Title
Specialized Learning and Memory Mechanisms for Foraging

Author
Seitz, Benjamin Michael

Publication Date
2022

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Specialized Learning and Memory Mechanisms for Foraging

A dissertation submitted in partial satisfaction of the requirements for the degree of Doctor of Philosophy in Psychology

by

Benjamin Michael Seitz

2022

ABSTRACT OF THE DISSERTATION

Specialized Learning and Memory Mechanisms for Foraging

by

Benjamin Michael Seitz

Doctor of Philosophy in Psychology

University of California, Los Angeles, 2022

Professor Aaron P. Blaisdell, Co-Chair

Professor A. Janet Tomiyama, Co-Chair

The study of memory is commonly associated with neuroscience, aging, education, and eyewitness testimony. This dissertation explores how eating behavior is also heavily intertwined—and yet considerably understudied in its relation to memory processes. Both are influenced by similar neuroendocrine signals (e.g., leptin and ghrelin) and are dependent on hippocampal functions. While learning processes have long been implicated in influencing eating behavior, recent research has shown how memory of recent eating modulates future consumption. In humans, obesity is associated with impaired memory performance, and in rodents, dietary-induced obesity causes rapid decrements to memory. Lesions to the hippocampus disrupt memory but also induce obesity, highlighting a cyclic relationship between obesity and memory impairment. In fact, the interconnected nature between learning and memory and eating may reflect the fact that learning and memory systems evolved primarily to aid in animals obtaining food. The chapters presented here explore this position and present evidence of unique “design features” of learning and memory systems that appear specialized for foraging. In Chapter 2, I show behavioral evidence consistent with innate metabolic

responses to novel flavors—putatively because flavors have historically been reliable signals of incoming calories and because an inadequate metabolic response to flavors could be costly. In Chapter 3, I show enhanced memory of eating relative to other similar but noneating behaviors and prioritized memory for eating high-calorie relative to low-calorie foods. Finally, in Chapter 4, I explore the neural basis of backward conditioning, a historically overlooked phenomenon that might be critical in allowing animals to learn relationships between food outcomes and related cues that can guide future foraging behavior. Using a range of animal models and experimental techniques, these chapters elucidate the ways in which the recurring struggle to obtain food has profoundly shaped learning and memory systems.

The dissertation of Benjamin Michael Seitz is approved.

Alan Dan Castel

Melissa J. Sharpe

Aaron P. Blaisdell, Committee Chair

A. Janet Tomiyama, Committee Chair

University of California, Los Angeles,

2022

This dissertation is dedicated to my parents—none of this would be possible without your love and support. Thank you for giving me roots and wings.

Table of Contents

List of Tables

List of Figures

Acknowledgements

I will remember my academic journey not by the publications, awards, or grants, but rather, the people I've met along the way. It takes a village; there are truly too many people who have been incremental in shaping my academic trajectory to list here—if you are reading this and think you made an impact on me, you most definitely did. That said, a few individuals deserve special recognition.

First and foremost, I'd like to thank Aaron Blaisdell who welcomed me to UCLA and his lab and not only accepted but encouraged my insatiable drive for exploring new topics—especially those outside our typical scientific wheelhouse. Aaron taught me how to formulate compelling research questions and then afforded me the freedom to develop those research questions on my own, always while knowing I had his support and expertise when needed. I cannot thank him enough for this. I next must thank Janet Tomiyama who has been an incredible mentor and also my biggest role model. Her ability to not only manage but excel in her research, mentorship, funding, service, and familial responsibilities is nothing short of breath-taking. Janet has made me a better scientist and a better person, and if I can accomplish half of the things she has accomplished at half of the level of expertise, I'll consider myself lucky. I would also like to thank Mel Sharpe, who took a chance on me, a late-stage grad student with minimal training in behavioral neuroscience, and pushed me to master difficult concepts and produce high-impact research at a rate I did not think was possible for myself. I learned so much in her lab and am incredibly proud of the work we produced. I am grateful for this experience and am a better researcher because of it. Finally, I'd like to thank a number of faculty in this department who have been exceptional mentors, colleagues, and friends. My dearest thanks to Martie Haselton, Alan Castel, Kate Wassum, Andrew Wikenheiser, Jesse Rissman, Alicia Izquierdo, Bob Bjork, and Michael Fanselow, as well as Ralph Miller and David Sloan Wilson for their support throughout my undergraduate and graduate career.

Beyond faculty, there are several amazing people whose help and friendship cannot be overstated. Thank you to Mary Flaim, Valeria González, Ivy Hoang, Lauren DiFazio, and Sam Millard, I am indebted to all of them in so many ways. I thank them for their support with everything, I could fill an entire dissertation with the questions and guidance I've asked of them. Tommer Schwarz, Arielle Pulverman, Josh Cain, and Jamie Mondello also deserve special recognition for their support and friendship throughout this process—how these years have passed is beyond me. Finally thank you to Amanda Johnson and Jennifer Butler who have brought an immense amount of joy to my life in the past few years.

I want to finish these acknowledgements by thanking my family who have been my biggest supporters throughout this process. I could not have asked for a better set of parents: Mom and Dad, I know you're reading this, I love you. I thank my brother, Aaron, who has been an incredible role model to me and source of guidance. He has instilled wisdom in me a PhD never could and I cherish that. Last but not least, I thank my partner Quinn. She has been by my side throughout this entire process, from dropping me off at the airport for my initial interview, to bringing me coffee (or beer) as I write these final paragraphs. Her love—and that from our lovely Poppy girl—has lifted me from my lowest lows and made the highest highs even more special.

To all these people and those I've left out, I am grateful beyond words.

Funding

This work was supported in part by NSF grant (BCS-1844144) to A.P.B., NSF CAREER grant (BCS-1454735), NIH grant (R01DK128575), and NIH grant (R01HL158555) to A.J.T., as well as NSF CAREER grant (NSF-2143910), BBRF award (BBRF30637), and a Society of Hellman Fellows award to M.J.S. Further support for this work was provided by NSF GRFP (DGE-1650604), the American Psychological Association of Graduate Students Psychological Science Research Grant, and the UCLA Graduate Summer Research Mentorship award to B.M.S.

Publications

Chapter 1: This chapter includes excerpts from the following two publications, reprinted with permission:

Seitz, B. M., Tomiyama, A. J., & Blaisdell, A. P. (2021). Eating behavior as a new frontier in memory research. *Neuroscience & Biobehavioral Reviews*, 127, 795–807. https://doi.org/10.1016/j.neubiorev.2021.05.024

Seitz, B.M., Blaisdell, A.P., Polack, C.W., Miller, R.R. (2019). The Role of Biological Significance in Human Learning and Memory. *The International Journal of Comparative Psychology.* 32. https://escholarship.org/uc/item/67k6r0n9

Chapter 2: This chapter is an adapted version of the following manuscript, reprinted with permission:

Seitz, B.M., Flaim, M.E., Blaisdell, A.P. (2020). Evidence that Novel Flavors Unconditionally Suppress Weight Gain in the Absence of Flavor-Calorie Associations. *Learning & Behavior.* 48, 351-363. https://doi.org/10.3758/s13420-020-00419-4

Chapter 3: This chapter is an adapted version of the following manuscript, reprinted with permission:

Seitz, B.M., Blaisdell, A.P., Tomiyama, A.J. (2021). Calories Count: Memory of Eating is Evolutionarily Special. *Journal of Memory and Language.* 117. https://doi.org/10.1016/j.jml.2020.104192

Chapter 4: This chapter is an adapted version of the following manuscript, reprinted with permission:

Seitz, B.M., Hoang, I.B., DiFazio, L.E., Blaisdell, A.P., Sharpe, M.J. (In press). Dopamine errors drive excitatory and inhibitory components of backward conditioning in an outcome-specific manner. *Current Biology*. https://doi.org/10.1101/2022.01.10.475719

Chapter 5: This chapter includes excerpts from the following manuscript, reprinted with permission:

Seitz, B. M., Tomiyama, A. J., & Blaisdell, A. P. (2021). Eating behavior as a new frontier in memory research. *Neuroscience & Biobehavioral Reviews*, 127, 795–807. https://doi.org/10.1016/j.neubiorev.2021.05.024

A Note on pronouns: The work reported here has come from several large-scale collaborative efforts. For clarity, I use the “I” pronoun in the introductory (1) and concluding (5) chapters but switch to “we” in the more empirical chapters (2-4).

Vita

Position

Doctoral Candidate (2017– Present)
University of California Los Angeles
Department of Psychology, Learning & Behavior

Head of Research Analysis (2018 – 2019)
100 Humans (Netflix) produced by Shed Media & Warner Bros. Entertainment

Education

University of California Los Angeles (2017 – 2018)
M.A. in Psychology

Binghamton University (2013 – 2017)
B.A. in Psychology *with departmental honors* and Evolutionary Studies
Magna Cum Laude

Selected Fellowships & Funding

National Science Foundation Graduate Research Fellowship (2019 – 2022)
APAGS Psychological Science Research Grant (2020)
Association for Psychological Science Travel Grant for ICPS, Paris (2018)
UCLA Grad Division: Graduate Summer Research Mentorship (2018)
UCLA Department of Psychology Fellowship (2017)

Selected Publications

Total Publications = 15 | First Authored = 12. *Represents mentored undergraduate

Seitz, B.M., Hoang, I.B., DiFazio, L.E., Blaisdell, A.P., Sharpe, M.J. (In press). Dopamine errors drive excitatory and inhibitory components of backward conditioning in an outcome-specific manner. *Current Biology*. https://doi.org/10.1101/2022.01.10.475719

González†, V.V., **Seitz†, B.M.,** Formaker*, R., Blaisdell, A.P. (2022). Elements of a compound elicit little conditioned responding. *Journal of Experimental Psychology: Animal Learning and Cognition.* https://doi.org/10.1037/xan0000296
†Equal contribution

Seitz, B.M., Blaisdell, A.P. & Sharpe. M.J. (2021). Higher-Order Conditioning and Dopamine: A new path forward. *Frontiers in Behavioral Neuroscience.* https://doi.org/10.3389/fnbeh.2021.745388

Seitz, B. M., Tomiyama, A. J., & Blaisdell, A. P. (2021). Eating behavior as a new frontier in memory research. *Neuroscience & Biobehavioral Reviews*, 127, 795–807. https://doi.org/10.1016/j.neubiorev.2021.05.024

Seitz, B.M., McCune, K.B, MacPherson, M., Bergeron, L, Blaisdell, A.P., Logan, C.J. (2021). Using Touchscreen Equipped Operant Chambers to Study Animal Cognition. Benefits, Limitations, and Advice. *PLOS ONE.* 6(2): e0246446. https://doi.org/10.1371/journal.pone.0246446

Seitz, B.M., Blaisdell, A.P., Tomiyama, A.J. (2021). Calories Count: Memory of Eating is Evolutionarily Special. *Journal of Memory and Language.* 117. https://doi.org/10.1016/j.jml.2020.104192

Seitz, B.M., Aktipis, A., Buss, D.M., Alcock, J., Bloom, P., Gelfand, M., Harris, S., Lieberman, D., Horowitz, B.N, Pinker, S., Wilson, D.S., Haselton., M.G. (2020). The Pandemic Exposes Human Nature: 10 Evolutionary Insights. *Proceedings of the National Academy of Sciences.* https://doi.org/10.1073/pnas.2009787117.

Selected Talks

National Institute of Health: Schoenbaum Lab	(2022)
UCLA: Behavioral Neuroscience Brown Bag Fall Quarter	(2021)
Harvard University: Phelps Lab	(2021)
UCLA: CogFog at Bjork Learning and Forgetting Lab	(2018)
UCLA: Learning & Behavior Brown Bag Fall Quarter	(2017)
University of Pennsylvania: Penn Lab for Experimental Evolutionary Psychology	(2016)

Chaired Symposium

Seitz, B.M. (2021, September). *The increasingly diverse role of midbrain dopamine neurons in reinforcement learning.* Symposium held at the Pavlovian Society's Annual Meeting 2021, Ann Arbor, M.I.

Selected Presentations and Posters

Total Presentations = 19 | First Authored = 12. *Represents mentored undergraduate

Seitz, B.M., Equita*, J., Kim*, J.S., Tomiyama, A.J., & Blaisdell, A.P. (2021). How participant sex and stimulus selection influence memory biases towards high-calorie food images. *Poster given at the Psychonomic Society Annual Meeting.* Virtual.

Seitz, B.M., Hoang, I.B., Blaisdell, A.P., Sharpe, M.J. (2021). Prediction(less) errors: Probing the role of midbrain dopamine in backward conditioning. *Talk given at Pavlovian Society's Annual Meeting 2021.* Ann Arbor, MI.

Seitz, B.M., Blaisdell, A.P., Tomiyama, A.J. (2021). Using the Memory of Eating Task (MEaT) to systematically study memory of eating. *Talk Given at Society for the Study of Ingestive Behavior Annual Meeting.* Virtual.

Seitz, B.M., Flaim, M.E., Blaisdell, A.P. (2019). Pavlovian Diet: Flavor-Calorie Associations and Their Role in Weight Gain and Food Consummatory Behaviors Using a Controlled Rat Model. *Poster Presented at The International Convention of Psychological Science.* Paris, France.

