Investigating the influence of environmental predictability on route planning using a novel foraging paradigm

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Abstract

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During self-guided behaviors animals rapidly identify constraints of the problems they face and adaptively employ appropriate strategies. In the case of foraging, animals must balance sensory-guided exploration of an environment with memory-guided exploitation of known resource locations. Here we show that animals adaptively shift cognitive resources between sensory and memory systems during foraging to optimize route planning under uncertainty. We demonstrate this using a new, laboratory-based discovery method to define the strategies used to solve a difficult route optimization scenario, the probabilistic "traveling salesman" problem. Using this system, we precisely manipulated the strength of prior information as well as the complexity of the problem. We find that rats are capable of efficiently solving this route-planning problem, even under conditions with unreliable prior information and a large space of possible solutions. Through analysis of animals' trajectories, we show that they shift the balance between exploiting known locations and searching for new locations of food based upon the predictability of food locations. When compared to a Bayesian search, we found that animal performance is consistent with an approach that adaptively allocates cognitive resources between sensory processing and memory, enhancing sensory acuity and reducing memory load under conditions in which prior information in unreliable. We also find that the complexity of this route planning problem can be finely titrated through manipulating the number of food locations, with greater numbers of locations leading to wider angles of approaches to pellets and increased head movements while foraging. Additionally, the influence of environmental predictability on hippocampal local field potentials is examined. We show that animals trained on unpredictable pellet distributions increase their theta power over the course of training, while animals trained on predictable pellet distributions exhibit location-specific decreases in theta power when they reach the first few pellets in an acquisition sequence. Our findings establish new approaches to understand neural substrates of natural behavior as well as the rational development of biologically inspired approaches for complex real-world optimization.

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For me

PROLOGUE

Rodents must develop complex strategies for foraging that make use of sparse, local sensory cues. Generally, they can either use sensory cues to navigate toward a source, use memorized possibilities of where that source could be, or a combination of both. There is a chief dichotomy in the literature between sensory-driven and habitual strategies (Dolan & Dayan, 2013). Sensory-driven behaviors are appropriate under conditions of uncertainty when the increased cognitive demand of the strategy is offset by the need to flexibly interact with the environment. Habitual strategies consume relatively less cognitive capacity yet result in behaviors that are not readily adaptable to changing contingencies in the environment. It is therefore important that animals maintain cognitive flexibility while foraging in their natural environment in order to execute the most efficient behaviors required for food procurement.

Optimal foraging theory argues that animals must balance the energy they take in from consuming food with the energy and time expended to locate and procure the food (Pyke et al., 1977). Additionally, they must make decisions about which areas to forage in and when it is optimal to leave a particular area and move on to a new one (Charnov, 1976). The ability of rodents to form internal representations of their environment could allow them to apply learned spatial information to dynamic environments, creating a map that would act to lessen the cognitive load required to use the complex sensory cues present during foraging and greatly increase the effectiveness and efficiency of searches (Slotnick, 2001; Zhang & Manahan-Vaughan, 2015). We aim to understand what strategies animals may employ in order to navigate for food in the most efficient manner possible.

Optimizing foraging paths is extremely difficult. Animals would need to know the locations of all targets, the distances between targets, how to get to these locations, and their position with respect to their targets. Some of this information is easier to come by than others. Animals can learn the locations of targets by attending to the sensory cues emanating from their source location, such as seeing or smelling the target. Or they could have visited the location previously and known that this is somewhere to reexamine in the future. Animals can learn how to get to these locations, and also learn their current location, by both allocentric and egocentric strategies. One common egocentric navigation strategy is path integration, which is when animals integrate self-motion cues in order to update their position in the environment (Etienne & Jeffery, 2004; McNaughton et al., 2006; Muller & Wehner, 1988). Animals are known to use multiple cues to aid in this process, such as wind direction (Buehlmann et al., 2012; Müller & Wehner, 2007; Wystrach & Schwarz, 2013), vestibular information (Chance et al., 1998), and kinesthetic feedback from their own body movements (Bakker et al., 1999). However, a major drawback to using only idiothetic self-motion cues is that they can build up errors over time if they are not updated with accurate information about the current position (Etienne et al., 2004; Hardcastle et al., 2015; Knaden & Wehner, 2006; Valerio & Taube, 2012). One way to update knowledge of one's position is to use allocentric spatial landmarks (Burgess et al., 2004; Ekstrom et al., 2014; Gleason & Rothblat, 1994). These are external cues in the environment that animals can use to orient themselves, whether they be visual, olfactory, auditory, or tactile (Espinosa & Ochaíta, 1998; Jensen et al., 2005; Karim et al., 2018; Steck et al., 2009; Werner et al., 1997). Though, even if you have perfect information about where rewards are located and how to get there, determining the shortest path between multiple locations is computationally very difficult. This becomes even more complex when the number of locations needed to visit increases and the probability of rewards being present at certain locations fluctuates.

It is known that animals use cues from their environment in order to inform decisions, but what strategies do animals use in order to get these cues? One possible behavior is casting. Casting, predominantly used during odor-guided navigation, is when an animal zigzags back and forth in an effort to sense odor cues (Kozlowski et al., 2001; Lei et al., 2009; Lochmatter et al., 2008). This behavior most often occurs when animals are tracking an odor trail to a source location, and is used in conjunction with changes in direction, speed, odor sampling rate, and head movements. Another possible behavior is known as vicarious trial and error. Vicarious trial and error behaviors occur at the deliberation stages of a task, such as choice points of a maze, and are when animals move their heads back and forth towards the different directions that they may choose from (Amsel, 1993; Goss & Wischner, 1956; E. C. Tolman, 1939). This type of head movement is often seen when animals are learning which cues are salient and need to be attended to, and often disappears once animals are well-trained. It is important to note that both of these behaviors involve head movements that are distinct from movements of the whole body. For this reason, it is important to study head movements in our foraging task to help elucidate how animals might be solving this difficult optimization scenario.

Spatial navigation can be defined as the ability of animals to use information gleaned from landmarks in space and from cognizance of egocentric body movements in order to travel to a chosen location (Ito, 2018). The hippocampus' essential role in spatial navigation is its role in creating a "cognitive map" of an animal's environment, used as a spatial and temporal scaffold for representing relationships and experiences (Eichenbaum, 2017; Lisman et al., 2017). Evidence shows that multiple navigational strategies are coded for in the hippocampus

(Rowland et al., 2016) suggesting its specific role is to integrate spatial information in order to form a cognitive space that memories can organize within (Eichenbaum, 2017). Hippocampal place cells fire in specific locations, known as place fields, as an animal traverses its environment (O'Keefe & Dostrovsky, 1971; O'Keefe, 1976). The role of place cells was first thought to help inform a neural spatial representation of an animal's environment in order to aid in navigation. However, recent research has shown that these place cells are modulated by a growing number of cues and stimuli besides landmarks in the environment. These cells have been shown to be modulated by context, direction, and speed Additionally, these cells can be modulated by non-spatial environmental stimuli, such as the probability of receiving a reward (Tryon, 2017).

Hippocampal neural activity has been shown to be modulated by neural oscillations in the theta frequency band (4-12 Hz) (Buzsáki & Moser, 2013; Lester et al., 2017). These neural oscillations are thought to aid in organizing information across spatially discrete structures, and have long been shown to play a role in spatial navigation. Furthermore, the hippocampus has been shown to organize sequences of visited locations through the patterned firing of place cells during specific phases of the theta oscillation (Fernández-Ruiz et al., 2017; Hasselmo & Stern, 2014; Kim et al., 2015). We are then interested in understanding what role the hippocampal theta oscillation plays during navigation among sequences of pellet locations that have varying levels of predictability.

There is a wealth of literature suggesting that rats use information about the probability of receiving a reward to inform future decisions. When presented with the choice between two options with differing probabilities of reward, rats consistently choose the option with the higher probability of being rewarded (Sul et al., 2010). There are times when rats will choose a larger reward that has a lower probability of occurring when it outweighs the gain of choosing a smaller reward that has a higher probability of occurring (St Onge & Floresco, 2009). Previous research also suggests that decreasing the probability of reinforcement leads to an increased variability in behavior (Stahlman & Blaisdell, 2011). They surmise that this variability produces new behaviors that may be rewarded on a greater scale. This suggests rats can learn information about probabilities that they then use to inform choice behavior, leading to them obtaining as much food as possible during a foraging bout.

The present study aims to investigate how animals use their memory of their environment to find food during a naturalistic foraging task. We developed a novel, fully-automated open field arena where we are able to have complete control over the foraging environment and create multiple probability distributions of where food rewards may be located. We show that rats balanced exploration for novel locations of food with exploitation of known food locations to solve this probabilistic "traveling salesman" task, with the balance between exploratory and exploitative strategies governed by the amount of information available regarding resource locations. We found that rats are able to increase their foraging efficiency when they have more knowledge of an environment and form an increasingly stereotyped trajectory as their familiarity with the pellet distributions increases. Additionally, we find that animals are able to travel much more directly to pellets when there are fewer locations to learn and these locations are predictable. Finally, we demonstrate how changes in hippocampal theta power are modulated by the predictability of the foraging environment. Our results show how animals utilize learned information about the predictability and complexity of their environment to solve complex, real-world route planning problems.

Chapter 1. Balancing Exploration & Exploitation During Probabilistic Route Planning

1.1 INTRODUCTION

Animals balance the ability to flexibly interact with their environment with the need to reserve energy while foraging. Foraging in natural environments can be particularly difficult due to the sparse and unreliable nature of sensory cues emanating from food sources. This is especially true when animals need to travel between multiple locations and it is unknown whether food will be present at these locations. Under conditions of high uncertainty it may be beneficial to rely upon sensory information during foraging and utilize a more exploratory approach, when the increased cognitive demand of this strategy is offset by the need to flexibly interact with the environment. Conversely, using a memory-based strategy to exploit known resource locations allows for the quick establishment of efficient stereotyped routes, yet result in behaviors that are not readily adaptable to changing contingencies in the environment. It is therefore important for animals to maintain cognitive flexibility while foraging in their natural environment in order to execute the most efficient behaviors required for food procurement (Dolan & Dayan, 2013). To this end, the ability to adaptively modify search strategy by using internal representations of the dynamic environment would serve to vastly increase the effectiveness of foraging bouts (Slotnick, 2001; Zhang & Manahan-Vaughan, 2015).

Animals must learn the constraints of their environment in order to determine how to optimize their foraging strategies, with the balance of exploration versus exploitation being vital in this context (Auh & Menguc, 2005; Gupta et al., 2006; Kramer & Weary, 1991; Mehlhorn et al., 2015). During exploration, animals sample from multiple food patches over the course of several foraging bouts. This allows them to construct an internal representation of different possible locations where they can find food, with the benefit being that their future foraging would be more resistant to reduced or noisy sensory cues. Exploitation of this information follows and relies on remembering bountiful patch locations so that animals have a framework to use for navigation. While benefits of exploitation include spending less energy traveling to locations where it is unknown whether food will be available, potential drawbacks would be that this strategy fails when resources have been exhausted or when resource locations change. Additional exploration after establishing resource location is thus most useful when new resource locations need to be discovered, such as when information regarding resource locations is found to be unreliable. Under the constraints of foraging in an unpredictable environment, it is more difficult to exploit reliable resource locations in order to reduce foraging costs and strategies should shift toward exploration.

The ability to rapidly solve complex problems, such as optimization of foraging strategies, is a defining feature of animal intelligence. Indeed, varieties of animals solve difficult optimization problems nearly instantaneously (Drea & Carter, 2009; Kenward et al., 2005; Wall & Balda, 1977; Zhang et al., 2015). However, it has been difficult to study route optimization during naturalistic foraging in a laboratory setting. Historically, many foraging tasks have been studied with apparatuses that do not explore the full behavioral repertoire of a natural forager. One issue is the difficulty of providing alternative possible paths for the animals when they are restricted to a track, such as a figure-8 maze (Pedigo et al., 2006). In these simplified tasks the space of available behaviors is limited to simple actions such as left and right turns. While other studies avoid these restrictions through the use of open field designs, these approaches necessarily reduce the precision and reproducibility of resource locations (Agarwal et al., 2014). We address these challenges by studying naturalistic foraging in a large, computer-controlled open field where food rewards can be precisely and reproducibly located anywhere in the environment.

Using our computer-controlled open field design we investigated the strategies rats use to solve a notoriously difficult optimization scenario, the probabilistic traveling salesman problem. In this problem, an agent must establish the most efficient (i.e., shortest) route between a finite number of locations and each location has a certain probability of containing pellets (Leipälä, 1978; Percus & Martin, 1999). We observed rats' ability to follow efficient acquisition sequences and measured how well animal performance correlated with memory-guided exploitative strategies or sensory-guided exploratory strategies as a function of the predictability of the pellet distributions upon which animals were trained. These precise behavioral experiments suggest animals adaptively shift their reliance on sensory information in response to the reliability of the foraging environment.

1.2 MATERIALS & METHODS

Subjects

The experiments in this study were performed on 12 male Long-Evans rats, purchased from Charles River Labs and housed individually. All animals were maintained on a 12-hour reverse light-dark schedule (lights off at 7:00am) with *ad libitum* access to water. After a weeklong habituation to the animal housing facility, all animals were then sustained at 85% of their free-feeding body weight in order to maintain motivation. All tests were performed between 9:00am and 6:00pm, during the dark phase of the light cycle. Zeitgeber Time (ZT, with ZT0 = lights on in the animal facility) of experiments was ZT 14 to ZT 23. To limit distal visual cues, all tests were performed under dim red light (~660 nm). All experimental procedures were approved by the Institutional Animal Care and Use Committee at the University of Washington.

Testing Apparatus

The foraging arena was a large, fully enclosed open-field measuring 2.5m in length, 1m in width, and 1m in height. The frame of the arena was constructed from T-slotted aluminum railings. The sides of the arena were constructed from 1.27cm thick clear acrylic, while the ceiling was 0.635cm in thickness. The floor was a sheet of 0.0635cm thick opaque white acrylic. The ends of the arena were made from a wire mesh to allow for air to circulate throughout. A nest area where the animals would remain during the inter-trial interval was attached to one end of the arena. The nest area was constructed from 1.27cm thick clear acrylic. Two synchronized cameras (The Imaging Source; DMK 23UP1300; frame rate 120 per second) were used to track the movement of the animals. An automated, custom-made pellet dispenser was used to bait the arena with 45mg sucrose pellets (Bio-Serv). An Arduino Uno controlled the movement of the motors running the pellet dispenser, allowing movement in the x- and y- coordinate plane.

Estimation of odor cues

Odor cue dispersal in the arena was directly measured using an ethanol source and miniature ethanol sensors (Tariq et al., 2019) that were scanned in a grid across the arena. The maximal signal detected at each sensor location over 30 seconds was normalized and reported in Figure 1.4. There was no flow imposed on the arena, which limited the dispersal of airborne odor cues.

Behavioral Paradigm

Before testing, all animals were habituated to the animal facility for 1 week. Animals then spent 2 days habituating to the attached waiting cage for ~15 minutes at a time. In order to motivate animals to return to the waiting cage, sucrose pellets were placed in the cage every 2 minutes when a 1 second, 1000Hz tone was played. They were then granted access to the test arena and were given 2-3 days to habituate to it. Animals were considered to have reached criterion when they were able to make 3 transitions between the waiting cage and test arena within 30 minutes.

Animals were placed into the waiting cage at the beginning of each testing session. Rats completed 1 session a day of 3 trials each. Before each trial, the automated pellet dispenser baited the arena with sucrose pellets organized into 3 clusters of approximately 3 pellets each. During foraging periods the dispenser was automatically lifted out of the arena so that the animals could not interact with it. Procedures differed only through the testing phase, when animals were assigned to forage within environments of high, medium, or low food location predictability. Animals trained on the environment with high food location predictability (n=4) were overtrained on a single distribution of pellet locations that stayed consistent across trials and sessions. Animals foraging in the environment with low food location predictability (n=4) were trained on unpredictable pellet distributions that changed across trials. All other animals (n=4) were trained on a moderately predictable distribution of pellet locations that changed slightly over time. All rats were given a maximum of 30 minutes to eat all of the sucrose pellets during the session. The entire testing period lasted for 30-35 days with approximately 5 sessions a week.

Experimental Design and Statistical Analysis

No explicit power analysis was conducted in order to determine sample sizes. However, the number of animals used is consistent with experiments in the current literature. All analyses were conducted using MATLAB (MathWorks) on PC workstations running under the Windows 10 operating system. A custom LabView (National Instruments) program was used to collect the behavioral data, also on a PC running the Windows 10 operating system. Significant differences between groups were assessed with the Mann-Whitney U test, followed by p-value adjustment with False Discovery Rate when multiple comparisons were made.

Predictability of pellet distributions was quantified using an across trial minimum distance metric, which, for each pellet in a given distribution reports the minimum distance from that pellet to all pellets in the immediately previous distribution. Relative entropy (RE) is equivalent to Kullback-Leibler Divergence and was calculated as: $RE(P||Q) = \int P(j)log(P(j)/Q(j))$ for all points j in the current trial's probability density function (P) and the probability density function calculated from all previous trials (Q). Prior to calculating the RE all distributions were convolved with a smoothing function, which was an averaging filter of width = 1 cm. RE is reported in bits.

For establishing optimal pellet acquisition sequences for each distribution we used a genetic algorithm developed by Joseph Kirk: Fixed Start Open Traveling Salesman Problem - Genetic Algorithm (https://www.mathworks.com/matlabcentral/fileexchange/21198-fixed-start-open-traveling-salesman-problem-genetic-algorithm). Briefly, this algorithm starts from a population of randomly generated paths that start at the entrance to the arena and travel to each pellet once. It then uses an iterative process wherein in each "generation" of solutions the fitness of every path in the population is evaluated; the objective function for fitness in this case is minimization of path length. The more fit (shorter) paths are selected, and each path's sequence of pellet locations is modified (recombined with other paths or randomly changed, or "mutated") to form a new generation. The new generation of candidate paths is then used in the next iteration of the algorithm. The algorithm can be terminated when either a maximum number of generations has happened or the path length reaches a small enough value.

Efficiency of foraging paths (Figure 1.3a) was calculated as $fe = lo/la$, where *lo* is the optimal path length, *la* is the animal's path length, and *fe* is foraging efficiency.

Bayesian search

For analyses conducted in Figure 1.5, we modeled rat behavior as a Bayesian search. Briefly, the search arena is divided into 2.8 cm squares resulting in a 40 x 80 grid of possible locations. This grid is then populated with the same pellet distributions that were used in the behavioral experiments. We start our analysis on day 10 of training, which provides an agent with up to the first 10 days of training data as a map of prior expectations regarding pellet locations (Figure 1.5a). The expression for prior expectation of pellet location is given by:

$$pe(x, y) = \Sigma_L^{t-1} rw\,(x, y)/(t - L)$$

Where t is the trial number, rw is the probability of a pellet being found at a given point, (x,y), over previous trials and pe is the resulting prior expectation from the previous pellet locations. L is based on the length of memory being used and is defined as $L = (t - md, 1)$, with md being memory depth in trials, with md >=1. To enforce the nearest-neighbor search strategy used by rats, this map of prior expectations is discounted by linear distance from the agent, resulting in decreased likelihood to search first in areas that are located at large distances from the agent. This results in the following expression at a point, (x, y) within the grid of possible pellet locations:

$$m(x, y) = pe(x, y) * ((max(d) - d(x, y))/max(d))$$

Where d is the distance from the agent and m is the memory-based map of prior expectations for pellet location adjusted by distance from the agent. The agent also uses sensory information that decays with distance to update their expectation of the possible pellet location,

$$s(x, y) = cr(x, y) * ((\max(d) - d(x, y))/\max(d))^{se}$$

where s is the sensory density function and cr is a map with the current location of all pellets set to 1 and all other locations set to 0. The term se is an exponent that determines the rate of decay of sensory information with distance. These two sources of information are weighted and then summed to result in a map that guides the agent's next step in the search path.

$$p(x, y) = s(x, y) * sw + m(x, y) * (1 - sw)$$

Where *p* is the probability map, *s* is the sensory density function and *m* is the memory-based map of prior expectations for pellet location. The term *sw* is the weight given to sensory information, $\{sw \mid 0 \leq sw \leq 1\}$. The agent makes its next step along the vector to the maximum point of p. The agent is considered to have perfect target detection at their location, such that after the agent moves to a new location, if a pellet is at that location it is always detected and if no pellet is at that location the probability of a target at that site is updated to 0. To fit parameters for the Bayesian search, we used a 3-dimensional coarse grid of values for *sw*, *se*, and *md*. We found the best fit for each animal in this grid and report these results in Figure 1.5.

For reported measures in Figure 1.5f, $sa = (1 - (se/(SE)) + sw)/2$, where *sa* is sensory acuity and *SE* is the set of values of *se* across all best fits for 12 animals, while $mi = (max(pr\{md > 0\}) - mean(pr\{md \leq 3\}))/(max(pr\{md > 0\}) - min(pr\{md > 0\}))$, where mi is long-term memory usage and *pr* is the correlation of the agent's performance with the animal's performance using *md* set to the indicated range of values.

1.3 RESULTS

Route planning revealed through controlling predictability of reward locations

We adapted the probabilistic traveling salesman problem for experimental investigation through the use of an automated system for precise, computer-controlled food pellet placement within a large foraging arena (Figure 1.1a). We divided a cohort of 12 rats into 3 equal groups that foraged within environments of high, medium, and low food location predictability (Figure 1.1b). Animals in each group were tested across precisely replicated pellet placements (Figure 1.1c) and all placements used had equivalent optimal path lengths (Figure 1.1d), as calculated through a genetic algorithm solution to the traveling salesman problem for each pellet placement (see methods). We generated sequences of pellet locations over days to create distributions that were extremely well-predicted by prior experience as well as distributions that were unable to be anticipated based upon prior pellet locations. To generate pellet placements with controlled levels of predictability we quantified the between trial minimum distance for each pellet of a given distribution and all pellets of the previous trial's distribution and set this value to be low for the computer-generated set of locations used for predictable conditions and to be high for the unpredictable condition (Figure 1.1e). The lower values for pellets in predictable distributions indicate that these pellets are in areas that are extremely close to where pellets were located on the previous trial, allowing animals to create an expectation over repeated searches. This is also demonstrated through a reduction of the relative entropy (a measure of surprise) of newly-encountered pellet distributions following multiple days of training for animals in high and medium predictability conditions. Animals could not develop such an expectation under low levels of predictability and relative entropy does not decrease with training for the unpredictable distribution (Figure 1.1f). In all conditions, animals searched for an average of 7 pellets, with the precise number on a given trial unknown to the animal (Figure 1.1g). This results in typically 7!, or 5,040 possible sequences of pellet acquisition, with most sequences being extremely sub-optimal. Examples of trajectories taken by animals on the first and last days of training demonstrate changes in search trajectories with learning (Figure 1.1h). After training, all animals favored a small subset of near-optimal acquisition sequences (Figure 1.2a), consistent with findings in non-probabilistic optimization across a number of species (Blaser & Ginchansky, 2012). We found that a simple nearest neighbor strategy (in which rats solve the task by traveling to the next nearest pellet) achieved strong performance on this task, often comparable to that of optimized routes (Figure 1.2b). Indeed, we found that animals achieved optimal performance only when the optimal solution was the same as a nearest neighbor approximating solution (Figure 1.2c), suggesting that the rats employed the nearest neighbor strategy to solve the task. Rats foraging in predictable environments were capable of employing a nearest neighbor strategy earlier during training, though all animals, even those in unpredictable environments, did increase the use of nearest neighbor routes while foraging (Figure 1.2d). However, animals in the highest predictability group were significantly more effective at ordering their search based on nearest neighbor relations of reward locations (Figure 1.2e, error relative to a nearest neighbor search: 16.9 +/- 0.5 cm for most predictable, 22.1 +/- 2 cm for moderately predictable, and 20.8 +/- 1.4 cm for least predictable, n = 4 animals per predictability group, see methods for statistical tests used for all comparisons). Examples of optimal, nearest neighbor, and animal sequences of pellet acquisition for animals in highly predictable and unpredictable environments are shown in Figure 1.2f.

