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Organization of exploratory behavior under dark conditions in female and male rats

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ABSTRACT

Sexually dimorphic performance has been observed across humans and rodents in many spatial tasks. In general, these spatial tasks do not dissociate the use of environmental and self-movement cues. Previous work has demonstrated a role for self-movement cue processing in organizing open field behavior; however, these studies have not directly compared female and male movement characteristics. The current study examined the organization of open field behavior under dark conditions in female and male rats. Significant differences between female and male rats were observed in the location of stopping behavior relative to a cue and the topography exhibited during lateral movements. In contrast, no sex differences were observed on measures used to detect self-movement cue processing deficits. These results provide evidence that female and male rats are similar in their use of self-movement cues to organize open field behavior; however, other factors may be contributing to differences in performance.

1. Introduction

Spontaneously occurring behaviors are highly organized and have provided robust tools to investigate the neurobiological basis of spatial and temporal processing (St. Peters, 2018; Thompson et al., 2018). For example, rodents exhibit sequentially organized movement when introduced to a novel environment. Movement in an open field has been characterized by sequences of stops and progressions that are focused around a discrete position in the environment, called a home base (Eilam and Golani, 1989). This movement organization is dependent on a rodent processing both environmental (Hines and Whishaw, 2005; Clark et al., 2006) and self-movement cues (Whishaw et al., 2001; Avni et al., 2006; Donaldson et al., 2019). Although this open field behavior has been used to investigate the neural mechanisms supporting spatial orientation, no work has characterized whether sexual dimorphisms are observed in this movement organization.

The vestibular system provides a crucial source of self-movement cues used to maintain spatial orientation (Potegal, 1982; Wallace et al., 2002b). Sexual dimorphisms in the anatomy of the vestibular system have been observed and may contribute to the increased rate of vestibular pathology reported in females (Ayyildiz et al., 2008; Marcus et al., 2013; Smith et al., 2019). Previous work has demonstrated a role for the vestibular system in organizing movement during open field behavior (Avni et al., 2009; Blankenship et al., 2017; Donaldson et al., 2019; Banovetz et al., 2021). Specifically, *tilted* mice are a genetic mouse model of vestibular pathology that exhibit increased path circuity and increased change in heading between progressions compared to control mice while moving through an open field (Blankenship et al., 2017). These abnormal behavioral patterns strongly parallel circuitous spiraling behavior observed in humans during moments of spatial disorientation (Schaeffer, 1928; Souman et al., 2009). Additionally, the vestibular system significantly influences the hippocampal cholinergic system. A growing body of literature has demonstrated a role for the hippocampal cholinergic system in processing self-movement cues provided by the vestibular system (Whishaw et al., 2001; Wallace and Whishaw, 2003; Martin et al., 2007; Martin and Wallace, 2007; Winter et al., 2013). For instance, stimulation of the vestibular system results in significantly increased hippocampal acetylcholine release (Horii et al.,

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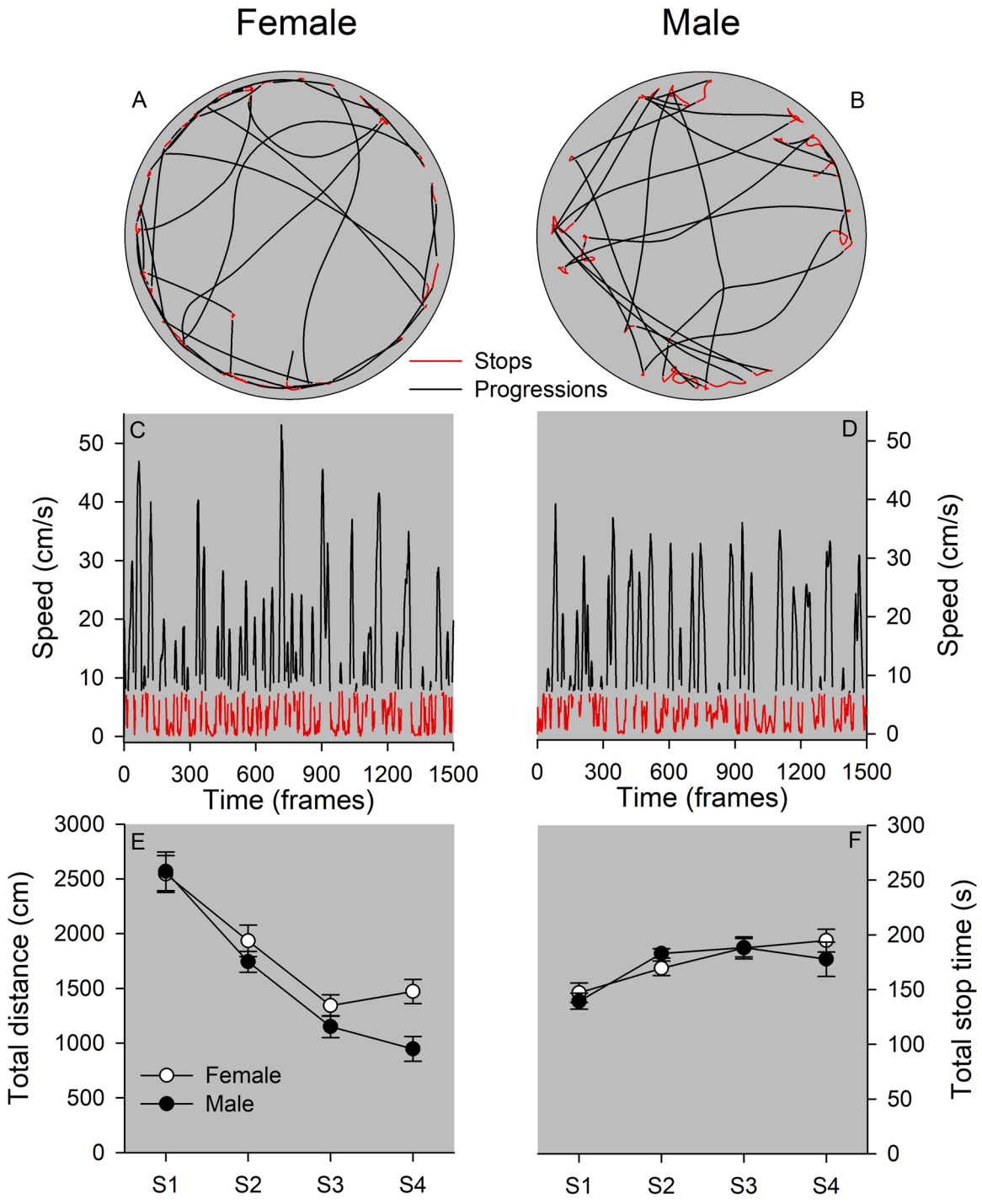

Fig. 1. Topographic profiles of progressions (black) and stops (red) are plotted for a representative female (A) and male (B) rat for one five-minute sample. Moment-to-moment speeds are plotted for the same female (C) and male (D) rats. No sex differences were observed on total distance traveled (E) or total stop time (F) across samples.

1994), and bilateral vestibular lesions result in a reduction of hippocampal cholinergic neurons (Aitken et al., 2016). Sexual dimorphisms observed in the structure, function, and pathology of the vestibular system across a range of behaviors (for a review see (Smith et al., 2019)) may be a significant contributing factor to sexual dimorphisms observed in spatial orientation.

