the table was cleaned with an alcohol (mice) or ammonia (rats) based solution, dried with paper towels, and rotated a varying amount of degrees to disperse any remaining odorants and to move the tab to a new position. All exploratory sessions occurred under completely dark conditions.

2.4. Behavioral analysis

Previous work has shown that rodents typically engage in grooming behavior within two minutes after being placed on the exploratory table (Blankenship et al., 2017; Donaldson et al., 2018) and this behavior is associated with home base establishment (Eilam and Golani, 1989). It is important to note that one report suggested that mice do not establish home bases as reliably as rats when exploring a novel environment (unpublished data described in (Gorny et al., 2002)) In contrast, mice in the present task, as well as mice in our recent study (Blankenship et al., 2017), showed robust home base establishment early in exploration. The goal was to compare the organization of mouse and rat exploratory behavior subsequent to home base establishment. Therefore sampling of exploratory behavior began three minutes after the rodent was placed on the table. Previous work has shown that rat open field movement significantly decreases 20 min after home base establishment, therefore a 20 min subset of a rodent's 40 min exploration session was captured for behavioral analysis. The 20 min were separated into four consecutive 5-minute samples. Ethovision 3.0 (Noldus, NL) was used to digitize the position of the rodent during the four samples. Behavior during each sample was segmented into progressions and stops. As with previous studies, progressions were defined as movement that was greater than or equal to 3.0 cm/s for two or more frames. Stops were defined as any movement that was less than 3.0 cm/s for two or more frames.

Several measures of exploratory behavior were used to describe mouse and rat levels of activity. The total distance traveled was calculated for each sample. It is possible that differences in body size may influence the travel distance. To examine this possibility, the number of body lengths were calculated by dividing each rodent's travel distance by either the average mouse (8.6 cm) or rat (21 cm) body length (Chakraborty et al., 2017; Clemens et al., 2014). Finally, the total amount of time spent stopping was recorded for each rodent.

2.4.1. Progression analysis

Several measures were developed to characterize the organization of behavior during progressions. First, the total number of progressions and total distance during progressions were recorded for each sample. Next, both the distance traveled and the Euclidean distance was calculated for all progressions. Both of these measures were used to quantify the topographical complexity of a progression or path circuity. Progression path circuity was calculated by dividing the Euclidean distance of a progression by the distance traveled on the progression. Path circuity values range from 0.0 to 1.0, with progressions becoming

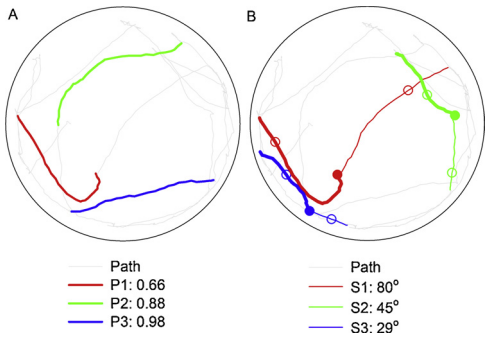

Fig. 1. Movement topography is plotted for a five minute sample of exploratory behavior (grey line). Three progressions are highlighted to illustrate variance in path circuity (panel A). Three progression-stop-progression sequences are plotted for the same five minute session (panel B). The first progression in a sequence is indicated by a heavy weight line. Progression peak speed (open circles) and stop location (filled circles) are plotted for each sequence. Note that change in heading from following a straight path varies across the three sequences.

more direct as values approach 1.0 (see panel A of Fig. 1). Previous work with rats (Wallace et al., 2006b) and mice (Blankenship et al., 2017) has demonstrated that progressions are typically non-circuitous paths through the environment, independent of access to visual cues. Finally, peak speed and movement scaling were used to assess kinematic characteristics of movement during progressions. Movement scaling involved calculating the correlation between a rodent's set of peak speeds and Euclidean distances for a five-minute sample. Previous work has demonstrated that rats consistently scale progression peak speeds to progression Euclidean distances independent of access to environmental cues (Wallace et al., 2006b).

2.4.2. Stop analysis

Previous work has suggested that hyperactivity may be attributed to decreased stop duration (Whishaw et al., 1994), and therefore several measures were developed to characterize behavior during stops. First, the total number of stops was recorded for each sample. Next, the total stop time and average stop duration were calculated for each sample. Finally, most of a rodent's change in heading along a path occurs during periods of slower movement or stops (Wallace et al., 2006b; Blankenship et al., 2017; Wallace, 2017; Donaldson et al., 2018). This change in heading was quantified by calculating the supplementary angle subtended by the following points: the preceding progression peak speed location, average stop location, and subsequent progression peak speed location (see panel B of Fig. 1). Change in heading ranged from 0 (continuing in a straight path) to 180 (complete path reversal). A rodent's resulting set of change in headings was averaged for each sample.