Chapter 1: Introduction

The scientific study of memory is close to 150 years old and has evolved greatly since the days of Ebbinghaus, Bartlett, and James (Bower, 2000). At the level of basic science, significant strides have been made in describing mnemonic processes (Baddeley, 2000; Bjork & Bjork, 1992), uncovering neurological underpinnings of memory formation (Bird & Burgess, 2008; Kandel, Dudai, & Mayford, 2014; Squire, 2004; Squire & Wixted, 2011), and computationally modeling memory systems (Burgess & Hitch, 2005; Kahana, 2020). The study of memory has also extended into applied settings. Elizabeth Loftus, for example, has done tremendous work detailing the role of false memories in the criminal justice system (Loftus, 1975; Loftus & Hoffman, 1989). Others have detailed the relation of memory and aging (Castel, Farb, & Craik, 2007; Hess, 2005; Park & Festini, 2017), and of course, an ongoing quest continues to search for behavioral or pharmaceutical interventions that can improve people's mnemonic capabilities. The themes outlined above are often found in basic textbooks of memory (e.g. Baddeley, Eysenck, & Anderson, 2014) and are what many would commonly associate with the scientific discipline of memory. However, memory researchers would be well-served to consider eating behavior as an emerging frontier in the study of memory. Not only do these two processes rely on similar neural architecture, namely the hippocampus (Stevenson & Francis, 2017), but recent work has demonstrated that memory processes affect eating behavior and eating behavior can similarly affect memory processes (Higgs & Spetter, 2018). The purpose of this dissertation, therefore, is to shed light on the recent intertwining of these (to many) seemingly distant areas of psychological science and illustrate to those interested in memory processes that there is much to glean by studying eating behavior.

A Lesson from the Study of Learning

Memory's sister discipline, learning, has been tied to eating behavior since Pavlov and his pioneering work on digestive processes. Pavlov famously discovered that neutral cues

(Conditional Stimuli [CS]) that preceded appetitive outcomes such as food or food odor (Unconditional Stimuli [US]) could elicit metabolic responses, such as the release of digestive enzymes, so long as the animal had properly learned the CS-US association. Moreover, he demonstrated that different food stimuli (e.g. bread or meat) influenced the amount and viscosity of saliva produced, suggesting metabolic responses are tailored to better digest previously encountered foods (Pavlov, 1910; Smith, 1995). Others have continued to demonstrate the influence of learning processes on eating behavior. Associations between flavors and their postingestive consequences create conditioned taste aversions and preferences. For example, Bolles, Hayward, and Crandall (1981) paired two different flavors with either flour (CS+) or chalk (CS-) and gave rats prolonged access to both mixtures. In a subsequent test, both flavors were paired with a flour/chalk mixture, but rats overwhelmingly preferred the flavor previously paired with the caloric flour outcome (CS+). Much of our recent understanding of conditioned taste preferences comes from the work of Anthony Sclafani and his colleagues who have, among other things, demonstrated the complex border parameters and neurobiology of this learning (for reviews see Myers, 2018; Sclafani, 2018). Similarly, flavors paired with illness on a single occasion can result in taste aversions to those flavors, even with extended temporal delays between experiencing the flavor and illness (Garcia, Kimeldorf, & Koelling, 1955). Evidence of these conditioned taste aversions exists even in fetal rats who then retain those aversions later in periadolescence (Gruest, Richer, & Hars, 2004; Stickrod, Kimble, & Smotherman, 1982). Learning typically requires multiple trials of the CS and US being paired in close temporal proximity and evidence of previous learning tends to wane over time. That conditioned taste aversion violates these norms suggests that learning processes differ when learning about food and postingestive consequences than when learning about other types of paired events. Indeed, though fear conditioning can occur following a single CS-US pairing, learning will not occur if the CS and US are not paired in close temporal proximity and even post-natal rats can acquire but not retain fear learning for prolonged periods of time (Sanders, Heroux, & Stanton, 2020). These

reviewed findings also demonstrate how simple Pavlovian relationships can have significant impacts on eating behavior.

Learning and disordered eating

Learning processes have more recently been invoked to understand disordered eating and its effects, such as overeating, anorexia nervosa, bulimia nervosa, and obesity. Berridge, Ho, Richard, and DiFeliceantonio (2010) outline a dissociation between food “liking” and “wanting” and suggest that alterations in reward learning contribute to overeating (for a recent review, see Morales & Berridge, 2020). Cues such as restaurant logos and scents gain incentive value as a consequence of becoming associated with food outcomes and then motivate eating behavior when later experienced. These motivated eating bouts represent increases in reward “wanting” but not necessarily hedonic reward “liking.” Such a dissociation is a hallmark feature of addiction phenotypes (Finlayson, King, & Blundell, 2007; Robinson, Fischer, Ahuja, Lesser, & Maniates, 2015; Robinson & Berridge, 2008). For instance, Watson, Wiers, Hommel, and de Wit (2014) taught human participants to press buttons for either chocolate or popcorn rewards. Satiating participants on one reward resulted in biased responding for the other. Nevertheless, even when satiated on chocolate for example, presenting a neutral cue that had previously been associated with chocolate increased the chocolate button key response, indicating an increased desire for the chocolate (i.e. Pavlovian to Instrumental Transfer). This type of habitual responding, in which responses are made simply because of an association with a stimulus, likely contributes to a significant amount of overeating, and can be contrasted to goal-directed behavior in which a response is made with the intention to receive a specific outcome (van’t Riet, Sijtsema, Dagevos, & de Bruijn, 2011). On the opposite side of the spectrum, anorexia nervosa (Foerde & Steinglass, 2017; Keating, 2010; Wagner et al., 2007) and bulimia nervosa (Grob et al., 2012; Wagner et al., 2010) are thought to be associated with impairments in reward learning, namely the ability to experience and learn from past rewarding events.

To conclude, learning theory and eating behavior have a long and rich history. It should be noted that the majority of the research combining these two areas has come at the hand of learning theorists and behavioral neuroscientists (for a review, see Boutelle & Bouton, 2015). Meanwhile, the recent linkages between memory and eating processes have almost exclusively been conducted by researchers who specialize in eating behavior. Their work has been instrumental in demonstrating the mnemonic control of eating but suggests that cognitive psychologists well-versed in mnemonic processes might offer a unique perspective to this new and growing arena.

Quantifying the Overlap Between Memory Processes and Eating Behavior

The aim of this dissertation is to highlight the interconnected nature of research on memory processes and eating behavior. To 'quantify' the extent of this overlap, we conducted a literature review in December 2020 using the database PubMed. Drawn from the overlapping topics to be discussed throughout this review, we created search terms to "measure" the relatedness of these *topics* of both our *bases*: memory processes and eating behavior. We used the number of returned articles as our metric of overlap size between each base with each topic. Note, the overlap between our bases and some topics (e.g., memory processes and hippocampal functions; eating behavior and obesity) is massive, and so it is not possible to stringently select articles based on any formal set of criteria. That said, the pure number of returned articles is still telling of the relative size of the overlap between each base and topic and can be used to make judgements of the relative size from one overlap to another. *Figure 1.1* illustrates the existing overlap between memory processes and eating behavior and the various topics we have identified in this review. The mnemonic control of eating, determinants of memory of eating, hippocampal contributions to eating, neuroendocrine influence on memory, and relationship between obesity and memory performance are all areas currently understudied and ripe for future research.

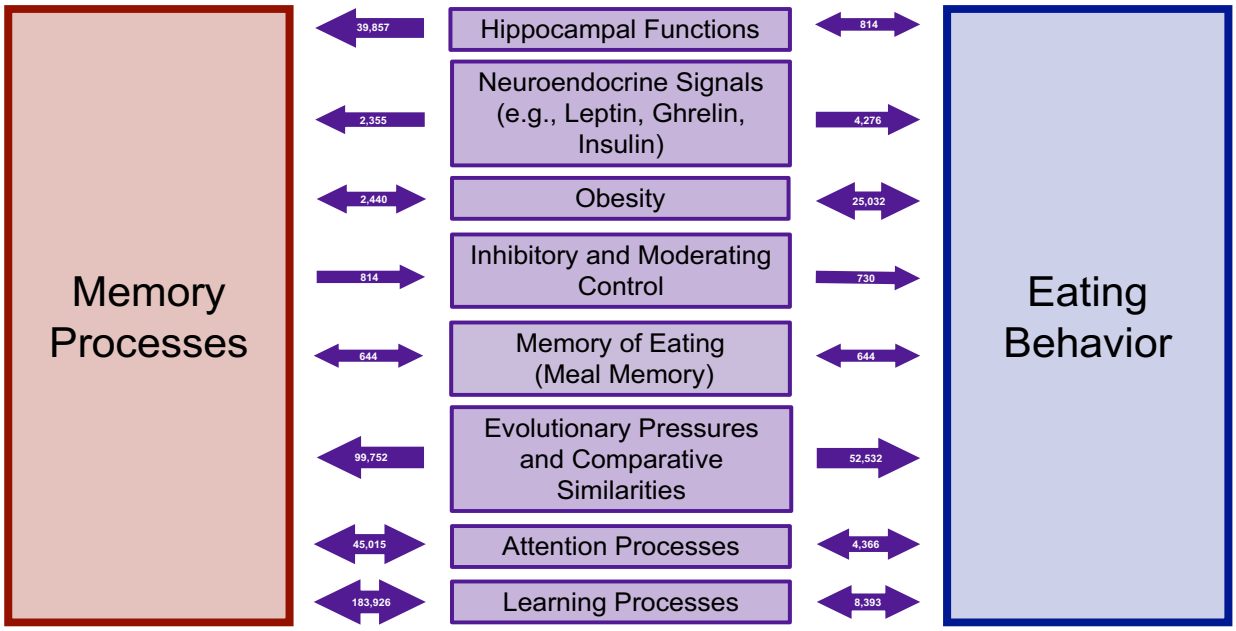

Figure 1.1: *Possible connections between memory processes and eating behavior supported by existing research. Arrow directionality indicates hypothesized causal relationship and arrow weight (log transformed) and value inside, indicates amount of existing research that supports each relationship. Intervening variables are not mutually exclusive.*

Memory's Effect on Eating

The first demonstration between declarative memory and eating behavior was a report by Hebben, Corkin, Eichenbaum, and Shedlack (1985) regarding the famous amnesiac patient H.M.. It was observed that his reports of hunger were not influenced by recent eating events. Amazingly, he was once documented to have eaten an entire meal just one minute after he had previously consumed the exact same full meal—although it was not initially recognized as being caused by deficits to memory of eating. This finding has since been shown in other amnesic patients, some of whom have consumed up to 3 full meals in under 90 minutes (over 1000 total calories) and points to the importance of memory of past eating events influencing current eating behavior (Rozin, Dow, Moscovitch, & Rajaram, 1998). Higgs, Williamson, Rotshtein, and

Humphreys (2008) followed up on this work and demonstrated that this effect is not due to impairments in sensory specific satiety.

Reduced memory of eating increases future eating

That memory affects eating behavior has also been demonstrated in healthy populations. Higgs (2002) cued participants to think about their most recent meal immediately before consuming a subsequent snack. In Experiment 1, participants in the control group received no cue, and in Experiment 2, participants in the control group were cued to remember their lunch from the previous day. In both experiments, only recalling one's most recent meal reduced eating at the subsequent snack test. This effect has now been replicated several times (Higgs, Williamson, & Attwood, 2008; Szypula, Ahern, & Cheke, 2020). Moreover, Vartanian, Chen, Reily, and Castel (2016) replicated the effect using the traditional retrospective approach but also by having participants imagine eating a future meal, which suggests that similar neural and cognitive processes underlie both retrospective memory and episodic future thinking (Schacter, Addis, & Buckner, 2007; Schacter, Benoit, & Szpunar, 2017) and that both contribute to the mnemonic control of eating. These data suggest that retrieval of a recent meal memory can modulate future eating.

Efforts and manipulations that target the encoding of meal memories similarly impact future eating. These studies typically involve an initial meal that is consumed while distracted or non-distracted, a follow up snack test, and finally, participants are asked to recall elements of the initial meal. For instance, Higgs and Woodward (2009) distracted participants while eating by having them watch television. At a later snack test, the distracted participants ate more than participants who did not watch television during the initial eating phase. The distracted participants also rated their memory of the initial meal as being less "vivid" than did the control participants. With that said, it is not necessarily clear that self-perceived memory vividness accurately relates to memory strength or accessibility. Mittal, Stevenson, Oaten, and Miller (2011) conducted a similar procedure but critically, asked participants to recall how much food

they consumed during the initial eating phase. They found that participants in the distracted eating group significantly underestimated the amount of food they had previously consumed compared to the non-distracted group, but this was confounded in that the distracted eating manipulation also caused those participants to consume more food in the initial eating task, thus increasing the likelihood for underestimation (Francis, Stevenson, Oaten, Mahmut, & Yeomans, 2017). Thus, future research should investigate how distracted eating affects recall of eating while holding the initial meal constant. Oldham-Cooper, Hardman, Nicoll, Rogers, and Brunstrom (2011) conducted such a study by having some participants play a video game to distract them. However, their memory test asked participants to remember the serial order of the foods they consumed during the initial eating event and not specifically how much of each food they had consumed. Nevertheless, distracted eating impaired serial-order memory relative to non-distracted eating, and all of these studies found distracted eating led to increased future snacking (for a review and meta-analysis, see Robinson et al., 2013).

Brunstrom et al. (2012) utilized a clever disappearing soup bowl mechanism to study the effect of memory on hunger. Participants were seated in front of a large or small portion of tomato soup. While some participants seated in front of the small portion consumed that small portion, others unknowingly consumed the large portion as it was covertly pumped into the bowl. Similarly, those seated in front of the large portion either ate the large portion or unknowingly ate the small portion as the soup was covertly siphoned out. Immediately after eating and one hour later, the amount of food actually consumed predicted self-reported hunger levels. However, two and three hours after eating the soup, self-reported hunger was predicted by memory of the portion size consumed (i.e. participants who were seated at the small portion were hungry regardless of how much they ate and participants seated at the large portion were less hungry regardless of how much they actually ate).