The current study evaluated the sequential movement organization in female and male rats in an open field under completely dark conditions. The topographic and kinematic organization of open field behavior has allowed for multiple measures to be used to characterize this movement (Eilam and Golani, 1989; Golani et al., 1993; Tchernichovski and Golani, 1995; Wallace et al., 2006). Measures of general locomotion, lateral movement during stops, and stop and progression characteristics were evaluated across four five-minute samples of open field behavior under dark conditions. This approach investigated if sexual dimorphisms in lateral movements contribute to sexually dimorphic measures of self-movement cue processing.

2. Materials and methods

2.1. Animals

Female (n = 11) and male (n = 12) eighty-day old Long Evans hooded rats (Rattus norvegicus) were obtained from the Northern Illinois University vivarium. Rats were pair housed in opaque plastic cages in a colony room maintained on a 12 h light/dark cycle at a consistent temperature (20−21 °C) and humidity (40–60 %) controlled climate. All experimental procedures were approved by the Northern Illinois University's Institutional Animal Care and Use Committee which follows standards set by the Office of Laboratory Animal Welfare.

2.2. Apparatus

The open field was a wooden circular table (198 cm in diameter, 130 cm above the floor) painted white and located in a room that was made completely dark. A rectangular piece of thick black plastic (8.9cm × 19cm) was attached to the edge of the table facing parallel to the surface of the table. The location (i.e., north, south, east, west) of the plastic tab remained in a stable position during an open field session but was varied between rats. The plastic tab was used to serve as a tactile cue to encourage home base establishment. A night vision camera was attached to the ceiling and provided a view of the entire table surface. Open field sessions were recorded on DVDs at 30 frames per second for offline analysis. Four infrared emitter banks illuminated the room to allow the testing to be visible on camera. Infrared is a wavelength that rats are unable to visually detect (Neitz and Jacobs, 1986). Night vision binoculars were used to place the rat on the center of the table and remove the rat after the conclusion of the session.

2.3. Procedure

The open field session under completely dark conditions occurred during the light portion of the rats' light/dark cycle. Rats were removed from the colony room and transported following a circuitous path in a covered opaque testing cage to prevent tracking the relationship between the colony and testing room. After entering the completely dark testing room, the rat was removed from the held cage and placed at the center of the table by the researcher. Each rat was left in the open field for 40-minutes. Upon completion of the session, the experimenter removed the rat from the table, placed it in an opaque transport cage covered by a towel, and left the experimental room in a circuitous path before returning the rat to the colony room. The arena and tab were sanitized between sessions with an ammonia-based cleaning solution to eliminate odor cues.

2.4. Behavioral analysis

Two minutes after a rat was placed on the table, four consecutive five-minute samples were captured for analysis. The two-minute delay was selected based on previous work demonstrating that rodents exhibit markers of home base establishment (grooming, rearing, circling) within two minutes of exposure to a novel environment (Blankenship et al., 2017; Donaldson et al., 2018, 2019). Segmenting the session into four five-minute samples allowed for an analysis of behavior across time. Ethovision XT 13 (Noldus) was used to digitize movement at five frames per second. The resulting digitized x- and y- coordinates were used to calculate moment-to-moment speeds. The average speed for an individual rat's entire session was used as a threshold for segmenting movement into progressions and stops. Progressions were classified as periods of movement greater than or equal to the rat's average speed for at least two frames per second. Stops were classified as periods of movement less than the rat's average speed for at least two frames per second. Multiple measures were used to quantify general and specific characteristics of open field behavior.

A variety of factors (e.g., emotional, locomotor) have been observed to influence behavior in the open field (Denenberg, 1969; Eilam and Golani, 1990). Several measures were included to assess these factors. The average speed, total distance traveled, and total stop time was calculated from the moment-to-moment speeds across the four samples (see Fig. 1). Average speed was calculated by averaging all movement across the four samples. Total distance traveled during a sample was calculated by summing all progression distances within that sample. Total stop time during a sample was calculated by summing all stop times within that sample. These measures describe general locomotion in the open field.

Rats exhibit lateral movements when changing heading during a stop. Sexual dimorphisms have been observed in lateral movements associated with food protection behaviors (Field et al., 1996, 2004). A similar analysis was adapted to examine whether sexual dimorphisms were observed in lateral movements during open field behavior. Two videos were captured (~30 Hz) from each of the four samples in which rats exhibited lateral movement during a stop. The first two lateral movements in each sample that did not include rearing were selected for analysis. Tracker motion capture software (Open Source Physics https://physlets.org/tracker/) was used to manually digitize the nose and base of the tail throughout the duration of the lateral movement. The resulting x- and y- coordinates were used to characterize topographic and kinematic features of lateral movements. First, determining the degree of lateral movement involved normalizing both coordinates on start and end frames such that the tail coordinates were set at the origin (0,0) and calculating the angle subtended by the location of the nose prior to beginning a lateral movement, origin of the tail, and the final location of the nose at the completion of a lateral movement. Next, the circuity of the path followed by the nose and tail during lateral movement was calculated as the ratio of the Euclidean distance to the total traveled distance for each body part. Path circuity ranged from one (direct path) to zero as the path became more circuitous. Finally, the distance traveled by the nose and tail was divided by the duration of the lateral movement to estimate the speed of movement of each body part.

Three measures were used to quantify the clustering of stopping behavior. Each second of a stop was equated to an observation relative to a cartesian x- and y- coordinate system. These cartesian coordinates were converted to a polar (theta, r) coordinate system with the center of the arena set as the origin. This allowed for an analysis of the direction of stopping behavior relative to the center of the table with values increasing from zero to 360 degrees counterclockwise. Descriptive circular statistics (Batschelet, 1981) were used to quantify the clustering of the directional heading (theta) of stops. Within-sample parameter of concentration and average heading was calculated for the four samples from each rat. The parameter of concentration ranges from zero (stop directional headings are uniformly distributed around the perimeter of the arena) to one (all stops have the same directional heading). The average heading from each sample provided four direction estimates of home base establishment that were used to calculate subsequent measures. Between-sample parameter of concentration was calculated from the four average headings and provided a measure of home base stability across samples (Blankenship et al., 2017; Donaldson et al., 2019). The average heading across the four sample heading directions was used to calculate the difference in heading between the home base and tactile cue, or how far stop clustering occurred from the cue location.

During the session, most changes in heading occurred during stops (Donaldson et al., 2019). Change in heading was calculated as the supplementary angle to the angle subtended by the preceding progression peak speed location, average stop location, and subsequent progression peak speed location. Change in heading values range from zero (no change in heading) to 180 (complete change in heading). All changes in headings associated with stops were averaged for each sample.

Progressions are relatively non-circuitous movement trajectories that vary in distance traveled. Progressions less than 20 cm in distance

Table 1
General Measures.

	df	F	p	η^2p
Total Distance				
Sample	1.98,41.53$^+$	66.968	<.001*	0.761
Sample x Sex	1.98,41.53$^+$	2.151	0.130	0.093
Sex	1,21	3.146	0.091	0.130
Total Stop Time				
Sample	3,63	12.215	<.001*	0.368
Sample x Sex	3,63	1.176	0.326	0.053
Sex	1,21	<1		

Note: *<.05, $^+$Greenhouse Geiser correction applied.

(approximately two body lengths) were excluded from the analysis to minimize small movements related to grooming, rearing, or turning behaviors (Drai et al., 2000; Drai and Golani, 2001). Three measures were used to evaluate changes in progression topographic and kinematic characteristics across the four samples. First, the distances of all progressions were averaged for each sample. Next, the path circuities of all progressions were averaged for each sample. Finally, the peak speeds for all progressions were averaged for each sample.