2.4.3. Stop clustering analysis

Location of home base establishment has been inferred from the distribution of stopping behavior within the environment (Eilam and Golani, 1989; Golani et al., 1993; Clark et al., 2005; Avni et al., 2006; Blankenship et al., 2017; Donaldson et al., 2018). Cartesian coordinates associated with each stop were converted to polar coordinates with the center of the table serving as the origin. Circular statistics (Batschelet, 1981) were used to characterize within-sample stop clustering and the stability of stop clustering across samples. The duration of each stop was converted into an individual observation at a specific heading (i.e., one second was equal to one observation). First order circular statistics (parameter of concentration and average heading) were calculated from all the stops a rodent made during a sample. The parameter of concentration was used as a measure of within-sample density of stop

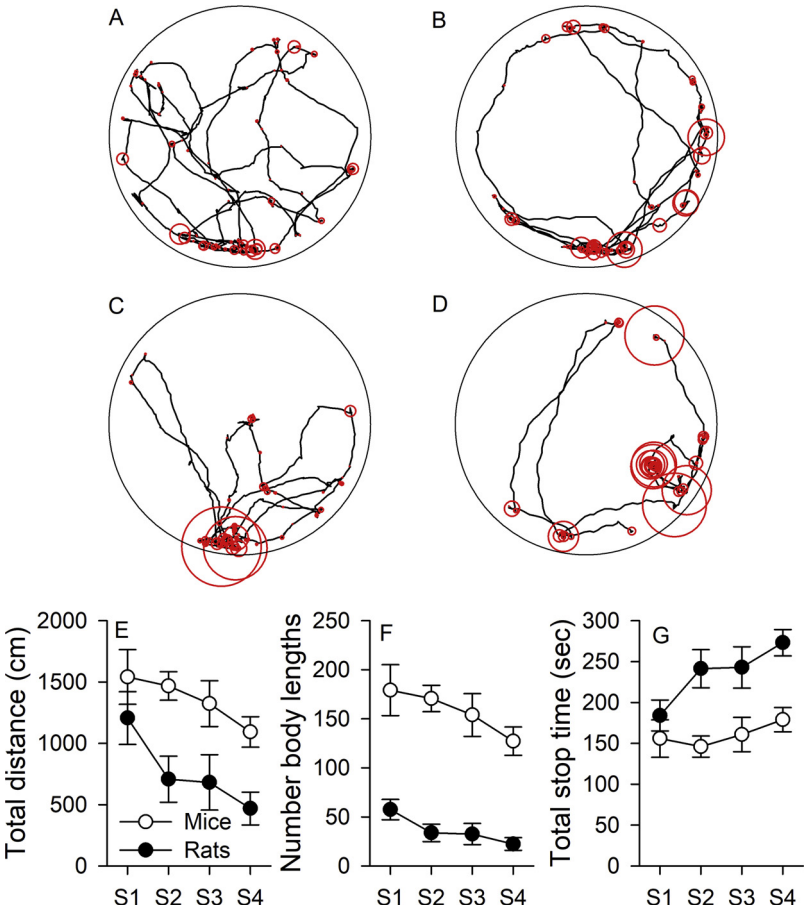

Fig. 2. The first (A and B) and the last (C and D) five minutes of the exploratory session are plotted for a representative mouse (A and C) and rat (B and D). The location of each stop is indicated by the red circle with diameter scaled relative to the duration of the stop. Total distance traveled (E), number of body lengths traveled (F), and total time spent stopping (G) are plotted for both species across the four samples. Error bars represent the standard error of the mean.

clustering. Second order circular statistics were applied to average stop heading from each sample. The resulting parameter of concentration was used as a measure of stability of stop clustering across samples.

2.4.4. Statistical analysis

Repeated measures ANOVAs were used to evaluate the main effects of species, sample, and species by sample interactions, with alpha set at 0.05. Partial eta squared values (η_p^2) were reported for each main effect and interaction as a measure of effect size. Linear trend analysis and Tukey's Honest Significant Difference (HSD) post-hoc tests were used to evaluate significant main effects and interactions. T-tests were used to assess species differences in second order parameter of concentration. Cohen's d was used as a measure of effect size. SPSS 25 (IBM) was used to calculate statistical results.

3. Results

Mice (see panels A and C of Fig. 2) and rats (see panels B and D of Fig. 2) engaged in exploratory behaviors during all four five-minute samples. The ANOVA conducted on total distance traveled during each sample revealed a significant main effect of species and sample; however, the species by sample interaction was not significant (see Table 1). Mice traveled significantly longer distances than rats (see panel E of Fig. 2). In addition, a significant linear trend analysis revealed that both species exhibited a significant reduction in travel distance across samples [$F(1,11) = 30.768$, $p < 0.001$, $\eta_p^2 = 0.737$].

The ANOVA conducted on number of body lengths traveled during each sample revealed a significant effect of species and sample; however, the species by sample interaction was not significant (see Table 1). Mice traveled significantly more body lengths than rats (see panel F of Fig. 2). In addition, a significant linear trend analysis revealed that the number of body lengths traveled decreased across samples for both species [$F(1,11) = 24.439$, $p < 0.001$, $\eta_p^2 = 0.690$].

The ANOVA conducted on total stop time during each sample revealed a significant main effect of species, sample, and species by sample interaction (see Table 1). Mice spent significantly less time stopping relative to rats (see panel G of Fig. 2). In addition, a significant linear trend analysis revealed that both species spent more time stopping across samples [$F(1,11) = 23.449$, $p = 0.001$, $\eta_p^2 = 0.681$]. Finally, species did not differ in total stop time during the first sample; however, mice spent less time stopping relative to rats on the last three samples (HSD, $p < 0.05$).

3.1. Progression analysis

Rats and mice organized their exploratory behavior into a sequence of progressions. The ANOVA conducted on the total number of progressions observed during each sample revealed a significant main effect of species, sample, and species by sample interaction (see Table 2). Mice exhibited significantly more progressions relative to rats (see panel A of Fig. 3). In addition, a significant linear trend analysis revealed that both species exhibited a decrease in the number of progressions observed across samples [$F(1,11) = 8.618$, $p = 0.014$, $\eta_p^2 = 0.439$]. Finally, species did not differ in the total number of progressions on the first sample; however, mice exhibited significantly more progressions relative to rats on the last three samples (HSD, $p < 0.05$).