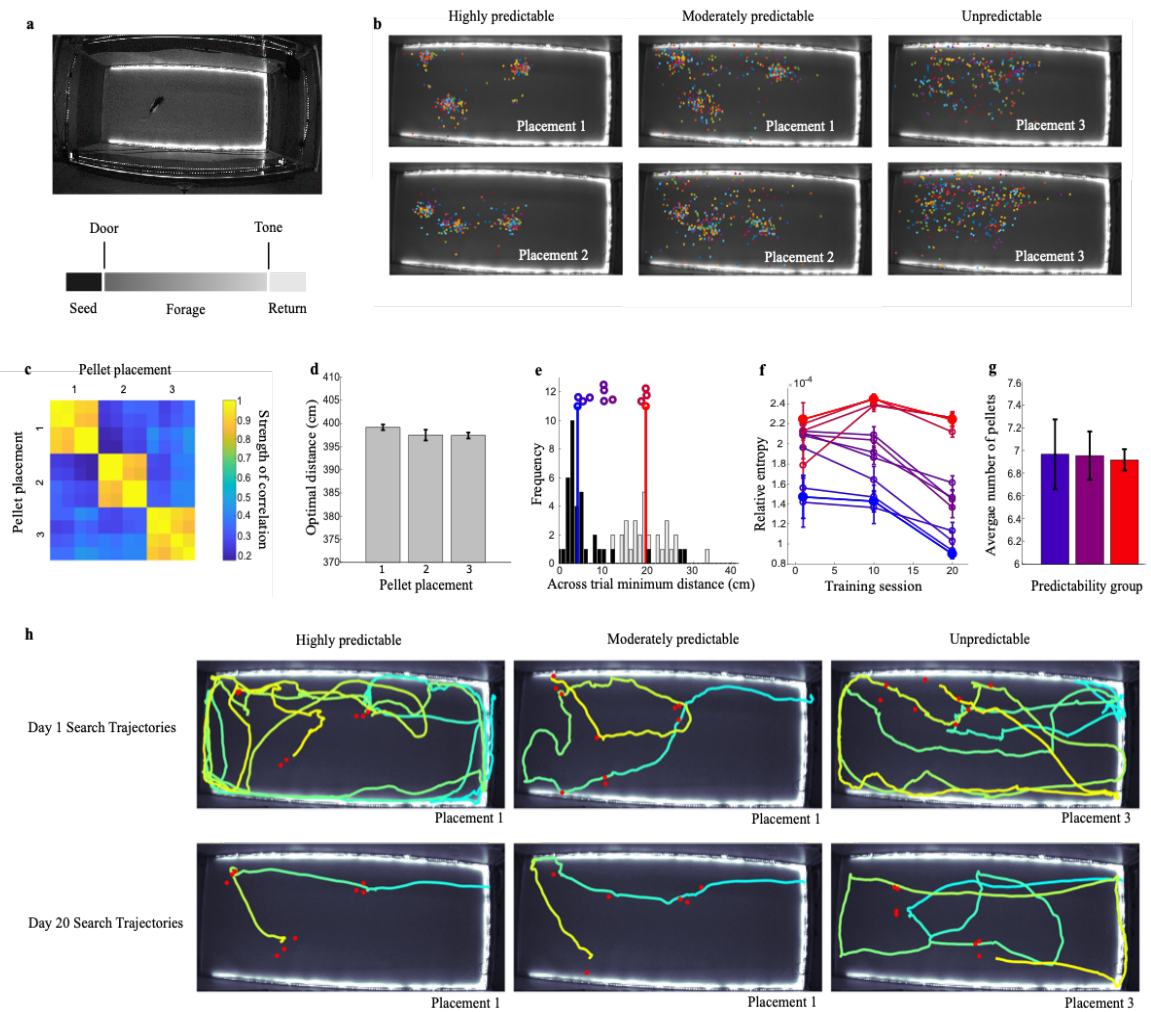


Figure 1.1: A computer-controlled probabilistic traveling salesman task enables direct tests of behavioral strategies under uncertainty.

a. **(top)** A large, automated arena with a rat shown for scale. **(bottom)** The temporal structure of a typical trial.
b. Rats forage for pellets in highly predictable **(left),** moderately predictable **(center),** and actively randomized **(right)** pellet placements. Placements are shown across all trials (20 days, 3 trials per day).
c. The automated system allows for reproducible pellet placement across animals. From the top to bottom of the matrix correlation coefficients are shown for two different predictable distributions and the single unpredictable distribution.
d. Pellet distributions from each placement shown in panels b) and c) have equivalent optimal path lengths.
e. Example histograms are shown for the most predictable (black) and least predictable (gray) distributions that were tested. Vertical colored lines show the mean for the predictable (blue) and unpredictable (red) distributions. The distributions for all animals are plotted as colored circles, with color corresponding to across trial minimum distance.

f. Relative entropy for each predictability grouping (high - blue; medium - purple; and randomized - red) across sessions of training. Higher values indicate higher entropy.
g. Average number of pellets per trial for each predictability level.
h. Examples of routes taken by rats on the first trial of the first day (top panels) and after 20 days of training (bottom panels). Color shifts from cyan to yellow as each animal's trajectory progresses.

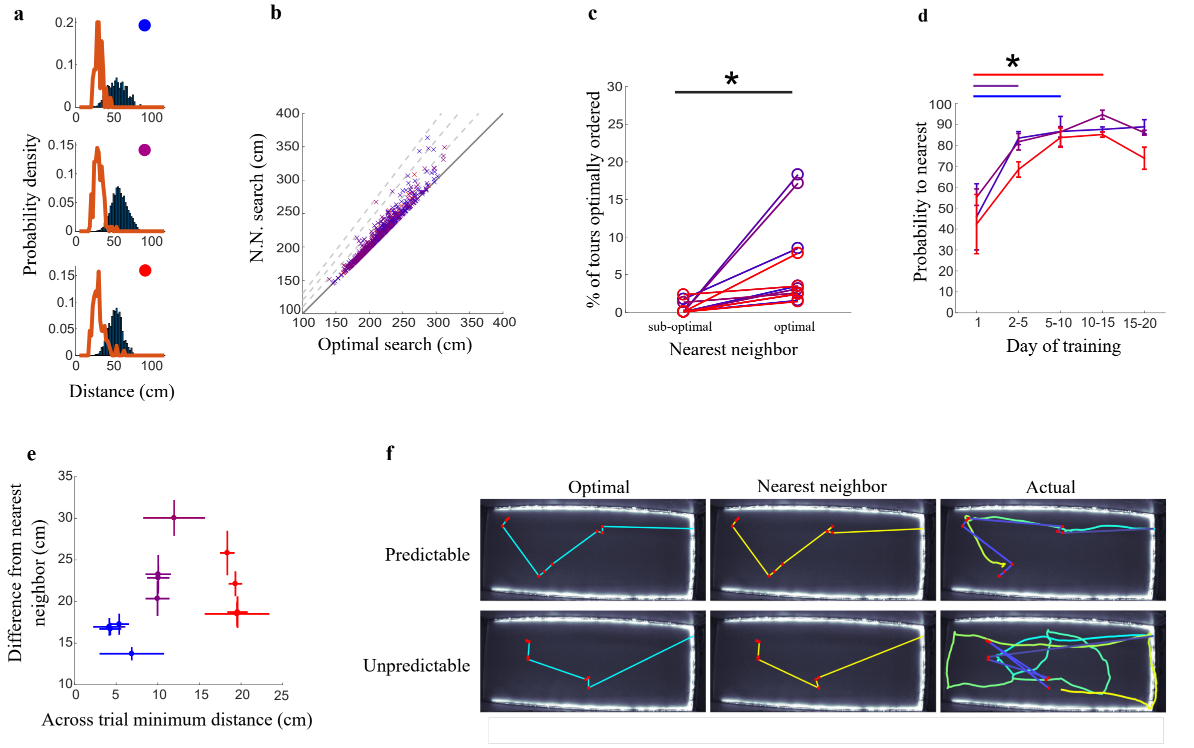


Figure 1.2: Search performance approaches a nearest neighbor search after experience with reward locations

a. Average distance per pellet. Rats acquire pellets in a sequence that is extremely efficient (red lines) compared to a random sampling of all possible sequences (blue bars). Predictability decreases from top to bottom.
b. Performance of a nearest neighbor strategy on all distributions tested in this study when compared to the optimal path length. Dashed lines represent 10, 20, and 30% above optimal.
c. Animal performance on trials in which a nearest neighbor search is optimal vs. trials in which a nearest neighbor search is sub-optimal.
d. The probability that rats in each predictability group acquire the nearest pellet during search increases during training for all groups.
e. Scatter plot showing the relation between predictability of distribution (x axis) and difference between animal acquisition sequence and nearest neighbor sequence (y axis) for all 12 animals.
f. Example of optimal and nearest neighbor pellet acquisition sequences, and the actual sequences and trajectories taken by animals. For the right panels, color shifts from cyan to yellow as the animal's trajectory progresses and from dark to light blue as the pellet acquisition sequence progresses.

Predictable environments enable enhancement of search routes

In our task, which involves probabilistic presence of pellets, this nearest neighbor search can be implemented through two different strategies: in a sensory-guided strategy animals use cues (odor or vision) to navigate towards the nearest detected target; in a memory-guided strategy animals use prior information to navigate towards the nearest, most likely locations of pellets. We next investigated which of the two alternative strategies might guide a nearest neighbor search within each level of uncertainty. Over training, animals across all predictability levels significantly increased their probability to travel to the nearest pellet during search (Figure 1.2d). However, the number of days of training taken for this to occur was dependent upon the predictability of the pellet distribution (Figure 1.2d; significant improvement on days 2-10 for highly and moderately predictable conditions, significant improvement not until days 10-15 for unpredictable conditions; $p < 0.05$ compared to day 1; n=4 for all groups). We found that animals searching in highly predictable environments were effective at enhancing the efficiency of their search across long distances (>40 cm) and learned to do this relatively early in training (days 5-10). Those in moderately predictable environments also learned to increase the efficiency of their search tours but required more training to do so (days 10-15), while those searching in unpredictable environments did not significantly increase the efficiency of their tours (Figure 1.3a,b). As the unpredictable nature, or "surprise value" of the environment increased, the ability of animals to increase the efficiency of their search tours decreased (Figure 1.3c ; R= -0.72 ; $p < 0.008$; n = 12). These results suggest that based upon the predictability of the environment rats employ two different strategies to find the next nearest pellet – one in which tours can be efficiently narrowed towards straight line paths and another in which paths between rewards are necessarily circuitous (see Figure 1.1h, lower panel for example tours after training).

In addition to supporting better-ordered search routes (Figure 1.2d-f) and efficient paths to the nearest target from farther away (Figure 1.3a-c), predictable distributions also enabled rats to enhance the speed of their travel between rewards. During training, the speed of the trajectories taken between pellets increased the most quickly for animals operating in the most predictable environments, though all animals eventually learned to decrease time between rewards by increasing speed (Figure 1.3d). Time spent pausing (speed < 1cm per second) and number of pauses per second did not significantly change with training (Figure 1.3e-f), suggesting consistent motivation to perform the task across all animals.

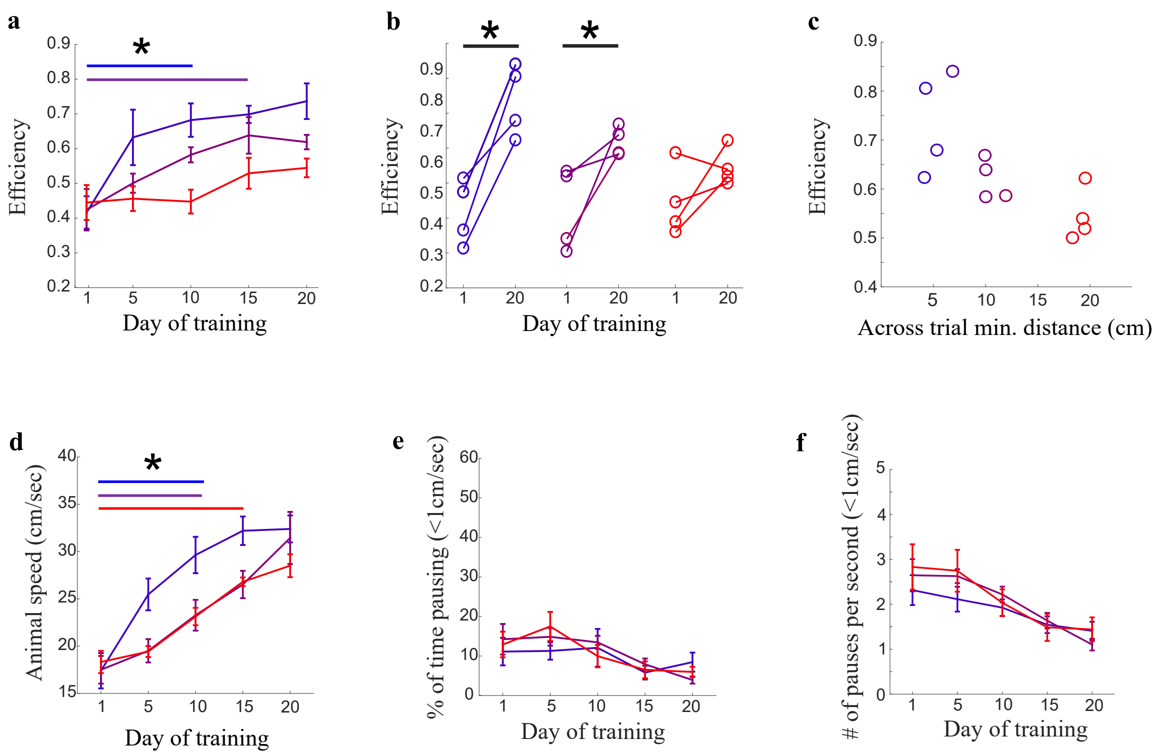


Figure 1.3: Predictability supports increased route efficiency.

a. Animals searching in predictable environments increase efficiency with training (see methods for efficiency metric). Efficiency was assessed on day 1 and then on blocks of 5 days until day 20.
b. Animals in both predictable groups significantly increased the efficiency of their search routes on the last block of training when compared to the first day.
c. Efficiency of search routes measured on the last block of training (days 15-20) show a strong negative correlation to the unpredictability of the foraging environment, here measured as the cross trial minimum pellet distance (see methods).
d. All animals increase speed during training. Average speed was taken without including pauses.
e. Animals spend a small amount of time pausing during the task and this does not significantly change with training.
f. The number of pauses per route as a function of training.

Analyzing shifting weightings between sensory- and memory-dominated strategies

We next sought to more precisely quantify the role of sensory information and memory in the navigation strategies used by animals under varying levels of uncertainty. To perform this analysis we simulated animal behavior by developing an agent that searched through foraging space using multiple free parameters related to exploratory and exploitative search characteristics (Elazary & Itti, 2010; McNamara et al., 2006). These parameters include the length of memory for the prior, the distance over which sensory signals from the pellets are detected, and the relative weighting of sensory and memory terms. We allowed these parameters to vary on a multidimensional grid and analyzed goodness of fit to actual animal performance as the correlation between trial-by-trial performance of the simulated searcher and the animal (Figure 1.5 and see methods). As expected, searches with long-range, noiseless sensory information lead to a perfect nearest neighbor search and do not correlate well with animal behavior (Figure 1.5b) since rats do not have access to perfect information and need to use local sensory information or learned locations to navigate (see Figure 1.4 for an examination of possible sensory cues used for this task). Similarly, searches with only a memory term also do not correlate well with actual behavior (Figure 1.5b). Consistent with animals under different levels of uncertainty using diverse search strategies, we found that any set of a wide range of parameters applied uniformly to all animals resulted in only moderate correlation with actual behavior (Figure 1.5c). We next allowed parameters to vary individually for each animal. While this approach will trivially result in a better fit due to the increased number of free parameters (Figure 1.5b-c ; $p < 0.01$; n= 12), we used the values of parameters obtained for these individual fits to examine the contribution of sensory and memory input to the simulated search that best matched each animal's performance. When varying the length of memory used by the searcher we found that simulated searches across the most predictable distributions benefited from increased memory with an increase in correlation to actual animal performance when the simulated searcher had access to cumulative memory of previous searches (predictable, single trial memory: R = 0.12 +/- 0.05 ; cumulative memory R = 0.66 +/- 0.03 ; $p<0.05$; n = 4). Searches across moderately predictable and unpredictable distributions did not show a significant increase in correlation with animal behavior with increased memory (Figure 1.5d). Consistent with these results, the impact of shuffling prior distributions on agent performance was directly related to the predictability of the data set (Figure 1.5e). To quantify the impact of sensory input on these searches we combined the weighting given to sensory input with the distance from which each agent could detect a target to create a measure of sensory acuity for each simulated agent (see methods). This measure was well correlated with increasing relative entropy of the training set, suggesting that animals increased sensory acuity under uncertainty (Figure 1.5f, left panel ; R = 0.8469 ; $p = 0.005$). We also used the length of memory for the best match to animal behavior to create a metric for long-term memory usage (see methods). We found a significant inverse correlation between relative entropy and long-term memory usage (Figure 1.5f, right panel ; R = -0.7252 ; $p = 0.0076$), suggesting that as the training set became more predictable animals relied more on long-term memory. Our results are consistent with a Bayesian search where searchers adaptively shift the weightings given to various locations (and thus, their likelihood to travel to these locations) based on their relative weightings of sensory and memory terms. For example, a searcher may shift the weighting of a given location based on being rewarded their many times in the past (exploitative, memory-guided strategy) or it may shift the weighting based on sensing cues emanating from a given location (exploratory, sensory-guided strategy).

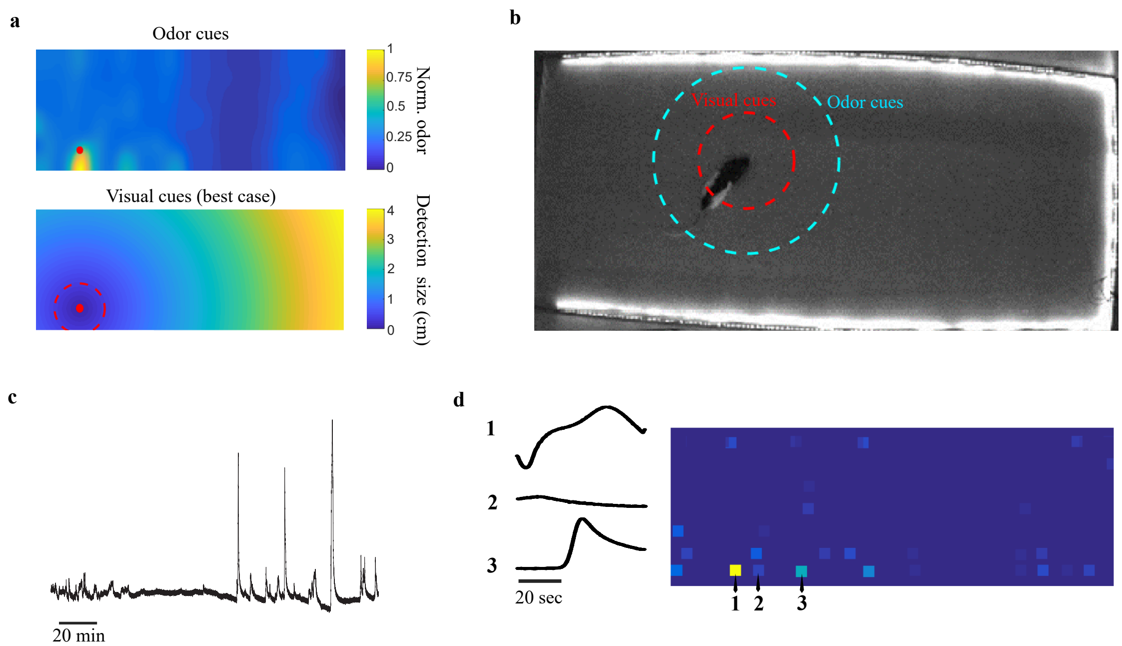


Figure 1.4: Sensory cues are local.

a. **Top:** Experimentally determined spread of odor in the foraging arena (see methods). **Bottom:** Calculated size of a pellet necessary for it to be visible for a foraging rat under bright, broad-spectrum lighting conditions with high contrast, based on reported values for rat visual acuity. The dashed red line indicates the actual size of the pellets used (and thus the distance for detection under ideal conditions). All experiments in the current study were done under dim red light using pellets matched in color to the arena floor, further limiting the range for visual detection.
b. Estimated best-case pellet detection distances for olfactory (cyan) and visual (red) sensory cues. Due to both the dim, red lighting conditions and the lightly odorized pellets actual detection distances are likely to be much smaller.
c. The entire time course of odor for one mapping experiment (approximately 180 minutes) used to establish the distribution in panel a. As the sensor is moved closer to the source (later in the experiment) odor fluctuations become much larger.
d. A grid of mean odor intensity values that were sampled during the experiment and convolved with a gaussian function to create the estimated odor density function in panel a. Odor sensor activation over time from the indicated locations (1,2 and 3) is shown to the left of the grid.

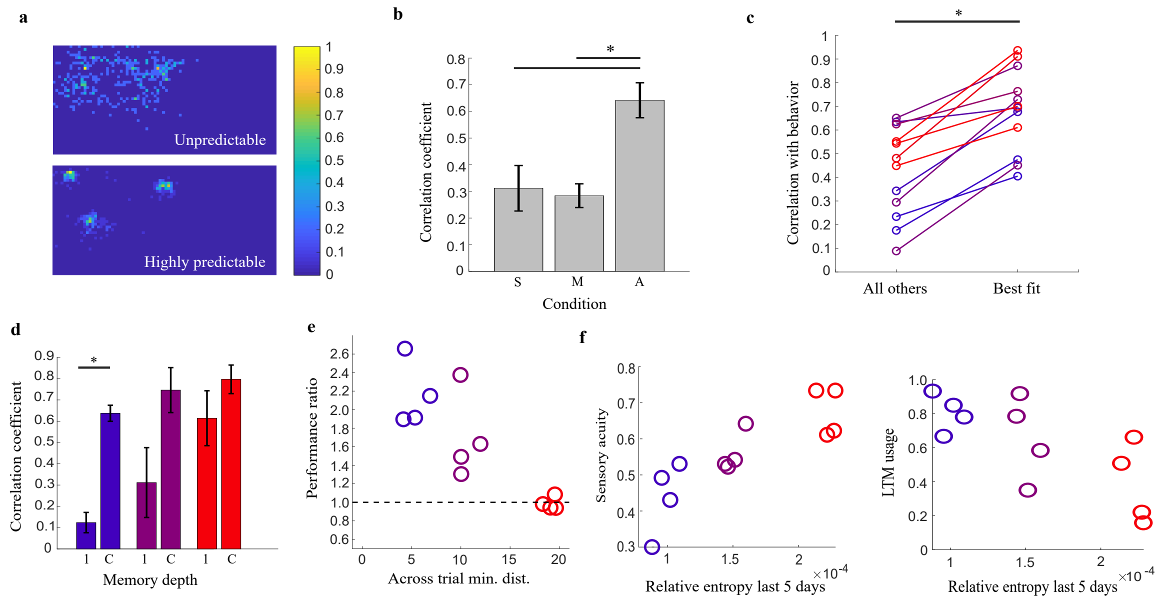


Figure 1.5: Modeling behavior as a Bayesian search with adaptive sensory acuity and memory depth explains performance under uncertainty.

a. Examples of prior distributions accumulated over all trials for one predictable and one unpredictable set of pellet locations.
b. Correlation to animal performance of models with parameters emphasizing sensory (S) or memory (M) guidance or an adaptive model (A) individually fit to each animal.
c. Correlation of agent's search performance with animal behavior when using parameters fit to other animals (All others) or the best fit to that specific animal (Best fit). The best fit is significantly better than the fits from other animals ($p = 0.0043$, $n = 12$).
d. Correlation between animal behavior and a Bayesian search with either single trial memory (1) or best performance with cumulative memory (C).
e. Performance ratio (Path length with priors from different distributions / Path length with correct prior) for all animals plotted as a function of the across trial minimum distance for the distributions presented to each animal (significant correlation: $R = -0.85$, $p = 0.0004$). A higher value for the performance ratio indicates longer path length with a shuffled prior. Agents searching with unpredictable distributions (red) show identical performance regardless of the prior used.
f. **(left)** Sensory acuity based on the best fit search parameters vs. relative entropy based on the distributions that animals have experienced. **(right)** Long-term memory usage vs. relative entropy of pellet distributions encountered.

1.4 DISCUSSION

Animals make use of appropriate cognitive strategies and behaviors to solve the many problems they are faced with during self-guided behaviors such as foraging (Marewski & Link, 2014). It is known that when animals are introduced to new environments with multiple food locations they may continually explore and sample the different options, or they may exploit a single, most profitable option (Krebs, 1978). However, it is not fully understood how animals balance exploratory behaviors against exploitative behaviors (Gupta et al., 2006). Our study revealed that rodents make use of their prior knowledge of the predictability of an environment to determine the extent that they rely on sensory cues during their foraging bouts. Our results are consistent with a strategy that increases sensory acuity and reduces memory load in direct relation to the level of uncertainty in an environment (Figure 1.6). This increased reliance on sensory input allows animals searching across unpredictable environments to employ an effective nearest neighbor strategy with nearly the same efficacy as animals that are operating in highly predictable environments, although due to the short-range nature of sensory cues a sensory-guided strategy fails at long distances and animals are unable to increase the efficiency of foraging trajectories over these distances (Figure 1.3). Conversely, animals operating in predictable environments reduce their reliance on sensory input in favor of stereotyped and efficient searches based on long-term memory, which allows them to enhance search tours over long distances. In short, in a sensory-dominated strategy animals approach the nearest sensed pellet, while in a memory-dominated strategy animals approach the nearest remembered location, enabling more efficient, planned routes to emerge. This result is consistent with the finding that humans integrate information from different sensory modalities and dynamically give greater weight to the modality that provides the stronger, most well-defined estimate (Ernst

& Banks, 2002). Taken together, these results suggest that animals assess the predictability of an environment to select appropriate strategies to allocate cognitive resources between sensory processing and memory while solving complex natural problems.

While it is difficult for animals to rapidly learn efficient paths for collecting rewards in the unpredictable environment, optimal paths in this environment are not more complex than those in predictable environments, as shown in Figure 1.1d. Indeed, animals in unpredictable environments do optimize their foraging behavior after many sessions, achieving a roughly equal ability to perform a nearest-neighbor solution to the task (Figure 1.2d). They may learn a general understanding of where pellets have never been found (such as along the boundaries of the arena) and may focus their search to the center of the arena in order to maximize getting close enough to pellets to then use sensory guidance to approach the reward locations (examples in Figure 1.1b,h). This suggests that while animals have a diminished, imperfect ability to rapidly learn efficient paths in unpredictable environments they are still capable of improving their foraging strategy, perhaps through a combination of coarse predictions and enhanced sensory guidance.

The differential weighting of sensory cues, specifically odor cues, is expected when the turbulent nature of odor plumes in natural environments is taken into account. Odor-guided searches are notoriously difficult due to the sparse and intermittent nature of odor plumes (Vickers, 2000). The ability of rodents to form internal representations of their environment could allow them to apply learned spatial information to dynamic environments, creating a map that would act to lessen the cognitive load required to use the complex sensory cues in odor plumes and greatly increase the effectiveness of odor-guided searches. So it follows that rodents would prefer to use a strategy that relies less on olfactory cues when instead they could navigate using the cognitive map of their familiar environment. This is in line with our results suggesting that under unpredictable conditions rats do not efficiently navigate to the next closest pellet when it is more than 40 cm from their current location (Figure 1.3a). Previous research suggests that 40cm is close to the threshold of rodents' ability to gain a directional benefit from the sparse odor cues emanating from an odor source (Gire et al., 2016; Liu et al., 2020). This difficulty is increased when rats have been trained on unpredictable environments and are unable to construct strong expectations of pellet location. Since there is no underlying structure of where pellets can be found that animals in the unpredictable environment can learn over time, the low weighting given to the memory terms in the Bayesian model reflects animals' discounting of information that will not be as useful as increasing their reliance on sensory cues. Animals then take advantage of the sensory cues emanating from food locations by increasing their weighting, which is in line with the results from our Bayesian model (Figure 1.5). Monitoring the trajectories of the rats allowed us to also determine that rats traveled in much more efficient paths when they were navigating under conditions of high predictability. This suggests that they are able to navigate directly to where pellets are located without having to resort to behaviors indicative of searching for olfactory cues, which typically result in more circuitous search trajectories (Figure 1.1h).