Previous work has demonstrated that differences in movement are dependent on an animal's heading direction relative to the home base. For example, progressions directed toward the home base are typically faster and less circuitous compared to progressions directed away from the home base (Tchernichovski and Golani, 1995; Whishaw et al., 2001). This work prompted a directional analysis of progression topographic and kinematic characteristics toward and away from the home base. Home base heading (defined by the between-sample stop clustering analysis) was used to define the 90-degree home base zone. Toward progressions were defined as those that originated outside of the home base zone and terminated within the home base zone. In contrast, away progressions originated in the home base zone and terminated outside of the home base zone. Four measures were used to separately assess sex differences in toward and away progressions. First, the progression path circuity was calculated as described above and averaged for each rat's set of away and toward progressions. Next, the progression peak speed was averaged for each rat's set of away and toward progressions. Further, the movement scaling, or correlation between a set of progression Euclidean distances and peak speeds, was obtained for the away and toward progressions. Finally, the peak error for toward and away progressions was obtained which reflects the absolute difference between 0.5 and the proportion of the progression of which the peak speed occurred. Peak error values start at 0.0, indicating the peak speed occurred at the midpoint of the progression and approach 0.5 as the peak speed deviates from the midpoint of the progression.

2.5. Statistical analysis

Repeated measures ANOVAs were used to evaluate main effects and interactions for between-subjects (sex) and within-subjects variables (samples, direction, or body part) with an alpha set at 0.05. The Greenhouse-Geisser correction was used in analyses in which the Mauchly's test indicated significant departure from the assumption of sphericity. Partial eta squared (η^2_p) values were reported for each main effect and interaction effect as a measure of effect size. Independent Samples t-tests were used to evaluate group differences in exploratory behavior with Cohen's *d* as a measure of effect size. Skew and kurtosis were used to characterize whether dependent variables significantly departed from normality. Across all measures, average absolute value for skew was 0.61 (Max: 2.12; Min: 0.01) and kurtosis was 1.21 (Max: 6.06; Min: 0.02). These values are within the range permitted for the assumption normality for the planned parametric statistics. All statistical analyses used JASP 0.12.2.0 (University of Amsterdam) to calculate results.

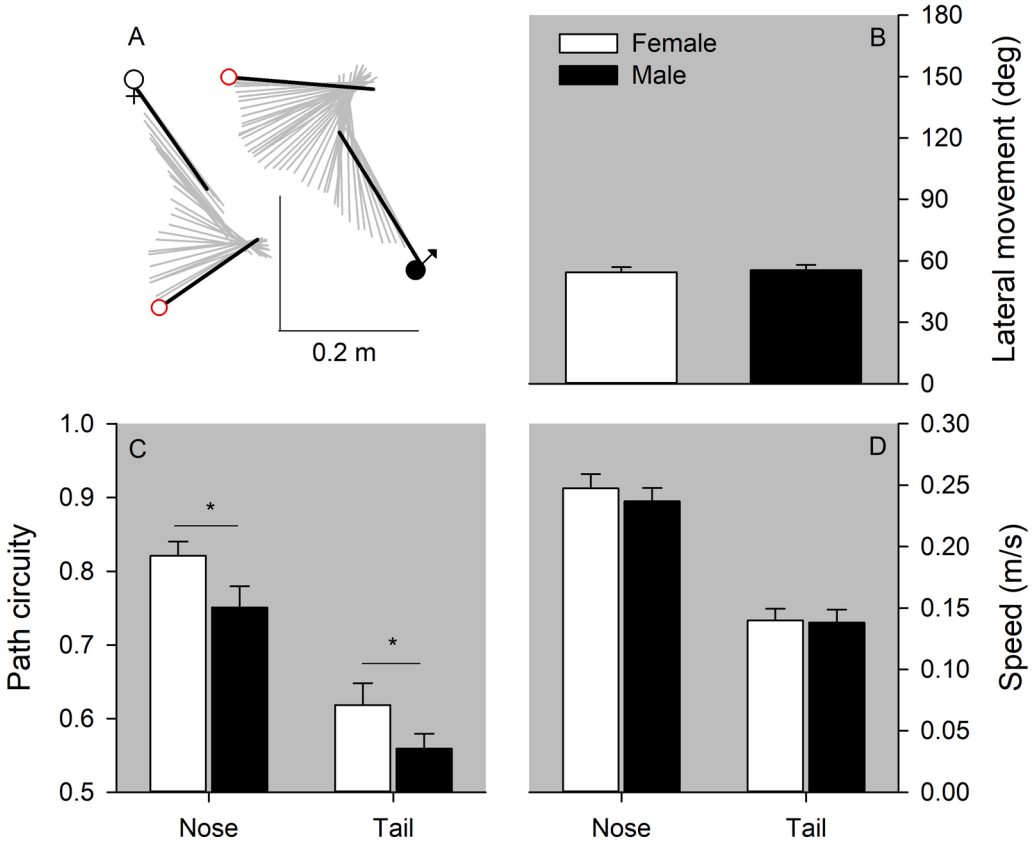

Fig. 2. Representative lateral movements are plotted for a female (♀) and male (♂) rat (A). The black symbols represent the starting position of the nose, and the red circles represent the final position of the nose. The gray lines represent each sample of movement between the beginning and end of a lateral movement. The degree of position change during lateral movements are graphed for female and male rats (B). The circuity of the paths followed by the nose and tail are graphed for both sexes (C). Male rats exhibited significantly more circuitous paths compared to female rats (p = 0.046*). Female and male lateral movement speeds are plotted for each body part (D).

Table 2
Lateral Movement Measures.

	df	F	p	η^2p
Lateral Movement Path Circuity				
Body Part	1,21	115.612	<.001*	0.846
Body Part x Sex	1,21	<1		
Sex	1,21	4.508	0.046*	0.177
Lateral Movement Speed				
Body Part	1,21	311.317	<.001*	0.937
Body Part x Sex	1,21	<1		
Sex	1,21	<1		

Note: *<.05, $^{+}$ Greenhouse Geiser correction applied.

3. Results

3.1. General behavior

Female (Fig. 1 panels A, C) and male (Fig. 1 panels B, D) rats organized their open field behavior under dark conditions into stops and progressions. Both sexes exhibited similar average speeds throughout the dark session [t (21) = 1.635, p = 0.117, d = 0.638]. Female and male rats traveled similar total distances that decreased across samples (Fig. 1 panel E). The repeated measures ANOVA with the Greenhouse-Geisser correction conducted on total distance traveled revealed a significant effect of sample; however, neither the effect of sex nor the Sex by Sample interaction was significant (Table 1). Female and male rats exhibited