Table 1
General Behavior ANOVA Statistical results.

Measure	Source	df	F	*P*	η_p^2
Total Distance	Species	1, 11	7.191	=0.021*	0.395
	Sample	3, 33	10.640	< 0.001*	0.492
	Species x Sample	3, 33	1.442	=0.248	0.116
Total body lengths	Species	1, 11	37.451	< 0.001*	0.773
	Sample	3, 33	7.391	= 0.001*	0.402
	Species x Sample	3, 33	0.969	= 0.419	0.081
Total stop time	Species	1, 11	9.985	= 0.009*	0.476
	Sample	3, 33	7.479	= 0.001*	0.405
	Species x Sample	3, 33	3.520	= 0.026*	0.242

* indicates significant result.

Table 2
Progression ANOVA Statistical results.

Measure	Source	df	F	*P*	η_p^2
Total progressions	Species	1, 11	18.666	= 0.001*	0.629
	Sample	3, 33	3.414	= 0.029*	0.237
	Species × Sample	3, 33	4.880	=0.006 *	0.307
Progression distance	Species	1, 11	0.091	=0.769	0.008
	Sample	3, 33	4.619	= 0.008*	0.296
	Species × Sample	3, 33	0.013	= 0.998	0.001
Progression Euclidean distance	Species	1, 11	0.134	=0.721	0.012
	Sample	3, 33	4.151	= 0.013*	0.274
	Species × Sample	3, 33	0.088	=0.966	0.008
Progression path circuity	Species	1, 11	0.169	=0.689	0.015
	Sample	3, 33	1.964	=0.141	0.150
	Species × Sample	3, 33	1.190	=0.329	0.098
Progression peak speed	Species	1, 11	10.320	= 0.008*	0.484
	Sample	3, 33	4.503	= 0.009*	0.290
	Species × Sample	3, 33	0.325	=0.808	0.029
Progression movement scaling	Species	1, 11	39.545	< 0.001*	0.782
	Sample	3, 33	0.540	=0.659	0.047
	Species × Sample	3, 33	1.727	=0.180	0.136

* indicates significant result.

Several measures were used to quantify the topographical organization of progressions (see panels B, C, and D of Fig. 3). First, the ANOVA conducted on average progression distance revealed a significant main effect of sample; however, neither the main effect of species, nor the species by sample interaction were significant (see Table 2). The linear trend analysis revealed that both species exhibited a significant decrease in average progression distance across samples [$F(1,11) = 10.840$, $p = 0.007$, $\eta_p^2 = 0.496$]. Next, the ANOVA conducted on average progression Euclidean distance revealed a significant main effect of sample; however, neither the main effect of species, nor the species by sample interaction were significant (see Table 2). The linear trend analysis revealed that both species exhibited a significant decrease in average progression Euclidean distance across samples [$F(1,11) = 11.049$, $p = 0.007$, $\eta_p^2 = 0.501$]. Finally, the ANOVA conducted on average progression path circuity failed to reveal a significant main effect of species, sample, or species by sample interaction (see Table 2). Rodents followed non-circuitous progressions across all samples.

Two measures were used to quantify species differences in the kinematic organization of progressions (see panels E and F of Fig. 3). First, the ANOVA conducted on average progression peak speed revealed a significant main effect of species and sample; however the species by sample interaction was not significant (see Table 2). Mice exhibited significantly faster progression peak speeds, relative to rats. A linear trend analysis revealed that both species peak speeds decreased across samples [$F(1,11) = 17.307$, $p = 0.002$, $\eta_p^2 = 0.611$]. Next, The ANOVA conducted on progression movement scaling revealed a significant main effect of species; however, neither the main effect sample, nor species by sample interaction were significant (see Table 2). Rats exhibited significantly stronger movement scaling, relative to mice.