Optimizing travel paths during navigation is a notoriously difficult problem to solve, especially when one considers the complexity of the traveling salesman problem. One must determine the shortest path between multiple locations in order to travel efficiently and conserve the most energy or increase the rate of reward per unit time. This problem is extremely difficult to solve optimally as the complexity of the problem scales unfavorably with the number of targets that must be visited. In our task, this problem is even more complex due to the fact that animals only have probabilistic information about whether food pellets will be present at target locations. While not optimal, simplifying heuristics enable solutions to such complex optimization problems to be reached in relatively short periods of time. Nearest neighbor tours are a common strategy used to solve the traveling salesman problem (Johnson, 1990; Tsai et al., 2004). Under this strategy, the agent simply travels to the next nearest target location until all targets have been visited. While not optimal, this approach is computationally simple, resulting in rapid solutions with time to solve scaling well with task complexity. Our results suggest that animals adopt a nearest neighbor strategy to procure all of the pellets; however, the degree to which the strategy resembles a perfect nearest neighbor strategy depends on the predictability of the environment. Animals trained in a predictable environment select a strategy that highly resembles a nearest neighbor search earlier on in training (Figure 1.2), which allows them to more effectively exploit pellet locations and increase efficiency (Figure 1.3a) and speed (Figure 1.3d) of their routes. In contrast, animals trained in unpredictable environments select a strategy that resembles a nearest neighbor search much later in training (Figure 1.2d). These differential time courses could reflect the time necessary to train the underlying memory or sensory networks in the brain, with sensory training requiring a longer training period.

The novel, fully-automated foraging arena we designed allows for new ways to study the balance between exploration and exploitation. Using an automated, moving pellet dispenser allows for food rewards to be placed in an unlimited number of different locations throughout the foraging arena. This allows us to instantaneously change any location in the arena into a reward location. Instead of being confined to defined locations, such as fixed near a feeder, we are able to create many different distributions of where food can be found, mimicking distributions that might occur in a more naturalistic setting. By combining this automated arena with computer-generated reward distributions we can also scale the difficulty of the task to address specific research questions. This allows us to study more complex behaviors that current experimental paradigms are not equipped to adequately explore. Through computer-aided creation of reward location sequences our new approach also supports direct testing of algorithms that could be used to perform self-guided optimization. This task also integrates extremely well with new advances in automated behavioral tracking (Nath et al., 2019). Finally, the self-guided nature of our task allows for future studies to elucidate neural mechanisms underlying complex behaviors, such as route optimization. Since animals trained on this task are not explicitly shaped or instructed on how to best perform, we are able to study how the brain changes as animals develop solutions to complex, natural problems.

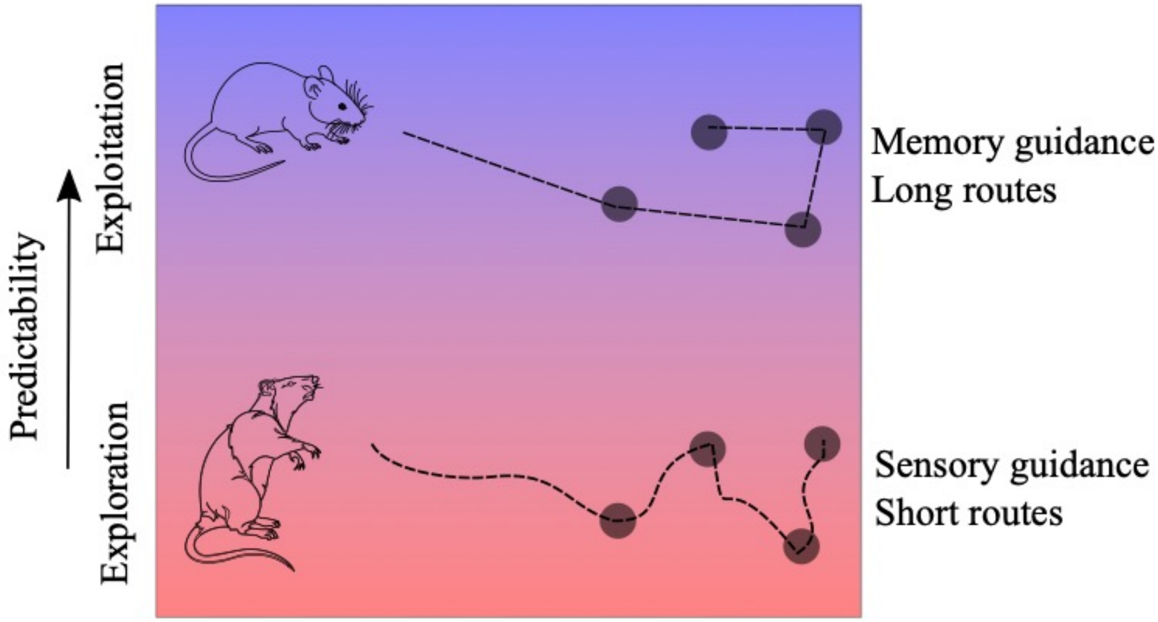


Figure 1.6: Schematic of two strategies selected to solve the probabilistic traveling salesman task.

A schematic of the main results, showing that animals adaptively change the strategies used for a search depending upon the level of uncertainty of the environment, here depicted as a spectrum from red (uncertain) to blue (predictable).

Chapter 2. Impacts of Environmental Complexity & Predictability On Body Poses & Approach Behaviors

2.1 INTRODUCTION

Animals have long been known to exhibit a diverse array of body movements and behavioral motifs when behaving naturally in the wild. Ethologists have noted a variety of movements when it comes to mating behaviors, foraging for food, searching for water sources, play behavior, and general exploration wild (Blanchard et al., 1986; Crabbe, 1999; Fonio et al., 2006; Himmler et al., 2013). However, research suggests that the repertoire of behavioral motifs displayed in natural environments are often distinct from the behaviors displayed in the laboratory (Holmes et al., 2000; Shettleworth, 1989; Troxell-Smith et al., 2016). This leads to a fundamental issue when trying to study behavior and body movements in the laboratory and then translate them to what would occur in natural environments. To this end, we have investigated specific behavioral motifs displayed during a semi-naturalistic foraging task and strive to understand how these vary with complexity of the foraging environment.

Historically, it has been difficult to study fine-grain behavioral pose tracking of animals in the laboratory due to technical limitations, such as camera quality, the need to physically attach markers to behaving animals, and the immense computing power needed to analyze sub-second movements. Additionally, the need to manually score videos to determine when specific behaviors have occurred consumes vast amounts of time and resources and can also be subject to observer bias (Hong et al., 2015; Tuyttens et al., 2014). We are now in a time where the technology underlying tracking has rapidly improved and we are able to achieve more fine grain analysis of behaviors with emerging technologies, such as DeepLabCut (Mathis et al., 2018). DeepLabCut is a software based tool for tracking fine-scale behaviors and movements using markerless pose estimations (Nath et al., 2019). We now have the ability to observe animals performing semi-natural foraging behaviors in the laboratory and track multiple points on their body in order to generate a more complete understanding of how specific movements relate to aspects of our foraging task.

Rodents are known to move their head in ways distinct from their body when navigating, with research suggesting this is most likely to aid in scanning for sensory cues (Choy et al., 2012). Early twentieth century research indicated that rodents performing a spatial navigation task would stereotypically move their heads left and right when arriving choice points on a maze (Tolman, 1948). This behavior, characterized as vicarious trial and error, was understood to derive from animals mentally investigating the possible outcomes of their future choices (Redish, 2016; Schmidt et al., 2013). It was also suggested that vicarious trial and error was a way for animals to attend to environmental stimuli in order to learn what exactly was salient to helping them reach their goal (Dudchenko et al., 2013). In addition to vicarious trial and error, rodents have been known to exhibit similar behaviors when navigating in environments where they must rely on local sensory cues. This behavior, known as casting, is often exhibited when animals are tracking an odor to the source (Cardé & Willis, 2008; Hayes et al., 2002; Khan et al., 2012; Lochmatter & Martinoli, 2009). Due to the turbulent nature of odor plumes (Moore & Atema, 1988; van Breugel et al., 2015; van Breugel & Dickinson, 2014), it is often the case that animals will experience frequent odor detections and losses (Weissburg & Zimmer-Faust, 1994). It is therefore prudent for them to routinely sample the area around their head in order to regain contact with odorants, allowing them to build an understanding of where the odor may be originating from. The sucrose pellets used in the present task that the animals forage for release weak odor signals that may not offer directional benefits at far distances. It is possible that animals can use their memory of where pellets are often found in order to get close to where they might currently be, and then display increases in head movements in order to exactly pinpoint where the pellets are located.

Task complexity has been shown to affect the range of behaviors displayed by animals completing the task (Balcombe, 2006; Juavinett et al., 2018; Winter, 2005). It was therefore prudent for us to investigate how task complexity, modulated by an increasing amount of possible locations needed to travel between, affects the repertoire of behavioral responses seen in our route planning-based foraging paradigm. In the present study we investigate the impacts of environmental predictability and complexity on the magnitude of head movements during foraging, how directly animals are able to approach pellet locations, and how efficient are the trajectories that animals take when navigating to specific pellets in an acquisition sequence.

2.2 MATERIALS & METHODS

Subjects

Twenty-two naïve Long-Evans rats (fourteen male and eight female), initially weighing 250-325g and procured from Charles River Laboratories, were housed individually in Plexiglas cages in a climate-controlled vivarium. The animals were maintained on a 12-hour reverse light/dark cycle (lights off at 7:00am) and all interactions took place during the dark phase between the hours of 9:00am through 6:00pm. Rats had *ad libitum* access to water and after a weeklong habituation to the vivarium were food-restricted to 85% of their free-feeding body weight. All experimental procedures were approved by the Institutional Animal Care and Use Committee at the University of Washington.

Apparatus

The foraging arena was a large, fully enclosed open-field measuring 2.5m in length, 1m in width, and 1m in height (Figure 2.1a-b). The frame of the arena was constructed from T-slotted aluminum railings (McMaster-Carr). The sides of the arena were constructed from 1.27cm thick clear acrylic, while the ceiling was 0.635cm in thickness. The floor was a sheet of 0.0635cm thick opaque white acrylic. The ends of the arena were made from a wire mesh to allow for air to circulate throughout. A nest area where the animals would remain during the intertrial interval was attached to one end of the arena. The nest area was constructed from 1.27cm thick clear acrylic. Two synchronized cameras (The Imaging Source; DMK 23UP1300; frame rate 120 per second) were used to track the movement of the animals. An automated, custom-made pellet dispenser was used to bait the arena during the intertrial interval with 45mg sucrose pellets (Bio-Serv). An Arduino Uno controlled the movement of the motors running the pellet dispenser, allowing movement in the x- and y- coordinate plane.

Foraging Task

Before testing, all animals were habituated to the vivarium for 1 week. Animals then spent 2 days habituating to the nest area attached to the foraging arena for ~15 minutes at a time. In order to motivate animals to return to the nest area, sucrose pellets were placed in the nest area every 2 minutes when a 1 second, 1000Hz tone was played. They were then granted access to the test arena and were given 2-3 days to habituate to it. Animals were considered to have reached criterion for experiment initiation when they were able to make 3 transitions between the nest area and foraging arena within 30 minutes.

Animals were placed into the nest area at the beginning of each testing session. Rats completed 1 session a day that lasted for 30 minutes at a time, resulting in 6 trials per session on average. Before each trial, the automated pellet dispenser baited the arena with plain sucrose pellets, or for a single experiment, banana-flavored pellets. These pellets were organized into 3 clusters for simple distributions and 6 clusters for complex distributions. Each cluster in the simple distribution consisted of 3 pellets each, while clusters in the complex distribution consisted of 2 pellets each. During foraging periods the dispenser was automatically lifted out of the arena so that the animals could not interact with it. Animals were then assigned to forage within environments of high or low food location predictability. Animals trained on the environment with high food location predictability (simple: $n = 8$; complex = $n = 6$) were overtrained on a single distribution of pellet locations that stayed consistent across trials and sessions. Animals foraging in the environment with low food location predictability (simple: $n = 4$; complex: $n = 3$) were trained on unpredictable pellet distributions that changed across trials. All rats were given a maximum of 30 minutes to eat all of the sucrose pellets during the session. The entire testing period lasted for 11-12 days with approximately 5 sessions per week.

Experimental Design and Statistical Analysis.

No explicit power analysis was conducted in order to determine sample sizes. However, the number of animals used is consistent with experiments in the current literature. All analyses were conducted using MATLAB (MathWorks). A custom LabView (National Instruments) program was used to collect the behavioral data. Significant differences between groups were assessed with either the Mann-Whitney U test, or a multi-factor ANOVA with Tukey's correction for multiple comparisons.

Predictability of pellet distributions was quantified using an across trial minimum distance metric, which, for each pellet in a given distribution reports the minimum distance from that pellet to all pellets in the immediately previous distribution.

For establishing optimal pellet acquisition sequences for each distribution we used a genetic algorithm developed by Joseph Kirk: Fixed Start Open Traveling Salesman Problem - Genetic Algorithm (https://www.mathworks.com/matlabcentral/fileexchange/21198-fixed-start-open-traveling-salesman-problem-genetic-algorithm). Briefly, this algorithm starts from a population of randomly generated paths that start at the entrance to the arena and travel to each pellet once. It then uses an iterative process wherein in each "generation" of solutions the fitness of every path in the population is evaluated; the objective function for fitness in this case is minimization of path length. The more fit (shorter) paths are selected, and each path's sequence of pellet locations is modified (recombined with other paths or randomly changed, or "mutated") to form a new generation. The new generation of candidate paths is then used in the next iteration of the algorithm. The algorithm can be terminated when either a maximum number of generations has happened or the path length reaches a small enough value.

Animal positions were tracked using custom DeepLabCut software (Mathis et al., 2018; Nath et al., 2019).

Efficiency of foraging paths was calculated as $fe = lo/la$, where *lo* is the optimal path length, *la* is the animal's path length, and *fe* is foraging efficiency.

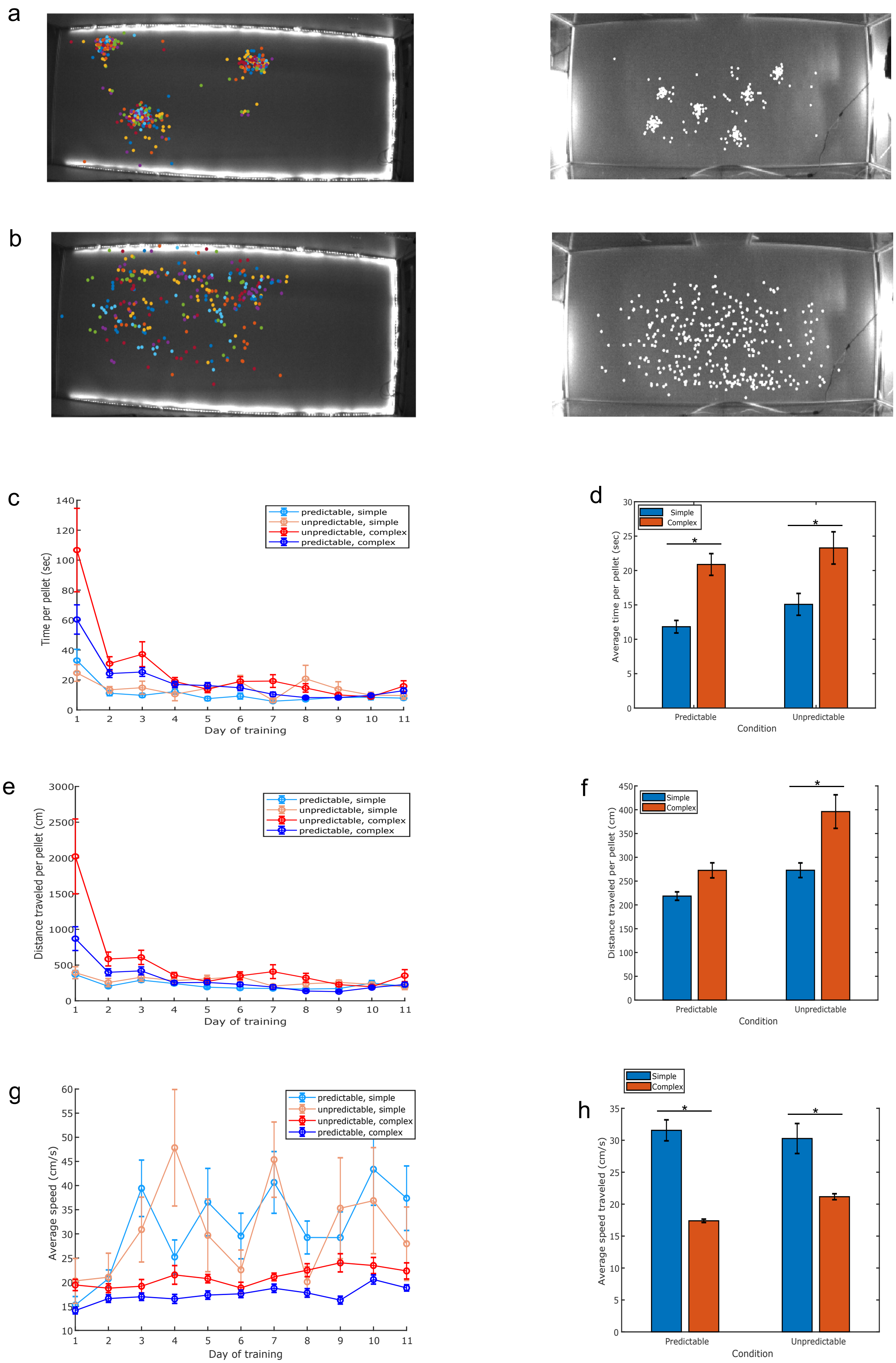
Head distance was calculated as the difference between the distance the head moved per frame and the distance the body moved per frame. Head variation is the coefficient of variation of the aforementioned head distances. Angles of approach are calculated from the vector between the animal's current position, the next target pellet, and the animal's position on the successive frame.

2.3 RESULTS

Investigating the impact of environmental complexity on search performance

In order to test the effects of task complexity on probabilistic foraging, animals were trained to forage for sucrose pellets in a large, open field arena. Animals were trained on either simple or complex pellet distributions, with simple distributions containing ~3 patches of pellets to visit and complex distributions containing ~6 patches to visit (Figure 2.1a-b). In addition to varying patch complexities, animals foraged in either predictable or unpredictable pellet distributions. Predictable distributions included pellets that were located in the same locations trial after trial, while unpredictable distributions had pellets randomly placed on every trial (Figure 2.1a-b).

All groups of animals reduced the amount of time needed to complete the task over training (Figure 2.1c). Animals foraging in complex distributions took significantly longer to procure all pellets under both predictable ($p < 0.01$) and unpredictable ($p < 0.01$) conditions (Figure 2.1d). All animals also reduced the distance they traveled to procure all of the pellets over the course of training (Figure 2.1e). Animals foraging in complex distributions traveled significantly farther than animals in simple distributions to procure all of the pellets when foraging in unpredictable conditions ($p = 0.022$), but not when foraging in predictable conditions ($p = 0.58$) (Figure 2.1f). Additionally, animals foraging in complex distributions traveled significantly slower during the task compared to animals trained on simple distributions (Figure 2.1g). This was true for animals trained on both predictable ($p < 0.01$) and unpredictable ($p < 0.01$) pellet distributions. These results suggest that increasing the number of foraging patch locations from 3 to 6 significantly increased the difficulty of the task, and animals were still able to improve their performance over time.



a
b
c
Time per pellet (sec)
Day of training
predictable, simple
unpredictable, simple
unpredictable, complex
predictable, complex
d
Average time per pellet (sec)
Simple
Complex
Predictable
Unpredictable
Condition
e
Distance traveled per pellet (cm)
Day of training
predictable, simple
unpredictable, simple
unpredictable, complex
predictable, complex
f
Distance traveled per pellet (cm)
Simple
Complex
Predictable
Unpredictable
Condition
g
Average speed (cm/s)
Day of training
predictable, simple
unpredictable, simple
unpredictable, complex
predictable, complex
h
Average speed traveled (cm/s)
Simple
Complex
Predictable
Unpredictable
Condition

Figure 2.1: Increased environmental complexity impairs search

a. Rats forage for pellets in a predictable distribution of pellet placements. Representative pellet placement showing pellet placements collapsed over time at the end of training for a simple distribution (left) and for a difficult distribution (right).
b. Rats forage for pellets in an unpredictable distribution of pellet placements. Representative pellet placement showing pellet placements collapsed over time at the end of training for a simple distribution (left) and for a difficult distribution (right).
c. Average amount of time taken by animals to procure all pellets in a trial. Animals trained on simple, predictable distributions are shown in light blue. Animals trained on complex, predictable distributions are shown in dark blue. Animals trained on simple, unpredictable distributions are shown in orange. Animals trained on complex, unpredictable distributions are shown in dark red. Error bars represent the standard error of the mean.
d. Comparing average time to complete the task for animals training in simple and complex pellet distributions. Asterisks represent $p < 0.01$, Mann-Whitney U-test.
e. Average distance traveled by animals to procure all pellets in a trial. Animals trained on simple, predictable distributions are shown in light blue. Animals trained on complex, predictable distributions are shown in dark blue. Animals trained on simple, unpredictable distributions are shown in orange. Animals trained on complex, unpredictable distributions are shown in dark red. Error bars represent the standard error of the mean.
f. Comparing average distance traveled during a trial for animals training in simple and complex pellet distributions. Asterisks represent $p < 0.01$, Mann-Whitney U-test.
g. Average speed traveled by animals to procure all pellets in a trial. Animals trained on simple, predictable distributions are shown in light blue. Animals trained on complex, predictable distributions are shown in dark blue. Animals trained on simple, unpredictable distributions are shown in orange. Animals trained on complex, unpredictable distributions are shown in dark red. Error bars represent the standard error of the mean.
h. Comparing average speeds during a trial for animals training in simple and complex pellet distributions. Asterisks represent $p < 0.01$, Mann-Whitney U-test.

Environmental complexity and predictability modulate head movements

We next wished to characterize how animals might move their heads during our probabilistic foraging task, especially as the environment becomes more complex. Using DeepLabCut we were able to simultaneously track the coordinates of both the animals' heads and bodies during our foraging task (Mathis et al., 2018; Nath et al., 2019). We were then able to determine whether animals' heads traveled further on a frame-by-frame basis compared to their bodies, which could be suggestive of head sweeps or casting. All animals displayed increased head movements compared to their body movements, suggesting they all engaged in casting behaviors (Figure 2.2a-b). Animals trained on both predictable ($p < 0.001$) and unpredictable ($p < 0.001$) pellet distributions exhibited significantly greater head movements when navigating in complex pellet distributions compared to simple distributions (Figure 2.2c-d). Animals in simple distributions showed no differences between predictable and unpredictable distributions ($p = 0.81$). Animals in complex unpredictable distributions displayed significantly greater head movements than animals in complex predictable distributions ($p = 0.017$).

We next wanted to determine if there were differences in the variation of the magnitude of head movements based on environmental complexity. By calculating the coefficient of variation (σ/μ), we found that animals trained on both simple predictable ($p < 0.001$) and unpredictable ($p < 0.001$) pellet distributions exhibited significantly greater variation of their head movements compared to animals trained on complex predictable and unpredictable distributions, respectively (Figure 2.2e-f). Additionally, animals trained on simple predictable distributions exhibited significantly less variation than animals trained on simple unpredictable distributions ($p = 0.020$), while animals trained on complex predictable distributions exhibited significantly greater variation compared to animals trained on complex unpredictable distributions (*p = 0.005*). These results suggest that animals trained on complex pellet distributions exhibit significantly larger head movements, but also display significantly reduced variation in the magnitude of these head movements.

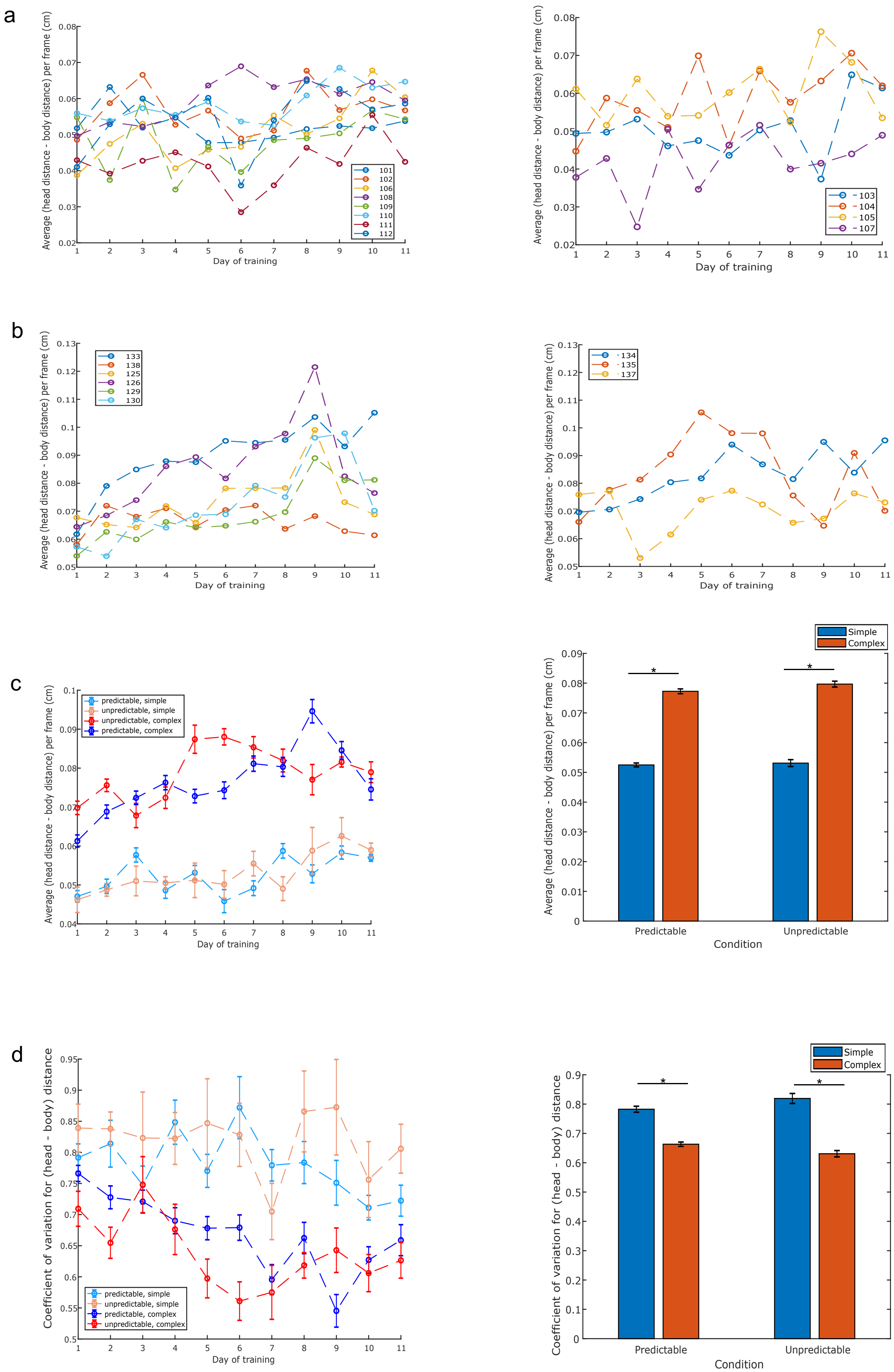

a
Average (head distance - body distance) per frame (cm)
Day of training
101
102
106
108
109
110
111
112
103
104
105
107
b
133
138
125
126
129
130
134
135
137
c
predictable, simple
unpredictable, simple
unpredictable, complex
predictable, complex
Simple
Complex
Predictable
Unpredictable
Condition
*
d
Coefficient of variation for (head - body) distance
predictable, simple
unpredictable, simple
predictable, complex
unpredictable, complex
Simple
Complex
Predictable
Unpredictable
Condition
*

Figure 2.2: Impact of environmental complexity on head movements during foraging

a. Average difference between the distance the head and the body moves per frame for individual animals trained on the simple predictable (left) and unpredictable (right) pellet distributions
b. Average difference between the distance the head and the body moves per frame for individual animals trained on the complex predictable (left) and unpredictable (right) pellet distributions
c. **Left**: Average difference per day between the distance the head and the body moves per frame for animals trained on simple predictable (light blue), complex predictable (dark blue), simple unpredictable (orange), and complex unpredictable (dark red) pellet distributions. **Right**: Animals trained on both predictable ($p < 0.001$) and unpredictable ($p < 0.001$) pellet distributions exhibited significantly greater head movements when navigating in complex pellet distributions compared to simple distributions. Animals in simple distributions showed no differences between predictable and unpredictable distributions ($p = 0.81$). Animals in complex unpredictable distributions displayed significantly greater head movements than animals in complex predictable distributions ($p = 0.017$).
d. **Left**: Average coefficient of variation per day for the difference in head movements compared to body movements for animals trained on simple predictable (light blue), complex predictable (dark blue), simple unpredictable (orange), and complex unpredictable (dark red) pellet distributions. **Right**: Animals trained on simple predictable pellet distributions exhibited significantly greater variation compared to animals trained on complex predictable distributions ($p < 0.001$). Animals trained on simple unpredictable pellet distributions exhibited significantly greater variation compared to animals trained on complex unpredictable distributions ($p < 0.001$). Animals trained on simple predictable distributions exhibited significantly less variation than animals trained on simple unpredictable distributions ($p = 0.020$). Animals trained on complex predictable distributions exhibited significantly greater variation compared to animals trained on complex unpredictable distributions ($p = 0.005$).