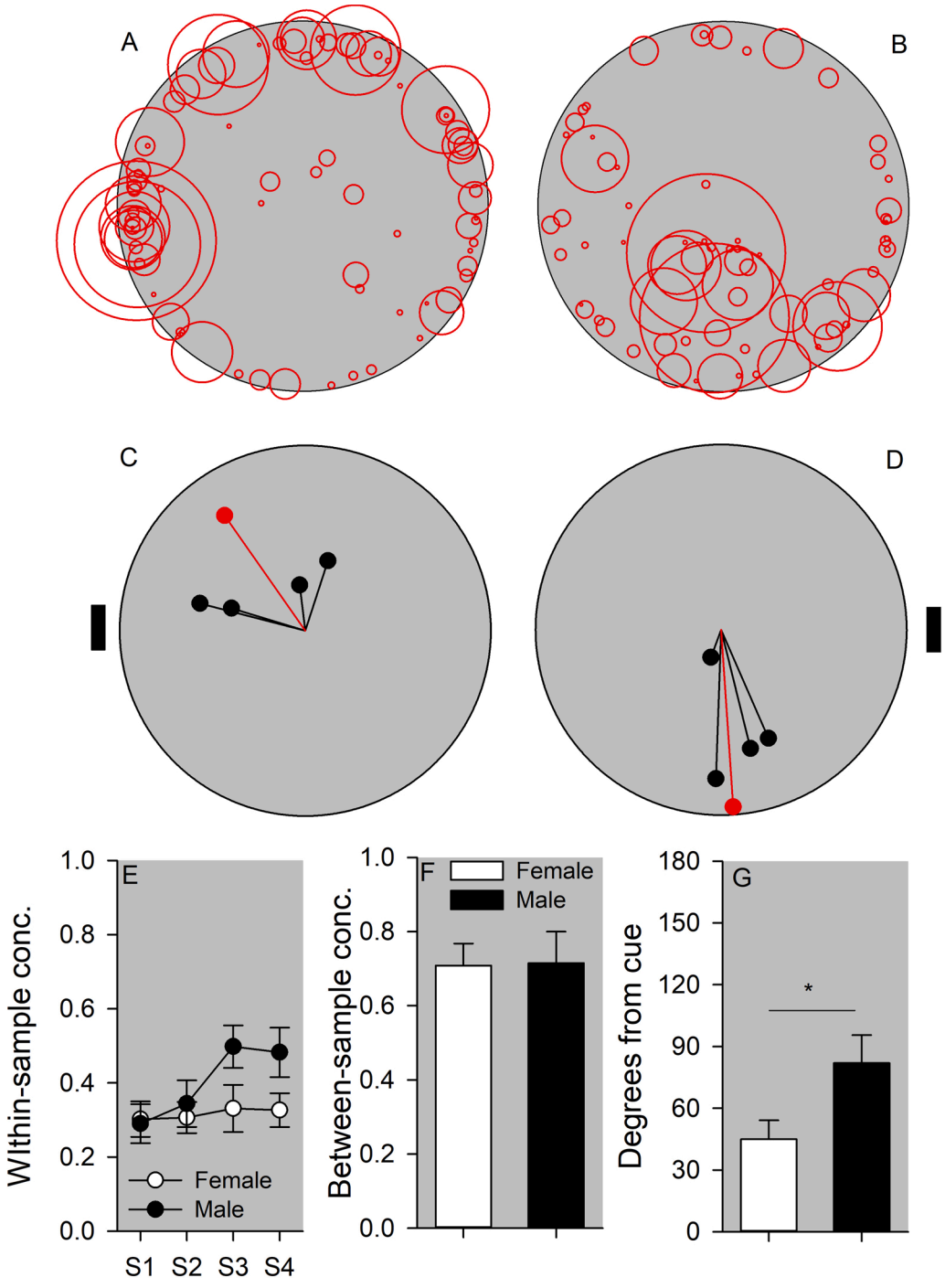

Fig. 3. Average position and duration (as represented by the diameter of red circles) of stops are plotted for a representative female (A) and male (B) rat. Average heading (direction of blackline) and parameter of concentration (length black line) are plotted for each sample from the same representative female (C) and male (D) rats. The between sample heading (direction of red line) and parameter of concentration (length of red line) are also plotted for both rats. The black rectangle outside of the circular arena represents direction of the cue. The average within (E) and between sample (F) concentrations are plotted for both groups. Female stop clustering occurred closer to the cue, relative to male stop clustering (G) (p = 0.038*).

Table 3
Stop Measures.

		df	F	p	η^2p
Within Sample Concentration					
	Sample	3,63	3.308	0.026*	0.136
	Sample x Sex	3,63	1.890	0.140	0.083
	Sex	1,21	2.371	0.139	0.101
Change in Heading					
	Sample	3,63	2.873	0.043*	0.120
	Sample x Sex	3,63	<1		
	Sex	1,21	2.593	0.122	0.110

Note: *<.05, $^{+}$Greenhouse Geiser correction applied.

similar stop times that increased in duration across samples (Fig. 1 panel F). The repeated measures ANOVA conducted on total stop time revealed a significant effect of sample (Table 1); however, neither the effect of sex nor the Sex by Sample interaction was significant (see Table 1). No sex differences were observed in these general measures of open field behavior.

3.2. Lateral movement

Representative lateral movement profiles are plotted for female (Fig. 2 panel A-left) and male (Fig. 2 panel A-right) rats. No sex differences [t (21) < 1] were observed in degree of lateral movement (Fig. 2 panel B). In contrast, significant differences were observed in the circuity of the path that each body part followed during lateral movements (Fig. 2 panel C). The repeated measures ANOVA conducted on path circuity for the nose and tail revealed significant effects of sex and body part; however, the Sex by Body Part interaction was not significant (Table 2). During lateral movements, rats moved their nose significantly faster than the base of the tail (Fig. 2 panel D). The repeated measures ANOVA conducted on peak speed for the nose and tail revealed a significant effect of body part; however, neither the main effect of sex nor the Sex by Body Part interaction was significant (Table 2). Lateral movements elicited sex differences in the circuity of the path followed by the nose and tail; however, no differences were observed in the speed of movement.

3.3. Stopping behavior

Female (Fig. 3 panels A, C) and male (Fig. 3 panels B, D) rats exhibited stopping behavior in which the direction of clustering remained stable within and between samples. Both sexes exhibited similar within-sample parameter of concentrations that increased in density across samples (Fig. 3 panel E). The repeated measures ANOVA conducted on the within-sample parameter of concentration revealed a significant effect of sample (Table 3); however, neither the effect of sex nor the Sex by Sample interaction was significant. Rats exhibited tightly clustered stopping resulting in high between-sample parameter of concentration values (Fig. 3 panel F) with no significant sex differences [t (21) < 1]. In contrast, female and male rats significantly differed in the number of degrees between the cue and the established home base (Fig. 3 panel G). Females established home bases closer to the cue [t (21) = −2.211, p = 0.038, d = −0.923)] relative to males. Although female and male rats established stable home bases similarly, female home bases were located closer to the tactile cue.

Most of the change in heading occurred during stops. Although female (Fig. 4 panel A) and male (Fig. 4 panel B) rats exhibited similar changes in heading between progressions, changes in heading were observed to decreased across samples (Fig. 4 panel C). The repeated measures ANOVA conducted on change in heading revealed a significant effect of sample; however, neither the effect of sex nor the Sex by Sample interaction was significant (Table 3). No sex differences were observed in the change in heading between progressions.