Enhanced memory of eating (sometimes) reduces future eating

Manipulations to enhance memory of eating have had mixed results in reducing future snacking. Several studies have found that instructing some participants to focus on sensory aspects of eating or to eat mindfully reduces later snacking compared to relevant controls (Allirot et al., 2018; Higgs, 2015; Higgs & Donohoe, 2011; Robinson, Kersbergen, & Higgs, 2014; Seguias & Tapper, 2018). Within these studies, there is also mixed evidence as to whether or not attentive eating manipulations enhances memory of eating (Higgs & Spetter, 2018). Additionally, more recent studies with attentive or mindful eating interventions have not reduced future snacking (Tapper & Seguias, 2020; Whitelock, Gaglione, Davies-Owen, & Robinson, 2019; Whitelock, Higgs, Brunstrom, Halford, & Robinson, 2018; Whitelock, Kersbergen, et al., 2019). Further research is needed to clarify the existence of this effect. One possible explanation of these inconsistencies is that memory for eating in the control conditions is already exceptionally strong, which would explain why memory for eating is not always enhanced by these manipulations, nor is future eating always reduced. Evidence in favor of this interpretation comes from a series of experiments covered in Chapter 3, showing that even distracted eating is better remembered than other similar behaviors (Seitz, Blaisdell, & Tomiyama, 2021). Thus, while it may be possible to reduce memory of eating through distraction, all things equal, eating events are likely to be well remembered (likely because of their evolutionary significance; see below).

Replication in an animal model and concluding framework

Advances in technological equipment in neuroscience have also demonstrated the role of memory in eating behavior. Using rats, Hannapel et al., (2019) optogenetically inhibited the dorsal and ventral hippocampus (dHC & vHC) before, during, or after an eating event, and then measured amount of future food consumed and latency to initiate subsequent eating. Only when either the dHC or vHC was inactivated after the meal was consumed, thus disrupting memory consolidation, did the rats increase their amount of future eating and also show a reduced duration between eating bouts. These results were found using lab chow, sucrose solution, and

saccharin solution as the main food variable. That rats who had their memory of eating the saccharin solution disrupted were quicker to initiate their next meal and consume more during that meal (relative to rats with an intact memory of eating the saccharin), suggests that it was not a lack of nutrients motivating the animal to eat (because saccharin contains no calories) but rather, their memory of their last meal. Thus, these results suggest a strong mediating relationship between memory of recent eating and future eating. In sum, there is considerable evidence that reducing meal memories, either through amnesia, distraction, deception, or optogenetics, increases future eating behavior and mixed evidence that attentive and/or mindful eating techniques can reduce future eating.

Eating Ailments and Memory

Given the global rise of eating related ailments (Hoek, 2016), and specifically obesity (Bentham et al., 2017), many have explored their effects on cognitive processes including memory. A number of correlational studies have established a negative correlation between Body Mass Index (BMI) and a variety of mnemonic capabilities. Cheke, Simons, and Clayton (2016) designed a novel “Treasure-Hunt Task” designed specifically to test definitive features of episodic memory. Their results show a negative correlation between BMI and episodic memory (but see Cole & Pauly-Takacs, 2017). Other studies with less sophisticated memory measures (e.g. wordlist recall, verbal list learning) have largely found deficits in memory associated with higher BMI (Cournot et al., 2006; Gunstad, Paul, Cohen, Tate, & Gordon, 2006; Prickett, Stolwyk, O’Brien, & Brennan, 2018), although not all studies have found this relationship (for reviews see Higgs & Spetter, 2018; Loprinzi & Frith, 2018; Prickett, Brennan, & Stolwyk, 2015). Neuroimaging studies also point to structural deficits and damage to memory associated areas being associated with overweight and obesity. For instance, numerous studies have shown reduced grey matter volume in hippocampus and prefrontal cortex in individuals with overweight and obesity (García-García et al., 2019; Herrmann, Tesar, Beier, Berg, & Warrings, 2019; Masouleh et al., 2016; Laurent et al., 2020; Medic et al., 2016; Raji et al., 2010; Willette &

Kapogiannis, 2015). It is, of course, important to note that this seemingly strong correlation between obesity and worsened memory performance poses a causal conundrum. Are individuals gaining weight because of their poorer mnemonic abilities or is weight gain causing deficits in memory? The relationship between weight gain and mnemonic deficits could also be cyclic. For instance, a one year longitudinal study with children (age 6-11) found that differences in some cognitive abilities (e.g. attention shifting, affective decision making) at the beginning of the study could predict BMI at the study's conclusion, but that initial BMI measures could also predict some cognitive abilities (e.g. working memory) at the study's conclusion (Groppe & Elsner, 2017). Non-human animal studies have therefore become important in understanding the causal and cyclic relationship between weight gain and memory impairments.

Evidence from non-human animal studies

The results from non-human animal studies tell a similar, albeit better controlled, story as those discussed above. A large number of studies in rats and mice have shown dietary induced obesity—or consuming diets known to cause obesity—results in rapid impairment on memory tasks, with the strongest deficits in spatial memory (Abbott, Arnott, Westbrook, & Tran, 2019; Cordner & Tamashiro, 2015). As an example, Kanoski and Davidson (2010) put rats on a diet high in fat and sugar (hereafter "Western diet") and showed impairments in a spatial memory task after only 72 hours and stable deficits to working memory were observed after 30 days on the diet. McLean et al. (2018) more recently demonstrated impaired episodic and contextual memory performance after just one day of exposure to a high fat diet, and others have found similar rapid impairments as a result of Western diets (Beilharz, Maniam, & Morris, 2014; Tran & Westbrook, 2015). Mechanistically, Western diets might impair mnemonic performance via neuroinflammation (Beilharz, Maniam, & Morris, 2015; Freeman, Haley-Zitlin, Rosenberger, & Granholm, 2014; Veniaminova et al., 2020), reduced neuroplasticity (Abbott et al., 2019; Morin et al., 2017; Spinelli et al., 2017), decreased blood brain barrier function (Davidson et al., 2012; Hargrave, Davidson, Zheng, & Kinzig, 2016; Kanoski, Zhang, Zheng, & Davidson, 2010), and

altered neuroendocrine (e.g., leptin, ghrelin, insulin) signaling (Kanoski & Grill, 2017; Suarez, Noble, & Kanoski, 2019). These diets might also impair memory performance through their effects on other cognitive processes, such as motivation (Blaisdell et al., 2014) and sustained attention (Blaisdell et al., 2017). While animal models provide ideal conditions for studying the effects of high fat and high sugar diets on memory, recent well controlled experiments in humans found sizable deficits in a number of memory tasks following just four days of eating a high fat and high sugar breakfast (Attuquayefio, Stevenson, Oaten, & Francis, 2017) and seven days of a high fat and high sugar diet (Stevenson et al., 2020). These data from studies in rodents, and now humans, make clear that dietary induced obesity, or simply consuming obesogenic diets, can cause deficits in memory processes.

The bidirectional relationship between obesity/poor diet and memory impairment

Despite mounting data that dietary induced obesity impairs memory, these data cannot entirely explain the correlation between human BMI and memory deficits. Just as inducing obesity begets memory impairments, studies in rodents similarly show that inducing memory impairments begets obesity. Forloni et al. (1986) and King et al. (1993) were among the first to demonstrate that lesions to the hippocampus result not only in memory deficits, but also hyperphagia. Davidson et al. (2009) provided a more precise and better controlled replication of this effect, demonstrating that destruction of the hippocampus results in increased food intake, body weight gain, and decreased general behavioral and metabolic activity. Damage to the hippocampus also results in impairments in detecting interoceptive cues related to hunger and satiety (Berriman et al., 2016; Davidson et al., 2010; Hebben et al., 1985; Kennedy & Shapiro, 2004).

This bidirectional relationship has been described by Terry Davidson and his colleagues as a “vicious cycle” of Western diet and cognitive decline (Davidson, Kanoski, Walls, & Jarrard, 2005; Davidson, Sample, & Swithers, 2014; Davidson, Jones, Roy, & Stevenson, 2019; Kanoski & Davidson, 2011). According to this model, there are both excitatory and inhibitory associations

between food cues and their postingestive consequences. The notion of competing excitatory and inhibitory associations is well documented in learning theory (Bouton, 2004; Rescorla, 1993; Seitz, Stolyarova, & Blaisdell, 2020). A unique component of Davidson's model is that the excitatory association is thought to be hippocampal-independent while the inhibitory association is thought to rely on hippocampal-dependent processes such as interoceptive cues and memory of recent eating. Competing activation strengths of both associations dictates eating behavior. This model is particularly illuminating in light of the fact that intake of a Western Diet leads to hippocampal dysfunction (reviewed above). Hippocampal dysfunction then results in an impaired ability to retrieve meal memories, detect interoceptive cues of satiety and hunger, and use other hippocampal dependent cognitive processes to appropriately inhibit eating behavior resulting in further intake of the Western diet, thus perpetuating the vicious cycle. This model adds nuance to the association between human BMI and memory deficits, and warns against the interpretation that poor diet simply causes obesity and cognitive impairments. Further, it suggests the need to develop separate intervention strategies aimed at targeting the hippocampal-independent excitatory and hippocampal-dependent inhibitory associations between food cues and their postingestive outcomes.

Determinants of Memory of Eating

The reviewed findings suggest memory of recent eating plays an important role in moderating future food consumption. Despite this, little is known about the factors that influence memory of eating. This should be the focus of future research because even small reductions in calorie consumption (e.g. 100 calories per day) could prevent weight gain in most of the population (Hill, Wyatt, Reed, & Peters, 2003, and see Hall et al., 2011, for more sophisticated estimates). For instance, when Higgs (2002) asked participants to recall their most recent meal prior to consuming a snack, they observed a 21% (Experiment 1, 61-85.5 kCal) and 49% (Experiment 2, 93.5-131.1 kCal) reduction in snacking compared to participants asked to think about anything (Experiment 1) or recall a meal from the day before (Experiment 2). Using a

similar manipulation and better powered study, Szypula et al. (2020) observed a 14% reduction, roughly equivalent to 70 fewer calories. Similarly, when Seguias and Tapper (2018) had some participants mindfully eat their lunch by focusing on the sensory properties of food, they observed a 91 calorie (~44%) reduction in subsequent snacking compared to a control group who focused on their heartbeat during the initial lunch. Thus, understanding the determinants of memory of eating may be insightful in designing interventions that enhance memory of eating and thus reduce unnecessary consumption and cue-induced eating.

Psychological and environmental determinants of memory of eating

Few studies have directly addressed what influences memory of eating in humans. New, Krasnow, Truxaw, and Gaulin (2007) had participants walk around a farmer's market and sample items from each of the vendors. Participants then entered an opaque tent where they were asked to point to where each vendor was. The pointing error was linearly related with caloric density of the food items, suggesting enhanced spatial memory for consuming high calorie foods. It should be noted that this is a somewhat crude measure of spatial memory, however the external validity of this measure and the study in general is impressive. Allan and Allan (2013) created a computer-based version of this task, where various food items were placed along a campus map. They found not only a spatial memory bias for high calorie foods but also that this bias was positively correlated with participant BMI, such that individuals with higher BMI showed a stronger bias towards remembering the spatial location of the high calorie images. Follow up work has replicated the enhanced spatial memory bias for high calorie food images and shown this effect is independent of personal experience with the food, duration of encoding, or hedonic evaluation of the food (de Vries, de Vet, de Graaf, & Boesveldt, 2020). While these studies suggest the caloric density of a food item might enhance spatial memory, they are correlational in nature, two have simply used food images, and they do not speak to whether caloric density influences memory for how much food was consumed—an episodic component of the memory separate from its spatial location. In chapter 3, I provide an

experimental test of the influence of caloric density on memory for how much food was consumed. Participants completed the Memory of Eating Task (MEaT) whereby they watched a video while being cued to eat every time a tone was sounded. This allowed the experimenters to manipulate exactly when and how often participants ate. Participants consumed the same amount (30 pieces) of either M&Ms, salted peanuts, or plain popcorn. When asked to recall how many pieces of food they consumed, participants who ate the two high calorie foods (around 5 calories per piece) were more accurate than those who ate the low-calorie popcorn (less than one calorie per piece). The results from these studies suggest one factor that influences memory of eating is the caloric density of the food item consumed. However, whether it is specifically the caloric density that is influencing memory of eating or some other component of the food that correlates with caloric density (e.g., nutrient content, texture, flavor) remains untested.

The speed/rate at which food is consumed might also be reasonably expected to influence memory for how much food was consumed. Distributing learning trials, by increasing the inter-trial-interval for example, yields better retention (Cepeda, Pashler, Vul, Rohrer, & Wixted, 2006; Underwood, 1961). Thus, slower or more distributed eating should result in better memory of the eating event than eating at a faster pace. This could potentially serve as a mechanism underlying the findings that slower pace of eating is associated with lower rates of obesity (Robinson, Almiron-Roig, et al., 2014), because of memory's moderating role on consumption. It could also explain why slower eating has been experimentally shown to reduce the amount of calories consumed during a meal (Bolhuis, Lakemond, de Wijk, Luning, & de Graaf, 2011; Martin et al., 2007; Scisco, Muth, Dong, & Hoover, 2011) and reduces post meal hunger levels (Andrade, Greene, & Melanson, 2008; Andrade, Kresge, Teixeira, Baptista, & Melanson, 2012). Ferriday et al. (2015) fed participants tomato soup via a modified feeding tube. Three hours later, participants were asked to pour into a bowl the amount of soup they remembered consuming, and those who consumed the soup slowly were more accurate at this

task than those who consumed the soup quickly. A limitation of this study was that consuming soup via a pump was a contrived and likely salient eating scenario which may have influenced memory performance and had limited applicability to actual eating behavior. Hawton et al., (2018) had participants consume a pasta dish either quickly (n=11) or slowly (n=10) and they controlled eating pace using an auditory cue. Two hours later, participants who ate slowly were more accurate in recognizing the correct portion size of their pasta dish in an array of images. One thing to note about this design and the design used by Ferriday et al. was that the memory test occurred several hours after consuming the food. This is important for understanding how memory of recent eating moderates future eating (which is expected to occur several hours after the initial eating event), but in terms of evaluating the strength of the initial encoded memory, it is possible that participant hunger levels may have influenced their responses. That is, just as memory of eating influences subsequent hunger levels (e.g. the disapearing soup bowl study discussed earlier Brunstrom et al., 2012), hunger levels might also influence reported memory of eating.