Investigating rate of increase in head movements over training

We next wanted to detail the time course over which these changes in head movements occurred. Using cumulative frequencies we were able to characterize the range of distances that animals' heads moved in excess of their body's movements, providing us with a useful metric of how this range shifts over time. For example, in Figure 2.3a, a cumulative frequency value of 0.6 on day 1 indicates that 60% of the distance values are less than ~0.0425 cm, which increases to ~0.0635 after 10 days of training. Animals trained on predictable pellet distributions (Figure 2.3a,c) display a more linear increase in the magnitude of head movements as training progresses, while animals trained on unpredictable pellet distributions exhibit much more variation in how the magnitude of head movements changes from day to day (Figure 2.3b,d).

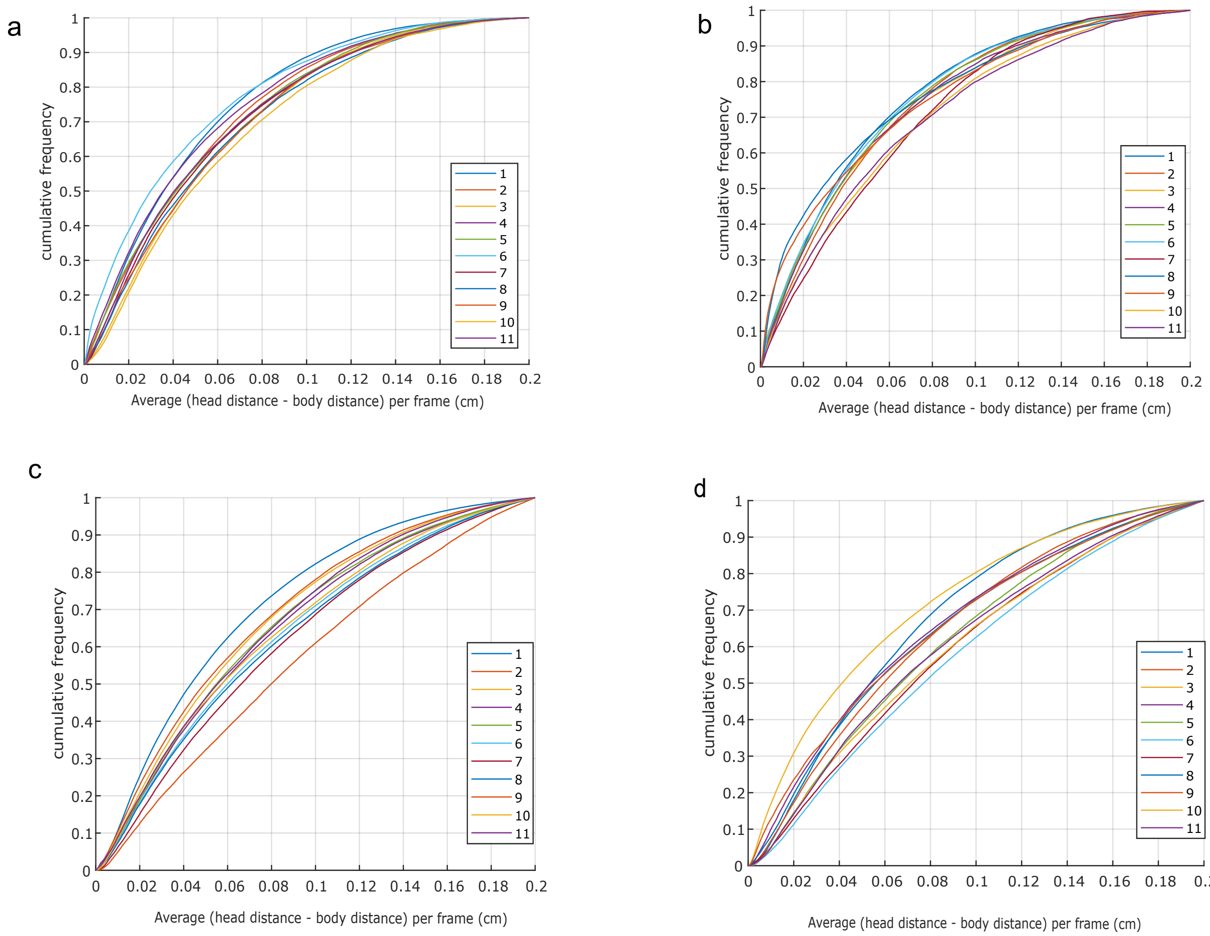


Figure 2.3: Environmental predictability affects rate of increase in performance

a. Cumulative frequency of the difference between head movements and body movements for animals trained on simple predictable pellet distributions over time. Figure legend indicates the day of training.
b. Cumulative frequency of the difference between head movements and body movements for animals trained on simple unpredictable pellet distributions over time. Figure legend indicates the day of training.
c. Cumulative frequency of the difference between head movements and body movements for animals trained on complex predictable pellet distributions over time. Figure legend indicates the day of training.
d. Cumulative frequency of the difference between head movements and body movements for animals trained on complex unpredictable pellet distributions over time. Figure legend indicates the day of training.

Elucidating relationships between head movements and behavioral performance

We next examined the correlations among task performance measures and the magnitude of head movements. Animals trained on simple predictable (r = 0.68, $p < 0.001$), complex predictable (r = 0.95, $p < 0.001$), simple unpredictable (r = 0.48, $p < 0.001$), and complex unpredictable (r = 0.97, $p < 0.001$) pellet distributions all exhibited significant correlations between the amount of time to complete the task and the distance traveled during the task (Figure 2.4a). Additionally, animals trained on simple predictable distributions exhibit significantly weaker correlations than animals trained on complex predictable (z = -11.39, $p < 0.001$), but significantly stronger correlations compared to animals trained on simple unpredictable (z = 2.66, $p = 0.0078$) pellet distributions. Animals trained on complex predictable distributions display significantly weaker correlations compared to animals trained on complex unpredictable pellet distributions (z = -2.58, $p = 0.0099$). Animals trained on simple unpredictable pellet distributions exhibit significantly weaker correlations than animals trained on complex unpredictable pellet distributions (z = -12.51, $p < 0.001$) (Figure 2.4a). The results of these correlations suggest that increasing the complexity of the foraging task increases the correlation of time to complete task and the distance traveled during the task.

Animals trained on simple predictable (r = -0.3683, $p < 0.001$), complex predictable (r = -0.3587, $p < 0.001$), simple unpredictable (r = -0.4252, $p < 0.001$), and complex unpredictable (r = -0.2865, $p < 0.001$) pellet distributions display significant correlations between the amount of time to complete the task and the average speed traveled during the task (Figure 2.4b). Additionally, animals trained on simple predictable distributions do not exhibit statistically different correlations compared to animals trained on complex predictable (z = -0.13, $p = 0.8966$) or simple unpredictable (z = 0.58, $p = 0.5552$) pellet distributions. Animals trained on complex predictable distributions do not exhibit statistically different correlations compared to animals trained on complex unpredictable distributions (z = -0.8, $p = 0.4237$). Animals trained on simple unpredictable pellet distributions do not exhibit statistically different pellet distributions from animals trained on complex unpredictable distributions (z = -1.27, $p = 0.2041$) (Figure 2.4b). This suggests that task complexity fails to affect the significant relationships between the time to complete the task and the average speed traveled.

Animals trained on complex predictable (r = -0.1654, $p = 0.0043$) and simple unpredictable (r = 0.1908, $p = 0.0411$) pellet distributions exhibited significant correlations between the distance traveled during the task and the average speed during the task (Figure 2.4c). Animals trained on simple predictable (r = 0.1213, $p = 0.0646$) and complex unpredictable (r = -0.1351, $p = 0.099$) pellet distributions do not exhibit significant correlations. Additionally, animals trained on simple predictable pellet distributions exhibited significantly different correlations compared to animals trained on complex predictable (z = 3.28, $p = 0.001$) but not compared to animals trained on simple unpredictable (z = -0.62, $p = 0.5353$) pellet distributions. Animals trained on complex predictable pellet distributions did not exhibit statistically different correlations compared to animals trained on complex unpredictable distributions (z = -0.3, $p = 0.7642$). Animals trained on simple unpredictable pellet distributions exhibited significantly different correlations compared to animals trained on complex unpredictable distributions (z = 2.62, $p = 0.0088$) (Figure 2.4c). Taken together, this suggests that task complexity shifts the relationship between the distance traveled and the average speed, with animals foraging in complex distributions moving slower as they travel longer distances.

Animals trained on simple predictable (r = -0.1591, $p = 0.0150$), complex predictable (r = -0.3786, $p < 0.001$), simple unpredictable (r = -0.4071, $p < 0.001$), and complex unpredictable (r

= -0.3358, $p < 0.001$) pellet distributions exhibit significant correlations between the amount of time to complete the task and the difference between head movements and body movements (Figure 2.4d). Additionally, animals trained on simple predictable distributions exhibit significantly weaker correlations compared to animals trained on complex predictable (z = 2.7, $p = 0.0069$) and simple unpredictable (z = 2.36, $p = 0.0183$) pellet distributions. Animals trained on complex predictable distributions do not exhibit statistically different correlations from animals trained on complex unpredictable distributions (z = -0.49, $p = 0.6241$). Animals trained on simple unpredictable pellet distributions do not exhibit significant differences from animals trained on complex unpredictable distributions (z = -0.66, $p = 0.5093$) (Figure 2.4d).

Animals trained on complex predictable (r = -0.3779, $p < 0.001$) and complex unpredictable (r = -0.2583, $p = 0.0014$) pellet distributions exhibit significant correlations between the distance traveled to complete the task and the difference between head movements and body movements (Figure 2.4e). Animals trained on simple predictable (r = 0.1047, $p = 0.1111$) and simple unpredictable (r = -0.1355, $p = 0.1487$) do not exhibit significant correlations. Additionally, animals trained on simple predictable exhibit significantly different correlations from animals trained on complex predictable (z = 5.71, $p < 0.001$) and simple unpredictable (z = 2.1, $p = 0.0357$) pellet distributions. Animals trained on complex predictable distributions did not exhibit statistically different correlations compared to animals trained on complex unpredictable distributions (z = -1.32, $p = 0.1868$). Animals trained on simple unpredictable distributions do not exhibit statistically different correlations from animals trained on complex unpredictable distributions (z = 1.02, $p = 0.3077$) (Figure 2.4e).

Animals trained on simple predictable (r = 0.1492, $p = 0.0227$), complex predictable (r = 0.2674, $p < 0.001$), simple unpredictable (r = 0.3855, $p < 0.001$), and complex unpredictable (r =

0.3175, $p < 0.001$) pellet distributions exhibit significant correlations between the average speed traveled and the difference between head movements and body movements (Figure 2.4f). Additionally, animals trained on simple predictable distributions do not exhibit statistically different correlations compared to animals trained on complex predictable distributions (z = -1.41, $p = 0.1585$), but they do exhibit significant differences from animals trained on simple unpredictable pellet distributions (z = -2.22, $p = 0.0264$). Animals trained on complex predictable distributions do not exhibit statistically different correlations compared to animals in complex unpredictable distributions (z = -0.54, $p = 0.5892$). Animals trained on simple unpredictable distributions do not exhibit significant differences from animals trained on complex unpredictable distributions (z = 0.62, $p = 0.5353$) (Figure 2.4f). Taken together, this suggests that, for animals foraging in predictable environments, increasing the complexity of the task leads to stronger correlations between the magnitude of head movements and amount of time and distance that animals travel to complete the task.

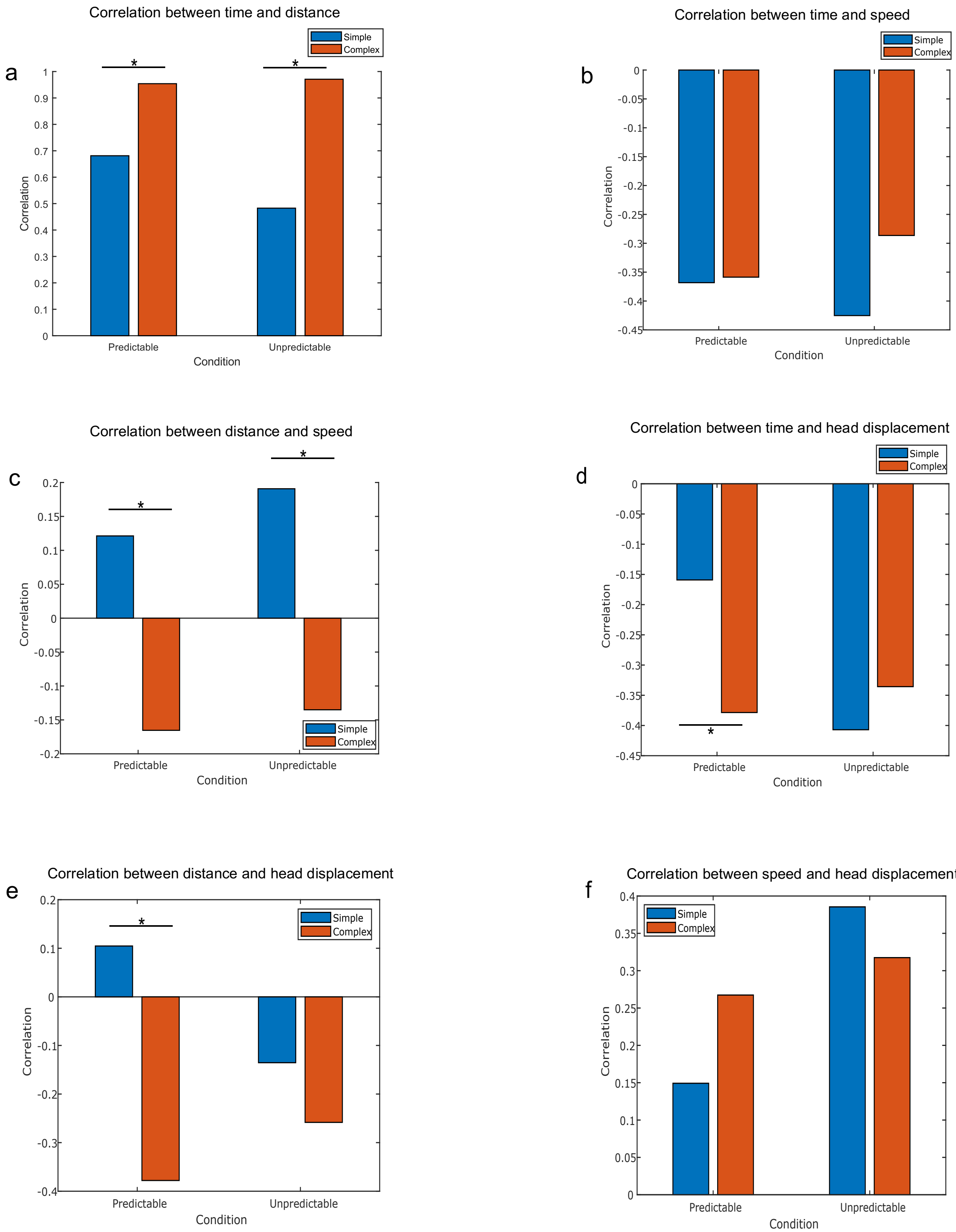

a
Correlation between time and distance
Simple
Complex
*
*
Correlation
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Predictable
Unpredictable
Condition
b
Correlation between time and speed
Simple
Complex
Correlation
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3
-0.35
-0.4
-0.45
Predictable
Unpredictable
Condition
c
Correlation between distance and speed
*
*
Correlation
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
Simple
Complex
Predictable
Unpredictable
Condition
d
Correlation between time and head displacement
Simple
Complex
Correlation
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3
-0.35
-0.4
-0.45
*
Predictable
Unpredictable
Condition
e
Correlation between distance and head displacement
Simple
Complex
*
Correlation
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
Predictable
Unpredictable
Condition
f
Correlation between speed and head displacement
Simple
Complex
Correlation
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
Predictable
Unpredictable
Condition

Figure 2.4: Influence of task complexity on correlations between behavioral measures of task performance

a. Correlation between the time to complete the foraging task and the distance traveled for animals trained on simple (blue) and complex (red) pellet distributions. Animals are separated by predictability. Asterisks indicate significant differences between groups, Fisher r-to-z transformation, $p < 0.05$.
b. Correlation between the time to complete the foraging task and the average speed traveled for animals trained on simple (blue) and complex (red) pellet distributions. Animals are separated by predictability. Asterisks indicate significant differences between groups, Fisher r-to-z transformation, $p < 0.05$.
c. Correlation between the distance traveled during the foraging task and the average speed for animals trained on simple (blue) and complex (red) pellet distributions. Animals are separated by predictability. Asterisks indicate significant differences between groups, Fisher r-to-z transformation, $p < 0.05$.
d. Correlation between the time to complete the foraging task and the average head displacement for animals trained on simple (blue) and complex (red) pellet distributions. Animals are separated by predictability. Asterisks indicate significant differences between groups, Fisher r-to-z transformation, $p < 0.05$.
e. Correlation between the distance traveled during the foraging task and the average head displacement for animals trained on simple (blue) and complex (red) pellet distributions. Animals are separated by predictability. Asterisks indicate significant differences between groups, Fisher r-to-z transformation, $p < 0.05$.
f. Correlation between the average speed during the foraging task and the average head displacement for animals trained on simple (blue) and complex (red) pellet distributions. Animals are separated by predictability. Asterisks indicate significant differences between groups, Fisher r-to-z transformation, $p < 0.05$.

Environmental complexity and predictability affect ability to navigate directly to pellets

In order to fully characterize how animals were navigating towards pellets, the angle of approach was also quantified. We focused our analysis on the 100 cm of foraging that immediately preceded a pellet acquisition and that did not include eating other pellets in order to limit interactions among multiple pellets. Animals trained on predictable pellet distributions displayed significantly narrower angles of approach to pellets (23.81° ± 0.58) compared to animals trained on unpredictable pellet distributions (28.00° ± 0.74) (2-way ANOVA, F (1, 1186) = 8.73, $p = 0.0032$), and animals trained on simple pellet distributions exhibited significantly narrower angles of approach to pellets (19.38 ° ± 0.86) compared to animals trained on complex pellet distributions (28.48° ± 0.51) (2-way ANOVA, F (1, 1186) = 83.46, $p < 0.0001$) (Figure 2.5a,d). Additionally, animals trained on complex predictable distributions (26.79° ± 0.68) exhibited significantly larger mean angles of approach than animals trained on both simple predictable (18.78° ± 0.99 ; $p < 0.0001$) and simple unpredictable (20.69° ± 1.67 ; $p = 0.0004$) pellet distributions, but significantly smaller angles of approach than animals trained on complex unpredictable distributions (30.73° ± 0.75 ; $p = 0.0019$). Animals trained on simple predictable distributions were not statistically different from animals trained on simple unpredictable distributions ($p = 0.65$) (Figure 2.5a,d).

We next wanted to characterize how the angle of approach to pellets changes as animals become more familiar with the foraging task. Animals trained on predictable pellet distributions exhibited significantly narrower angles of approach at the end of training (20.34° ± 1.11) compared to the beginning of training (31.23° ± 1.46) (2-way ANOVA, F (1, 297) = 42.42, $p < 0.001$) (Figure 2.5b). Specifically, animals in the simple distribution significantly narrowed their angle of approach from early (25.93° ± 2.26) to late (16.08° ± 1.78) in training ($p = 0.0006$).

Animals trained on complex pellet distributions also significantly narrowed their angle of approach from early (36.29° ± 1.66) to late (23.52° ± 1.32) in training ($p < 0.0001$). Early in training, animals trained on complex distributions exhibited significantly larger angles of approach (36.29° ± 1.66) compared to animals trained on simple distributions at both early (25.93° ± 2.26 ; $p = 0.0003$) and late (16.08° ± 1.78 ; $p < 0.0001$) stages of training (Figure 2.5b). Similar results were found for animals trained on unpredictable pellet distributions, where they exhibited significantly narrower angles of approach at the end of training (23.65° ± 1.57) compared to the beginning of training (32.13° ±2.49) (2-way ANOVA, $F(1, 142) = 18.53$, $p < 0.0001$) (Figure 2.5c). Animals trained on the complex unpredictable distribution significantly decreased their angle of approach from early (42.06° ± 3.34) to late (30.04° ± 1.59) in training ($p = 0.0017$), however animals trained on the simple unpredictable distribution did not significantly change their angle of approach from early (22.84° ± 2.84) to late (13.88° ± 2.32) in training ($p = 0.0577$). Late in training, animals trained on complex unpredictable distributions exhibited significantly larger angles of approach (30.04° ± 1.59) compared to animals trained on simple unpredictable distributions at both early (22.84° ± 2.84 ; $p < 0.0001$) and late (13.88° ± 2.32 ; $p < 0.0001$) stages of training (Figure 2.5c). Taken together, training on simple predictable pellet distributions allows for animals to navigate more directly to pellet locations, and more direct approaches can emerge over training for all groups as animals become more familiar with the foraging environment.