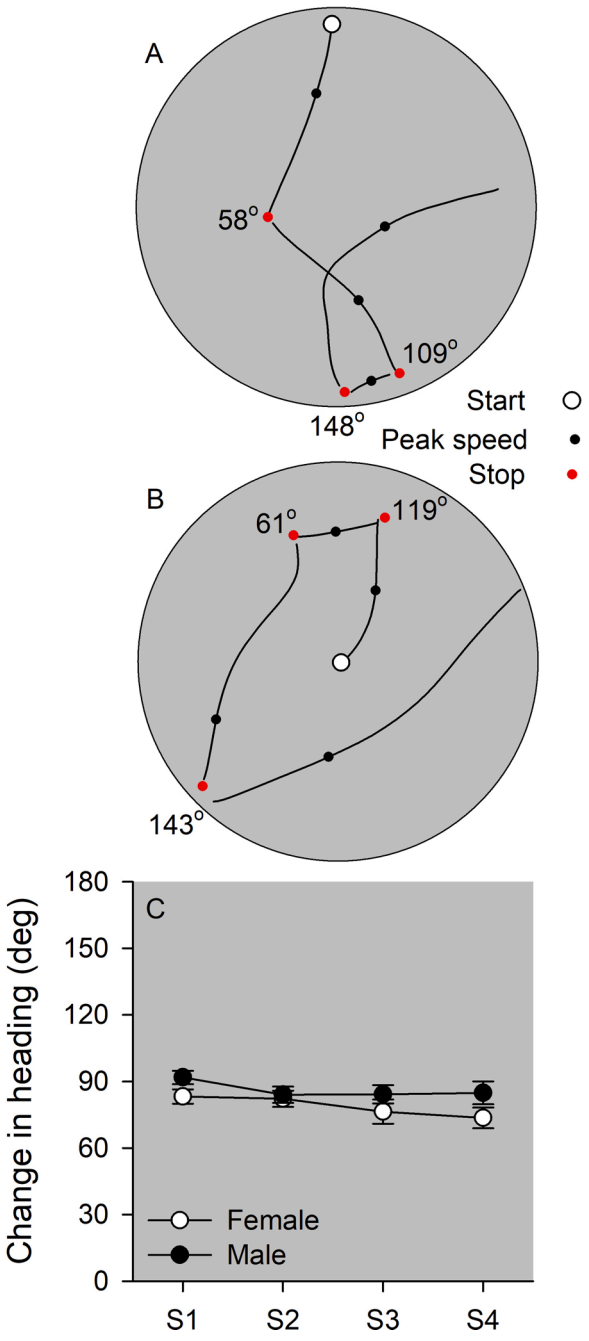

Fig. 4. A sequence of four progressions is plotted for a representative female (A) and male (B) rat. The white circles indicate the starting point, the black circles represent the location of peak speeds in the progression, and the red circles represent the stop locations. Degree of change in heading between each stop is indicated near the red circle. Average change in heading across samples is plotted for both sexes (C).

3.4. Progression behavior

Several measures were used to investigate sexual dimorphisms in progression characteristics across samples. Female and male rats traveled similar distances during progressions, with travel distance decreasing for both sexes across samples (Fig. 5 panel A). The repeated measures ANOVA conducted on average progression distance revealed a significant effect of sample; however, neither the effect of sex nor the Sex by Sample interaction was significant (Table 4). Female and male rats exhibited similar path circuity with paths becoming less circuitous across samples (Fig. 5 panel B). The repeated measures ANOVA

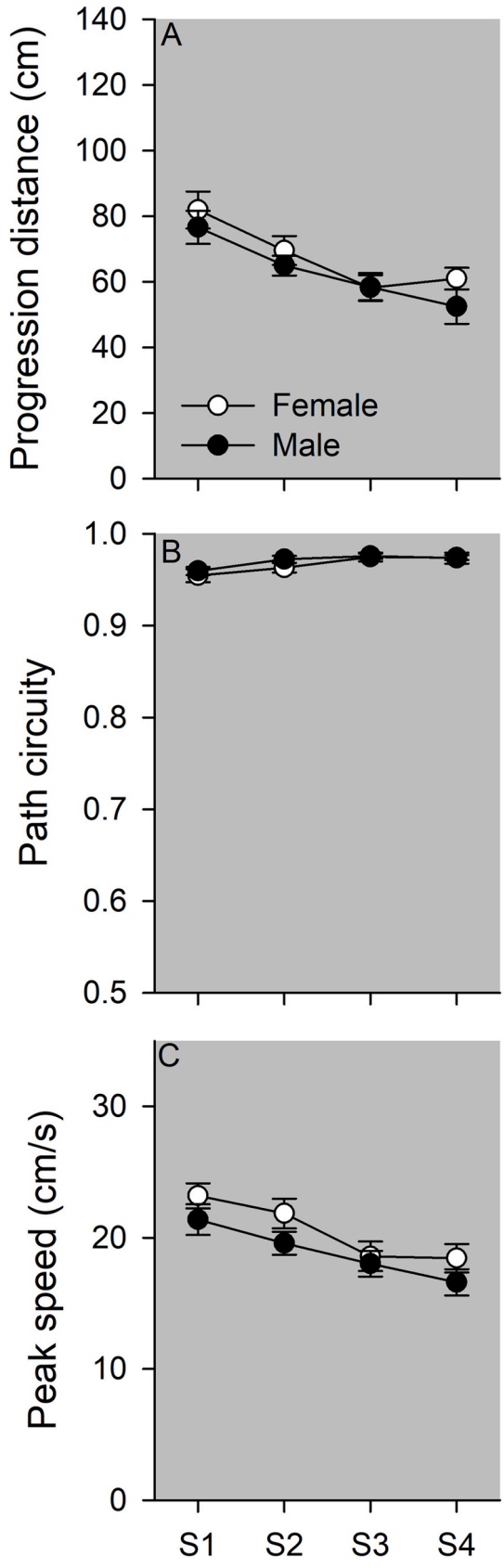

Fig. 5. Average progression distance traveled (A), path circuity (B), and peak speed (C) are plotted for both sexes across the four samples. Across samples, progressions were observed to become shorter, more direct, and exhibited slower peak speeds.

Table 4
Progression Measures.

	df	F	p	η^2p
Progression Distance				
Sample	3,63	15.550	<.001*	0.425
Sample x Sex	3,63	<1		
Sex	1,21	1.093	0.308	0.049
Progression Path Circuity				
Sample	3,63	7.912	<.001*	0.274
Sample x Sex	3,63	<1		
Sex	1,21	<1		
Progression Peak Speed				
Sample	2.21,46.31^{+}	21.725	<.001*	0.508
Sample x Sex	2.21,46.31^{+}	<1	0.562	0.028
Sex	1,21	1.738	0.202	0.076

Note: *<.05, $^{+}$ Greenhouse Geiser correction applied.

conducted on path circuity revealed a significant effect of sample; however, neither the effect of sex nor the Sex by Sample interaction was significant (Table 4). Female and male rats exhibited similar progression peak speeds, with peak speeds decreasing across samples (Fig. 5 panel C). The repeated measures ANOVA conducted on peak speed with the Greenhouse-Geisser correction revealed a significant effect of sample; however, neither the effect of sex nor the Sex by Sample interaction was significant (Table 4). Overall, progressions became shorter, more direct, and slower across samples; however, no sex differences were observed.

Progressions directed away or toward the home base may be differentially influenced by sexual dimorphisms. In general, away and toward progressions were non-circuitous (Fig. 6 panels A, B) and progressions toward the home base had higher peak speeds throughout the session (Fig. 6 panels C, D). Female and male rats did not exhibit differences in path circuity for away or toward progressions (Fig. 6 panel E). The repeated measures ANOVA conducted on progression path circuity did not reveal a significant effect of sex, direction, or Sex by Direction interaction (Table 5). In contrast, progressions directed toward the home base had faster peak speeds relative to progressions away from the home base (Fig. 6 panel F). The repeated measures ANOVA conducted on progression peak speed revealed a significant effect of direction; however, neither the effect of sex nor Sex by Direction interaction was significant (Table 5). Peak speeds typically occur at the midpoint of the progression (Fig. 7 panels A, B) and are scaled to the Euclidean distance of the progression (Fig. 7 panels C, D). Both female and male rats exhibited strong movement scaling across the away and toward progressions (Fig. 7 panel E). The repeated measures ANOVA conducted on movement scaling failed to reveal a significant effect of sex, direction, or Sex by Direction interaction (Table 5). Both female and male rats exhibited peak speeds that occurred relatively close to the midpoint of progression (Fig. 7 panel F). The repeated measures ANOVA conducted on peak error failed to reveal a significant effect of sex, direction, or Sex by Direction interaction (Table 5). Sexual dimorphisms were not observed on any of the measures for away or toward progressions.