To test immediately after encoding and speak specifically to the retrieval strength of the encoded memory of eating (Bjork & Bjork, 1992), Seitz et al. (2021) used the MEaT task (described above and in chapter 3) to investigate how eating rate influences memory of eating immediately following the initial eating event. Participants picked up the food item and placed it in their mouths—in contrast to food being pumped into their mouths and the memory test involved recall of how many M&Ms were consumed. As hypothesized, participants who completed a slow version of the MEaT, consuming 30 M&Ms on average once every 45 s, were significantly more accurate in remembering how many M&Ms they consumed compared to participants who consumed 30 M&Ms quickly (on average once every 15 s) (Seitz et al., 2021). Thus, slower and more distributed eating appears to effectively enhance memory of eating, although its downstream effects on later food consumption are less known.

The extant studies suggest that the caloric density of the food item consumed and rate at which it is eaten affects later recall. Still though, there remain a host of additional factors related to the food items themselves (e.g. nutrient density, flavors, novelty, etc.), and nature of the eating experience (alone vs with others, time of day, meal size, etc.) that may also influence memory of eating. Future research is needed to uncover additional determinants of memory of eating and how such changes in memory of eating influence its regulatory control of future eating.

Source monitoring and reality monitoring also likely influence memory of eating. Source monitoring involves determining the origin of memories and may be particularly difficult for eating behavior given its frequent and ritualistic occurrence (Bradburn, Rips, & Shevell, 1987). Children—who typically exhibit more errors in source monitoring, were found to report a high number of intrusions (i.e., memory for things they did not eat) when asked to report their breakfast from 24-hours prior (Baxter, Hardin, Royer, Guinn, & Smith, 2008). Reality monitoring involves determining whether memories are based on external or internal sources and could be a challenge for individuals who often think about food and eating events and those with so called “food addiction” (Gearhardt, Corbin, & Brownell, 2009). Both processes are relevant to individuals trying to remember the content and quantity of their recent meals and yet, to our knowledge, have not been specifically studied in relation to eating behavior.

Physiological and neuroendocrine determinants of memory of eating

While the psychological determinants of memory for eating are still largely unknown, much work has demonstrated the physiological and neuroendocrine signals that influence memory of eating. Leptin is a gut-derived hormone that communicates with the hypothalamus to effectively induce feelings of fullness and cease eating (Farooqi et al., 1999). Receptors for leptin are also found in the hippocampus (Lathe, 2001) and leptin administration to the hippocampus generally enhances memory function (Malekizadeh et al., 2017; Oomura et al., 2006). Paradoxically however, leptin administration to the hippocampus decreases learning

about food relevant information. For instance, in rats, leptin administration to the ventral (but not dorsal) hippocampus impairs memory consolidation for the spatial location of food (Kanoski et al., 2011) and systemic leptin administration attenuates conditioned place preference for sucrose (Figlewicz et al., 2004; Shimizu et al., 2017). Leptin, therefore, may aid in encoding the reward value of food, with high volumes of leptin in the vHPC resulting in the attenuation of food's value and decreased leptin resulting in enhanced value assigned to food (Davis et al., 2011; Domingos et al., 2011; Hommel et al., 2006). Alternatively, it is possible that high volumes of leptin in the vHPC may promote learning of food relevant information with feelings of satiety that can then suppress the excitatory association between the food relevant information and rewarding food outcomes (Davidson, Jones, Roy, & Stevenson, 2019). Thus, animals might not demonstrate CPP because the "place" has been associated with feelings of fullness or nonrewarding food intake which prevents expression of any excitatory associations between the "place" and food (Kanoski et al., 2011). By either account, because leptin serves as a satiety signal, high levels of leptin in the brain might indicate to the animal that it is not necessary to remember eating related information (perhaps to prioritize learning about other information) or indicate that a food cue will no longer be followed by a reinforcing outcome—either of which would reduce certain aspects of memory of eating.

Less is known how leptin influences memory in humans. While leptin serves as a signal of fullness, a paradoxical finding is that individuals with obesity reliably exhibit higher concentrations of serum leptin (Francisco et al., 2018; Zimmet et al., 1996). This is thought to be the result of impaired transport of leptin across the blood-brain barrier (BBB) (Münzberg, Björnholm, Bates, & Myers, 2005) and/or weakened leptin receptor sensitivity, and is why obesity is said to be associated with *leptin resistance* (Myers, Leibel, Seeley, & Schwartz, 2010; Scarpace & Zhang, 2009). Because leptin administration to the vHC is thought to devalue food reward, the lack of leptin reaching the vHC and perhaps other critical regions may inflate the rewarding value of food outcomes. Suggestive of this, exogenous leptin concentrations (high

concentrations being indicative of insulin insensitivity) were correlated with greater activation of striatal-limbic regions when viewing food images (Grosshans et al., 2012; Jastreboff et al., 2014). Despite these intriguing results, little research in humans has directly addressed the role of leptin in learning about and remembering food versus nonfood information.

Ghrelin is another gut-derived hormone implicated in both homeostatic regulation of eating as well as having contributions to learning and memory. Ghrelin is often referred to as the hunger hormone because its signaling to the hypothalamus is believed to induce hunger (Müller et al., 2015). Following training on a passive avoidance assay, rats given ghrelin administration to the cerebral ventricles (Carlini et al., 2002) and hippocampus (Carlini et al., 2004) improved memory performance in a dose-dependent fashion. Ghrelin knockout mice demonstrate impairments in a novel object recognition task but this deficit is attenuated following subcutaneous ghrelin replacement (Diano et al., 2006). Ghrelin also appears to play a role in spatial and contextual memory as ghrelin antagonists disrupt conditioned place preferences with food rewards (Chuang et al., 2011; Perello et al., 2010). At a neurobiological level, leptin knockout mice show reductions in hippocampal spinal density (Cahill, Hatchard, Abizaid, & Holahan, 2014) but peripheral ghrelin administration increases hippocampal spinal density in ghrelin deficient mice (Diano et al., 2006). Recent work has begun to implicate ghrelin in human memory formation. Intravenous ghrelin administration increases cerebral blood flow in the hippocampus, amygdala, orbito-frontal cortex, and striatum when viewing food stimuli but not nonfood stimuli (Malik, McGlone, Bedrossian, & Dagher, 2008). Similarly, intravenous ghrelin enhances cue-food reward learning by increasing connectivity between the hippocampus and ventral striatum (Han et al., 2018). This suggests ghrelin may enhance the rewarding value of food cues in both humans and rodents or that ghrelin enhances the memorability of food relevant information. That said, these studies in humans have limitations due to their procedural indices of enhanced learning. As an example, the reported finding of intravenous ghrelin enhancing the formation for cue-food reward learning was demonstrated by pairing an image

with a food odor and then finding faster reaction time in answering a descriptive question about the image paired with food vs non food odors (e.g. whether the image is composed of straight or curvy lines). Thus, there is need to demonstrate the effects of ghrelin on the formation of food relevant memories using additional procedures and measures of memory.

While we have focused on just leptin and ghrelin as neuroendocrine determinants of memory of eating, others may be implicated as well (e.g. insulin, CCK, Glucagon-Like Peptide 1, Neuropeptide Y). There is growing evidence of this in rodents (for an exhaustive review, see Suarez et al., 2019), but little work has addressed these mechanisms in humans. Collaborations between human memory researchers and neuroendocrine specialists would be particularly fruitful in moving forward.

Evidence of specialized learning and memory mechanisms that aid in foraging

How does learning and remembering food relevant information differ, if at all, from learning and remembering other information? Central to this question is the notion of equipotentiality—the assumption that any two events (e.g., cue-outcome or cue-response) have equal potential to be learned about and associated with one another. Equipotentiality fueled many early learning theorists' attempts to derive general laws of learning (Bolles, 1993; Escobar & Miller, 2004; Miller & Escobar, 2002). It also arguably influenced many of the early and influential models of memory (e.g., Multi-Store [Atkinson & Shiffrin, 1968], Parallel Distributed Processing [Rumelhart & McClelland, 1986], Levels of Processing [Craik & Lockhart, 1972], Working Memory Model [Baddeley, 1992]). The first process that occurs in all of these models is that 'information' or 'input' enters the memory system and therefore, there is no way for these models to make *a priori* predictions regarding how some information might be inherently better remembered than other information (Seitz, Blaisdell, Polack, & Miller, 2019). But much work has challenged the notion that learning and memory systems are such *Tabula rasa*. Garcia and Koelling (1966) famously showed rats are more capable of learning associations between flavors and malaise than they are flavors and tactile pain and evidence of these selective

associations is also seen in humans (Öhman, Eriksson, & Olofsson, 1975; Öhman, Fredrikson, Hugdahl, & Rimmö, 1976; Öhman & Mineka, 2001). Recent studies show biases to the human memory system that appear to be reflective of evolutionary pressures. As an example, simply imagining oneself performing fitness relevant tasks, such as surviving in the grasslands or parenting a child, while encoding information, can result in increased retention of that information (Nairne, Thompson, & Pandeirada, 2007; Seitz, Polack, & Miller, 2018). There are also reported biases towards remembering potential sources of contamination (Bonin, Thiebaut, Witt, & Méot, 2019; Fernandes, Pandeirada, Soares, & Nairne, 2017), future mates (Pandeirada, Fernandes, Vasconcelos, & Nairne, 2017), and potentially untrustworthy individuals (Hou & Liu, 2019; Kroneisen, 2018). Thus, it appears the evolutionary significance of encoded information potentiates its ability to be later recalled (Seitz, Blaisdell, Polack, et al., 2019). If true, information relevant to eating and foraging should be incredibly well learned about and remembered given the obvious survival relevance of these acts.

The chapters that follow evaluate the hypothesis that learning and memory systems are optimized to learn about and remember food relevant information. Specifically, in a number of experiments, I seek to identify features of learning and memory systems that appear specialized to aid animals in foraging. In Chapter 2, I explore the role of innate metabolic responses to novel flavors and argue their existence is likely due to a long evolutionary history of flavors being paired with caloric outcomes. In Chapter 3, I compare memory for the act of eating to other similar but non-eating behaviors, and show prioritized memory for the act of eating and for eating high-calorie food items relative to low-calorie food items. Finally, in Chapter 4, I explore the role of midbrain dopamine neurons in learning backward relationships between food rewards and cues that can later be used to guide behavior in ways that indicate these cues have become associated with detail-rich representations of the food rewards. Such findings revise current conceptualizations of dopamine's contribution to learning and also broadens the way with which learning Pavlovian relationships can help aid a foraging animal understand their

environment. Collectively, I argue these findings, in addition to many others, are at least suggestive of the hypothesis that learning and memory systems evolved primarily to assist animals in finding and obtaining food.

Chapter 2: Evidence that Novel Flavors Unconditionally Suppress Weight Gain in the Absence of Flavor-Calorie Associations

The obesity epidemic currently poses a major health (Williams, Mesidor, Winters, Dubbert, & Wyatt, 2015) and financial threat (Tremmel, Gerdtham, Nilsson, & Saha, 2017) to societies around the world. Rates of obesity have increased dramatically over the past several decades, with environmental factors being strongly implicated (Apovian, 2016). As food intake and nutrient digestion are necessary factors in weight gain, a deeper understanding of the mechanisms that govern food consumption and metabolic processes is needed in order to address possible interventions to treat obesity.

Beginning with Pavlov (1927), there has been great interest in the role of associative learning in eating behavior, including the regulation of appetite. Food choice and foraging decisions are influenced by associative learning about food cues. Such learning aids in discriminating food from non-food (e.g., as food preferences and aversions), readies digestion (e.g., through the release of digestive enzymes), and regulates post-prandial energy regulation (e.g., through insulin signaling). For example, Pavlov (1910) found that the viscosity and amount of saliva that was elicited by the presentation of a food stimulus differed depending on what that food stimulus was. Moreover, he found sham feeding, a procedure in which surgical manipulations prevent chewed and swallowed food from reaching the stomach, lasted longer and resulted in more gastric secretion for meat than for bread (Pavlov, 1910; Smith, 1995).

Many others have attempted to use Pavlovian principles of conditional relationships to understand a variety of aspects related to eating behaviors. For instance, a flavor can serve as a conditioned stimulus (CS) that signals incoming calories which serve as an unconditioned

stimulus (US). Once conditioned, flavor CSs tend to be preferred over flavors not associated with calories (Capaldi, 1996; Capaldi, Hunter, & Lyn, 1997; Sclafani, 2001). In a simple demonstration of this effect, Bolles, Hayward, and Crandall (1981) gave rats access to a flavor paired with flour (CS+) while a different flavor was paired with chalk (CS-; "+" and "-" indicate the presence or absence of the caloric US). Rats had access to both of these mixtures for several days and were then presented with the flavors combined with a mixture of flour and chalk. Rats consumed more of the mixture that contained the CS+ flavor than that which contained the CS- flavor. Mehiel and Bolles (1984) conducted a similar experiment in which they paired flavors with either sucrose or saccharin (both sweet tasting) in a solution to rule out the possibility that rats simply were avoiding the potentially aversive chalk. Rats overwhelmingly preferred the solutions containing sucrose over saccharin. Acquired preferences for flavors that had been paired with calories has also been demonstrated in humans (Birch, McPhee, Steinberg, & Sullivan, 1990; Brunstrom & Mitchell, 2007, but see Brunstrom, 2007, and Yeomans, 2012). The past several decades of research, much of it led by Anthony Sclafani and his colleagues, has demonstrated the complex border parameters and neurobiology that govern flavor-outcome learning (for recent reviews see, Myers, 2018; Sclafani, 2018). For instance, a flavor CS paired with sweetness may become preferred not only because it is reinforced with the caloric outcome (US), but also because it is reinforced with the sweet taste outcome (US). Thus, precise experimental designs and procedures have been developed to dissociate the reinforcing effects of both outcomes, and post oral hedonic and postingestive nutrient outcomes appear to reinforce flavors in dissociable ways (Myers & Hall, 1998).