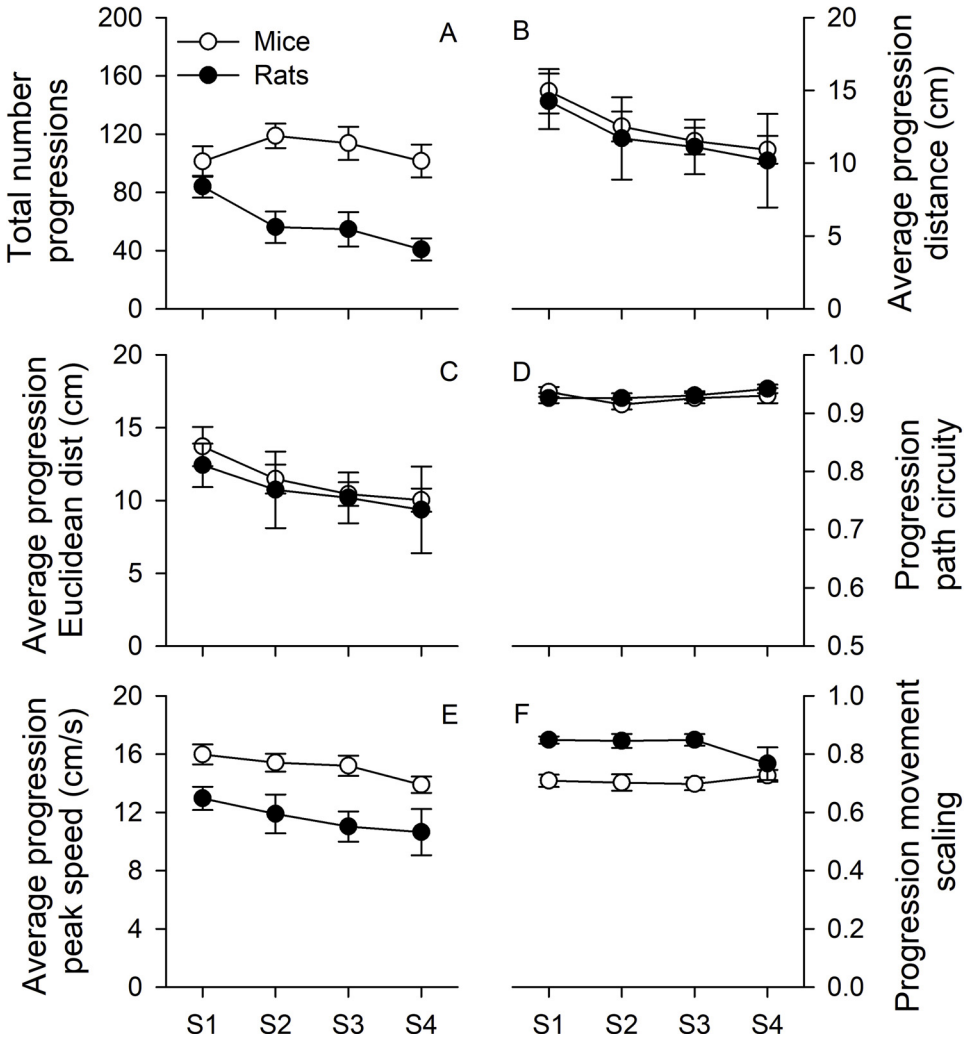

Fig. 3. Average total number of progressions are plotted for both species (A). Measures of progression topography (B, C, and D) and kinematics (E and F) are plotted for both species. Error bars represent the standard error of the mean.

3.2. Stop analysis

Several measures were used to quantify behavior during stops (see Fig. 4). First, the ANOVA conducted on total number of stops revealed a significant main effect of species and species by sample interaction; however, the main effect of sample was not significant (see Table 3). Mice made significantly more stops than rats; however, this observation was specific to the last three samples (HSD, $p < 0.05$). Next, the ANOVA conducted on average stop duration revealed a significant main effect of species; however, neither the main effect of sample, nor the species by sample interaction were significant (see Table 3). Rats exhibited significantly longer average stop durations, relative to mice. Finally, the ANOVA conducted on the average change in heading failed to reveal a significant main effect of species, sample, or species by sample interaction (see Table 3). Rats and mice were similar in their average change in heading observed across samples.

3.3. Stop clustering

Mice (see panels A and C of Fig. 5) and rats (see panels B and D of Fig. 5) clustered their stops with similar levels of concentration across samples. The ANOVA conducted on the first order parameter of concentration failed to reveal a significant main effect of species, sample, or species by sample interaction (see Table 3). Although not significant, mice (M: 0.507; CI: 0.318 to 0.696) and rats (M: 0.770 CI: 0.566 to 0.974) exhibited a similar tendency to cluster their stopping behavior within samples (see panel E of Fig. 5). Next, an independent samples *t*-test conducted on second order parameter of concentration failed to reveal a significant difference between species [$T(11) = 0.945$, $p = 0.365$, $d = 0.5411$]. Mouse and rat stop clustering was highly consistent between samples (see panel F of Fig 5).

4. Discussion

The current study investigated the organization of exploratory movements in mice and rats under dark conditions. Several differences in movement organization were observed between species. First, mice exhibited longer travel distances relative to rats. This increase in distance was related to an increase in total number of progressions, but not average progression length. Next, mice spent less time stopping relative to rats. This difference was mediated by mice exhibiting a larger number of stops that were shorter in duration. Finally, mice exhibited faster progression peak speeds relative to rats. Despite mice reaching high peak speeds, they exhibited weaker movement scaling on progression relative to rats. In contrast, no differences were observed in progression path circuity, change in heading, within sample stop clustering, and among sample stop clustering. This pattern of results is consistent with species exhibiting differences in general levels of activity, while self-movement cue processing is highly conserved between species.