4. Discussion

The current study investigated sexual dimorphisms in movement organization during open field behavior under dark conditions. Sexual dimorphisms were observed in the location of stopping behavior relative to a cue. Female rats established home bases closer to the cue. Additionally, sexual dimorphisms were observed in path circuity during lateral movements. Female nose and tail body parts followed more direct paths during lateral movements compared to male rat body parts. In contrast, no sexual dimorphisms were observed in measures sensitive to vestibular pathology which is indicative of self-movement cue processing. These results provide evidence that sexually dimorphic performance observed in traditional spatial tasks is not mediated by differential self-movement cue processing.

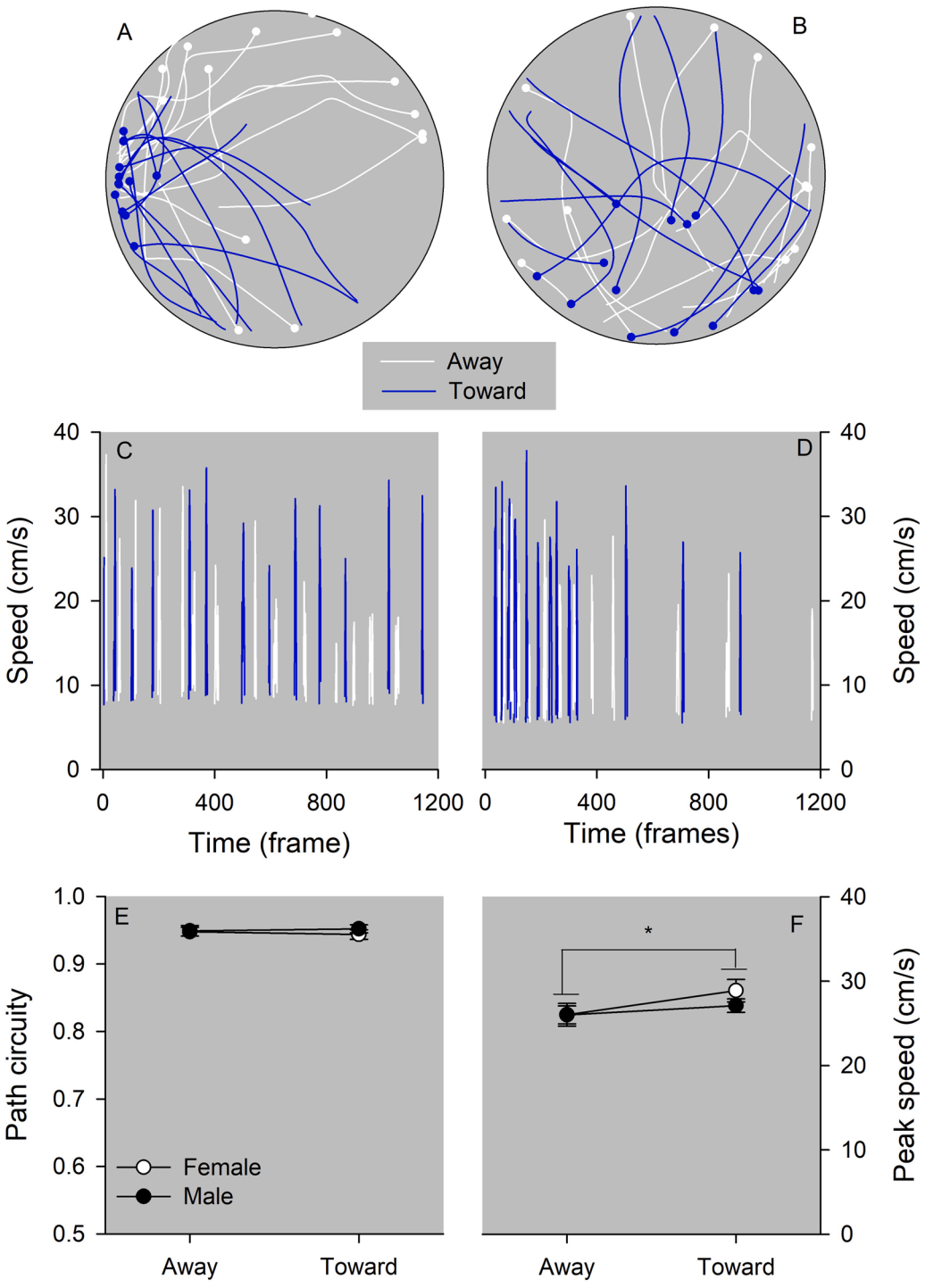

Fig. 6. Topographic profiles for progressions directed away (white) or toward (blue) the established home base are plotted for a representative female (A) and male (B) rat. Filled circles indicate the progression end point. Moment-to-moment speeds are plotted for progressions directed toward or away from the home base for a representative female (C) and male (D) rat. The average progression path circuity (E) and peaks speed (F) are plotted for both sexes, relative to the direction of the home base. Rats exhibited significantly faster peak speeds in progressions directed toward the home base relative to progression directed away from the home base ($p = 0.006$*).

4.1. *Factors influencing sexually dimorphic performance*

Sexually dimorphic performance in spatial tasks have been well documented across a range of species; however, the nature of these differences continues to be debated. One possibility is that sexually dimorphic information processing contributes to differences observed in spatial performance. These sexual dimorphisms may involve differences in processing environmental cues (e.g., visual), self-movement cues (e.g., vestibular), or both. Several lines of evidence support this possibility. For example, work with humans has demonstrated that when participants are prompted to give directions, females tend to use egocentric terms (e.g., turn right at the landmark), whereas males more frequently use allocentric terms (e.g., move north for two blocks, then turn east) (Ward et al., 1986; Galea and Kimura, 1993; Lawton, 1994; Saucier et al., 2002). In addition, neonatal manipulation of androgens has been shown to influence performance in spatial tasks (Stewart et al., 1975) and bias the use of either egocentric or allocentric navigational strategies (Williams et al., 1990). This work has been complemented by studies demonstrating that androgens have been shown to produce anatomical sexual dimorphisms in the limbic system (Madeira and Lieberman, 1995). The hippocampus is a structure within the limbic system that traditionally has been viewed as the neural basis for encoding allocentric representations in an environment, or the cognitive map (O'keefe and Nadel, 1978; Morris et al., 1982; Morris et al., 1990; Pearce

Table 5
Away and Toward Measures.

	df	F	p	η^2p
Path Circuity				
Direction	1,21	<1		
Direction x Sex	1,21	<1		
Sex	1,21	<1		
Peak Speed				
Direction	1,21	9.281	0.006*	0.306
Direction x Sex	1,21	1.803	0.194	0.079
Sex	1,21	<1		
Movement Scaling				
Direction	1,21	<1		
Direction x Sex	1,21	1.219	0.282	0.055
Sex	1,21	<1		
Peak Error				
Direction	1,21	<1		
Direction x Sex	1,21	<1		
Sex	1,21	<1		

Note: *<.05.

et al., 1998; Goodrich-Hunsaker et al., 2010). A major component lacking from these studies, and many other studies investigating sexual dimorphisms in spatial orientation, are procedural techniques that dissociate environmental and self-movement cue processing. Two exceptions to this limitation have been investigated in humans navigating a virtual environment (Mahmood et al., 2009) and in rats carrying a food item to a nest (Köppen et al., 2015). These two studies, parallel to the current study, did not find evidence of sexual dimorphisms in self-movement cue processing. Although sex differences in processing of environmental cues may contribute to sexually dimorphic performance observed in studies not restricting animals to self-movement cues, other factors may play a role.