While there are many examples of learned flavor preferences, there also exists evidence of unconditioned preferences for certain tastes. Note there is a difference between a taste and a flavor, as a flavor requires an olfactory component (Small & Prescott, 2005). Also note that we use the term unconditioned instead of innate due to the challenge of proving a response to have occurred in the absence of experiential input (e.g. prenatal and postnatal development). Of

course, proving a response to be truly unconditioned is difficult as well because it requires knowledge of all previous encounters with various stimuli. Fortunately, using a rodent model and unique flavors allows for this possibility, hence our use of the term unconditioned. Infant rats demonstrate likings to sweet and moderately salty tastes as well as aversion to bitter and sour tastes (Bartoshuk & Beauchamp, 1994; Birch, 1999; Myers & Sclafani, 2006; Vigorito & Sclafani, 1988). Even fetal rats on day 19 of gestation have shown aversions to lemon infusions and preferences towards milk infusions (note milk has both taste and flavor components) (Smotherman & Robinson, 1987). While there exists evidence of unconditioned preferences to certain tastes as well as to flavors specific to milk in mammals, whether there are unconditioned preferences and/or responses to non-species relevant flavors is underexplored. By non-relevant, we mean flavors that are not naturally found in the substances (e.g., milk) that a species (e.g., mammals) should be prepared to consume starting from a very early age. As with many behaviors, metabolic responses to flavors likely reflect a combination of unconditioned and learned responses.

The role of Pavlovian conditioning in appetite regulation

As a novel flavor is repeatedly paired with calories, such as when an omnivorous animal consumes a novel food, the development of flavor-calorie associations increases the amount of food consumed during an eating bout (i.e., a meal). The initial intent of our research was to document the effect of the development of flavor-calorie associations on general food consumption and weight gain in animals that received a new flavor paired with calories compared to animals just receiving flavors or calories separately. A surprising but reliable result emerged, however, which led us to continue to explore the role of novel flavors that were or were not paired with calories on appetite and body weight over a three-week period. The following series of experiments, therefore, examines the effect of novel flavors, consumed in solutions containing either plain water or sugar water, on appetite and weight regulation over a three-week interval.

We developed a protocol to isolate the learning event (exposure to flavors and/or calories) from its potential effects on appetite and body weight[‡]. A diagram of the treatment is depicted in Figure 2.1. Rats were given *ad libitum* access to lab chow and water for 20 hours each day. During their active period, water and food access were restricted for two 90-minute flavor-free and calorie-free windows. Following the first window, rats were given 60-minutes of access to a small amount of liquid containing some combination of flavor or no flavor, and calories or no calories. Another 90-minute window of no flavor or calories followed the one-hour access, and ended with the return of water and chow until the next treatment 20 hours later. This procedure was repeated daily for 21 days which should be sufficient time for the development of flavor-calorie associations to have their effects on the dependent measures of interest (appetite and body weight). It should be noted that sucrose solution contains a small but detectable amount of flavor, at least for rats (Rhinehart-Doty, Schumm, Smith, & Smith, 1994). Nevertheless, adding a salient flavor should greatly enhance the effects of flavor-calorie associations compared to the sugar water condition in which sugar flavor is of low salience. Furthermore, the 2 (flavor vs. no flavor) by 2 (sugar vs no sugar) design of this experiment allows us to tease apart any effect of the flavor of sugar from its taste.

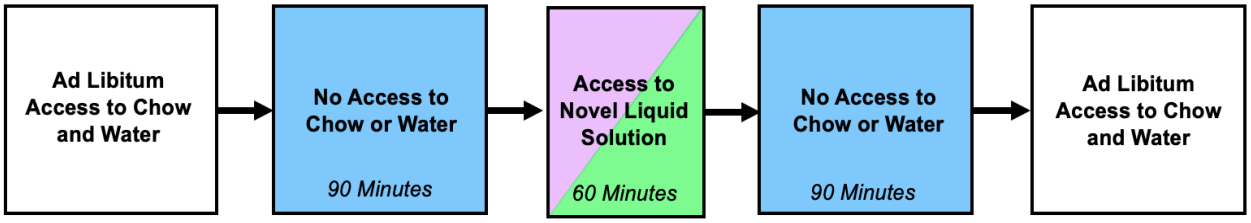

Figure 2.1: *Schematic of the daily procedural timeline for Experiments 1, 2, & 3.*

Experiment 1

In this experiment, rats received either plain water, sugar water, water with a pomegranate-berry flavor added, and sugar water with the pomegranate-berry flavor added. Rats received their daily access to their proscribed liquid following the protocol described above (Figure 2.1) for 21 consecutive days.

***Subjects*:** 32 female Long Evans rats (Envigo) were used in this experiment. Subjects were single-housed in transparent plastic tubs with a wood-shaving substrate. Subjects were housed in a vivarium maintained on a reverse 12-hour light cycle (lights off at 7am). Immediately preceding this study, all subjects had participated in a study involving exposure to audiovisual cues, footshock, and a 20% sucrose solution. During that training, animals were kept at 85% of their free feed weight and pair-housed. After that experiment concluded, animals were individually housed and given *ad libitum* food access for six days before the diet intervention procedure of Experiment 1 began. Our decision for reusing these rats reflects ethical considerations in regards to the three R's of animal research (Fenwick, Griffin, & Gauthier, 2009), but it is acknowledged as a potential confound of this study, which we discuss further in the conclusion.

***Materials*:** Mio Liquid Water Enhancer (Kraft Foods, Berry Pomegranate) was used as the novel flavor additive. The solution contains zero calories and is sweetened by a combination of sucralose, acesulfame potassium, and less than 2% natural flavors. This flavor additive was initially chosen for its lack of calories but is confounded by the fact that it has the properties of a sweet taste. We elaborate on this further in the discussion and also choose a different flavor additive (peppermint extract) in Experiments 2 and 3. Four solutions were created using separate equipment for the production and dispersion of each to reduce contamination of flavors and calories. Each of the flavored solutions contained 3% Mio Flavoring, the rest being tap water. Each of the caloric solutions contained 20% sucrose. Rats were randomly assigned to treatment group. Mean initial body weight per group was 248.12 +/- 2.91 grams.

***Procedure*:** Rats were first individually caged for six days and given access to standard lab chow and filtered water ad libitum. This six-day period allowed subjects to adjust to the novel single-housed environment. Following this six-day adjustment period, access to food and water was restricted each day from 1-5 pm. *Figure 2.1* displays a complete outline of the daily procedure during this 4-hour period. In each condition, a 90-minute period elapsed where rats

had no access to food or water. When removing food and water from each subject's home cage, care was taken to remove any food hidden within the cage, particularly in the wood shavings. At the conclusion of this 90-minute period, each subject received access to a bottle containing 30 ml of their group-assigned liquid solution (water, flavored water, sugar water, or flavored sugar water) for 60 minutes. At the conclusion of this 60-minute access to the bottle, the solution was removed for another 90 minutes before having their normal water bottle and chow returned. Although each bottle contained 30 ml, the angle at which it was placed in the cage only allowed access to about half of the solution (i.e. ~15 ml). Rats typically consume around 10-15% of their body weight in water (Kuribara et al., 1978) in a daily period, and so even if our rats (average starting weight = 248 g) consumed all of the liquid, it would only be around half of their daily typical water intake. Body weight measurements and food consumption measurements were made during the first and second 90-minute period respectively. This procedure was repeated for 21 consecutive days.

***Results and Discussion*:** Measurements of body weight were taken daily and analyses were conducted using 2-day blocks (Figure 2.2a). A mixed ANOVA with a Greenhouse-Geisser correction and with Block as a repeated measure, and Flavor (present or not present) and Sugar (present or not present) as between-subject factors conducted on body weight revealed a main effect of Block, $F(5.197,147.511) = 11.821$, $p < 0.001$, $\eta^2 = 0.019$, indicating that body weight significantly changed over the course of the intervention. This analysis also revealed an interaction between Block and Flavor, $F(5.197,147.511) = 5.399$, $p < 0.001$, $\eta^2 = 0.009$, but no interaction between Block and Sugar, $F(5.197,147.511) < 1.0$, nor was there a three way interaction, $F(5.197,147.511) < 1.0$.

Mean body weights differed between groups at the start of the intervention. Therefore, to better assess the effect of the intervention on changes in body weight, we calculated body weight percent change over the course of three weeks (Figure 2.2b). A mixed ANOVA with a Greenhouse-Geisser correction and with Block as a repeated measure, and Flavor (present or

not present) and Sugar (present or not present) as between-subject factors conducted on body weight percent increase revealed a main effect of Block, $F(5.433,152.130) = 14.465$, $p < 0.001$, $\eta^2 = 0.105$, an interaction between Block and Flavor, $F(5.433,152.130) = 6.069$, $p < 0.001$, $\eta^2 = 0.044$, but no interaction between Block and Sugar, $F(5.433,152.130) < 1.0$, nor was there a three way interaction, $F(5.433,152.130) = 1.186$, $p = 0.318$, $\eta^2 = 0.009$.

Due to these interactions, and because we were more interested in the final percentage of weight gain or loss from the intervention, a 2 (flavor vs. no flavor) by 2 (sugar vs. no sugar) ANOVA conducted on body weight percent change in the 10th block (i.e. the last two days, Figure 2.2c) of the intervention procedure revealed a main effect of Flavor, $F(1,28) = 6.260$, $p = 0.018$, $\eta^2 = 0.180$. No effect of Sugar was found, $F(1,28) < 1.0$, nor was there a Flavor x Sugar interaction on weight gain, $F(1,28) < 1.0$. Thus, when the liquid solution contained Mio flavoring, natural weight gain associated with the removal of restricted feeding was attenuated. Interestingly, the presence of sugar in the flavored liquid solutions did not affect this attenuation in weight gain, $F < 1.0$, nor did it cause increased weight gain for the sugar water condition compared to the water condition, $F < 1.0$.

Measurements of daily food consumption were also taken. Following the daily intervention procedure, rats were always given access to 85 grams of Purina Lab Chow. The following day, we weighed the amount of remaining food after we had removed it from the animal's cage and subtracted that value from 85 to compute daily consumption. Food consumption was also analyzed in two-day blocks (Figure 2.2d). While the development of flavor-calorie associations has been shown to increase consumption of food containing that specific flavor, the effects of these associations on general food consumption is unclear. Roberts (2004) theorized that learning flavor-calorie associations should increase general appetite after detection of the flavor, because it serves as a signal that high quality food is available and should be consumed, but this has yet to be adequately tested. Nevertheless, because we observed differences in weight gain, we were not only interested in how the amount

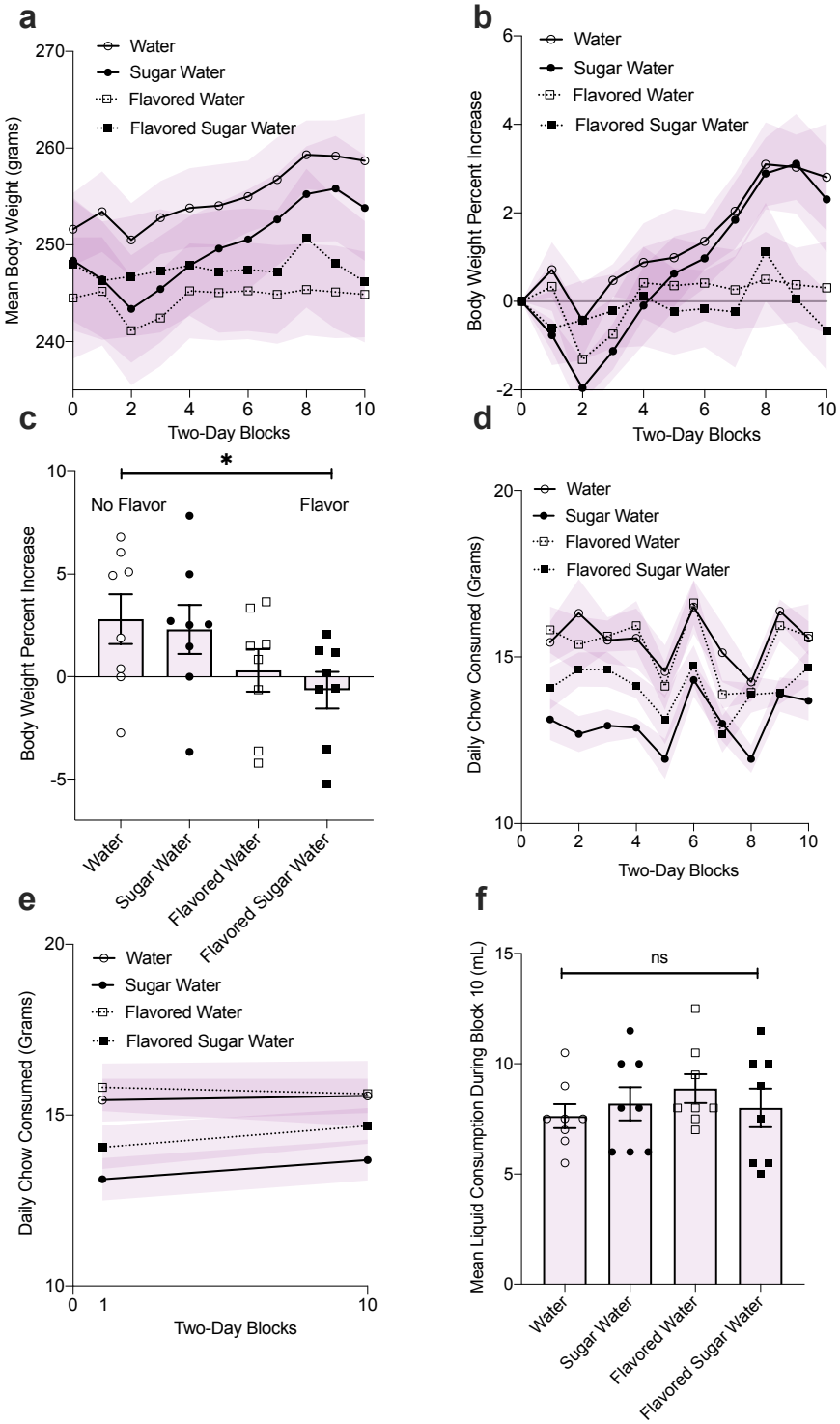

Figure 2.2: *Data from Experiment 1 using Mio Berry Pomegranate flavoring. Error bars represent SEM. * = p value < .05, ** = p value < .01, *** = p value < .001. a) Mean body weight (grams) following liquid intervention in two-day blocks as a function of each liquid-intervention group. b) Mean body weight converted to percent increase c) Mean body weight increase on final block of liquid intervention. d) Daily food consumption in two-day blocks. e) Change in daily food consumption from block 1 to block 10. f) Mean consumption of the intervention liquid for one hour during block 10.*