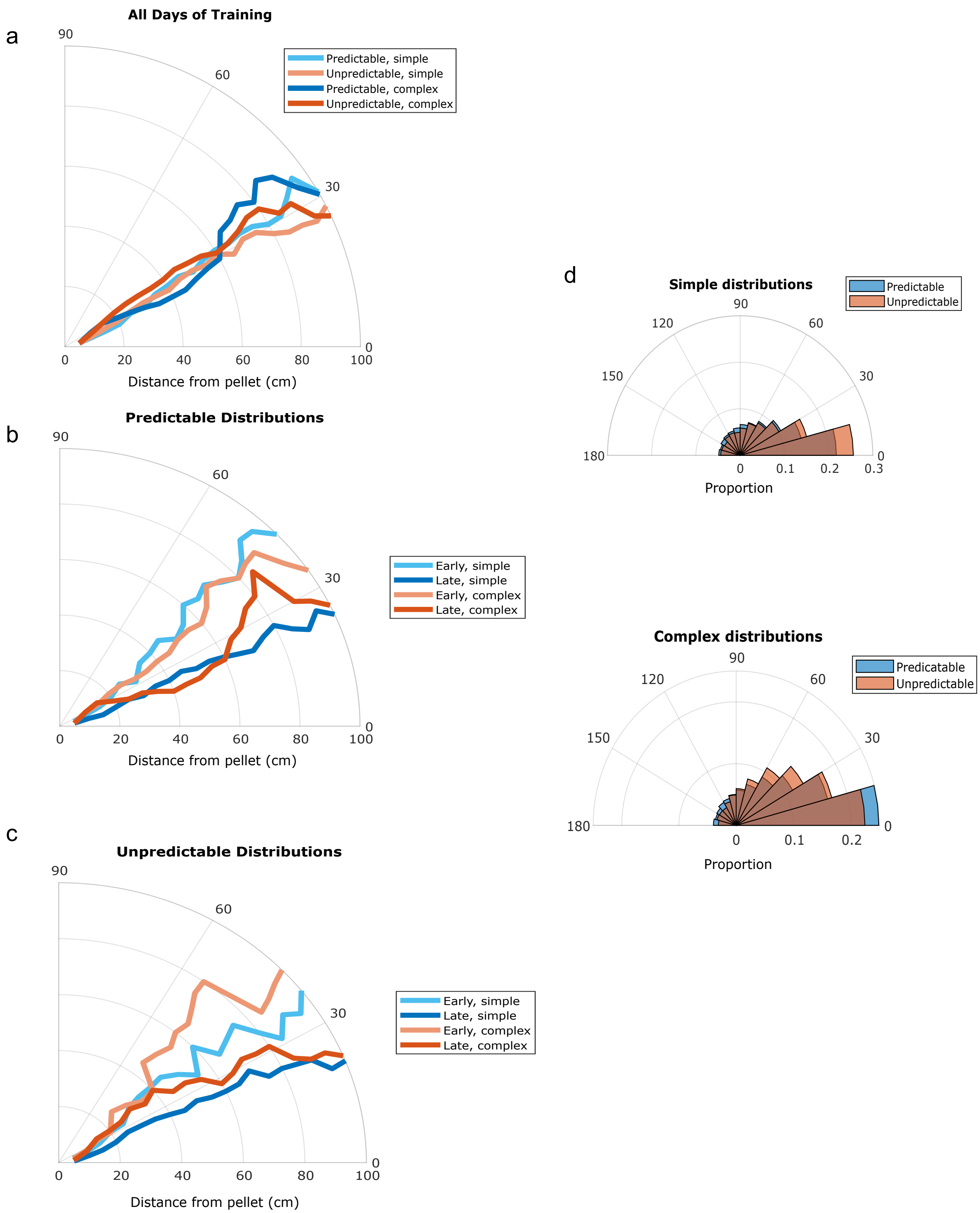

a
All Days of Training
Predictable, simple
Unpredictable, simple
Predictable, complex
Unpredictable, complex
90
60
30
0
0 20 40 60 80 100
Distance from pellet (cm)
b
Predictable Distributions
Early, simple
Late, simple
Early, complex
Late, complex
90
60
30
0
0 20 40 60 80 100
Distance from pellet (cm)
c
Unpredictable Distributions
Early, simple
Late, simple
Early, complex
Late, complex
90
60
30
0
0 20 40 60 80 100
Distance from pellet (cm)
d
Simple distributions
Predictable
Unpredictable
90
120
60
150
30
180
0
0 0.1 0.2 0.3
Proportion
Complex distributions
Predicatable
Unpredictable
90
120
60
150
30
180
0
0 0.1 0.2
Proportion

Figure 2.5: Increasing environmental complexity reduces direct approaches to pellets

a. Mean angle between the current position of the animal's head, the position of the animal's head on the next frame, and the position of the target pellet for all animals. Animals trained on simple predictable (light blue), complex predictable (dark blue), simple unpredictable (orange), and complex unpredictable (dark red) are represented. Only trajectories that met the following criteria were included for analysis: at least 100 cm, the animal did not eat any other pellet during this 100 cm trajectory, and the trajectory ended in successfully finding/eating a pellet.
b. Mean angle between the current position of the animal's head, the position of the animal's head on the next frame, and the position of the target pellet for animals trained on predictable distributions. Animals trained on simple distributions early in training (light blue) and late in training (dark blue) are represented, along with animals trained on complex distributions early in training (orange) and late in training (dark red). Only trajectories that met the following criteria were included for analysis: at least 100 cm, the animal did not eat any other pellet during this 100 cm trajectory, and the trajectory ended in successfully finding/eating a pellet.
c. Mean angle between the current position of the animal's head, the position of the animal's head on the next frame, and the position of the target pellet for animals trained on unpredictable distributions. Animals trained on simple distributions early in training (light blue) and late in training (dark blue) are represented, along with animals trained on complex distributions early in training (orange) and late in training (dark red). Only trajectories that met the following criteria were included for analysis: at least 100 cm, the animal did not eat any other pellet during this 100 cm trajectory, and the trajectory ended in successfully finding/eating a pellet.
d. Histogram of all angles during approaches to pellets for simple distributions (top) and complex distributions (bottom). Animals trained on predictable pellet distributions are represented in blue and animals trained on unpredictable pellet distributions are represented in red.

Predictable environments allow for increasing the efficiency of pellet acquisitions

We next sought to understand how animals were ordering their pellet acquisitions when foraging in complex environments, particularly how close their trajectories resembled the optimal trajectory and whether their paths were efficient. Path efficiency was calculated as the ratio of the animals' actual distance traveled to a pellet to the shortest distance between pellets (also see methods). A multi-factor ANOVA revealed main effects for day of training ($F(2,299) = 56.04$, $p < 0.0001$), pellet number in acquisition sequence ($F(5, 299) = 6.95$, $p < 0.0001$), and predictability ($F(1, 299) = 31.07$, $p < 0.0001$). We found that animals trained on complex predictable distributions significantly increased their efficiency when traveling to the first 3 pellets by the end of training when compared to the first day of training (first pellet: $p < 0.0001$, second pellet: $p = 0.0052$, third pellet: $p = 0.0205$), while animals trained on unpredictable distributions were only able to increase their efficiency for navigating to the first pellet ($p < 0.0001$) (Figure 2.6a-b). As indicated by the larger, yellower dots, animals trained on simple pellet distributions were better able to travel in efficient paths between pellet locations (Figure 2.6b), decrease the distance they traveled to resemble the optimal distance (Figure 2.6c), and acquire pellets in a progression that resembles the optimal sequence (Figure 2.6d). These results indicate that animals trained on simple pellet distributions are better able to adopt an optimal foraging strategy. Moreover, animals trained on predictable distributions are better able to increase the efficiency of their paths further into a search sequence.

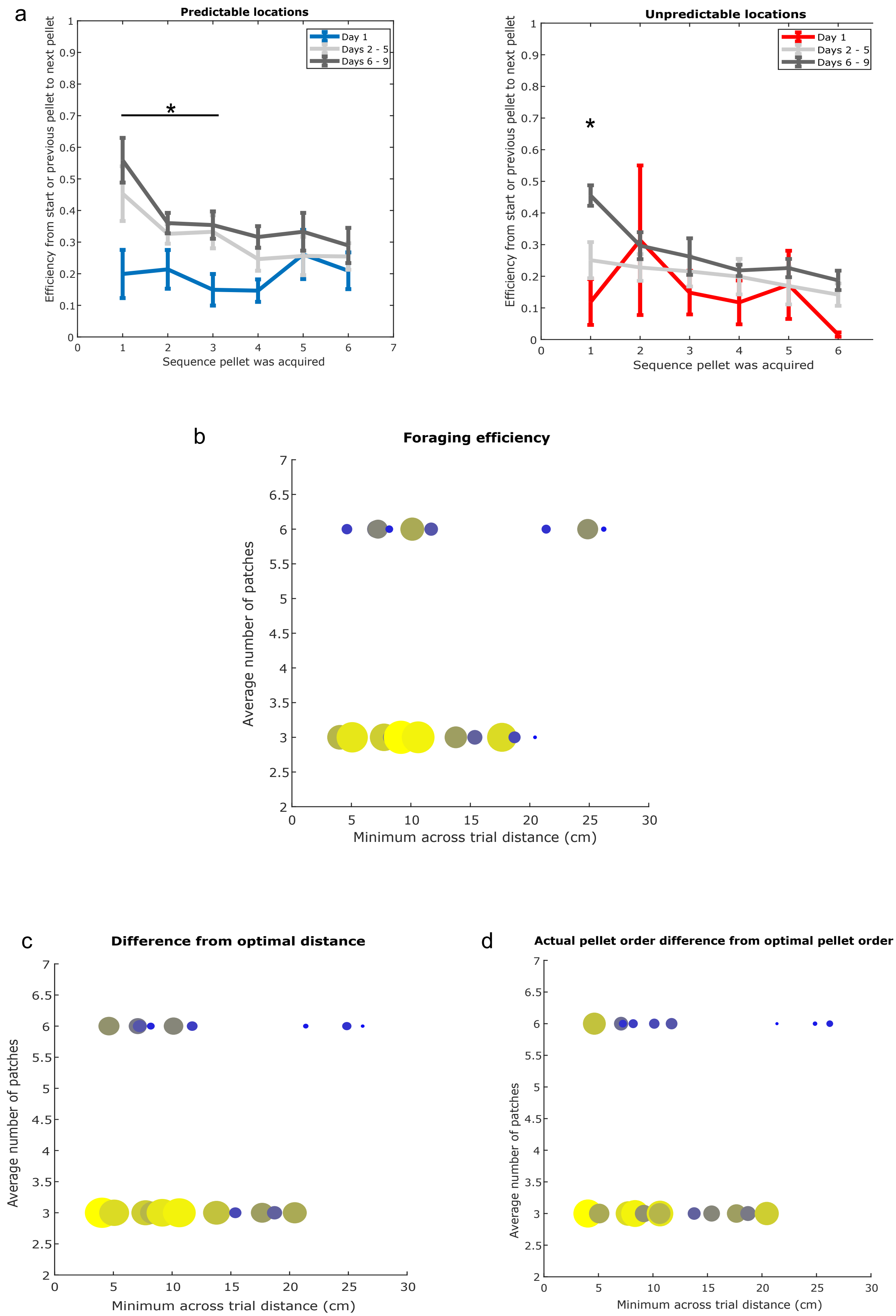

a
Predictable locations
Day 1
Days 2 - 5
Days 6 - 9
*
Efficiency from start or previous pellet to next pellet
Sequence pellet was acquired
Unpredictable locations
Day 1
Days 2 - 5
Days 6 - 9
*
Efficiency from start or previous pellet to next pellet
Sequence pellet was acquired
b
Foraging efficiency
Average number of patches
Minimum across trial distance (cm)
c
Difference from optimal distance
Average number of patches
Minimum across trial distance (cm)
d
Actual pellet order difference from optimal pellet order
Average number of patches
Minimum across trial distance (cm)

Figure 2.6: Predictability supports increased route efficiency between individual pellets

a. Foraging path efficiency for animals trained on complex predictable (left) or complex unpredictable (right) pellet distributions. For the first pellet in each trial, path efficiency is calculated for the trajectory between the animal first entering the arena and procuring the first pellet. For subsequent pellets, path efficiency is calculated for the trajectory between the current and previous pellet acquisition. Efficiency is calculated as the shortest distance between pellets (or the position at the start of foraging and the first pellet) divided by the actual distance that the animal traveled to get to the next pellet. Panels show the average of the first day of training, days 2-5, and days 6-9. Asterisks indicate $p < 0.01$.
b. Visualization for path efficiency as a function of foraging complexity and predictability. Path efficiency is calculated as the shortest distance between pellets (or the position at the start of foraging and the first pellet) divided by the actual distance that the animal traveled to get to the next pellet. Predictability of pellet distributions was quantified using an across trial minimum distance metric, which, for each pellet in a given distribution reports the minimum distance from that pellet to all pellets in the immediately previous distribution. The lower values for pellets in predictable distributions indicate that these pellets are in areas that are very close to where pellets were located on the previous trial, allowing animals to create an expectation over repeated searches. Larger and yellower dots indicate more efficient performance.
c. Visualization for how closely animals' trajectories resemble optimal paths. Performance is calculated as follows: (distance traveled by animal - optimal distance to procure all pellets) / optimal distance.
d. Visualization for how closely animals' pellet acquisition sequence resembles the optimal pellet acquisition sequence. Performance is calculated as follows: (shortest distance between pellets in the order the animal procured them - shortest distance between pellets in optimal order) / shortest distance between pellets in optimal order.

Increased odor cues augment direct approaches to pellets

In order to test whether odor-intensity had an effect on foraging, animals were trained to forage for banana-scented sucrose pellets in both simple predictable and simple unpredictable pellet distributions (Figure 2.7). A multi-factor ANOVA with the factors of distance (close and far) and predictability revealed a significant effect of both distance (F = 17.16, $p = 0.003$) and predictability (F = 19.69, $p = 0.001$) on angle of approach when navigating to regular-scented pellets (Figure 2.7a,c). However, there was neither a significant effect of distance (F = 0.006, $p = 0.81$) nor predictability (F = 2.65, $p = 0.11$) when navigating to banana-scented pellets (Figure 2.7b,c). These results suggest that an increase in odor cues from the banana-scented pellets narrows the angle of approach and facilitates more direct paths to pellets.

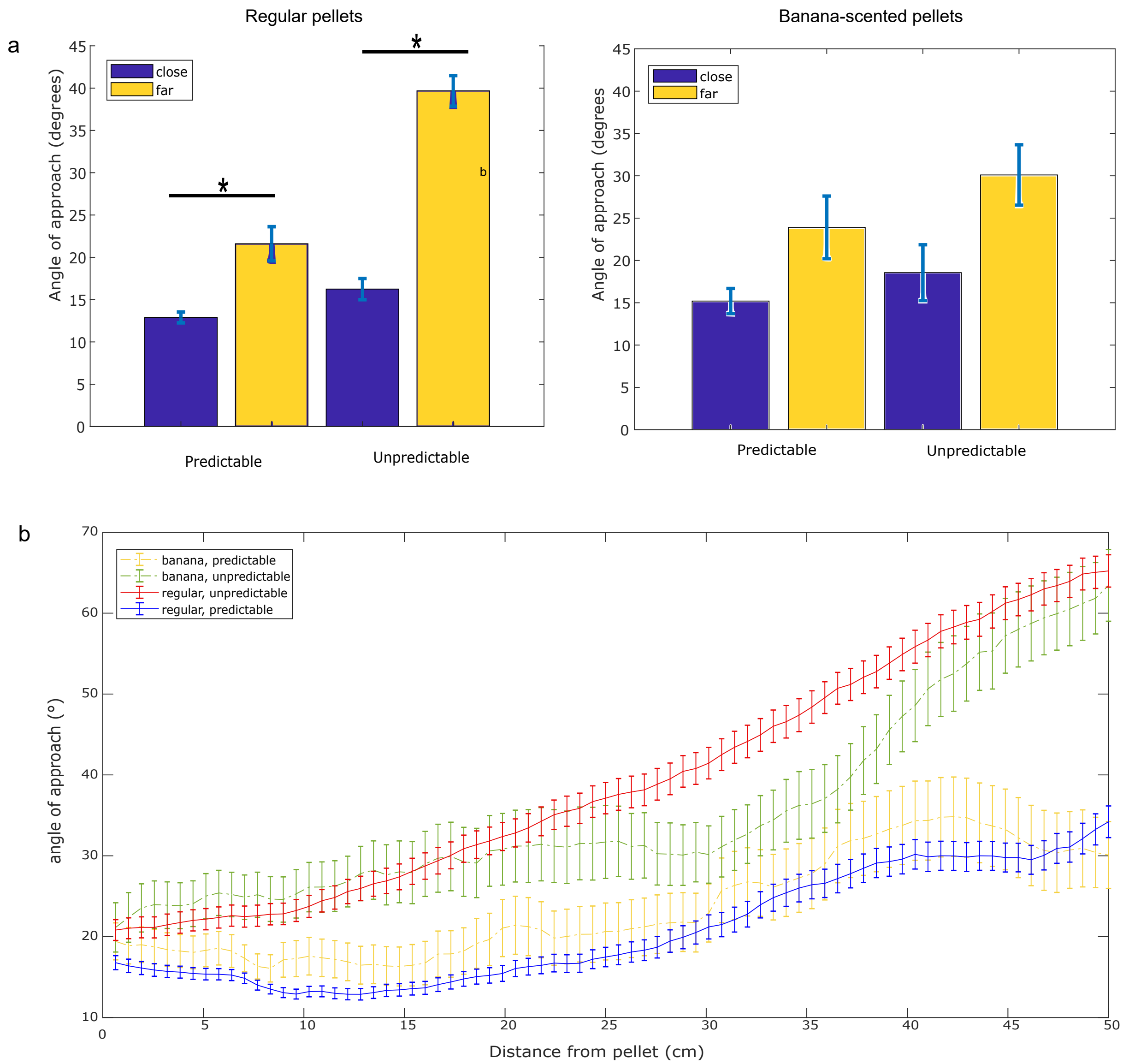


Figure 2.7: Increasing odor cues augments direct approaches to pellets

a. Mean angle of approach towards regular sucrose pellets (left) and banana-scented sucrose pellets (right).
b. Using banana-scented pellets positively impacted search from far distances when navigating to pellets in unpredictable locations. Asterisks indicate significance at $p < 0.05$, 2-way ANOVA.

2.4 DISCUSSION

The results described in this chapter demonstrate that task difficulty in our foraging paradigm can be titrated by modulating the number of pellet locations that animals are required to visit. Animals trained to visit 6 pellet patch locations took more time, traveled farther, and moved slower compared to animals trained to visit 3 pellet locations. Compared to animals trained on simple pellet distributions, these animals displayed much larger head movements during foraging, suggesting a more active searching strategy. Furthermore, animals trained on complex pellet distributions exhibited wider angles of approach to individual pellets, regardless of whether they were trained on predictable or unpredictable distributions. Animals trained on predictable pellet distributions were also able to maintain an efficient path for much further into foraging bouts than animals trained on unpredictable distributions. Taken together, these results indicate that animals are able to utilize information about the probability of finding rewards in known locations even when the number of locations and possible paths are vast.

In our task we found that animals foraging within complex pellet distributions displayed significantly larger movements of the head compared to animals foraging in simple environments, which could be due to a multitude of reasons. Firstly, these animals might be able to utilize sensory cues from pellets more often due to the increased number of pellets in the environment, so it is possible that these animals would regularly end up in locations that are close to multiple patches of pellets. Secondly, due to the larger number of patch locations it is possible that the increased head movements we found are an artifact of the animals just needing to turn their heads more often to orient towards the different patches. This interpretation would be consistent with our results showing that animals foraging in the complex environments had significantly less variation in the magnitude of their head movements, suggesting that these larger head movements could be due to stereotyped turning between known pellet locations. For this reason it would also be interesting to investigate changes in head angular velocity. Thirdly, due to the need to renovate the foraging arena in order to prepare it for facilitating neural recordings, we had to change our illumination tactic in order to reduce electrical noise. As such, the animals foraging in the complex distributions were subject to mostly infrared lighting while the animals foraging in the simple distributions were subject to far-red lighting. While the infrared lighting would make it even more difficult for the animals to use visual cues, these animals were possibly able to use the ambient light from the computer monitors as a distal cue to orient to (Rudy et al., 1987).

An animal's ability to optimize their foraging paths is adaptive, allowing for the least amount of energy to be wasted during extraneous searches (Pyke, 1978). Our results demonstrate how animals may utilize their experience with their environment in order to exploit known food locations and navigate more directly to them. When the foraging environment is more predictable it allows for animals to plan the path they will take ahead of time, reducing the time spent fruitlessly searching in barren locations. We found that animals foraging in predictable environments were able to utilize more efficient trajectories over training when navigating to the first three pellets of a sequence, but animals in unpredictable environments were only able to do this for the first pellet. For this reason I believe our task could be a great tool for studying how animals learn sequences, especially considering there is no definitive “wrong” answer.

Quantifying the paths that animals take to navigate towards pellets using the angle of approach is an important metric for studying the balance between memory use and sensory guidance while foraging. Our results show that animals foraging in predictable environments, as well as animals foraging in simple environments, approached pellets with a significantly narrower angle of approach compared to animals foraging in unpredictable and complex environments, respectively. This suggests that animals can use their memory of where pellets have previously been located to navigate more directly to them on subsequent foraging bouts, and this ability decreases as the number of pellet locations increases. Future studies should aim to quantify the sequences of pellet acquisitions in our foraging task and how these sequences are affected by increasing the number of locations needed to travel between.

Head sweeps and casting behaviors are difficult to quantify in tasks where the range of behavioral responses an animal can make are large. Historically, these behaviors have been studied in more constrained tasks containing fixed tracks and discrete choice points. Our task introduces a novel way of studying head movements through the fine-scale tracking of both head and body trajectories during semi-naturalistic foraging. The tracking software we used, DeepLabCut, has now implemented mechanisms for three-dimensional tracking of behaviors, allowing for the capture of a more robust data set of behavioral motifs (Mathis et al., 2018; Wiltschko et al., 2015). Future studies utilizing our foraging paradigm should incorporate three-dimensional tracking in order to observe a larger number of nuanced exploratory behaviors, such as rearing and whisking.

Chapter 3. Investigating Hippocampal Oscillations During Probability-Based Foraging In Complex Environments

3.1 INTRODUCTION

The critical roles of medial temporal lobe structures in spatial navigation have been well studied, including the hippocampus and entorhinal cortex (Hasselmo, Hay, et al., 2002; J. O'Keefe & Dostrovsky, 1971; Penner & Mizumori, 2012). These structures contain populations of neurons that have been found to respond to and represent multiple aspects necessary for successful navigation, such as place cells (Diba & Buzsáki, 2007; O'Keefe, 1976), grid cells (Boccara et al., 2010; McNaughton et al., 2006; Moser et al., 2008), head direction cells (Goodridge & Taube, 1995; Taube et al., 1990), and speed cells (Hinman et al., 2016; Kropff et al., 2015; Ye et al., 2018). These populations work in tandem to integrate both self-motion cues as well as external sensory cues in order to track where an animal is in their environment and also how to navigate from their current location to a target (Eichenbaum & Cohen, 2014; Hargreaves et al., 2005; Squire et al., 2004). Previous research has shown how place cells in the hippocampus preferentially fire when animals are located in specific areas of their environment, known as the cell's place field (Foster & Knierim, 2012; Kentros et al., 2004; Lee et al., 2012; R. Muller et al., 1994). Following these initial discoveries, experiments have shown how place cell activity can be modulated by a multitude of factors, such as context (M. I. Anderson & Jeffery, 2003; Smith & Mizumori, 2006), experience (Ekstrom et al., 2001; Pfeiffer & Foster, 2013), age (Mizumori et al., 1996; Oler & Markus, 2000; Shen et al., 1997; Wilson et al., 2003), reward probability (Ambrose et al., 2016; Tryon et al., 2017), attention (Fenton et al., 2010; Hölscher et al., 2003), and threat (Kim et al., 2015). Previous studies have also suggested that hippocampal place cell representations of environments become more stable once experience in the environment increases and it becomes more familiar (Muller et al., 1987; Thompson & Best, 1990). However, there is a dearth of evidence elucidating how these representations change when animals gain more experience in an environment but their ability to predict target reward locations changes.

Moreover, a large majority of these tasks take place in experimental apparatuses that restrict the paths that animals can navigate with and the locations where animals may find rewards, done as a way to induce reproducibility of behaviors and ease of analysis. As such, the repertoire of behavioral responses can be limited and may not accurately reflect behaviors exhibited in natural settings. To combat this, the present study utilizes a semi-naturalistic open-field foraging arena to elucidate the neural correlates of foraging, specifically under conditions of varying food location predictability. Importantly, this task allows for reward locations to be presented anywhere throughout the arena, with the repeatability of reward locations being precisely computer-controlled. In addition to ensuring our task can be solved using multiple strategies and animals are not explicitly penalized for suboptimal solutions, it allows us to analyze the extent to which animals may optimize their foraging paths to increase efficiency.

It has long been hypothesized that neural oscillations are a possible mechanism for communication between distal structures (Buzsáki & Moser, 2013), and oscillations are especially pertinent in structures such as the hippocampus, entorhinal cortex, and prefrontal cortex (Buzsáki, 2002; Colgin & Moser, 2010). Particularly, oscillations in the theta frequency band (4-12 Hz) have long been implicated to synchronize neural activity of coordinated structures to the activity of the hippocampus, especially in situations important to memory retrieval or encoding (Anderson et al., 2010; O'Neill et al., 2013). In addition, these oscillations are known to provide a structure for organizing the firing of neurons (Ward, 2003; Wehr & Laurent, 1996). In particular, research indicates that one role is to provide a mechanism for sequencing the firing of place cells (Colgin et al., 2009; O. Jensen & Colgin, 2007; Lasztóczi & Klausberger, 2016). In a process known as phase precession, studies have shown that place cells fire in bursts in specific phases of the theta oscillation, and this firing moves to earlier and earlier phases of theta as animals move through a place cell's place field (Lisman, 2005; Skaggs et al., 1996). In addition to theta amplitude correlating with running speed (Fuhrmann et al., 2015; McFarland et al., 1975; Sławińska & Kasicki, 1998), studies have shown that impairments in the hippocampal theta rhythm through lesions of medial septal nucleus have led to deficits in spatial navigation (Winson, 1978). Studies have also found that hippocampal theta power is increased when animals visit salient locations in their environment, such as decision points in a maze (Tryon et al., 2017). Taken together, these results suggest a distinct role of the hippocampal theta rhythm in aiding spatial navigation. Nonetheless, experiments have yet to elucidate what role hippocampal theta oscillations play in probability-based foraging in environments with varying levels of predictability.

In the present study, we investigate the relationship between theta oscillations in the hippocampus and environmental predictability. Specifically, we analyze how theta power correlates with different aspects of overall task performance. Additionally, we examine how theta power changes as animals navigate further into single foraging bouts and whether the sequence in which animals encounter reward pellets affects the power of theta oscillations.

3.2 MATERIALS & METHODS

Subjects

Five naïve Long-Evans rats (three male and two female), initially weighing 275-325g and procured from Charles River Laboratories, were housed individually in Plexiglas cages in a climate-controlled vivarium. The animals were maintained on a 12 hour reverse light/dark cycle (lights off at 7:00am) and all interactions took place during the dark phase between the hours of 9:00am through 6:00pm. Rats had *ad libitum* access to water and after a weeklong habituation to the vivarium were food-restricted to 85% of their free-feeding body weight. All experimental procedures were approved by the Institutional Animal Care and Use Committee at the University of Washington.

Apparatus

The foraging arena was a large, fully enclosed open-field measuring 2.5m in length, 1m in width, and 1m in height (Figure 3.1a). The frame of the arena was constructed from T-slotted aluminum railings (McMaster-Carr). The sides of the arena were constructed from 1.27cm thick clear acrylic, while the ceiling was 0.635cm in thickness. The floor was a sheet of 0.0635cm thick opaque white acrylic. The ends of the arena were made from a wire mesh to allow for air to circulate throughout. A nest area where the animals would remain during the inter-trial interval was attached to one end of the arena. The nest area was constructed from 1.27cm thick clear acrylic. Two synchronized cameras (The Imaging Source; DMK 23UP1300; frame rate 120 per second) were used to track the movement of the animals. An automated, custom-made pellet dispenser was used to bait the arena during the inter-trial interval with 45mg sucrose pellets (Bio-Serv). An Arduino Uno controlled the movement of the motors running the pellet dispenser, allowing movement in the x- and y- coordinate plane.

LFP Recording Device

Tetrodes used during recordings were constructed from 0.0005” thick polyimide coated nickel-chromium wires (Sandvik-Kanthal) and mounted to a custom-made movable drive that could be lowered to the desired depth. The 16 tetrodes were then connected to a 64-channel Open Ephys electrode interface board. Tetrode tips were gold-plated multiple times to reduce impedances to 175-300 MΩ. During recording experiments, the electrode interface board was connected to an active commutator (Alpha Omega, AlphaComm-I-H2), which was connected to an acquisition board (Open Ephys), which was then connected to a PC workstation running under the Windows 10 operating system.