Odors can be salient environmental cues; however, several studies discount the role for olfaction guiding movement in the current study. First, there are qualitatively different kinematic profiles during navigation guided by olfactory vs self-movement cues (Wallace and Whishaw, 2003). Specifically, rats tracking odor exhibit uniform sequences of moment-to-moment speeds. In contrast, rats in the current study exhibited a progressive increase in moment-to-moment speeds followed by a symmetrical decrease. This profile is not consistent with the head scans typically observed during odor tracking behaviors. Second, previous work has demonstrated that olfactory bulbectomized rats are still able to establish a home base and make direct returns to this location (Hines and Whishaw, 2005). Finally, when odor cues from a rat's refuge location are displaced in completely dark conditions, rats will exhibit direct returns from the open field to the refuge (Whishaw et al., 2001). Although rats have been observed to learn to use odor cues to guide navigation (Wallace et al., 2002a), they are neither necessary nor primarily relied upon to guide movement in the open field.

Independent of spatial orientation, the open field has been observed to elicit sexually dimorphic levels of locomotor behavior. Specifically, female rats are typically more active in the open field relative to males (Valle, 1970; Blizard et al., 1975; Beatty and Fessler, 1976; Seliger, 1977; Masur et al., 1980; Elliott and Grunberg, 2005; Gould et al., 2009; Seib et al., 2018). In the current study, no sex differences were observed in general measures of locomotion. Several procedural differences may have contributed to the absence of sex differences. First, changes in illumination differentially influence locomotion, as higher levels of illumination tend to suppress locomotion more in males than females (Valle, 1970; Seliger, 1977). Therefore, absence of sexual dimorphisms in general locomotor function in the current study may reflect conducting the open field under completely dark conditions. Next, the amount of time an animal is exposed to the open field has been observed to influence the magnitude of sexual dimorphisms in locomotion. Typically, the open field test involves exposing a rat to the arena for two to five minutes (Blizard et al., 1975; Beatty and Fessler, 1976; Seliger, 1977; Masur et al., 1980). When given repeated exposure to the same arena, measures of locomotion typically decrease (Igarashi and Takeshita, 1995; Rebouças and Schmidek, 1997; Alstott and Timberlake, 2009). In the current study, rats were exposed to the open field for two minutes prior to capturing movement for 20 min. This was done to provide time for the rats to establish a home base prior to analyzing movement organization. However, it is possible that these temporal differences in exposure to the open field may have also attenuated locomotor behavior. Adding an extended exposure to the open field under completely dark conditions may be sufficient to attenuate sex differences in locomotor behavior.

Sexually dimorphic stress responses have been posited to influence performance in both physical and virtual spatial navigation tasks. Compared to males, females exhibit higher basal serum corticosterone levels, and acute stressors increase these levels at significantly higher rates compared to males (Kant et al., 1983). Studies that have manipulated corticosterone levels in rats through adrenalectomies or pretraining procedures have demonstrated an attenuation of sexually dimorphic performance in Morris water task performance (Beiko et al., 2004; Anderson et al., 2013). It is possible that sexually dimorphic stress responses generated from open field dark conditions contributed to the group differences observed in the location of stopping relative to the cue in the current study. Female rats exhibited stopping behavior significantly closer to the cue than male rats. Previous work has demonstrated that when rats are given benzodiazepines prior to placement in the elevated zero maze with one wall, time spent near the wall is significantly reduced (Pickles and Hendrie, 2013). Additionally, previous studies have demonstrated that when rats are given benzodiazepines prior to open field exploration, corticosterone levels are attenuated, and rats spend less time thigmotaxing in a novel environment (Treit and Fundytus, 1988). Therefore, it is possible that a sexually dimorphic stress response mediated stopping behavior such that female rats stopped closer to the cue compared to male rats, even though rats explored the environment for two minutes prior to recording movement. However, these potential differences in corticosterone levels did not influence performance on measures of self-movement cue processing. Future work should examine whether necessary conditions exist for a stress response to impact measures of spatial orientation while moving in an open field.

Movement patterns that differ between females and males have been reported in many non-reproductive behaviors (Beatty, 1992). For example, sexual dimorphisms in food protection turning behavior depend on the position of the pivot point during lateral movement (Field et al., 1996, 2004). The female pivot point is focal to the pelvis, whereas the male pivot point is centered near the mid-point of the body. This sexual dimorphism in lateral movements during food protection behavior prompted the topographic analysis of lateral movements in the current study. Female rats exhibited less path circuity during lateral movements compared to male rats. This could be explained by several factors. First, general anatomical differences may have contributed. The location of the pivot point may influence the ability to steadily control movement during a turn. It is possible that the pelvis provides more support strength to control body position during lateral movements. Second, it is possible that body length contributes to path circuity. The increased length of male rats compared to female rats results in a greater distance traveled by males during lateral movements. Previous work has demonstrated that longer distances traveled are associated with more circuitous paths (Drai and Golani, 2001). Interestingly, the greater path circuity exhibited by male rats during lateral movements did not translate to greater path circuity throughout the open field session. Therefore, it is unlikely that sexual dimorphisms in path circuity during lateral movement affect self-movement cue processing during movement in an open field. Instead, the degree of change in heading during lateral movements would be more likely to contribute to deficits in self-movement cue processing (Blankenship et al., 2017; Donaldson et al., 2018). Specifically, rats exhibit approximately an 80 degree