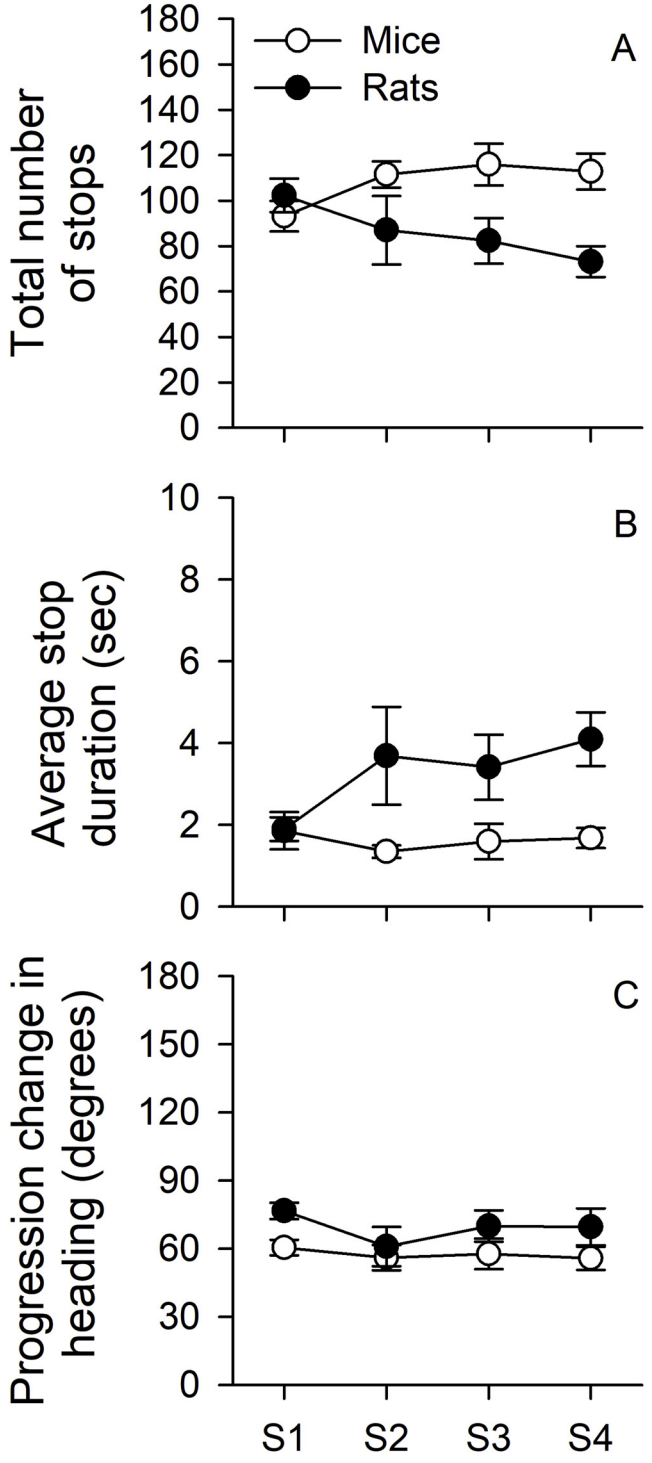

Fig. 4. Average total number of stops (A), stop duration (B), and change in heading (C) are plotted for both species across the four, five-minute samples. Error bars represent the standard error of the mean.

Table 3
Stop ANOVA Statistical results.

Measure	Source	df	F	*p*	η_p^2
Total stops	Species	1, 11	5.244	= 0.043*	0.323
	Sample	3, 33	0.408	=0.748	0.036
	Species × Sample	3, 33	5.624	=0.003*	0.338
Stop duration	Species	1, 11	9.170	=0.011*	0.455
	Sample	3, 33	1.365	=0.271	0.110
	Species × Sample	3, 33	2.386	=0.087	0.178
Change in heading	Species	1, 11	3.444	= 0.090	0.238
	Sample	3, 33	1.455	=0.245	0.117
	Species × Sample	3, 33	0.502	=0.684	0.044
Parameter of concentration	Species	1, 11	4.335	=0.061	0.283
	Sample	3, 33	1.649	=0.197	0.130
	Species × Sample	3, 33	1.591	=0.210	0.126

* indicates significant result.

4.1. Topographical organization of exploratory behavior

Organization of rodent exploratory behavior depends on maintaining spatial orientation. The home base anchors movements by providing an origin for estimates of direction and distance. While moving through an environment, multiple sources of information can be used to update a representation of direction and distance to the home base. Self-movement cues provide an important source of information to guide movement when environmental cues are either not available or unfamiliar (Gallistel, 1990). However, self-movement cue processing is prone to the accumulation of errors (Barlow, 1964). Restricting access to familiar landmarks compounds this accumulation of errors by attenuating the resetting of these estimates, and the resulting spatial disorientation is associated with spiral movements. For example, early work demonstrated that blindfolded human participants instructed to follow a straight-line exhibit spiral movements while walking, driving a car, or swimming (Schaeffer, 1928). In addition, recent work has observed spiral movements in human participants walking in various environments (forest on an overcast day, desert at night without the moon) without access to salient landmarks (Souman et al., 2009; Yaski et al., 2009; Eilam, 2014). Finally, spiral movements have been associated with impaired direction estimation during an ambulatory dead reckoning task in human participants (Wallace et al., 2006a). Therefore, spiral movements may provide a behavioral index of an animal's current level of spatial orientation.

The vestibular system has been observed to significantly contribute to neural signals of direction (for reviews, see (Yoder et al., 2011; Yoder and Taube, 2014)(. Vestibular pathology has been observed to disrupt the organization of exploratory movements (Avni et al., 2009; Blankenship et al., 2017; Donaldson et al., 2018). For example, mice typically organize exploratory movements under dark conditions into non-circuitous progressions with most of the change in heading occurring during stops. In contrast, *tilted* mice that have dysfunctional otolith organs exhibit more circuitous progressions with larger changes in heading during stops (Blankenship et al., 2017). These changes in exploratory behavior organization are consistent with the mice following more spiral paths, and provide evidence that the impaired self-movement cue processing associated with vestibular pathology is preventing accurate updating of estimated direction to the home base, resulting in spiral movements. Interestingly, when *tilted* mice are provided access to visual cues there is an attenuation of the spiral pattern of movement. This is consistent with a spared ability of the *tilted* mice to use environment cues to update their perceived direction leading back to the home base, even though *tilted* mice have degraded head direction signals (Yoder and Taube, 2009) and are impaired at using visual cues to solve several spatial tasks (Yoder and Kirby, 2014; Yoder et al., 2015). These observations provide support for a strong relationship between self-movement cue processing and spatial orientation in both visual and non-visual environments.