of chow consumed differed between groups, but also how the consumption differed within condition over time due to the respective treatments. A mixed ANOVA was conducted on food consumption data with two between subject factors (Sugar and Flavor) and one within subject factor (Blocks 1 & 10; Figure 2.2e). A main effect of Sugar was found, $F(1,28) = 10.352$, $p = 0.003$, $\eta^2 = 0.258$, such that rats that drank liquid solutions containing sugar consumed less food than rats that drank liquid solutions without sugar. This could be explained by the fact that the animals were receiving additional calories from their sugar in their liquid intervention solution. There was no main effect of Flavor, $F(1,28) = 1.235$, $p = 0.276$, $\eta^2 = 0.031$, nor an interaction between Flavor and Sugar, $F(1,28) < 1.0$. We also did not see any evidence that learning a flavor-calorie association affected food consumption. No main effect of Block (1 *vs*. 10) was found, $F(1,28) < 1.0$, nor was there an interaction between Block and Sugar, $F(1,28) < 1.0$, or Block and Flavor, $F(1,28) < 1.0$, nor a three way interaction between Block x Sugar x Flavor, $F(1,28) < 1.0$. Daily chow consumed, therefore, does not appear to explain the group differences in weight gain. Critically, though the animals that drank flavored solutions did not gain weight as much as did animals that drank non-flavored solutions, these animals did not eat any less food than the animals who gained weight.

Is it possible that these differences in weight gain could reflect differences in the amount of liquid consumed (e.g., overconsumption or no consumption) during the one-hour intervention period? We believe this to be unlikely given the small amount of liquid (~15 ml) that was given in a relatively short period of time. To test this, we took pre and post bottle weight measurements on the last two days of the intervention procedure for all rats. These data are displayed in Figure 2.2f, and a one-way ANOVA revealed no effect of condition on amount of liquid consumed during the 10th block of intervention, $F(3,28) < 1.0$. Interestingly, while rats drank more of the sugar water compared to the unsweetened water, this difference was not as large as one might expect given rats typically prefer sweetened water. This is possibly the result of rats having previous exposure to the sucrose solution but could also be due to the small amount of liquid

that was provided to already thirsty rats. Further, that all rats consumed about the same amount of liquid during the intervention period suggests the observed patterns in weight gain are due to contents of the liquid solution and not how much of it was consumed.

The animals that drank the flavored solutions did not gain weight, yet they also did not consume any less food than the non-flavor controls. This suggests there may have been differences in metabolic responses evoked by the flavored solutions. Specifically, the 3% Mio flavored solutions, which were sweet and flavorful, may have evoked a large metabolic response from the rats. For the flavored water condition, no calories followed this flavor exposure, and so metabolism could only operate on the body's existing energy stores (e.g., glycogen and lipids). Similarly, given the strong sweetness and flavor of the Mio-flavored sugar solution, the magnitude of the metabolic response may have exceeded the appropriate response magnitude for that amount of incoming calories. In the absence of a direct measure of metabolic response, this interpretation is speculative. This interpretation is also similar in principle to research that demonstrates the potential downsides of artificial sweeteners from a learning perspective (T L Davidson & Swithers, 2004; Swithers, 2013; Swithers & Davidson, 2008). Through experience, or perhaps evolved predispositions, sweetness is a strong signal of incoming calories. Frequent consumption of artificially-sweetened foods therefore, can result in sweetness becoming an unreliable signal of incoming calories, thereby lowering the magnitude of metabolic responding to sweet tastes. In turn, when one actually consumes a high-sweet, high-calorie food item, the metabolic response is insufficient to metabolizing the calories and the excess is stored, potentially resulting in weight gain. Thus, in our experiment, an unconditioned or learned association between sweetness and calories may have resulted in the Mio-flavored solutions eliciting a large metabolic response for either no incoming calories (Flavored Water) or fewer incoming calories than was expected given the level of sweetness (Flavored Sugar Solution). While the Mio flavoring was entirely novel to the subjects at the start of the experiment, all rats had prior experience with a sweetened liquid solution that contained calories

(20% sucrose water). This creates some difficulty in drawing inferences about the extent to which the metabolic response to the Mio flavoring was due to some sort of unconditioned metabolic response to flavors or to generalization because the rats had learned that other sweet solutions contain calories. Additionally, that Mio contains acesulfame potassium is also troubling because this substance has been shown to increase consumption and weight gain under some conditions (Swithers, Baker, & Davidson, 2009). To obviate these confounding factors, in Experiment 2, we replicated the procedure of Experiment 1 using a peppermint extract as the flavor additive. The peppermint extract on its own was not sweet.

Experiment 2

The surprising result from Experiment 1 was the suppressing effect on weight gain by consuming an initially novel flavor, despite no change in daily amount of food consumed. These unexpected findings raise the hypothesis that novel flavors might unconditionally elicit metabolic responses, even if those novel flavors exist in liquid solutions that contain no calories. To investigate this hypothesis and rule out any effect of the sweetness of the novel flavor used in Experiment 1, we replicated the procedure of Experiment 1 with new rats, and used peppermint extract as the novel flavoring agent. Critically, none of the animals had prior experience with the peppermint flavoring, and this flavor was highly distinct from any other flavors the animals had previously experienced.

***Subjects*:** 32 female Long Evans rats (Envigo) were used in this experiment. Rats had similar prior experience with cues, footshock, sucrose solution, and food restriction as did rats in Experiment 1. Housing and acclimation were as described for Experiment 1.

***Materials*:** The materials used in Experiment 2 were nearly identical to those used in Experiment 1, with the exception being that flavored solutions were flavored with 0.039% McCormick peppermint extract. Rats were pseudo randomly assigned to group and care was taken to ensure there were minimal initial differences in mean body weight between the 4 groups (all groups mean initial body weight was 254.5 +/- 0.76 grams).

***Procedure*:** The procedure was identical to that used in Experiment 1 (Figure 2.1).

Results and Discussion: Mean body weight over the three-week period is displayed in Figure 2.3a. A mixed ANOVA with a Greenhouse-Geisser correction with Block as the repeated measure and Flavor (present or not present) and Sugar (present or not present) as between-subject factors conducted on body weight revealed a main effect of Block, $F(4.390,122.920) = 20.210$, $p < 0.001$, $\eta^2 = 0.017$, indicating that body weight significantly changed over the course of the intervention. There was a significant interaction between Block and Flavor, $F(4.390,122.920) = 2.525$, $p = 0.006$, $\eta^2 = 0.002$, but no interaction between Block and Sugar, $F(4.390,122.920) = 1.133$, $p = 0.356$, $\eta^2 = 0.001$, nor a three way interaction, $F(4.390,122.920) < 1.0$. We then performed similar analyses after converting body weight to body weight percent increase (Figure 2.3b) and found a main effect of Block, $F(4.682,131.096) = 18.079$, $p < 0.001$, $\eta^2 = 0.119$, but no interactions between Block and Flavor, $F(4.682,131.096) = 1.811$, $p = 0.120$, $\eta^2 = 0.012$, between Block and Sugar, $F(4.682,131.096) = 1.182$, $p = 0.322$, $\eta^2 = 0.008$, nor a three way interaction, $F(4.682,131.096) < 1.0$.

We were most interested in the final effect of the intervention on body weight. A two (flavor *vs*. no flavor) by two (sugar *vs*. no sugar) ANOVA conducted on the body weight data from the 10th block (i.e. last two days) of the intervention (Figure 2.3c) revealed a main effect of Flavor, $F(1,28) = 10.273$, $p = 0.003$, $\eta^2 = 0.242$. There was no effect of Sugar, $F(1,28) = 2.339$, $p = 0.137$, $\eta^2 = 0.055$, nor was there an interaction between Flavor and Sugar, $F(1,28) = 1.866$, $p = 0.183$, $\eta^2 = 0.044$. While flavor and sugar did not interact, the flavored water condition appeared to gain less weight than the flavored sugar water condition. Indeed a simple effect of sugar was found for flavored liquids, $F(1) = 4.191$, $p = 0.050$. These results replicate what was found in Experiment 1, that repeated consumption of a novel flavored liquid solution during a window of no access to other flavors or calories attenuated weight gain. Unlike in Experiment 1, this effect in Experiment 2 appears to be specific to the flavored water solution, because it was

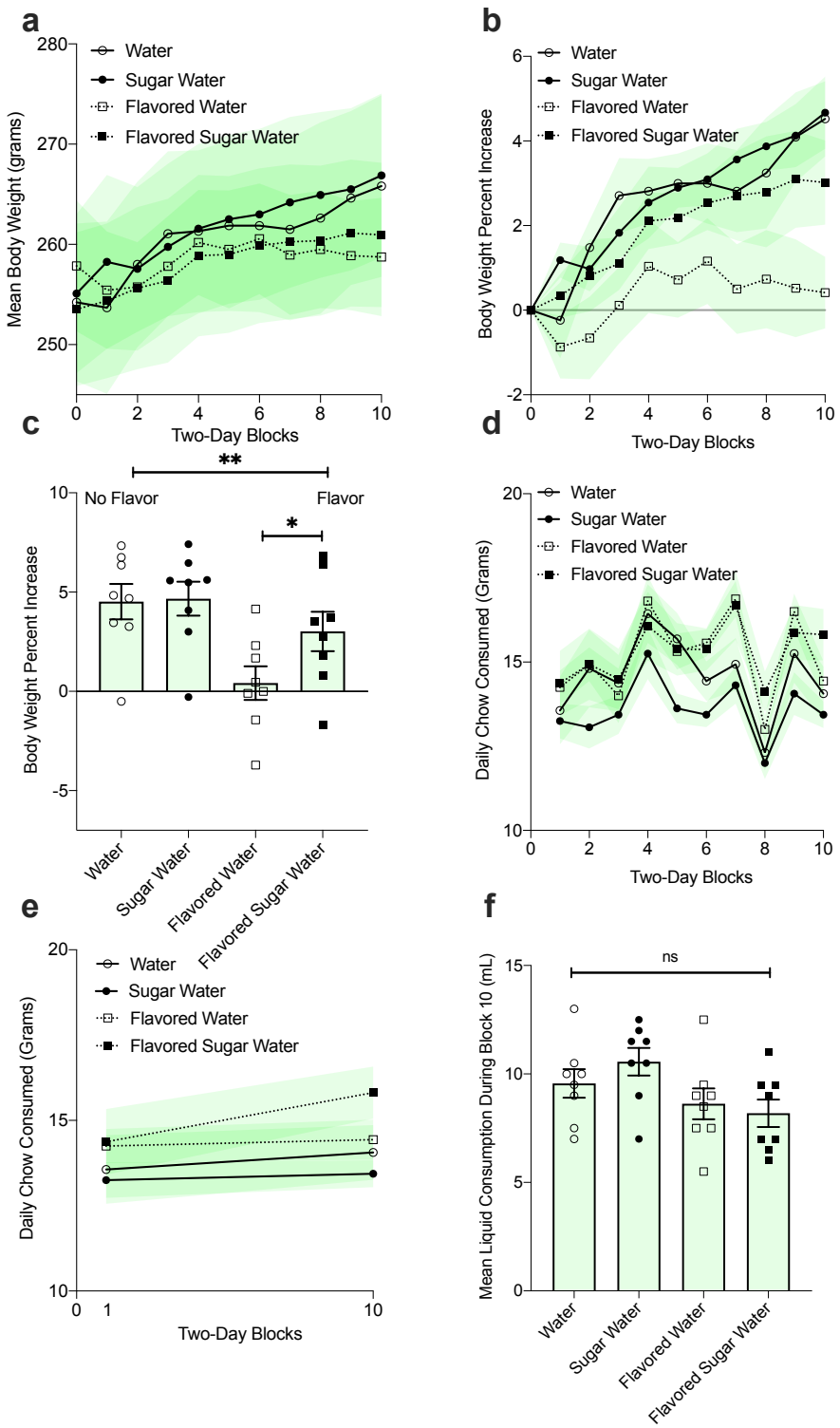

Figure 2.3: *Data from Experiment 2 using McCormick peppermint extract as flavoring. Error bars represent SEM. * = p value < .05, ** = p value < .01, *** = p value < .001. a) Mean body weight (grams) following liquid intervention in two-day blocks as a function of each liquid-intervention group. b) Mean body weight converted to percent increase c) Mean body weight increase on final block of liquid intervention. d) Daily food consumption in two-day blocks. e) Change in daily food consumption from block 1 to block 10. f) Mean consumption of the intervention liquid for one hour during block 10.*

not found in rats consuming the flavored sugar solution (but note the lack of significant interaction between flavor x sugar). Additionally, this replicated effect was achieved using peppermint as a flavor additive which is quite different than the Pomegranate Mio flavor solution used in Experiment 1, thereby demonstrating the generality of the effect of novel flavors.