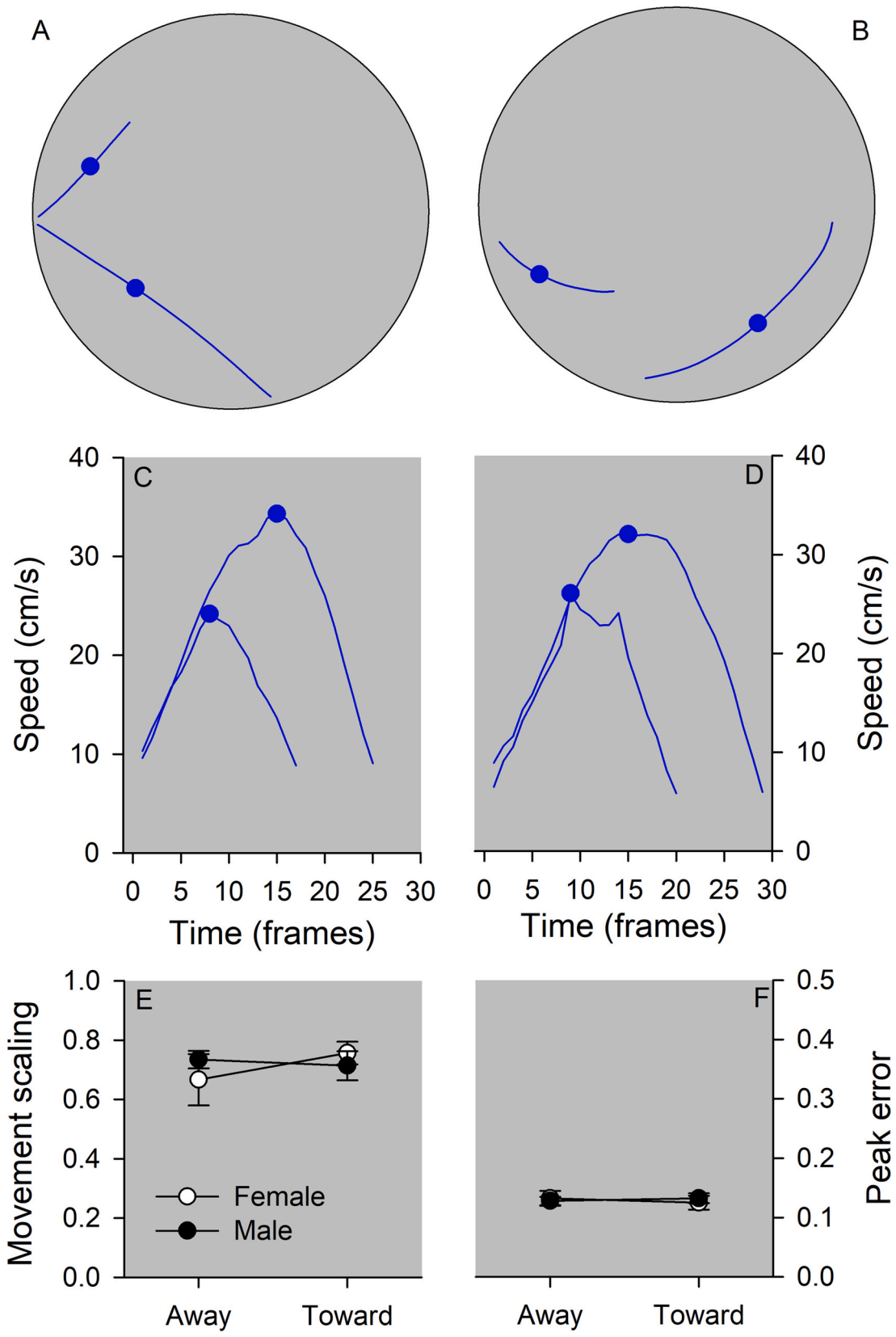

Fig. 7. Topographic (A, B) and kinematic (C, D) profiles of two progressions are plotted for a representative female (A, C) and male (B, D) rat. The location of the peak speed along a progression is indicated by the filled blue circle. In general, peak speeds were scaled to the length of the progression (i.e., longer progressions have higher speeds) and typically occur near the mid-point of a progression. Average movement scaling (E) and peak error (F) are plotted for both sexes relative to the direction of the progression.

change in heading between progressions during open field behavior (Donaldson et al., 2019), whereas rats typically exhibit a 175 degree change in heading during food protection behavior (Whishaw and Tomie, 1987). The varied degree of change in heading during lateral movements between open field and food protection behaviors may be mediated by levels of motivation or aggression elicited from task demands. Both factors have been shown to produce sexually dimorphic performance (Beatty, 1992); however, cognitive and emotional factors, such as motivation and aggression, are not likely to contribute to specific measures of open field behavior. Therefore, it is likely that anatomical differences, such as body length, contributed to differences observed in lateral movement path circuity.

Finally, hormonal factors may mediate sexual dimorphisms in lateral movement. Previous work has demonstrated that rats ovariectomized prior to the development of pubertal hormonal levels exhibit similar lateral movement behavior to male rats during food protection behavior; however, pregnant females exhibit female-typical lateral movements (Field et al., 1996). The current study did not track the estrous cycle throughout testing. Therefore, it is possible that varying levels of estradiol were circulating throughout open field behavior and may have contributed to the differences observed in path circuity during lateral movements. A caveat to this possibility, however, is that wide variability was not observed in female rat path circuity values during lateral movements as would be expected if the estrous cycle influenced this behavior. In fact, similarly small variability was observed in both female and male rats during lateral movement path circuity. Therefore, it is unlikely that the estrous cycle contributed to the sexual dimorphisms observed in lateral movement. Rather, it is likely that sexual dimorphisms in lateral movement path circuity reflect differences in body size or location of the pivot point during lateral movements. Further work is needed to characterize the influence of the estrous cycle on sexual dimorphisms observed during specific open field behaviors.

4.2. Sexual dimorphisms in vestibular and neural systems

The vestibular system provides a source of self-movement cues which are necessary for maintaining spatial orientation under dark conditions (Potegal, 1982; Wallace et al., 2002b). Recent work has demonstrated that genetic mouse models of vestibular pathology disrupt the organization of open field behavior (Avni et al., 2009; Blankenship et al., 2017; Donaldson et al., 2018). For example, otoconia deficient mice exhibit greater path circuity and larger changes in heading between progressions relative to control mice. Given the fact that previous work has demonstrated males exhibit larger lateral movements during food protection behavior, and have different vestibular anatomy compared to males, it was expected that focal impacts would be observed on the organization of behavior in the open field. However, this was not observed in the current study. Considering that sexual dimorphisms are present in vestibular anatomy (Ayyildiz et al., 2008; Marcus et al., 2013), and female humans have a significantly higher prevalence of vestibular pathology (Smith et al., 2019), further work is needed to investigate sexually dimorphic susceptibility to vestibular insult and how this may affect spatial orientation.

The hippocampal formation receives significant input from the vestibular system and has a critical role in processing self-movement cues. Damage to the hippocampus (Wallace and Whishaw, 2003; Winter et al., 2013) or selective damage to hippocampal cholinergic projections (Martin et al., 2007) has been shown to disrupt the organization of open field behavior under dark conditions. Specifically, progressions to the home base become more circuitous and variable in temporal pacing of moment-to-moment progression speeds which may be attributed to impaired processing of self-movement cues. Therefore, sexual dimorphisms in the hippocampal cholinergic system would have been expected to produce focal disruptions to self-movement cue processing; however, this was not observed in the current study. Previous work has demonstrated that sexual dimorphisms in the hippocampal cholinergic system are present early in development and reemerge in senescence. Female rats exhibit an earlier maturation of hippocampal cholinergic function (Darlington, 2010), whereas loss of function for this system occurs earlier in males throughout the aging process (Loy and Sheldon, 1987). It is possible that the current rats, aged 80 days, were in a similar window of hippocampal cholinergic function. Future work should evaluate the effects of age on open field behavior and movement organization. The current study sets a foundation for future work to examine the effects of aging hippocampal cholinergic function on processing self-movement cues.

5. Conclusions

The current study examined movement organization during open field behavior under completely dark conditions in female and male rats. Sexual dimorphisms were observed in the location of stopping behavior relative to a cue, as well as topography exhibited during lateral movements; however, sexual dimorphisms in measures previously used to detect self-movement cue processing deficits were not observed. This work provides evidence that sexual dimorphisms observed in many navigational tasks are not dependent on differences in self-movement cue processing. Further work is needed to evaluate if sexual dimorphisms in self-movement cue processing emerge following vestibular and hippocampal pathology as well as with aging.

CRediT authorship contribution statement

Jenna R. Osterlund Oltmanns: Conceptualization, Methodology, Writing - original draft, Writing - review & editing, Formal analysis. **Megan H. Lipton:** Investigation, Writing - review & editing. **Natalie Adamczyk:** Investigation, Writing - review & editing. **Rami I. Lake:** Software. **Ashley A. Blackwell:** Conceptualization, Writing - original draft, Writing - review & editing. **Ericka A. Schaeffer:** Conceptualization, Investigation, Writing - original draft, Writing - review & editing. **Shih-Yen Tsai:** Conceptualization, Writing - original draft, Writing - review & editing. **Gwendolyn L. Kartje:** Conceptualization, Writing - original draft, Writing - review & editing. **Douglas G. Wallace:** Supervision, Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing.

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