In the current study, mice and rats appear to be equivalent in using self-movement cues to maintain spatial orientation. Both species were observed to follow non-circuitous progressions while exhibiting similar changes in heading during stops. In addition, no differences in stop clustering were observed within (first order) or among (second order) samples. This topographic organization of movement is different from

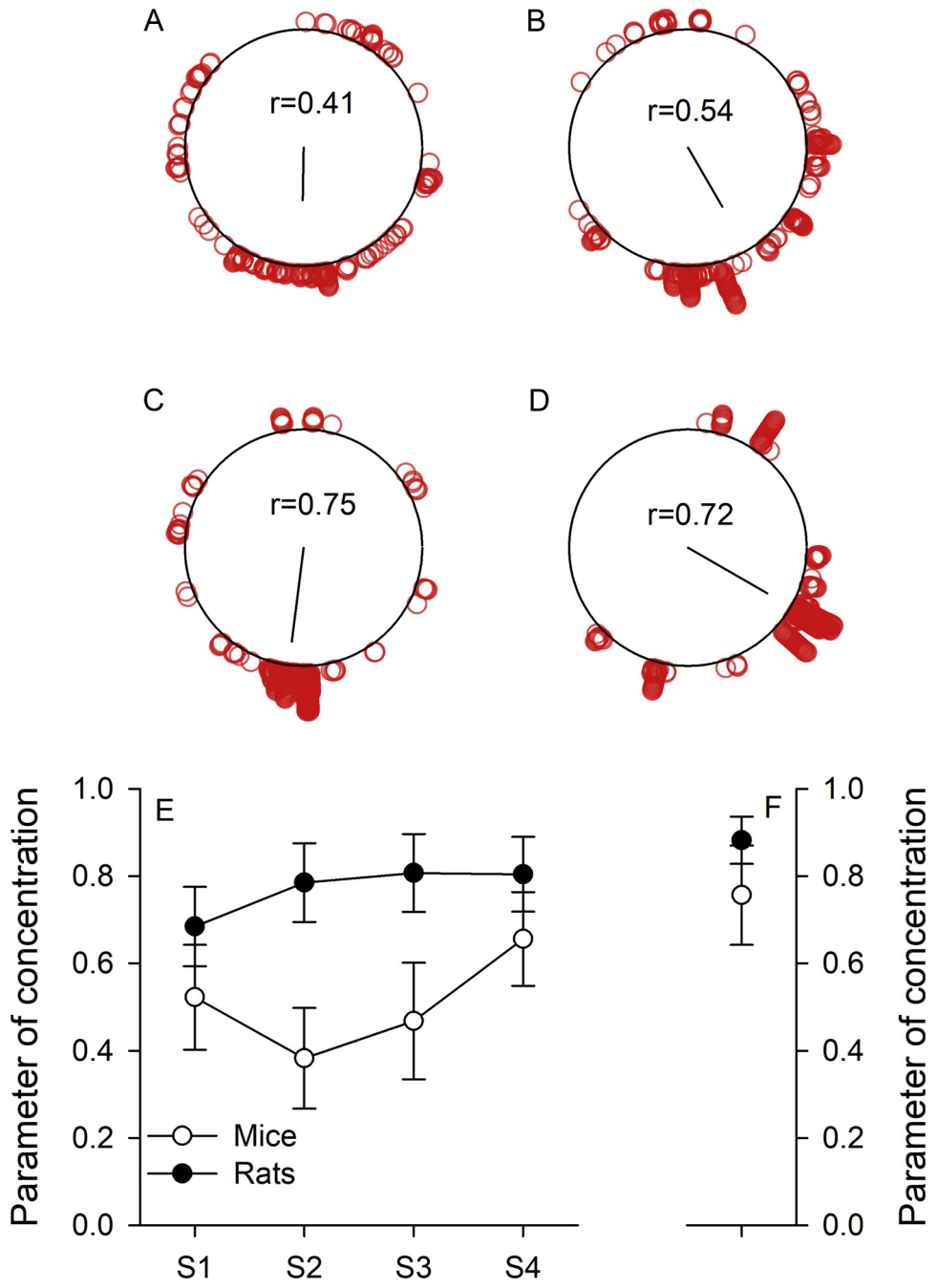

Fig. 5. Stop clustering is plotted for the first (A and B) and the last (C and D) five minutes of the exploratory session from a representative mouse (A and C) and rat (B and D). The length and direction of line in each polar plot represents concentration and direction of stop clustering for a five-minute sample, respectively. The first order parameter of concentration (i.e., within sample magnitude of stop clustering) is plotted for both species (E). The second order parameter of concentration (i.e., between sample consistency of stop clustering) is plotted for both species (F). Error bars represent the standard error of the mean.

the more spiral movements associated with vestibular pathology. The absence of spiral movements is consistent with the interpretation that both species use self-movement cues to update the representation of their current position relative to a home base.

The structural characteristics of the environment may have also influenced the organization of rodent exploratory behavior observed in the current study. For example, rats exploring circular arenas under dark conditions exhibit more spiral movements relative to exploring square arenas of equivalent size (Yaski et al., 2011). It should be noted these differences are also observed on paths that cross the center of the arena. In addition, the symmetry of object placed in the environment influences the organization of exploratory behavior (Weiss et al., 2012). It remains to be determined whether these environmental effects are sufficient to influence spatial orientation. Therefore, the similarity in mouse and rat exploration observed in the current study may not generalize to other more complex environments. Further work is needed to examine the extent that both species exhibit a similar sensitivity to changes in structural characteristics of the environment.