A summary of daily food consumption as a function of intervention condition is displayed in Figure 2.3d. A mixed ANOVA was conducted with two between subject factors (Sugar and Flavor) and Block (1 & 10) as a repeated measure to examine trends in daily food consumption over the three-week period (Figure 2.3e). Unlike in Experiment 1, there was no main effect of Sugar, $F(1,28) < 1.0$, though the sugar water condition did again nominally consume the least amount of food. There was a marginal effect of Flavor, $F(1,28) = 3.519$, $p = 0.071$, $\eta^2 = 0.108$, such that rats that drank flavored beverages ate slightly more food. There was no significant interaction between Sugar and Flavor, $F(1,28) = 1.004$, $p = 0.325$, $\eta^2 = 0.031$. We also failed to observe any change in eating as a result of learning, as there was no difference in consumption between the first and last Block, $F(1,28) = 2.168$, $p = 0.152$, $\eta^2 = 0.020$, and there was no interaction between Block and Sugar, $F(1,28) < 1.0$, Block and Flavor, $F(1,28) < 1.0$, and no three way interaction between Block x Sugar x Flavor, $F(1,28) < 1.0$. While the flavored sugar water group increased daily food consumption over training, this difference was not significant, $t(7) = 1.475$, $p = 0.184$. We again measured the amount of liquid consumed during the one-hour intervention period on the last two days of the intervention and did not find differences between the conditions, $F(3,28) = 2.55$, $p = 0.076$, $\eta^2 = 0.215$ (Figure 2.3f).

The findings from Experiment 2 strengthen our interpretation of the data in Experiment 1, that consuming a novel flavor results in the elicitation of metabolic responses that then metabolize existing stored energy in the absence of incoming calories. This is one plausible explanation of the main effect of flavor in both experiments despite no differences in daily food consumption. It might also explain why the presence of sugar did not affect weight gain in Experiment 1 but did in Experiment 2. That is, the sugar solution flavored with Mio may have

evoked a metabolic response much larger than was needed for the calories within that solution. In Experiment 2, the potentially less salient and certainly more novel peppermint flavor may have elicited a slightly smaller metabolic response, and so when the flavored solution also contained calories those calories were less readily metabolized by the evoked responses. If this interpretation of the data is correct, it would suggest that metabolic responses can be elicited by entirely novel flavors, even prior to learning about its postingestive consequences. While learning processes can certainly affect the magnitude and identity of these responses, it would also make sense for organisms to have, *a priori*, a baseline metabolic response to novel flavors, to maximize nutrient absorption and due to the potentially lethal consequences that could follow ingesting a novel food. To investigate the existence of these potential unconditioned metabolic responses to novel flavors, we reasoned that varying the intensity of the flavor of the liquid intervention may affect the intensity of the evoked metabolic response.

Experiment 3

A viable interpretation of the data from Experiments 1 and 2 is that unconditioned metabolic responses are elicited by the consumption of a flavor, even in the absence of learned caloric consequences of that flavor. Here we test whether varying the intensity of the flavor will vary the intensity of its unconditioned effects off suppression of weight gain in free-feeding rats. We repeated the water only and peppermint water group treatments form Experimental 2, but for the peppermint water manipulation we gave rats access to a solution containing either a weak flavor, a medium flavor, or a strong flavor.

***Subjects*:** 32 female Long Evans rats (Envigo) were used in this experiment. Rats had similar prior experience with cues, footshock, sucrose solution, and food restriction as did rats in Experiment 1. Housing and acclimation were as described for Experiment 1.

***Materials*:** McCormick peppermint extract was again used as the flavoring agent. The medium flavor condition was given a solution containing 0.039% flavoring which is the same amount of flavor as used in the flavor water condition from Experiment 2. Rats in the strong

condition were given twice that concentration of flavoring (0.077%) and the weak condition was given half the concentration of flavoring as the medium condition (0.019%). Rats were pseudo randomly assigned to each condition and care was taken to ensure there were minimal initial differences in mean body weight between the 4 groups (all groups mean initial body weight was 259.1 +/- 0.79 grams).

***Procedure*:** The procedure was identical to that used in Experiment 2 (Figure 2.1). After 21 days of daily liquid intervention, rats in the medium flavor condition and water condition were given a preference test for the medium flavored solution or water. Each rat (*n*s=16) received simultaneous access to both solutions and the time spent drinking from each bottle was recorded for 5 minutes. The amount of liquid consumed from each bottle after one hour was measured by subtracting pre and post bottle weights.

Results and Discussion: Mean body weight over the three-week period is displayed in Figure 2.4a. A mixed ANOVA with a Greenhouse-Geisser correction conducted on body weight data with Block as a repeated measure and Group as a between subject factor revealed a main effect of Block, $F(3.651, 102.242) = 12.522$, $p < 0.001$, $\eta^2 = 0.017$, indicating that body weight significantly changed over the course of our intervention. There was also a significant interaction between Block and Group, $F(3.651, 102.242) = 2.715$, $p = 0.004$, $\eta^2 = 0.011$. After converting body weight to body weight percent increase (Figure 2.4b), we conducted identical analyses and found a main effect of Block, $F(3.566, 528.4) = 7.518$, $p < 0.001$, $\eta^2 = 0.080$, and an interaction between Block and Group, $F(3.566, 528.4) = 2.686$, $p = 0.005$, $\eta^2 = 0.086$. We were most interested in the overall effect of the intervention on weight gain, and so we conducted a one (Group) way ANOVA on the 10^{th} block of body weight (Figure 2.4c) which revealed a main effect of Group, $F(3,28) = 6.713$, $p = 0.001$, $\eta^2 = 0.418$. While we did not observe a strong dose-dependent response function, all groups with a flavored liquid solution showed attenuation of weight gain compared to the water group. Tukey HSD post hoc analyses support these observations. Compared to the water group, rats gained less weight in Group Strong flavor,

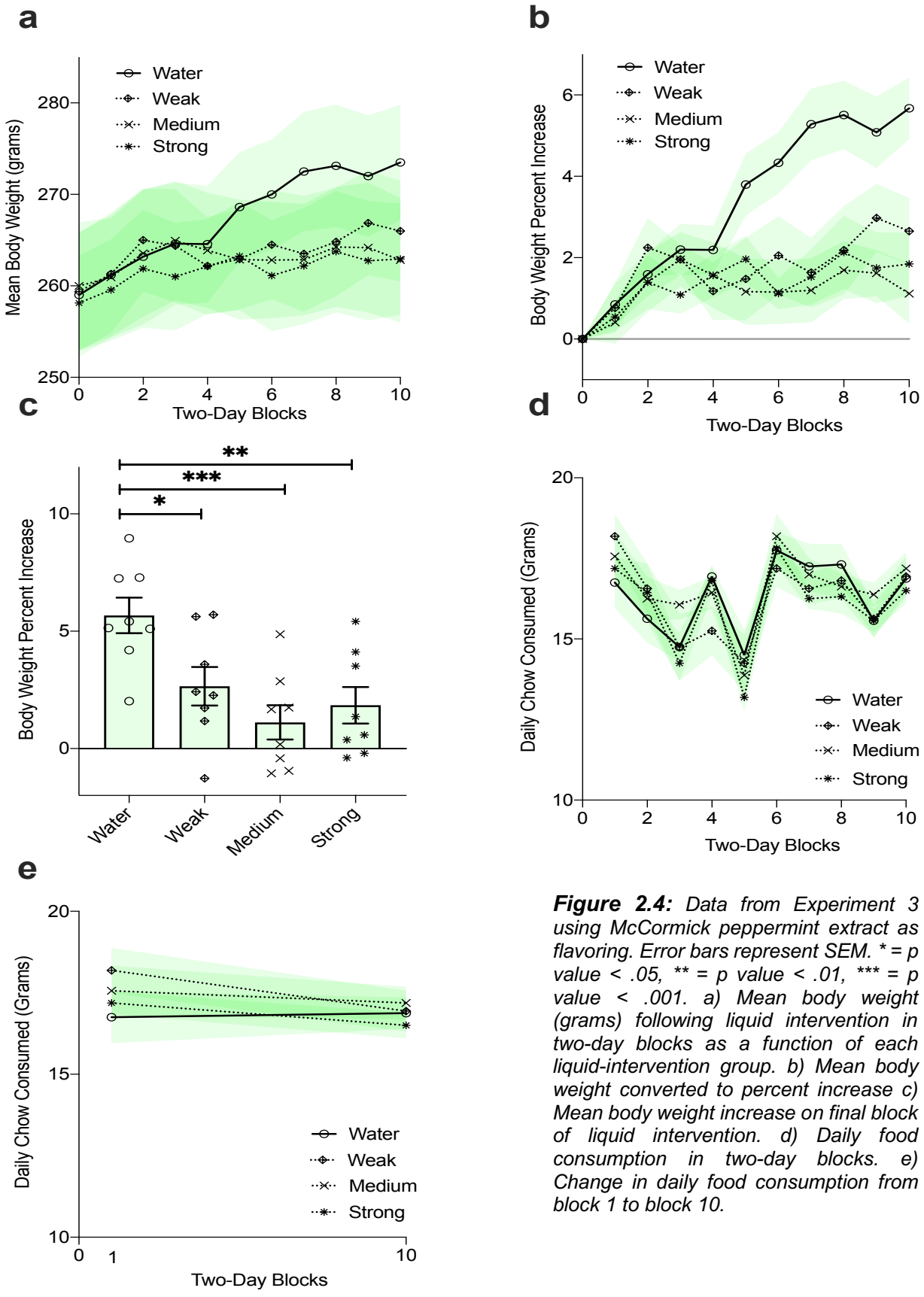

Figure 2.4: *Data from Experiment 3 using McCormick peppermint extract as flavoring. Error bars represent SEM. * = p value < .05, ** = p value < .01, *** = p value < .001. a) Mean body weight (grams) following liquid intervention in two-day blocks as a function of each liquid-intervention group. b) Mean body weight converted to percent increase c) Mean body weight increase on final block of liquid intervention. d) Daily food consumption in two-day blocks. e) Change in daily food consumption from block 1 to block 10.*

t = 3.503, p = 0.008, Cohen's d = 1.763, Group Medium flavor, t = 4.171, p = 0.001, Cohen's d = 2.163, and Group Weak flavor, t = 2.763, p = 0.047, Cohen's d = 1.353. These results suggest an apparent role of the peppermint flavoring in reducing weight gain.

A mixed ANOVA with one between-subject factor (Group) and Block (1 & 10) as a repeated measure conducted on food consumption revealed no effect of Block, $F(1,28) = 2.157$, $p = 0.153$, $\eta^2 = 0.068$, and critically, no effect of Group, $F(3,28) < 1.0$ (Figures 5d and 5e). There was also no interaction between Block and Group, $F(3,28) < 1.0$. The differences in body weight gain despite the lack of differences in food consumption suggests evoked metabolic responses by the consumption of a novel flavor, despite it not signaling a caloric outcome (US).

An alternative explanation of these data could be that the rats found the peppermint flavored liquid solutions aversive, and that the lack of liquid consumption during the 60-minute exposure interval was responsible for the lack of weight gain. We had anecdotal reasons to doubt this, because we often observed the rats eagerly approach the liquid solutions, presumably because they were thirsty following 90 minutes of no access to food or water. Additionally, in Experiments 1 and 2, we found no group differences in the amount of liquid consumed during the 1-hour intervention period on the 10th block. Nevertheless, to empirically demonstrate with a different procedure that the rats did not find the Peppermint flavored water aversive, we restricted rats from food and water for 120 minutes, and then gave the rats in Group Medium flavor simultaneous access to the medium flavored Peppermint solution and a water solution after completing 21 days of access to the medium flavored Peppermint solution. We measured the amount of time spent drinking from each bottle during a 5-minute observation period, and the pre and post bottle weights following one-hour access to both bottles. A paired samples T-test revealed no difference in the amount of time spent at each bottle during 5 minutes of observation, $t(7) < 1.0$. In addition, there was no difference in the amount of liquid solution consumed from each bottle following an hour exposure with simultaneous access, $t(7) < 1.0$. We also ran an identical procedure for rats in the water condition, thus allowing them

access to the medium flavored solution for the very first time, along with access to water. Again, we saw no difference in amount of time spent drinking from either bottle, $t(7) < 1.0$, nor was there a difference in the amount of liquid consumed after 60 minutes access, $t(7) < 1.0$. These data support our anecdotal experience of the rats willingly consuming the flavored solution during the 60-minute intervention period, and rules out dehydration or over hydration as explanations for the lack of weight gain observed in the flavored solution conditions. It also shows that the Peppermint flavor wasn't unconditionally aversive as rats that had previously had access only to water showed no avoidance to the Peppermint solution the first time they were given access.

Conclusions

Across three experiments, we report consistent evidence that the consumption of flavored liquids in between calorie-free and flavor-free windows can attenuate weight gain. Because there were no differences in the amount of daily food consumed, we speculate that these data can be interpreted as evidence for unconditioned metabolic responses to consuming a flavor. We found no evidence that an acquired flavor-calorie association in the flavored sugar water group resulted in any change in body weight or daily food consumption of normal chow, which does not support Roberts (2004) theory. The effect of an initially novel flavor was replicated three times and with two flavors (Berry Pomegranate and Peppermint). The lack of an effect of flavor-calorie associations on body weight and food consumption was replicated twice, once for each type of flavor.