Surgery

Each rat was placed in an induction chamber and deeply anesthetized using isoflurane (5% mix with oxygen at a flow rate of 1L/min). While the animal was unconscious their skull was shaved, they were placed in a stereotaxic instrument (David Kopf Instruments) to maintain a fixed placement for the skull, and they were given the analgesic Carprofen (2.5mg/kg) and the topical anesthetic Lidocaine (0.15mL of a 20mg/ml solution). After exposing the skull with an incision, the anesthesia was lowered to its maintenance level of a 2.5% mix with oxygen and delivered via a nosecone attached to the stereotaxic mechanism. The tissue overlying the skull was cleared and the skull placement was adjusted to place bregma and lambda into the same horizontal plane. A hole was drilled over the left dorsal CA1 of the hippocampus (unilateral coordinates from bregma: -3.7mm posterior, -2.8mm lateral, and -2.1mm ventral from the surface of the dura mater) and a custom-built microdrive array was implanted. The recording array was secured in place with anchoring screws and dental cement.

Histology

At the completion of the experiment, electrolytic currents were applied to each tetrode of anesthetized rats to confirm placement within the brain. All rats were then euthanized using carbon dioxide and perfused intracardially with 0.9% saline followed by 10% phosphate-buffered formaldehyde. Extracted brains were stored in a 10% formaldehyde solution for 24 consecutive hours and refrigerated. The following day the brains were transferred to a 30% sucrose solution until they sank to the bottom of the jar. Coronal sections through the hippocampus were sliced at 40μm using a frozen microtome. Further histological evaluation was unable to be completed due to COVID-19 restrictions on entering the laboratory.

Foraging Task

Before testing, all animals were habituated to the vivarium for 1 week. Animals then spent 2 days habituating to the nest area attached to the foraging arena for ~15 minutes at a time. In order to motivate animals to return to the nest area, sucrose pellets were placed in the nest area every 2 minutes when a 1 second, 1000Hz tone was played. They were then granted access to the test arena and were given 2-3 days to habituate to it. Animals were considered to have reached criterion for experiment initiation when they were able to make 3 transitions between the nest area and foraging arena within 30 minutes.

Animals were placed into the nest area at the beginning of each testing session. Rats completed 1 session a day that lasted for 30 minutes at a time, resulting in 6 trials per session on average. Before each trial, the automated pellet dispenser baited the arena with sucrose pellets organized into 6 clusters of approximately 2 pellets each. During foraging periods the dispenser was automatically lifted out of the arena so that the animals could not interact with it. Procedures differed only through the testing phase, when animals were assigned to forage within environments of high or low food location predictability. Animals trained on the environment with high food location predictability (n = 2) were overtrained on a single distribution of pellet locations that stayed consistent across trials and sessions. Animals foraging in the environment with low food location predictability (n = 3) were trained on unpredictable pellet distributions that changed across trials. All rats were given a maximum of 30 minutes to eat all of the sucrose pellets during the session. The entire testing period lasted for 18-20 days with approximately 5 sessions per week.

Experimental Design and Statistical Analysis

No explicit power analysis was conducted in order to determine sample sizes. However, the number of animals used is consistent with experiments in the current literature. All analyses were conducted using MATLAB (MathWorks) on PC workstations running under the Windows 10 operating system. A custom LabView (National Instruments) program was used to collect the behavioral data, also on a PC running the Windows 10 operating system. Significant differences between groups were assessed with the Mann-Whitney U test. Correlations are reported as Pearson's *r*.

LFP analysis: Values for power were analyzed during phases when animals were inside of the foraging arena during testing sessions. Raw local field potentials were collected at a sampling rate of 30,000 Hz and measured in microvolts. They were then filtered using MATLAB's Hampel identifier for outlier removal using a window of 30,000 samples. Power was calculated using MATLAB's periodogram function to determine the power spectral density estimate of the input signal for frequencies between 1-100 Hz. Values were converted to decibels using the MATLAB function 10*log10(data). For specific analysis, the theta proportion of the total power was used instead of the total or average theta power. This was calculated by dividing each theta frequency's power level by the integrated sum of power at all frequencies between 1-100 Hz, then summing these values to get a trial value for the integrated theta power proportion. The theta frequency band used during analysis is 4-12Hz, analyzed in steps of 0.5 Hz. Power was averaged across trials or days when needed for particular analyses.

3.3 RESULTS

Behavioral performance in complex environments increases over the course of training

A total of 5 implanted rats were trained to forage in a large, automated foraging arena for 45mg sucrose pellets (Figure 3.1a-b). Two animals were trained on predictable pellet distributions that had pellets placed in the same locations during each trial (Figure 3.1c), while three animals were trained on unpredictable pellet distributions that had pellets placed in random locations for each trial (Figure 3.1d). Animals trained on both predictable ($p < 0.01$) and unpredictable ($p < 0.01$) pellet distributions significantly decreased the amount of time necessary to complete the task when comparing the first day of training to the last day of training (Figure 3.1e). Additionally, animals in the predictable condition took significantly less time to complete the task late in training ($p < .05$) compared to animals in the unpredictable condition. To investigate how animals might reduce their time to complete the task, we looked at the distances they are traveling and also the average speed they are moving. Animals trained on both predictable pellet distributions ($p < 0.01$) and unpredictable pellet distributions ($p < 0.05$) significantly decreased the distance traveled in order to procure all of the pellets when comparing the first day of training to the last day of training (Figure 3.1f). Additionally, animals trained on predictable distributions traveled significantly shorter distances to complete the task late ($p < 0.01$) in training compared to animals in the unpredictable condition. There was no significant difference between the average speed animals traveled while training on predictable ($p > 0.05$) or unpredictable ($p > 0.05$) pellet distributions when comparing early days of training to later days of training (Figure 3.1g). Further, animals in both conditions did not differ statistically in their average speeds at either early or late stages of training.

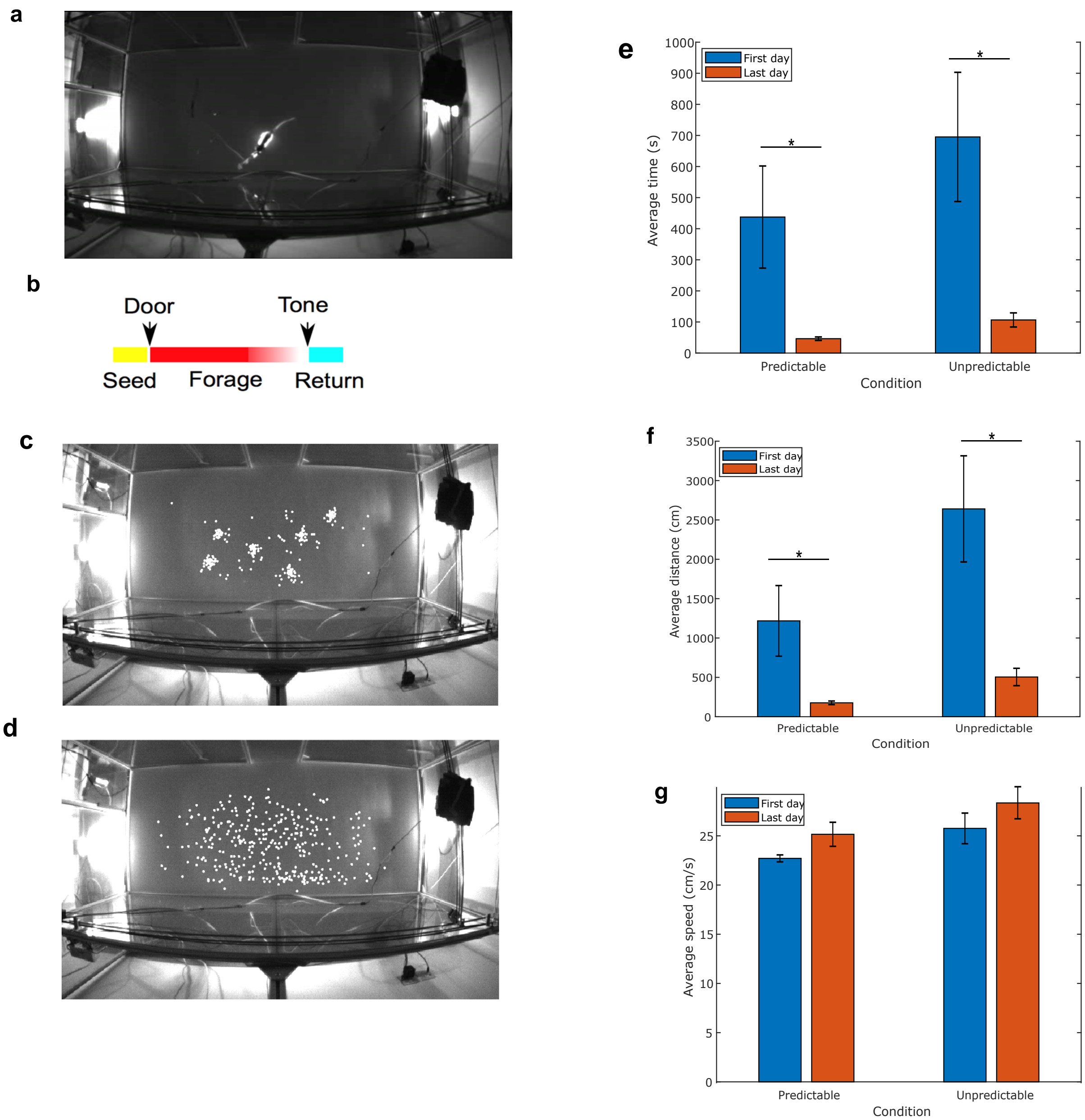


Figure 3.1: Behavioral performance increases over the course of training

a. A large, automated foraging arena with an implanted rat shown for scale.
b. The temporal structure of a typical trial.
c. Rats forage for pellets in a predictable distribution of pellet placements. Representative pellet placement showing pellet placements collapsed over time at the end of training.
d. Rats forage for pellets in an unpredictable distribution of predictable pellet placements. Representative pellet placement showing pellet placements collapsed over time at the end of unpredictable training.
e. Animals trained on both predictable *($p = 1.077e\text{-}4$)* and unpredictable *($p = 0.0034$)* distributions significantly decreased their time to procure pellets by the end of training. Additionally, animals

trained on predictable distributions took significantly less time to complete the task late in training compared to animals in the unpredictable condition *($p = 0.049$)*.

f. Animals trained on both predictable *($p = 1.077e-4$)* and unpredictable *($p = 0.032$)* distributions significantly decreased their distance traveled during foraging bouts by the end of training. Additionally, animals trained on predictable distributions traveled significantly shorter distances to complete the task late in training compared to animals in the unpredictable condition *($p = 0.0087$)*.

g. Animals trained on neither predictable distributions ($p = 0.49$) nor unpredictable distributions ($p = 0.65$) significantly increased their speed by the end of training. There was no significant difference in the average speed late in training *($p > 0.05$)*.

Broad-spectrum hippocampal power changes during probabilistic foraging

It is well known that the hippocampus plays a large role in the spatial navigation ability of animals (Eichenbaum & Cohen, 2014; J. O'Keefe & Dostrovsky, 1971; John O'Keefe, 1976; Penner & Mizumori, 2012). For this reason we decided to investigate what changes might be occurring in the hippocampal local field potential as animals forage under these conditions of varying predictability of food locations (Figure 3.2a). We found that animals foraging under predictable conditions did not significantly change their local field potential power when comparing the first day of training to the last day of training (Figure 3.2b). However, we did find that animals trained on unpredictable conditions did exhibit a significant increase in their local field potential for many frequencies within the 1-100 Hz range (Figure 3.2c). We found that many of these significant increases occurred in the theta frequency band (4-12 Hz), specifically at 4 Hz ($p = 0.036$), 4.5 Hz ($p = 0.029$), and 11.5 Hz ($p = 0.0052$). Additionally, we found that animals foraging in unpredictable distributions displayed significantly less total power of frequencies between 1-100 Hz compared to animals foraging in predictable conditions ($p < 0.001$). These differences were significant at the early stage of training ($p < 0.05$), but not significant later in training ($p > 0.05$) (Figure 3.2d). Due to theta's known role in spatial navigation (Belchior et al., 2014; Buzsáki & Moser, 2013; Hasselmo & Stern, 2014), as well as seeing significant changes in the theta power for animals in the unpredictable condition, we decided to focus further local field potential analysis on this frequency band. We found the total theta power to be significantly decreased for animals in the unpredictable condition overall ($p < 0.001$), and at early ($p < 0.01$) but not late ($p > 0.05$) in training (Figure 3.2d). We found the average theta power to be significantly decreased for animals in the unpredictable condition overall ($p < 0.001$) and at early in training ($p < 0.001$), but not significant later in training ($p >$

0.05) (Figure 3.2e). To ascertain whether the changes we found in the theta range were due to actual changes in theta or to general, broad-spectrum changes in the local field potential, we calculated the theta power proportion of the total power. We found the average theta proportion of the total power to be significantly higher for animals in the unpredictable condition compared to the predictable condition ($p < 0.01$) (Figure 3.2f). This suggests that although animals in the unpredictable condition exhibit lower theta power levels than animals in the predictable condition, the proportion of the theta power to the total power is actually higher in these animals.

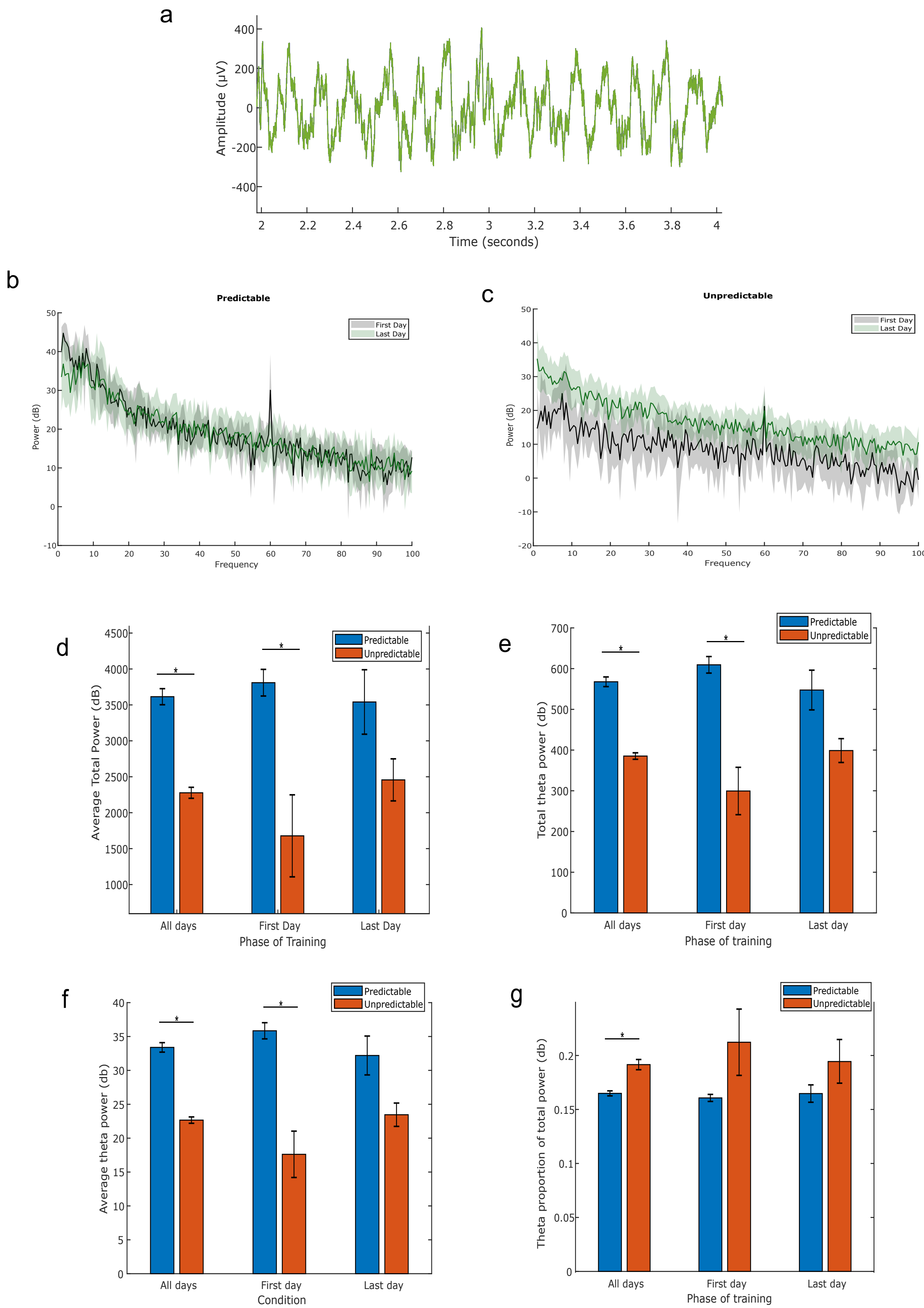

a
Amplitude (μV)
Time (seconds)
b
Predictable
First Day
Last Day
Power (dB)
Frequency
c
Unpredictable
First Day
Last Day
Power (dB)
Frequency
d
Predictable
Unpredictable
Average Total Power (dB)
All days
First Day
Last Day
Phase of Training
e
Predictable
Unpredictable
Total theta power (db)
All days
First day
Last day
Phase of training
f
Predictable
Unpredictable
Average theta power (db)
All days
First day
Last day
Condition
g
Predictable
Unpredictable
Theta proportion of total power (db)
All days
First day
Last day
Phase of training

Figure 3.2: Changes in power as a function of foraging environment predictability

a. Representative raw trace of the local field potential recorded from the CA1 region of the hippocampus. Oscillations in the theta frequency range are clearly visible.
b. Periodogram power spectral density estimate for frequencies between 1-100 Hz during trials on the first day of training compared to the last day of training for animals trained of predictable distributions. Animals show no significant differences in power at any theta frequency (4-12 Hz).
c. Periodogram power spectral density estimate for frequencies between 1-100 Hz during trials on the first day of training compared to the last day of training for animals trained of unpredictable distributions. Animals show significant increases in power by the end of training at the following theta frequencies: 4 Hz ($p = 0.036$), 4.5 Hz ($p = 0.029$), and 11.5 Hz ($p = 0.0052$).
d. Average total power of local field potentials between the frequencies of 1-100 Hz at all days of training, at the beginning of training, and at the end of training for animals trained on predictable (blue) and unpredictable (red) pellet distributions.
e. Average total theta power between frequencies of 1-100Hz at the beginning of training compared to the end of training for animals trained on predictable (blue) and unpredictable (red) pellet distributions.
f. Average theta (4-12 Hz) power level at the beginning of training compared to the end of training for animals trained on predictable (blue) and unpredictable (red) pellet distributions.
g. Average theta (4-12 Hz) proportion of total power (1-100 Hz) at the beginning of training compared to the end of training for animals trained on predictable (blue) and unpredictable (red) pellet distributions.

Relationship between theta proportion of total power and behavioral performance

We next wanted to characterize the relationships between hippocampal theta and performance in the foraging task. For each trial we calculated the correlation between the amount of time taken to complete the task, the distance traveled during the task, and the average speed during the trial and correlated these performance measures with the average theta proportion of the total power for each trial. Animals trained on both predictable (left: r = -0.32, $p < 0.001$) and unpredictable (right: r = -0.23, $p < 0.01$) distributions exhibit significant negative correlations between time to complete the task and the integrated theta proportion (Figure 3.3a). Similarly, there were significant negative correlations between the average distance traveled and the integrated theta proportion for animals trained on both predictable (left: r = -0.24, $p < 0.01$) and unpredictable (right: r = -0.19, $p < 0.05$) pellet distributions (Figure 3.3b). However, significant positive correlations were found between the average speed during the trial and the integrated theta proportion for animals trained on both predictable (left: r = 0.68, $p < 0.001$) and unpredictable (right: r = 0.45, $p < 0.001$) pellet distributions (Figure 3.3c). Taken together, there are many interesting significant correlations between the integrated theta proportion and behavioral performance, though pellet distribution predictability had no differential effect on these correlations.

In order to determine whether animals were able to more quickly solve the task due to differences in the theta proportion of the total power, trials were split into groups of short and long based on the median trial time (9 seconds for animals trained on predictable distributions, 14 seconds for animals trained on unpredictable distributions). On short trials, animals in both the predictable ($p < 0.01$) and unpredictable ($p < 0.05$) conditions exhibited significantly higher theta proportions compared to long trials (Figure 3.4a). Additionally, animals in predictable conditions had significantly lower theta proportions for longer trials compared to animals in the unpredictable condition ($p < 0.05$). Also, on short trials, animals in both the predictable ($p < 0.001$) and unpredictable ($p < 0.001$) conditions exhibited faster average speeds compared to the longer trials (Figure 3.4b). Animals trained on predictable pellet distributions were significantly slower than animals trained on unpredictable pellet distributions during both short ($p < 0.01$) and long ($p < 0.01$) trials. Animals trained on predictable distributions also exhibited significant negative correlations between the amount of time taken to procure all of the pellets and the integrated theta proportion of the total power during short trials (top: r = -0.54, $p < 0.001$), whereas there was no significant correlation for animals trained on unpredictable distributions (top: r = -0.19, $p > 0.05$) (Figure 3.5a-b). Long trials did not have significant correlations between the time to complete the task and the theta proportion (Figure 3.5a-b, bottom). Additionally, no predictability condition exhibited significant correlations between distance and theta proportion regardless of trial length (Figure 3.5c-d). However, animals in both predictable and unpredictable conditions displayed significant correlations between average speed and integrated theta proportion of the total power for both short and long trials (Figure 3.5e-f). These results suggest that some aspect of having higher proportions of theta in the hippocampal local field potential is beneficial to solving the task more quickly when foraging under predictable conditions.

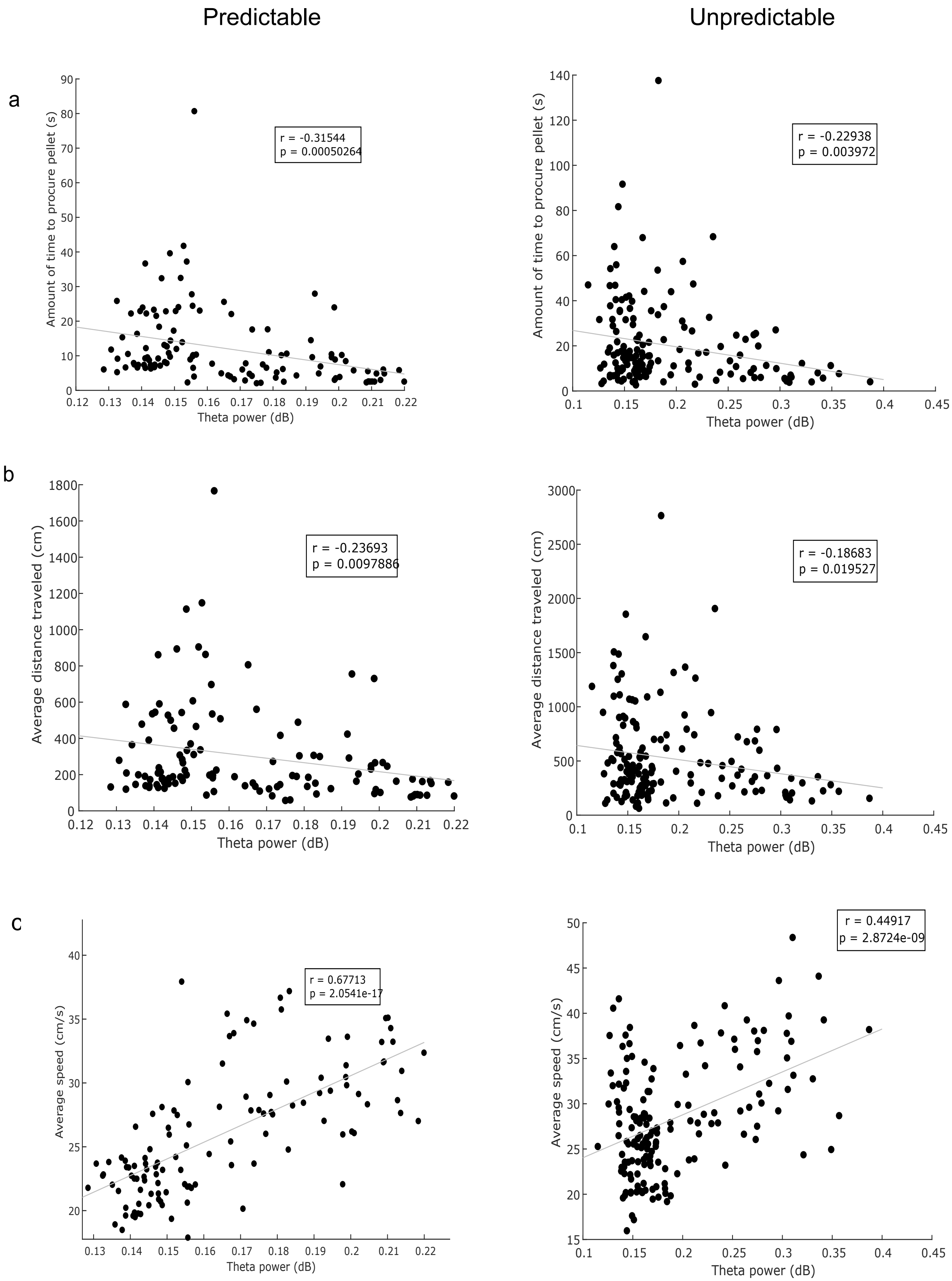

Predictable
Unpredictable
a
b
c
Amount of time to procure pellet (s)
Average distance traveled (cm)
Average speed (cm/s)
Theta power (dB)
r = -0.31544
p = 0.00050264
r = -0.22938
p = 0.003972
r = -0.23693
p = 0.0097886
r = -0.18683
p = 0.019527
r = 0.67713
p = 2.0541e-17
r = 0.44917
p = 2.8724e-09

Figure 3.3: Effect of pellet distribution predictability on theta proportion correlations with behavior

a. Animals trained on both predictable pellet distributions (left; r = -0.32, $p = 0.00050$, n = 118 trials) and unpredictable pellet distributions (right; r = -0.23, $p = 0.0040$, n = 156 trials) exhibit significant negative correlations between time to complete foraging task and the theta proportion of the total power. There is no significant difference between the correlations of the predictable and unpredictable conditions ($p > 0.05$, Fisher r-to-z transformation).
b. Animals trained on both predictable pellet distributions (left; r = -0.24, p = 0.0098, n = 118 trials) and unpredictable pellet distributions (right; r = -0.19, p = 0.020, n = 156 trials) exhibit significant negative correlations between the distance traveled during the foraging task and the theta proportion of the total power. There is no significant difference between the correlations of the predictable and unpredictable conditions ($p > 0.05$, Fisher r-to-z transformation).
c. Animals trained on both predictable pellet distributions (left; r = 0.68, p = 2.1e-17, n = 118 trials) and unpredictable pellet distributions (right; r = 0.45, p = 2.9e-9, n = 156 trials) exhibit significant positive correlations between the average speed traveled during the foraging task and the theta proportion of the total power. Additionally, animals trained on predictable distributions have significantly stronger correlations between speed and theta proportion of total power compared to animals trained on unpredictable distributions (p = 0.0058, Fisher r-to-z transformation).