These observations demonstrate a role for self-movement cues and the structure of the environmental to influence the organization of exploratory behavior. A lesion-based approach may determine whether each source of information is influencing a common or parallel processes related to spatial orientation. For example, damage localized to neural systems involved in processing self-movement cues may result in

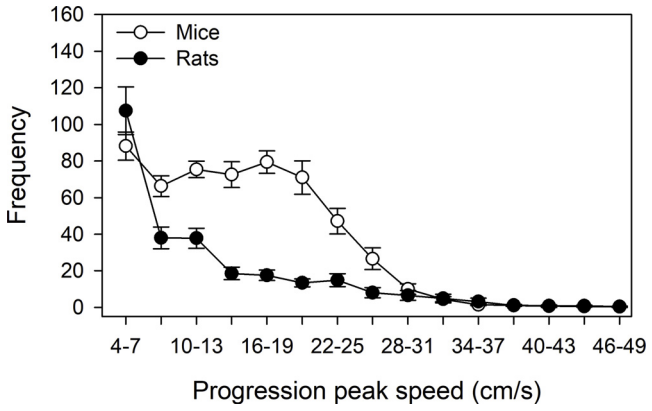

Fig. 6. Distribution of progression peak speeds is plotted for both species across the four, five-minute samples. Error bars represent the standard error of the mean.

spiral movements; however, the structure of the environment continues to influence the organization of exploration. This outcome would be consistent with separate processing of both sources of information. Further work in this area is needed to understand how these sources of information contribute to maintaining spatial orientation.

4.2. Kinematic organization of exploratory behavior

Most of the species differences are revealed by the movement kinematics observed during progressions. Previous work examining the distribution of progression peak speeds has suggested that rodents travel in three different gears (Drai et al., 2000; Drai and Golani, 2001; Drai et al., 2001). The first gear reflects stopping or lingering in a restricted spatial location. The second and third gears are associated with slow and relatively faster modes of travel throughout the environment, respectively. Application of a gear analysis to progression peak speeds depends on capturing movement at 10 Hz or higher (Drai and Golani, 2001). Although the exploratory behavior in the current study was captured at 5 Hz, our investigation revealed that mice and rats exhibit different distributions of progression peak speeds (see Fig. 6). Specifically, mice exhibited a broader distribution of peak speeds, relative to the narrower distribution observed in rats. This broad distribution may result from the availability of a greater range of possible speeds from which to choose, given that mice are capable of much greater running speeds than rats (13 km/h for mice vs. 9.7 km/h for rats; (Garland, 1983)). However, no evidence is currently available to support a relation between an animal's maximum speed and the observed distribution of peak speeds within a fixed arena (but see discussion of arena size, below).

The relation between peak speed and distance traveled (movement scaling) is an important characteristic of planned movements across several species. Rats appear to scale their peak speed relative to the Euclidean distance of the progression, where higher peak speeds are associated with longer Euclidean distances (Wallace et al., 2006b). A similar relationship has also been observed in human non-visually guided planar reaching (Gordon et al., 1994). In both cases, the movement organization has been attributed to the use of a prospective code for estimated distance to be moved. Although mice and rats exhibited a strong correlation between progression peak speed and Euclidean distance, the relationship is significantly weaker in mice. There are at least two explanations for these differences between mice and rats. First, morphological differences in body size may produce varied patterns of locomotion, particularly if the environmental boundaries prevent animals from reaching maximum running speed. Indeed, the upper limit of peak speeds observed here is considerably lower than the maximum running speed reported previously for both mice and rats (Garland, 1983). Therefore, the relatively short distance between start and stop locations could have limited our ability to accurately evaluate movement scaling. A larger arena may encourage greater progression distances in mice and rats, given that studies in voles revealed that increases in arena size results in an increase in average progression length (Eilam, 2003; Eilam et al., 2003). A second explanation for reduced movement scaling is that mice may have more error in their prospective code for movement distance, relative to rats. However, our previous studies of rodent navigation suggest mice's prospective coding is similar to that of rats, as indicated by the point of peak speed occurring near the midpoint of a ballistic movement for both species (Yoder et al., 2015; Wallace et al., 2006b). A caveat to this interpretation is that both of these studies involved relatively small arenas, thus limiting our analysis to relatively short excursions. If mice are impaired at prospective distance coding, increases in progression length (in a larger arena) would amplify these errors, resulting in a weaker correlation between progression peak speed and Euclidean distance. Further work is therefore needed to determine the extent that changes in arena size influence the distribution of progression peak speeds in mice and rats, and whether movement scaling is maintained up to the maximum running speed in each species.

4.3. Other factors influencing exploratory behavior

Exploratory behavior characterized in the current task parallels behavior observed in the traditional open field studies. Behavior observed in open field arenas has been extensively used to investigate a range of psychological phenomena, such as anxiety, and it is possible that differences in mouse and rat exploratory behavior reflect variations in anxiety. Specifically, mice may be less anxious than rats, resulting in their greater total distance traveled. If true, then manipulations that reduce anxiety should have a greater effect on rat navigation than mouse navigation. Indeed, administration of benzodiazepines has been shown to have differential effects on mouse and rat open field behavior (Prut and Belzung, 2003). An increase in open field locomotion was observed in rats administered benzodiazepines, consistent with the anxiolytic effects of this class of drugs (Christmas and Maxwell, 1970). In contrast, one study found that administration of benzodiazepines to mice had no effect on open field locomotion (Choleris et al., 2001). However, another study found that benzodiazepines decreased open field locomotion (Jakaria et al., 2016). These conflicting results provide evidence that anxiety level is not a parsimonious account of the species differences in exploratory behavior, although the influence of anxiety on other factors, such as mnemonic functions, may alter locomotion characteristics.

Next, between species variation in mnemonic function may have influenced the distance traveled during exploration. Several studies have shown that locomotor activity decreases over time within sessions, between sessions, and across days, in rats and mice in an open field environment (Bronstein et al., 1974; Terry, 1979; Bolivar et al., 2000; Bailey and Crawley, 2009). This reduction of locomotor behavior is thought to result from habituation to the environment. If habituation depends on encoding information experienced while exploring an environment, and if mnemonic systems contribute to habituation differently between species, then disruption of neural systems mediating these mnemonic functions would be expected to have a greater effect on habituation in mice or rats. Several studies have evaluated locomotion after administration of MK-801, a selective NMDA receptor antagonist that has been shown to influence performance in memory tasks (Butelman, 1989; Heale and Harley, 1990). Interestingly, MK-801 produced increases in open field locomotion in both rats (Carey et al., 1997) and mice (Diana and Sagratella, 1994), providing indirect evidence for similar mnemonic contribution to habituation to the environment, as indicated by distance traveled. The differences in distance travelled between rats and mice in the present study persisted over a more protracted time frame, suggesting that other factors may have influenced performance.

Finally, varying levels of hyperactivity may have contributed to the species differences in exploratory behavior. Distance traveled is typically used to assess the general locomotor activity of rodents in the open field (Paulus et al., 1999). Amphetamines have been demonstrated to increase locomotion in both rats (Briegleb et al., 2004; Siviy et al., 2015) and mice (Yates et al., 2007) in a dose dependent manner in the open field. These observations are consistent with species differences in endogenous dopamine neurotransmission (i.e., DA levels or receptors) contributing to the persistent variation in distance traveled, regardless of anxiety levels or mnemonic functions.

Species differences in the organization of exploratory movements may be mediated by a combination of factors. Previous work has suggested a potential benefit of using the organization of exploratory behavior to phenotype various rodent models (Eilam et al., 1989; Kafkafi et al., 2003). The current study demonstrates that mice and rats are equivalent in using self-movement cues to maintain spatial orientation; however, the observed species differences are likely related to varying levels of emotional, mnemonic, or locomotor function. Combining the sequential analysis of exploratory behavior with pharmacological manipulations may provide further insight to the neural systems that mediate these species differences.

4.4. The role of stops in exploratory behavior

The frequency and distribution of stops provide insight into the information processing that occurs during exploratory behavior. In environments with access to visual cues, stops may serve as moments during which the animal pauses to examine the spatial cues available to guide navigation (Whishaw et al., 1994). These stop locations appear to be encoded into memory, as indicated by mice frequently returning to previous stop locations (i.e., stop clustering) in an open-field environment (Dvorkin et al., 2008). These memories for stop locations may contribute to an overall representation of the environment – or cognitive map – that can be called upon at a later time to enable efficient navigation among locations within that environment (Tolman, 1948; O'Keefe and Nadel, 1978). In environments without access to visual cues, such as darkness, the animals are prevented from forming memories for stop locations relative to visual cues. Instead, the stops may serve as moments during which the animal updates its perceived position relative to a safe location like the home base, and uses this information to reorient toward a desired goal. If true, then stops may be a ubiquitous component of exploration and may facilitate the integration of available visual and/or non-visual cues.

Both mice and rats showed similar numbers of stops and similar stop clustering, suggesting that both species process information similarly during stops. Similar processing across species is hardly surprising, given that both rats and mice are able to accurately track their positions during non-visual exploration and to use this information to guide their return trajectories in homing tasks (Wallace et al., 2002; Yoder et al., 2015). However, following the initial time sample of the present task, mice made more stops of shorter duration than rats. Frequent, short-duration stops are characteristic of rats with fimbria-fornix lesions (Whishaw et al., 1994), which also show impaired performance on non-visual homing tasks (Whishaw and Gorny, 1999). In mice, the frequent short stops do not appear to be associated with impaired homing, given that path circuity and changes in heading were similar between species in the present task. The similarity of behaviors surrounding stops suggests that both species process a similar amount of information across stops, and the tendency for mice to stop more frequently than rats may simply reflect mice's need to reflect on their position more frequently than rats. Additional work is therefore warranted to precisely determine the nature of the information processed during stops within each species, as well as the implications of this information processing for various aspects of navigational performance. Nevertheless, this is the first direct cross-species comparison of non-visual exploration on the same task, and the results suggest that non-visual navigation may be more similar across species than visual navigation, where mice and rats perform differently on some task (Whishaw and Tomie, 1996). These results further suggest that the overall accuracy of non-visual navigation may not be specific to rats or mice, and general processes can be inferred from studies involving either species.

4.5. Conclusion

Mouse and rat exploratory behavior is organized into stops and progressions. Group differences in exploratory movements are consistent between species variance in general performance variables (i.e., hyperactivity, habituation, anxiety). No species differences were observed on several aspects of exploratory behavior that depend on vestibular function. This work establishes a translational basis to investigate neural systems that mediate self-movement cue processing related to maintaining spatial orientation.

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