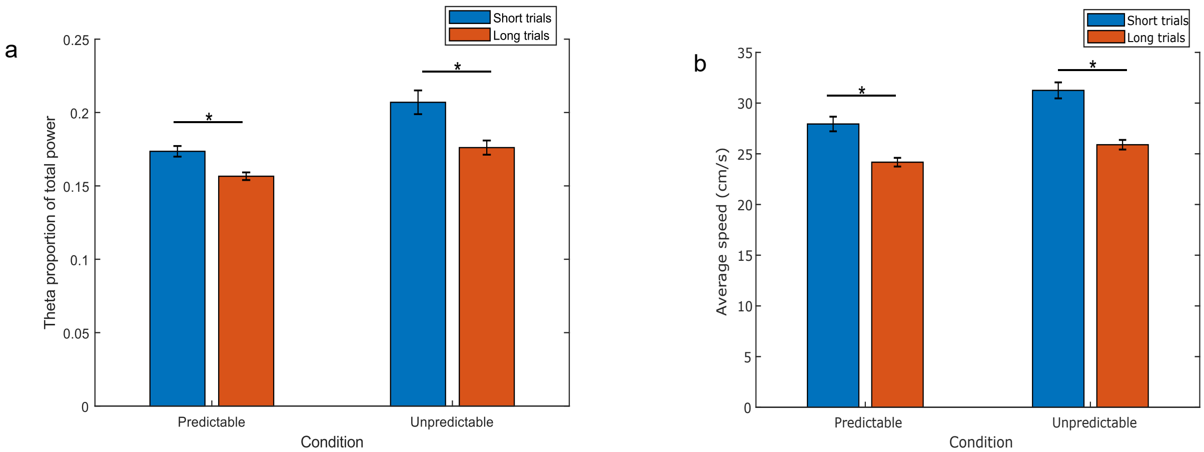
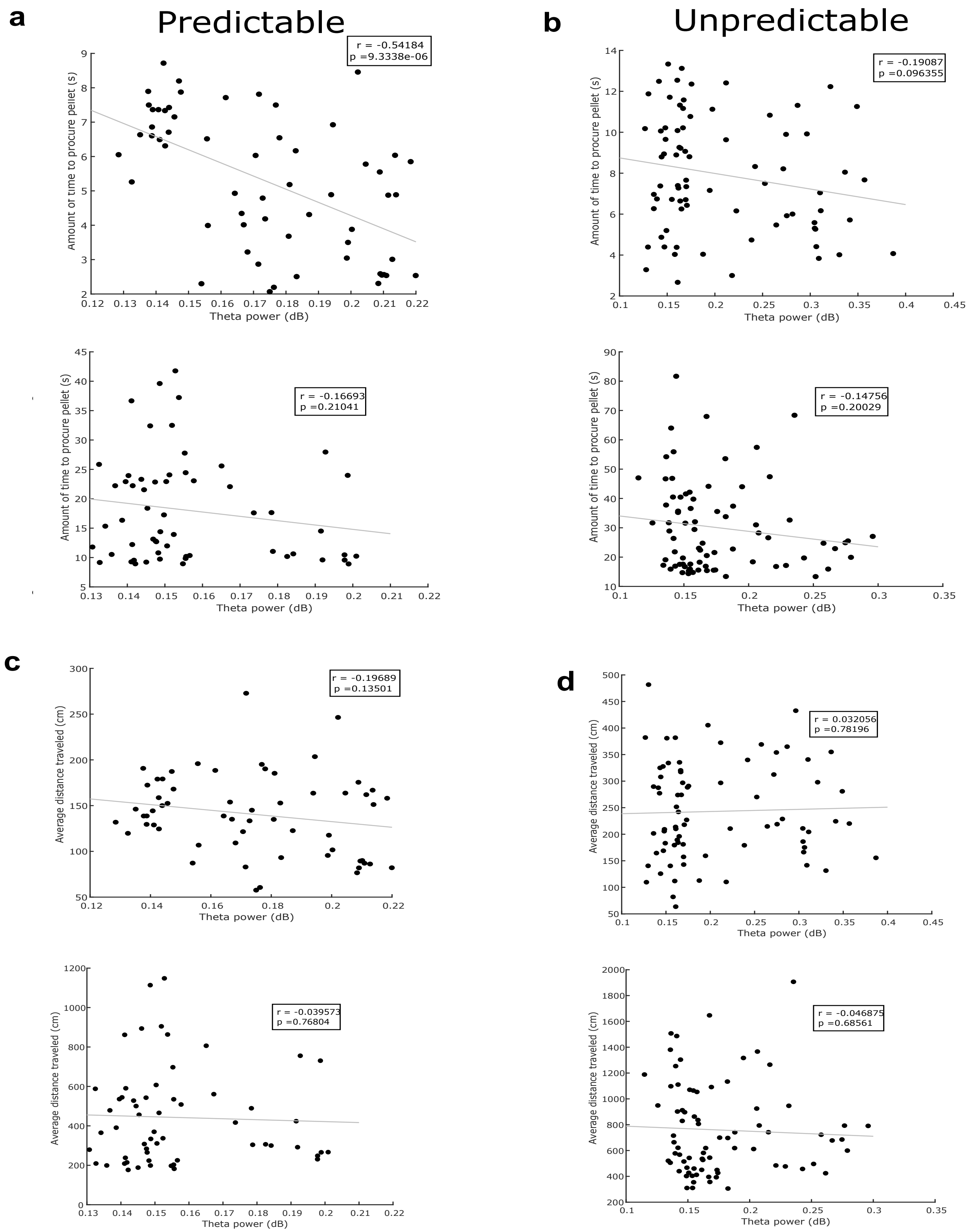


Figure 3.4: Impact of trial duration on theta proportion and trial speed

a. Comparing the theta proportion of the total power for trials shorter and longer than the median time to complete the task. Median time for animals trained on predictable pellet distributions is 9 seconds, while the median time for animals trained on unpredictable pellet distributions is 14 seconds.
b. Comparing the average speed for trials shorter and longer than the median time to complete the task. Median time for animals trained on predictable pellet distributions is 9 seconds, while the median time for animals trained on unpredictable pellet distributions is 14 seconds.


a
Predictable
b
Unpredictable
r = -0.54184
p =9.3338e-06
Amount of time to procure pellet (s)
Theta power (dB)
r = -0.19087
p =0.096355
r = -0.16693
p =0.21041
r = -0.14756
p =0.20029
c
d
r = -0.19689
p =0.13501
Average distance traveled (cm)
r = 0.032056
p =0.78196
r = -0.039573
p =0.76804
r = -0.046875
p =0.68561

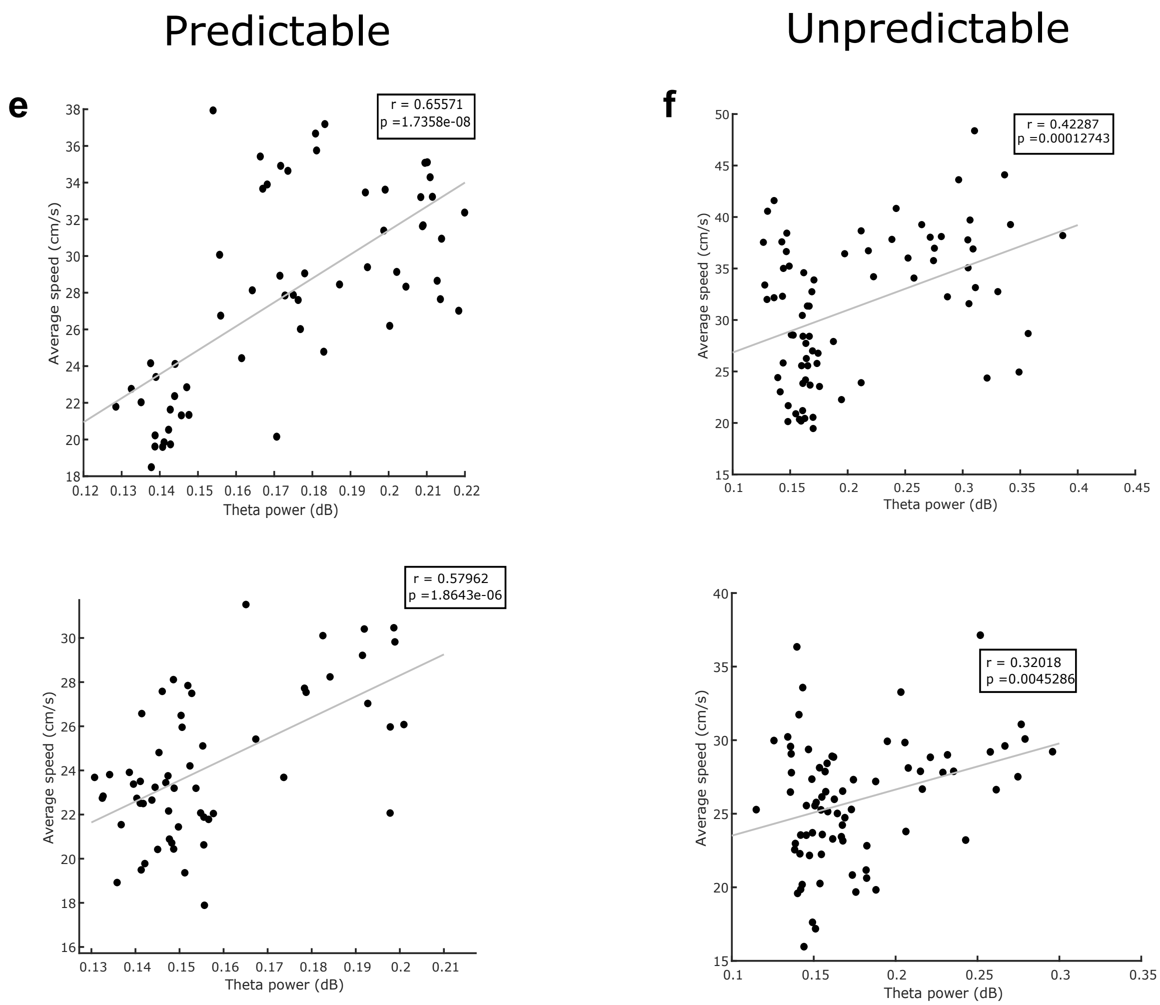


Figure 3.5: Effect of trial duration on theta proportion correlation with behavior

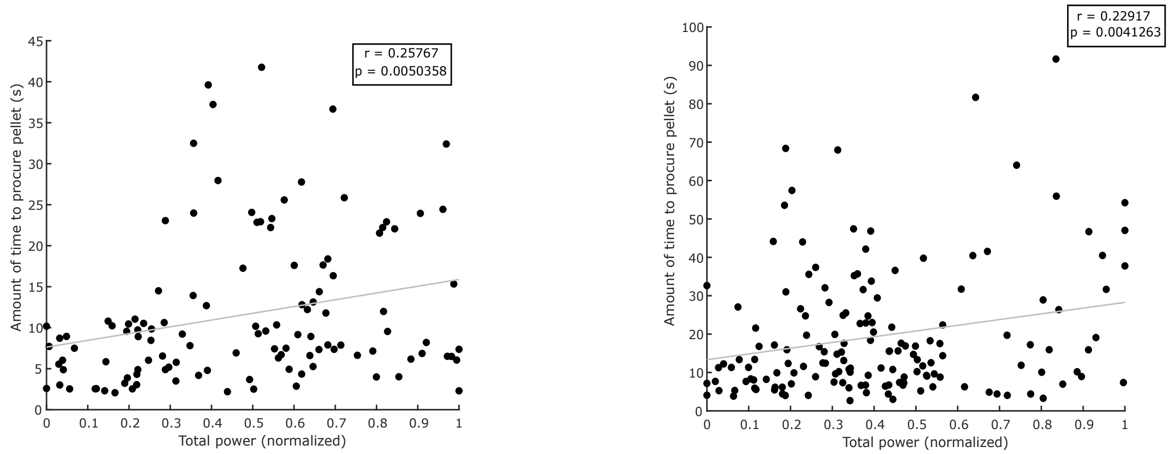
a. Animals trained on predictable pellet distributions exhibit a significant negative correlation between the amount of time to complete the foraging task and the theta proportion of the total power for trials shorter than the median trial length (top; r = -0.54, p = 9.3e-6). However, they exhibit no significant correlation between time and theta proportion when trials are longer than 9 seconds (bottom: r = -0.17, p = 0.21).
b. Animals trained on unpredictable distributions exhibit no significant correlation between time to complete the task and the theta proportion of total power for both short trials (top; r = -0.19, p = 0.10) and longs trial (bottom; r = -0.15, p = 0.20).
c. Animals trained on predictable distributions exhibit no significant correlation between the distance traveled during foraging bouts and the theta proportion of total power for both short trials (top; r = -0.20, p = 0.14) and long trials (bottom; r = -0.040, p = 0.77).
d. Animals trained on unpredictable distributions exhibit no significant correlation between the distance traveled during foraging bouts and the theta proportion of total power for both short trials (top; r = 0.032, p = 0.78) and long trials (bottom; r = -0.047, p = 0.69).

e. Animals trained on predictable pellet distributions exhibit significant positive correlations between the average speed traveled during the foraging task and the theta proportion of the total power for both short trials (top; $r = 0.66$, $p = 1.74e\text{-}8$) and long trials (bottom: $r = 0.58$, $p = 1.9e\text{-}6$).
f. Animals trained on unpredictable pellet distributions exhibit significant positive correlations between the average speed traveled during the foraging task and the theta proportion of the total power for both short trials (top; $r = 0.42$, $p = 0.00013$) and long trials (bottom: $r = 0.32$, $p = 0.0045$).

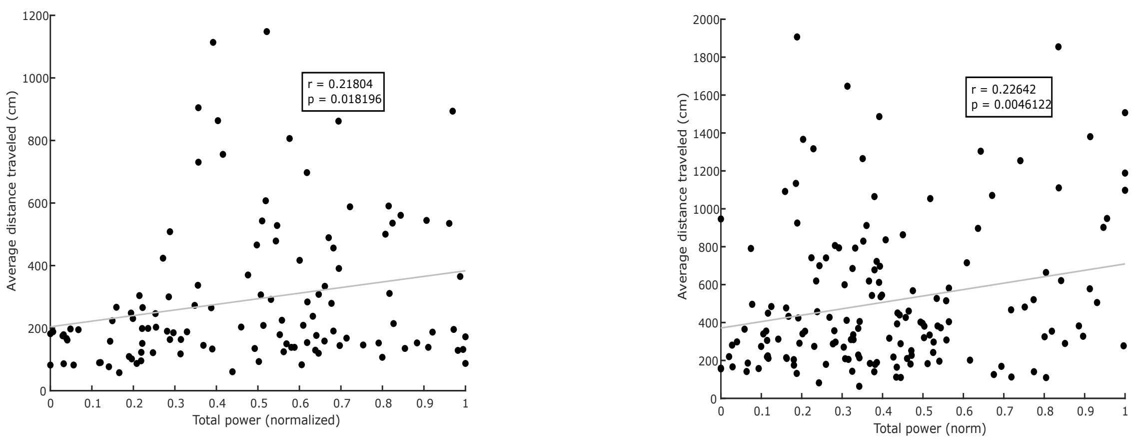
Relationship between total hippocampal power and behavioral performance

To determine whether the relationships seen were specific to the theta band or to broad spectrum changes, we also looked at correlations between task performance and the total power of the hippocampal local field potential. For each animal, total power rescaled using min-max normalization due to a wide range of total power values across animals. Animals trained on both predictable (left: r = 0.26, $p < 0.01$) and unpredictable (r = 0.23, $p < 0.01$) pellet distributions exhibited significant positive correlations between the amount of time needed to procure all of the pellets and the total power of the local field potential (Figure 3.6a). This positive correlation was also significant when analyzing the relationship between the distance traveled and the total power (predictable, left: r = 0.22, $p < 0.05$; unpredictable, right: r = 0.23, $p < 0.01$) (Figure 3.6b). However, animals trained on predictable pellet distributions displayed a significant negative correlation between total power and average speed (r= -0.27, $p < 0.01$) (Figure 3.6c). Taken together, these results suggest environmental predictability failed to shift correlations between the total hippocampal local field potential power and task performance, with the exception of the relationship between speed and total power. This suggests that foraging in predictable environments provides an opportunity for some relationship between running speed and total power in the local field potential to form.

a


r = 0.25767
p = 0.0050358
Amount of time to procure pellet (s)
Total power (normalized)
r = 0.22917
p = 0.0041263
Amount of time to procure pellet (s)
Total power (normalized)

b


r = 0.21804
p = 0.018196
Average distance traveled (cm)
Total power (normalized)
r = 0.22642
p = 0.0046122
Average distance traveled (cm)
Total power (norm)

c

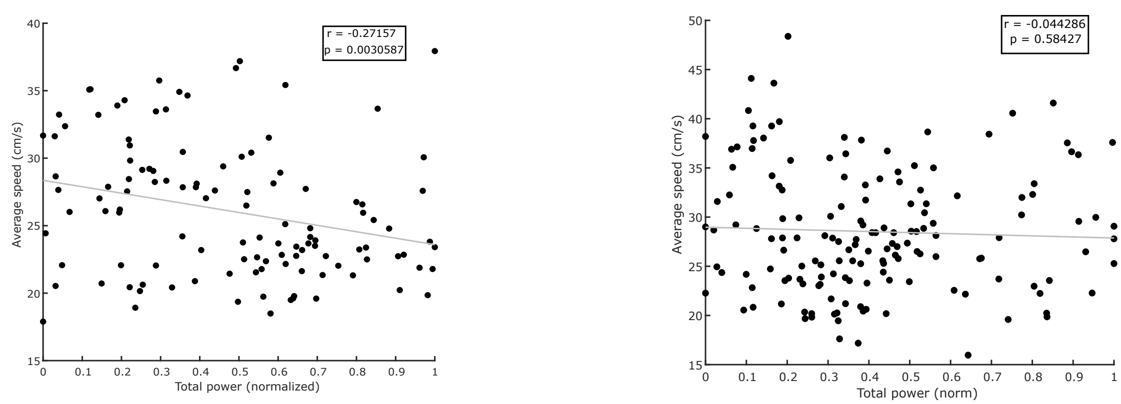

r = -0.27157
p = 0.0030587
Average speed (cm/s)
Total power (normalized)
r = -0.044286
p = 0.58427
Average speed (cm/s)
Total power (norm)

Figure 3.6: Effect of pellet distribution predictability on total power correlations with behavior

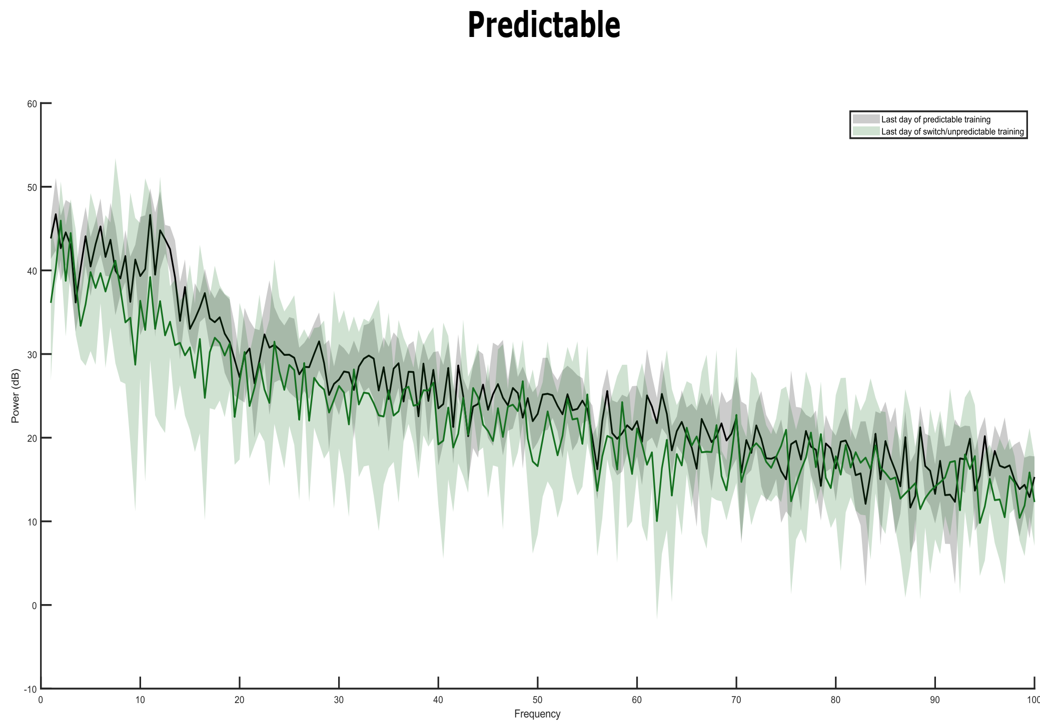
a. Animals trained on both predictable pellet distributions (left; $r = 0.26$, $p = 0.0050$) and unpredictable pellet distributions (right; $r = 0.23$, $p = 0.0041$) exhibit significant positive correlations between time to complete foraging task and the total power of the hippocampus. There is no significant difference between the correlations of the predictable and unpredictable conditions ($p > 0.05$, Fisher r-to-z transformation).
b. Animals trained on both predictable pellet distributions (left; $r = 0.22$, $p = 0.018$) and unpredictable pellet distributions (right; $r = 0.23$, $p = 0.0046$) exhibit significant positive correlations between the distance traveled to complete foraging task and the total power of the hippocampus. There is no significant difference between the correlations of the predictable and unpredictable conditions ($p > 0.05$, Fisher r-to-z transformation).
c. Animals trained on predictable pellet distributions (left; $r = -0.27$, $p = 0.0031$) exhibit significant positive correlations between time to complete the foraging task and the total power of the hippocampus. Animals trained on unpredictable pellet distributions (right; $r = -0.044$, $p = 0.58$) exhibit no significant correlation between average speed during trials and the total hippocampal power. There is no significant difference between the correlations of the predictable and unpredictable conditions ($p > 0.05$, Fisher r-to-z transformation).

Analyzing performance once animals switch their foraging distributions

To ascertain whether the effects seen would carry over after the foraging distribution changes, we switched the pellet distributions that the animals were trained on after 11 days of training. One animal switched from a predictable distribution to an unpredictable distribution, while three animals trained on unpredictable distributions were switched to predictable distributions. The animal switched to the unpredictable distribution exhibited no significant differences in the theta range when comparing the last day of the original predictable distribution training and the subsequent unpredictable training (Figure 3.7a). In contrast, the animals switched to the predictable distribution exhibited significant decreases in theta power at 6 Hz ($p < 0.05$), 10.5 Hz ($p < 0.05$), 11.5 Hz ($p < 0.01$), and 12 Hz ($p < 0.01$) (Figure 3.7b). Interestingly, this is the opposite of the change in theta power seen when these animals initially began their training on unpredictable pellet distributions (Figure 3.2b).

The results do indicate there is an effect of condition on theta proportion correlation with task performance after switching from one distribution to another. While the animal that switched from a predictable pellet distribution to an unpredictable distribution did not exhibit any significant correlations between the theta proportion of the total power and behavioral measures of task performance (Figure 3.8a, c, e), the animals that switched from unpredictable distributions to predictable distributions displayed significant correlations for time to complete the task ($r = -0.46$, $p < 0.001$), the distance traveled during the task ($r = -0.37$, $p < 0.001$), and the average speed traveled ($r = 0.57$, $p < 0.001$) (Figure 3.8b, d, f).

a


Predictable
Last day of predictable training
Last day of switch/unpredictable training
Power (dB)
Frequency

b

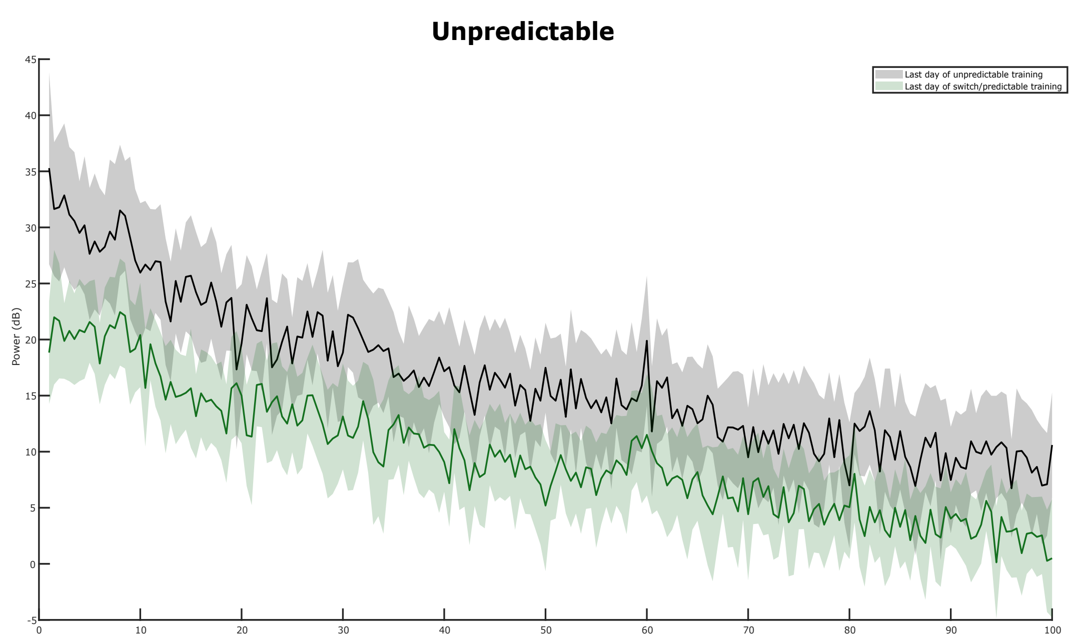

Unpredictable
Last day of unpredictable training
Last day of switch/predictable training
Power (dB)
Frequency

Figure 3.7: Switching predictability distributions differentially affects theta power

a. Periodogram power spectral density estimate for frequencies between 1-100 Hz during trials on the last day of training (gray) on predictable distributions compared to the last day of training (green) after switching to unpredictable distributions. No significance at frequencies within the theta range.
b. Periodogram power spectral density estimate for frequencies between 1-100 Hz during trials on the last day of training (gray) on unpredictable distributions compared to the last day of training (green) after switching to predictable distributions. Animals show significant decreases in power by the end of training at the following theta frequencies: 6 Hz ($p = 0.011$), 10.5 Hz ($p = 0.024$), 11.5 Hz ($p = 0.0082$), and 12 Hz ($p = 0.0058$).

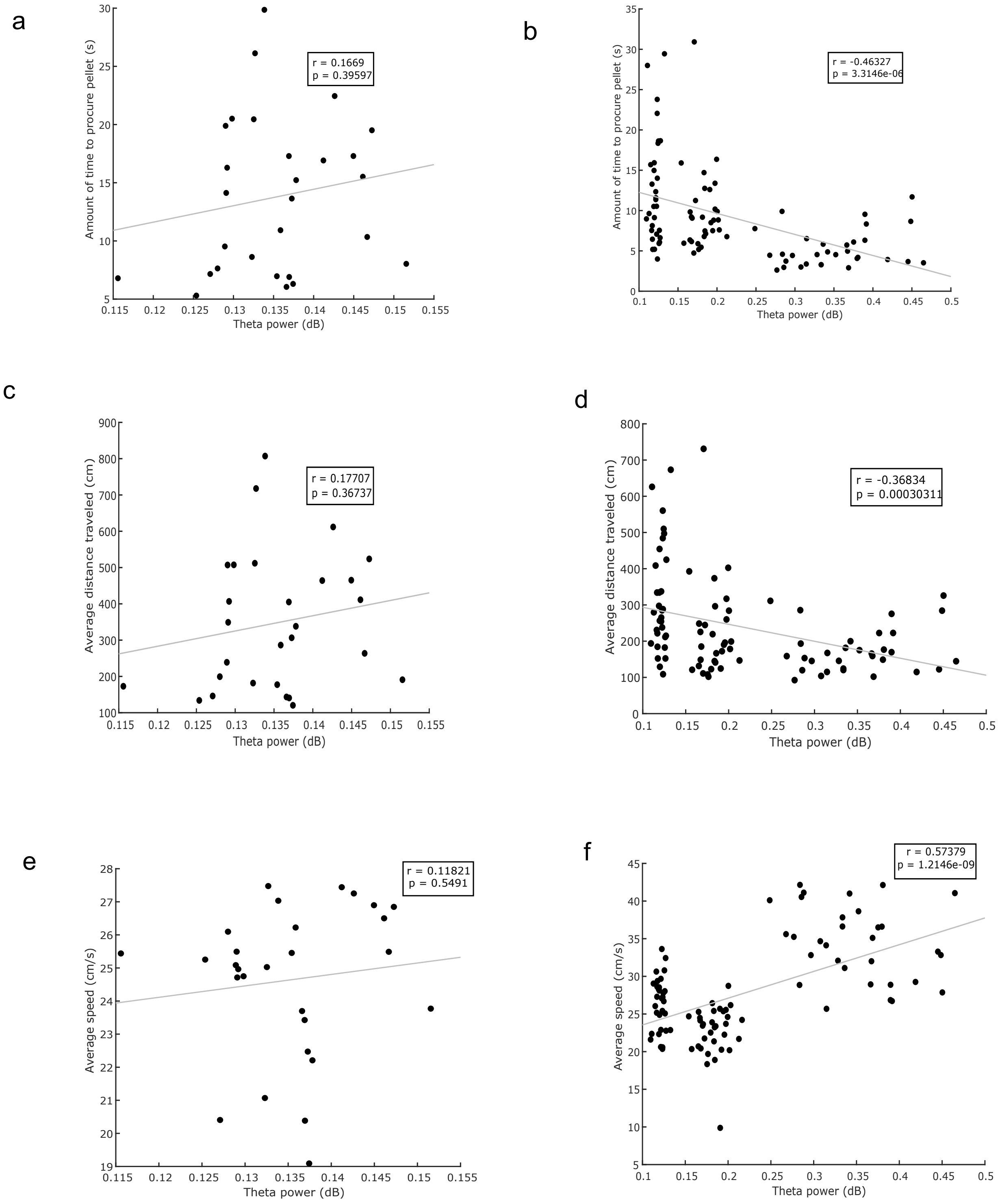

a
Amount of time to procure pellet (s)
Theta power (dB)
r = 0.1669
p = 0.39597
b
Amount of time to procure pellet (s)
Theta power (dB)
r = -0.46327
p = 3.3146e-06
c
Average distance traveled (cm)
Theta power (dB)
r = 0.17707
p = 0.36737
d
Average distance traveled (cm)
Theta power (dB)
r = -0.36834
p = 0.00030311
e
Average speed (cm/s)
Theta power (dB)
r = 0.11821
p = 0.5491
f
Average speed (cm/s)
Theta power (dB)
r = 0.57379
p = 1.2146e-09

Figure 3.8: Impact of switching predictability of pellet distributions on correlations between theta power and task performance

a. After switching to an unpredictable distribution after training originally on a predictable distribution, there was an insignificant positive correlation between the amount of time to complete the foraging task and the theta proportion of the total power ($r = 0.17$, $p = 0.39$).
b. After switching to a predictable distribution after training originally on an unpredictable distribution, there was a significant negative correlation between the amount of time to complete the foraging task and the theta proportion of the total power ($r = -0.46$, $p < 0.01$).
c. After switching to an unpredictable distribution after training originally on a predictable distribution, there was an insignificant positive correlation between the distance traveled to complete the foraging task and the theta proportion of the total power ($r = 0.18$, $p = 0.37$).
d. After switching to a predictable distribution after training originally on an unpredictable distribution, there was a significant negative correlation between the distance traveled to complete the foraging task and the theta proportion of the total power ($r = -0.37$, $p < 0.01$).
e. After switching to an unpredictable distribution after training originally on a predictable distribution, there was an insignificant positive correlation between the average speed traveled during the foraging task and the theta proportion of the total power ($r = 0.12$, $p = 0.55$).
f. After switching to a predictable distribution after training originally on an unpredictable distribution, there was a significant positive correlation between the average speed traveled during the foraging task and the theta proportion of the total power ($r = 0.57$, $p < 0.01$).

Order of pellet acquisition contributes to changes in theta power

We next investigated whether environmental predictability affected theta power at individual pellet encounters during foraging bouts. For this analysis, the power of the hippocampal local field potential was calculated for the 2 seconds preceding pellet encounters. This 2 second window was selected due to the average inter-pellet interval being at least this duration, allowing for this power to be calculated based on single pellet encounters. The first 6 pellets encountered during a trial were included for analysis, and grouped into pellets 1-3 (first) and pellets 4-6 (last). Pellets were grouped in this way due to the differences in duration of time between pellet encounters. For pellets 1-3, the amount of time between the previous pellet (or start of trial when calculating for pellet 1) and the current pellet was exponentially distributed and skewed towards times 3 seconds and shorter. For pellets 4-6, this duration resembled a normal distribution with an average around 4 seconds. Additionally, pellets were grouped in this way due to the different increases in efficiency we saw for the first 3 pellets for animals trained on predictable distributions (Figure 2.6). Animals trained on predictable distributions exhibited significantly decreased power during encounters with the first few pellets on the last day of training at the following theta band frequencies: 4 Hz ($p = 0.0089$), 4.5 Hz ($p = 0.0017$), 5 Hz ($p = 0.0030$), 5.5 Hz ($p = 0.0016$), 6 Hz ($p = 9.39e\text{-}5$), 6.5 Hz ($p = 0.029$), 7 Hz ($p = 0.0015$), 7.5 Hz ($p = 3.29e\text{-}5$), and 8 Hz ($p = 0.0026$) (Figure 3.9a). However, these animals did not display significantly different theta power at the end of training for the last few pellets encountered during a foraging bout (Figure 3.9b). Additionally, animals trained on unpredictable pellet distributions did not exhibit significant changes in theta power during encounters with either the first or last few pellets (Figure 3.9c-d).

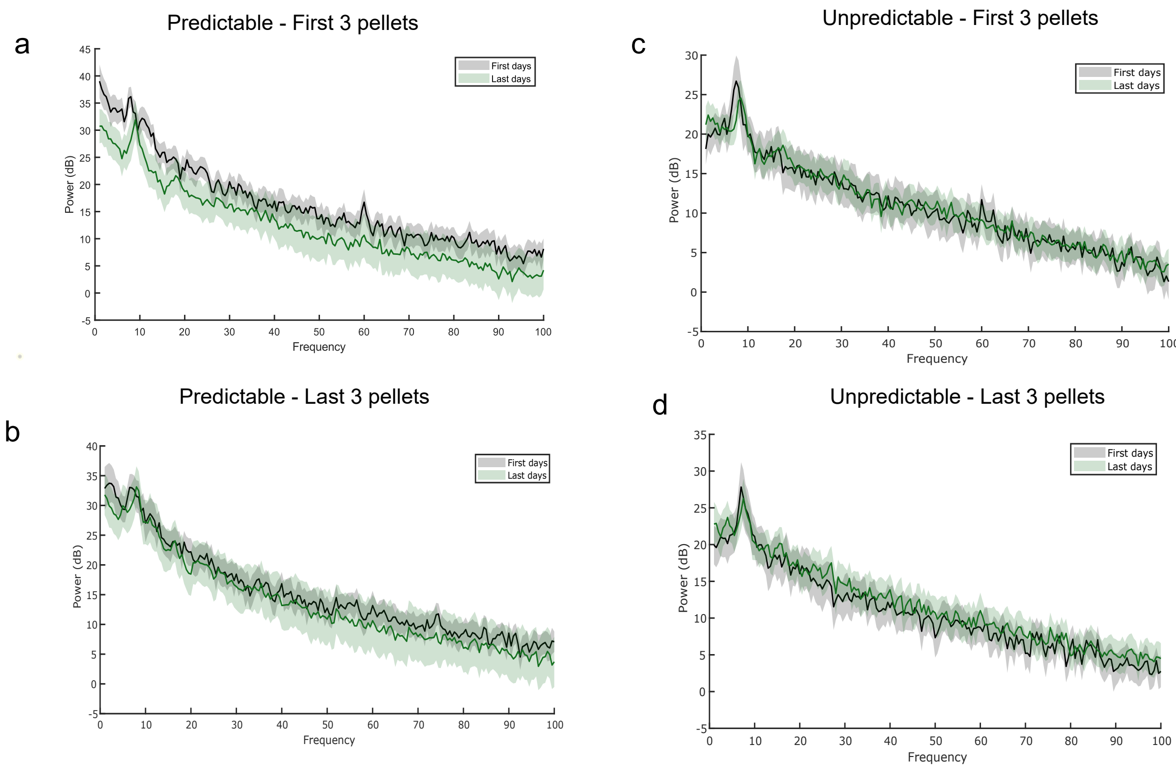


Figure 3.9: Order of pellet acquisition contributes to changes in theta power

a. Periodogram power spectral density estimate for frequencies between 1-100 Hz for the first three pellets encountered on the first day (gray) of training on predictable distributions compared to the last day (green) of training on predictable distributions. Significant differences exhibited at 4 Hz ($p = 0.0089$), 4.5 Hz ($p = 0.0017$), 5 Hz ($p = 0.0030$), 5.5 Hz ($p = 0.0016$), 6 Hz ($p = 9.39e-5$), 6.5 Hz ($p = 0.029$), 7 Hz ($p = 0.0015$), 7.5 Hz ($p = 3.29e-5$), and 8 Hz ($p = 0.0026$).
b. Periodogram power spectral density estimate for frequencies between 1-100 Hz for the last three pellets encountered on the first day (gray) of training on predictable distributions compared to the last day (green) of training on predictable distributions. No significant differences exhibited.
c. Periodogram power spectral density estimate for frequencies between 1-100 Hz for the first three pellets encountered on the first day (gray) of training on unpredictable distributions compared to the last day (green) of training on unpredictable distributions. No significant differences exhibited.
d. Periodogram power spectral density estimate for frequencies between 1-100 Hz for the last three pellets encountered on the first day (gray) of training on unpredictable distributions compared to the last day (green) of training on unpredictable distributions. No significant differences exhibited.

Investigating individual variability during searches

The animals included in this analysis exhibited a lot of variation in performance as well as hippocampal power (Figure 3.10). It was therefore prudent to include individual data for the animals included in this chapter of the study, especially for the animals that switched pellet distributions at the end of training. One interesting observation is that some animals exhibited decreases in the theta proportion of the total power over training, while other animals exhibited increases in the theta proportion (Figure 3.10a). These trends of either decreases or increases continued even when the animals were switched to the other pellet distribution. While animals' speed did not vary much over the course of training (Figure 3.10c), the animals trained on unpredictable distributions displayed decreases in the time to complete the task at every phase of training (Figure 3.10b). The animal initially trained on the predictable distribution (138) increased the amount of time necessary to complete the task after switching to an unpredictable pellet distribution. We also found that the majority of animals switched from either positive to negative correlations or negative to positive correlations between the theta proportion and the amount of time taken to complete the task when comparing the beginning of training to the end of training (Figure 3.10d), suggesting there is no single relationship for all animals as they become more familiar with their environment. We also observed a transition from stronger correlations between the theta proportion and speed to weaker correlations when comparing the beginning of training to the end (Figure 3.10e), irrespective of the direction of the correlation. In conclusion, the variation in the results for individual animals is a strong reason for deeper study of how hippocampal local field potentials relate to behavior in this complex task without limited spatial constraints.

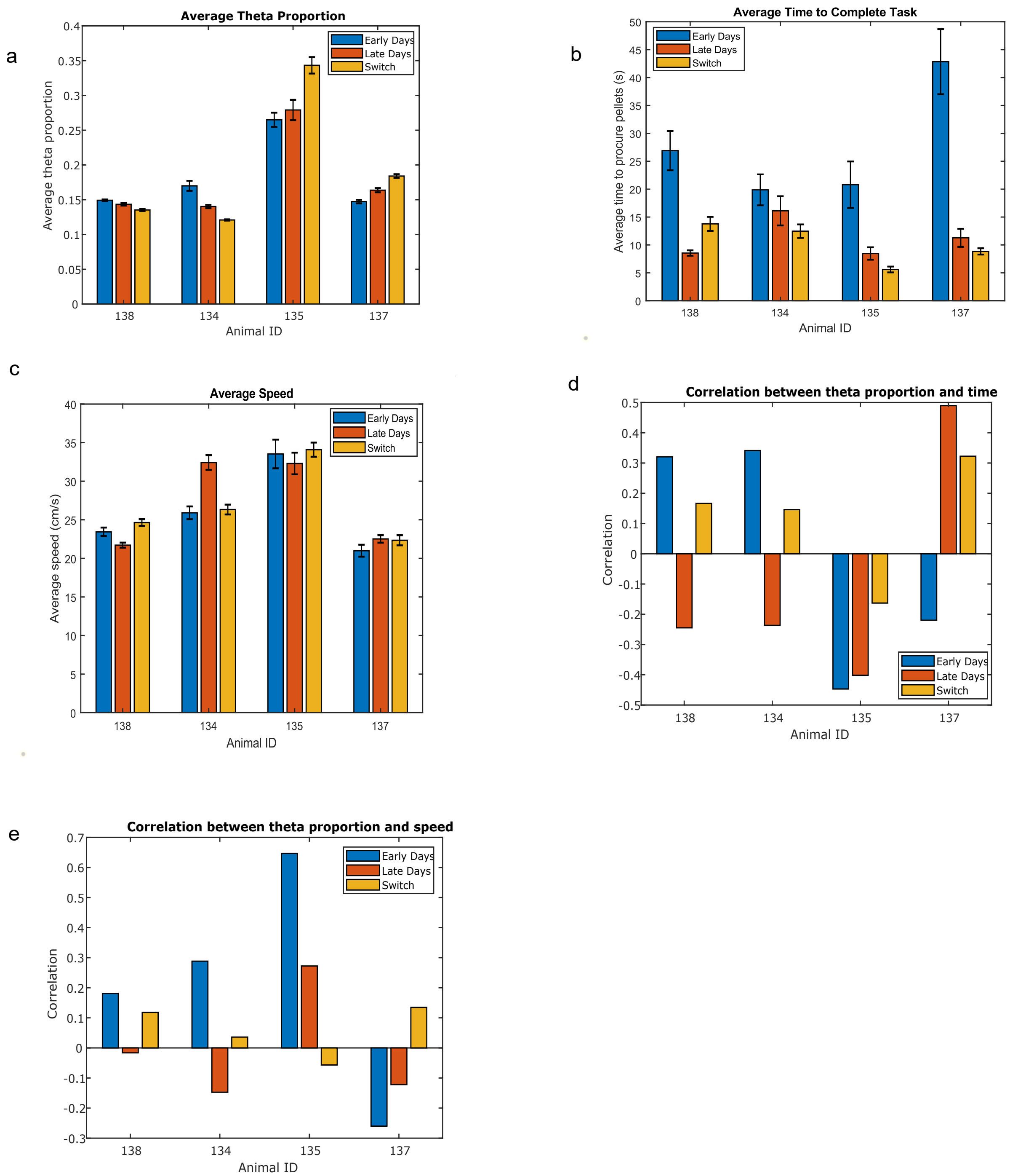


Figure 3.10: Examining individual variability during searches

a. Average theta proportion of the total hippocampal power for individual animals across all trials. 133-138 are animals trained on a predictable distribution and 134-137 are animals trained on unpredictable distributions.
b. Average theta proportion of the total hippocampal power for individual animals as a function of the early days of training, the late days of training, and the days during switched distributions.

138 is an animal trained on a predictable distribution and 134-137 are animals trained on unpredictable distributions.

c. Average time to complete the foraging task in seconds. 138 is an animal trained on a predictable distribution and 133-137 are animals trained on unpredictable distributions.
d. Average time to complete the foraging task during early days of training, late days of training, and after switching distributions.
e. Average speed traveled during the foraging task in centimeters per second.
f. Average speed during the foraging task during early days of training, late days of training, and after switching distributions.
g. Individual animal correlations between theta proportion of the total power and the amount of time needed to complete the foraging task. Animal 135 exhibits a significant correlation between time and theta proportion ($r = -0.53$, $p < 0.001$).
h. Individual animal correlations between theta proportion and time divided into early in training, late in training, and during the switch training. Animal 137 exhibits a significant correlation between time and theta proportion late in training ($r = 0.49$, $p = 0.024$).
i. Individual animal correlations between theta proportion of the total power and the average speed during the foraging task. Animals 134 ($r = -0.31$, $p = 0.026$) and 135 ($r = 0.37$, $p = 0.0066$) exhibit significant correlations between speed and theta proportion.
j. Individual animal correlations between theta proportion and speed divided into early in training, late in training, and during the switch training. Animal 135 exhibits a significant correlation during the early days of training ($r = 0.65$, $p = 0.012$).

3.4 DISCUSSION

There have been many studies researching the relationship between hippocampal activity and spatial navigation, including how knowledge of goal areas affects oscillatory and place cell activity (Belchior et al., 2014; Hollup et al., 2001; Wikenheiser & Redish, 2015). It has long been known that place fields often appear in salient areas of one's environment and also become more stable as an animal becomes overtrained (Muller et al., 1994; O'Keefe & Dostrovsky, 1971; O'Keefe, 1976). Additionally, previous research indicates hippocampal oscillations, especially in the theta frequency range, are involved in spatial memory task performance (Buzsáki, 2002; Moser et al., 2008). However, it has remained unclear what role hippocampal theta may play for animals foraging in environments without defined reward locations, where the probability of finding rewards throughout these environments is variable. The present study employed a semi-naturalistic, fully-automated foraging environment to specifically test how environmental predictability impacts hippocampal oscillatory activity and local field potentials during this self-guided task. This study demonstrates how theta power differentially varies depending on the predictability of the foraging environment in which animals are being trained, with this change being dynamic across different phases of training. Although we found that, in most cases, environmental predictability failed to shift the relationship between theta power and task performance, animals trained on unpredictable pellet distributions did exhibit increased theta power at specific frequencies as training progressed. Interestingly, the increases in theta power were reversed once these animals were switched to predictable pellet distributions. Taken together, these results suggest a specific utility of the theta oscillation when navigating in unpredictable environments.

Previous studies have shown how changes in theta amplitude affects performance in spatial navigation tasks. It has been shown that eliminating the hippocampal theta rhythm led to impairments in spatial memory on a circular maze (Winson, 1978). There is also evidence that increases in theta power are correlated with improvements in memory and performance in spatial navigation tasks (Belchior et al., 2014; Ekstrom et al., 2005). It is thought that theta oscillations could be a mechanism that the brain uses to communicate across distal structures, such as with the prefrontal cortex (Anderson et al., 2010; O'Neill et al., 2013; Ward, 2003). Additionally, the theta rhythm is hypothesized to function in a way to aid in encoding of information and aligning spike sequences (Hasselmo, Bodelón, et al., 2002; Hasselmo & Stern, 2014; Manns et al., 2007). In this study, we found that specific theta frequencies significantly increased their power as training increased for animals in the unpredictable condition. One reason for this could be that animals foraging in unpredictable environments need to maintain behavioral flexibility and are consistently updating their environmental cognitive map whenever they encounter new reward locations. Also, it has been indicated that hippocampal theta oscillations can be increased through novel stimulation (Penley et al., 2013), and it can be argued that the unpredictable foraging environment contains more novelty than the predictable foraging environment. We did not see similar changes in theta power for animals foraging in predictable environments, possibly because these animals were able to quickly understand the context of their environment and shifted to a habitual strategy. If this is the case then it is expected that the animals initially trained on unpredictable distributions, then switched to predictable distributions, would also not exhibit these changes in theta power if again switched back to unpredictable distributions.

It has long been established that running speed is significantly correlated with the power of theta in the hippocampus (Fuhrmann et al., 2015; McFarland et al., 1975; Sławińska &

Kasicki, 1998). Indeed, in this study the theta proportion of the total power was significantly correlated with running speed for both the predictable and unpredictable conditions. Therefore, it may be possible that the increased theta proportion for animals in the unpredictable condition is due to their significantly higher running speeds. However, this does not account for the differential changes in power observed at specific theta frequencies. For instance, in animals trained on unpredictable distributions, power at 11.5 Hz significantly increases by the end of training, but significantly decreases from its increased level once training switches to predictable distributions. It is important to note here that running speed does not significantly change from the end of training to the beginning of the switched distribution training. This suggests that at least some of the changes observed in the hippocampal theta power can be explained by reasons other than running speed. Additionally, previous studies suggest that hippocampal local field potentials exhibit layer-specific characteristics, such as differential amplitude and relative phase (Artemenko, 1972; Kocsis et al., 1999; Mizuseki et al., 2011; Montgomery et al., 2009). Due to the inability to definitively conclude where in the hippocampal CA1 the recording tetrodes were located, it is possible that this contributed to the prevalence of individual variability found in our task. It is also interesting to investigate the relationship between theta power and task performance on the scale of individual animals. It would therefore be prudent to look further into individual differences in the hippocampal local field potential, specifically in the theta frequency band, during this probabilistic foraging task.

Future studies should investigate differences in place cell activity during this task. For animals trained in predictable foraging environments, it is hypothesized that place fields would be smaller, more stable, and more accurately reflect previous reward locations compared to animals trained on unpredictable pellet distributions. It has previously been reported that place fields can modulate their spatially selective firing based on factors besides just location, such as context (M. I. Anderson & Jeffery, 2003; Smith & Mizumori, 2006). Therefore, it is not far-fetched to expect changes in place field structure and stability across environments where reward locations are either well-defined or effectively randomized. Additionally, for animals foraging in predictable environments, it would be interesting to continue investigating changes in hippocampal theta during encounters with pellets that are found in unexpected areas of the arena. Although there were no significant changes in the theta power for animals originally trained on predictable distributions once they switched to unpredictable distributions, it is possible that this effect would be too subtle to notice with one animal. It would also be interesting to divide trials based on theta power and examine whether better task performance occurs on trials with higher power, which could be likely due to the significant correlations between the time needed to complete the task and the average theta proportion of the total power.

EPILOGUE

The studies presented herein demonstrate that animals adaptively shift cognitive resources between sensory and memory systems and optimize performance under uncertainty. We demonstrate this using a new, laboratory-based discovery method to define the strategies used to solve a difficult optimization scenario, the probabilistic "traveling salesman" problem. Using this system, we precisely manipulated the strength of prior information available to animals as well as the complexity of the problem. We find that rats efficiently solve the probabilistic traveling salesman problem, even under conditions in which prior information is unreliable and the space of possible solutions is large. We compared animal performance to a simulated Bayesian agent and found that performance is consistent with an approach that adaptively allocates cognitive resources between sensory processing and memory, enhancing sensory acuity and reducing memory load under conditions in which prior information is unreliable. This increased reliance on sensory input allows animals searching across unpredictable environments to employ an effective nearest neighbor strategy with nearly the same efficacy as animals that are operating in highly predictable environments, although due to the short-range nature of sensory cues a sensory-guided strategy fails at long distances and animals are unable to increase the efficiency of foraging trajectories over these distances. Our findings set the foundation for new approaches to understand the neural substrates of natural behavior as well as the rational development of biologically inspired approaches for complex real-world optimization.

The second study quantified how animals approach single pellets and optimize their pellet acquisition sequence when foraging in more complex distributions. We found that animals trained on predictable pellet distributions approach pellets from a much narrower angle than animals trained on unpredictable distributions, which was consistent for both simple and complex distributions. This is consistent with our initial finding that animals trained on predictable distributions are able to use their memory of previous pellet locations to navigate more directly to them. We also observed that animals navigating in complex environments exhibit significantly larger head movements than animals navigating in simple environments, with animals foraging in unpredictable distributions exhibiting the largest head movements. This finding suggests that complexity and unpredictability interact to increase animals' searching for cues, leading to more zigzagging sweeps of the head. This is consistent with the literature that suggests animals increase head movements when they are still learning about the task and/or when they are searching for odor cues with which to aid in navigating to the source. Future research may benefit from real-time monitoring of odor cues as animals forage using our paradigm. A more focused odor-guided task could be valuable in this context due to the changes in approach strategy we observed when using scented pellets, perhaps by investigating the performance of anosmic animals.

Finally, the role of hippocampal theta activity was examined during our probabilistic foraging task. We found that animals navigating in unpredictable environments selectively increased power at specific theta frequencies over the course of training, suggesting a specific utility of the theta oscillation when navigating in unpredictable environments. Surprisingly, these same frequencies decreased their power once these animals were switched to predictable pellet distributions at the end of training. Although, in most cases, we found that environmental predictability failed to shift the correlational relationships between theta power and task performance, this task is still valuable for investigating the role of the hippocampus during route planning in a probabilistic foraging task.

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