Finally, the lack of any discernable preference for or avoidance of the flavored water compared to plain water suggests that the suppressing effects of flavor water exposure on body weight cannot be explained by rats preferring or avoiding either water or the peppermint flavored solutions.

Taken together, these data suggest that the ingestion of unpaired flavors can unconditionally suppress weight gain, at least under the strict parameters of our experimental

design (see Figure 2.1). We believe this can be explained by unconditioned metabolic responses that are elicited by the consumption of flavors. While learning processes have been demonstratively shown to influence the magnitude and identity of metabolic responses, the existence of an unconditioned, reflexive metabolic response to novel-flavor consumption in the absence of calories is likely adaptive given the paradox of feeding (Woods, 1991). The paradox of feeding is that while feeding is a necessary behavior for survival, consuming food threatens some aspects of homeostasis by introducing exogeneous substances into the body, some of which can be harmful. Even vital nutrients are only physiologically tolerable within a restricted range. Thus, postingestive metabolic and other physiological responses are critical to an organism's survival and are unlikely to be entirely dictated by learning processes because relying solely on learned responses could have fatal consequences. An analogy can be drawn to the emergency self-braking feature in many modern cars. When faced with an incoming object, the driver can choose to apply the brake at an appropriate level based on his/her experience. Nevertheless, even if the brake is not pressed, the emergency self-braking system will stop the car, though not always in a well calibrated or smooth manner. Thus, well calibrated metabolic responses to flavors may dominate when the organism has learned about the postingestive consequences of a flavor, but it would be problematic for an organism not to have any metabolic response to the detection of a flavor, because a whole host of postingestive consequences could potentially follow. This potential unconditioned metabolic response to flavors may also reflect some sort of *prepared learning*, as it is likely that the vast majority of flavors ever detected by an organism and its ancestors were followed by a caloric outcome (Seligman, 1970). That said, to our knowledge, little evidence exists to accurately assess the possibility of unconditioned metabolic responses to flavors.

One limitation to our interpretation is that we are indirectly inferring metabolic responses due to observed differences in weight gain in the absence of differences in food consumption. This was the result of our initiating these experiments for separate reasons, but then continuing

to interrogate the emerging behavioral patterns. A more direct way to measure unconditioned metabolic responses to a novel or familiar flavor would be to directly measure a metabolic response following exposure to a novel flavor that does not contain calories. Ideally, these measurements would occur during both the first exposure to the flavor and after 21 days of daily exposure to it, and would be compared to those same measurements but to a flavor that is paired with calories. There are various measurements that more directly target the potential metabolic response(s) responsible for this effect, including insulin release, thermoregulation, and energy expenditure. None of these targets work in isolation and may be individually or collectively responsible for this effect, though measuring metabolic response is notoriously challenging (Speakman, 2013). Supportive of our interpretation, Dhillon, Lee, and Mattes (2017) measured Cephalic Phase Insulin Responses to both sucrose (a caloric sweetener) and sucralose (an artificial sweetener with minimal calories) in humans and found no differences in the magnitude of insulin response to liquid solutions that contained either of these sweeteners, even after a two-week period of repeated daily exposure to those liquids. While the Dhillon et al. procedure utilizes a sweet taste, it may be that our non-caloric, and in Experiments 2 and 3 non-sweet flavors also elicited a metabolic response that failed to habituate after a three-week period. It is possible that with more time, these responses may eventually habituate, but their apparent lack of habituation in our 3-week procedure may reflect the strength of these responses and/or their evolutionary significance (i.e., resistance to habituation).

An additional limitation of these studies is our use of rats that had previous experimental experience with a small amount of sugar water. Our decision to re-use rats reflects commitments to, as outlined by the 3 Rs (Fenwick et al., 2009), reusing animals when possible in experimental animal research. This may have had some influence on liquid consumption because in Experiments 1 and 2 we did not observe a sizeable difference in drinking sugar compared to regular water. However, this may be due to other reasons like the short period of time rats had with these solutions as well as the small amount of liquid actually given. Further,

the lack of differences in liquid consumption support our view that it was critically the contents of the liquid solution that influenced weight gain or lack thereof, and not the amount consumed. Finally, we did not measure water consumption in the *ad libitum* period which may potentially explain or illuminate the observed effects.

A tempting conclusion of these experiments may be that they support the use of diet sodas or other flavored but calorie-free beverages (e.g., peppermint tea or other floral teas) as part of a weight-loss strategy. We caution against this interpretation, primarily due to a number of studies suggesting that regular consumption of artificial sweeteners renders sweetness an unreliable predictor of calories, resulting in an inadequate metabolic response following consuming foods that are sweet and also calorically dense (Swithers, 2013; Swithers & Davidson, 2008; Swithers, Martin, & Davidson, 2010, but see Rogers et al., 2016, for an important discussion on human vs animal models). Additionally, our results were obtained by having animals consume the non-caloric flavor in the middle of an extended flavor and calorie free windows, which is not often how artificially sweetened beverages are consumed (i.e., as a part of a larger meal). Extended use of this method might also be susceptible to habituation which was not observed in our three-week intervention period.

While the reported studies were initially motivated by the literature on Pavlovian learning and appetite (Myers, 2018; Roberts, 2004, 2006; Sclafani, 2018) we failed to observe an effect of learning a Pavlovian relationship between flavor and calories on weight gain or daily food consumption. Instead, we appear to have discovered that novel flavors can unconditionally suppress weight gain, which we speculate may be caused by metabolic responses that are elicited by entirely novel (at first introduction) flavor stimuli, despite those stimuli not containing calories. While it may be possible to conceive dieting intervention strategies based on these results, more proximally, this knowledge further demonstrates an interaction between unconditioned and learned responses that guide animals to successfully navigate their environments.

Chapter 3: Calories Count: Memory of Eating is Evolutionarily Special

"Our stomachs are bad at math, and what's more, we get no help from our attention or our memory. We don't register how many pieces of candy we had from the communal candy dish at work, and whether we ate 20 French fries or 30. It gets even worse when we're out dining with our friends and family. Five minutes after dinner, 31 percent of the people leaving an Italian restaurant couldn't even remember how much bread they ate, and 12 percent of the bread eaters denied having eaten any bread at all."– Wansink (2006)

The quote above is from Brian Wansink's *Mindless Eating.* We now know the integrity of these data is shaky at best (Lee, 2018; van der Zee, 2017)—but the idea raised here is interesting: how well do we remember eating? A number of studies (e.g., Armstrong et al., 2000; Baxter, Thompson, Litaker, Frye, & Guinn, 2002; Fries, Green, & Bowen, 1995) appear to support Wansink's claim and show that participants often underestimate how much food they consumed 24-hours prior. This proclivity to underestimate consumption has led some in the nutritional and medical communities to proclaim that self-reported dietary assessment techniques "offer an inadequate basis for scientific conclusions" (Archer, Marlow, & Lavie, 2018; Schoeller et al., 2013). It remains unclear however, if this underestimation bias in memory is unique to eating behavior, as it may be the case that similar behaviors are also misremembered. Is it true that when it comes to eating, "we get no help from our attention or our memory?"

Memory researchers have long recognized the adaptive benefits of forgetting (Anderson & Schooler, 2000; Bekinschtein, Weisstaub, Gallo, Renner, & Anderson, 2018; Kuhl, Dudukovic, Kahn, & Wagner, 2007). What's more, if the main goal of memory is to predict future events (Josselyn & Tonegawa, 2020; Mullally & Maguire, 2014; Schacter et al., 2007; Suddendorf & Corballis, 2007), there may be little need to be able to easily recall minute details of everyday experiences. Misra, Marconi, Peterson, & Kreiman (2018) provided a recent test of this.

Participants wore a video-camera combined with an eye-tracker while walking several routes in Cambridge Massachusetts. The next day, participants completed an old/new recognition memory test where they were shown clips of their own walking experience or those of other participants. Participants were only slightly above chance in recognizing their own walking experiences compared to others, which suggests memory for the minor details of everyday events is poor. In light of this, it is reasonable to suspect that memory for eating should be no different than memory for any other behavior—which is, as it turns out, often poor and inaccurate due to the benefits of forgetting erroneous information.

Alternatively, it could be that memory for eating is more accurately remembered than other behaviors. That is, this underestimation bias that has worried some nutritional scientists may actually be fairly conservative relative to memory for other behaviors. There are three theoretical reasons to suggest this may be the case.

First, comparative studies in non-human animals suggest that episodic memory may have evolved in animals to benefit foraging. Birds such as Black-capped chickadees and Scrub Jays provide evidence as such as they, via enlargement and specialization of the hippocampus, can remember the exact location and even contents of food cached up to several months prior (Balda & Kamil, 1992; Clayton & Dickinson, 1998; Roberts et al., 2008; Sherry, Jacobs, & Gaulin, 1992). In rodents, episodic-like memory is shown as rats are tasked with remembering specific details about food, some of which has been devalued (Babb & Crystal, 2006; W. A. Roberts et al., 2008; Zhou & Crystal, 2009). These findings are suggestive of the idea that episodic memory evolved to benefit animals in foraging and obtaining food. Thus, memory of eating and for food relevant information may be particularly strong, as it reflects one of the main tasks the memory system was selected for.

Second, evolutionary influences on human memory are abundant. For more than a decade, researchers have observed preferential memory for fitness relevant stimuli or neutral stimuli processed in such a manner to make them fitness relevant. Nairne, Thompson, &

Pandeirada (2007) provided the first demonstration of this, showing that neutral items processed on the basis of their relevance to an imagined survival scenario were better recalled than those exact same items processed based on their relevance to the non-evolutionarily important scenario of moving to a foreign land. A similar mnemonic benefit also exists for processing information based on its relevance to an imagined scenario involving the evolutionarily-important task of parenting/raising a child (Seitz, Polack, & Miller, 2018), as well as selecting a future mating partner (Pandeirada et al., 2017). Neutral items can be made more memorable if described as being touched by a sick individual compared to those same items touched by a healthy individual (Bonin et al., 2019; Fernandes et al., 2017). Faces deemed to be trustworthy or untrustworthy are better remembered than neutral faces in an imagined survival scenario (Hou & Liu, 2019). Such findings demonstrate that the evolutionary significance of the information being encoded affects its ability to be subsequently recalled, which suggests the act of eating should be well remembered (Seitz, Blaisdell, Polack, & Miller, 2019). However, all of these studies rely on hypothetical or imagined scenarios. To truly understand the role of adaptation on selective memory, and to move the 'adaptive memory' literature forward, studies of actual behavior are needed. While it is well known that performing actions is better remembered than simply imagining them (Engelkamp, 1998), a functional perspective of memory predicts that actions more relevant to evolutionary fitness (e.g., eating) should be better recalled than actions less relevant to evolutionary fitness.

Third, memory of eating appears to play an important role in moderating future food consumption—which to do so, likely relies on enhanced memory of eating. Interfering with memory of eating, either through optogenetics in rats (Hannapel et al., 2019), or by distracting humans while they eat (Higgs & Woodward, 2009; Mittal, Stevenson, Oaten, & Miller, 2011; Oldham-Cooper, Hardman, Nicoll, Rogers, & Brunstrom, 2011), results in earlier onset of eating and increased amount of food consumed in the subsequent meal. By contrast, increasing memory of a meal, by instructing participants to focus on sensory aspects of the food and/or

eating mindfully (Allirot et al., 2018; Higgs, 2015; Higgs & Donohoe, 2011; Robinson, Kersbergen, & Higgs, 2014; Seguias & Tapper, 2018) or cuing them to remember their last meal (Higgs, 2002; Szypula, Ahern, & Cheke, 2020), reduces total volume consumed during a following eating opportunity. Note that some manipulations aimed at enhancing attention during eating have not resulted in less subsequent snacking (Tapper & Seguias, 2020; Whitelock, Higgs, Brunstrom, Halford, & Robinson, 2018). If, however, memory of eating is already particularly strong—as we hypothesize—it may be the case that these enhancements in attention do not strengthen memory of eating significantly more than the control conditions (i.e., a ceiling effect). Thus, it may be easier to demonstrate that distracting participants during eating worsens memory of eating and leads to greater consumption rather than demonstrating that enhancements to memory of eating reduces future snacking. In any event, it is not unreasonable to suspect that given the important role that memory of eating plays in moderating future consumption, memory of eating may be particularly well remembered, either through enhancements in encoding, storage, or retrieval.

Thus, these three separate literatures inform the prediction that the act of eating should be well remembered. However, there is also reason to suspect memory of eating is no different than memory of any other behavior, or as some nutritional scientists might think, that memory of eating is surprisingly poor and inaccurate. In fact, some memory researchers might make the latter prediction, as the repetitive nature of eating three meals a day might make eating a particularly habitual behavior (White & McDonald, 2002) and one that is prone to much interference (Wixted, 2004). In this study, we created a novel task to test how memory of eating differs from memory of other similar procedural behaviors. Next, we investigated several factors that might influence memory of eating. As enhanced memory of eating is thought to reduce future food consumption, understanding what influences meal memories might help reduce overconsumption. The following experiments, therefore, represent early investigations into the strength and determinants of memory of eating.

Experiment 1

The objective of this experiment was to assess differences in memory for three similar behaviors—one that involved eating, another that involved handling food, and another that involved handling nonfood items. All participants completed what we henceforth refer to as the Memory of Eating Task (MEaT). The task is conceptually similar to that used by Morewedge, Huh, & Vosgerau (2010) who had participants imagine eating M&Ms or moving quarters, except that in our task all participants actually performed an action. In brief, the task involves participants watching a video and cueing them to perform one of the three previously described behaviors every time a tone is sounded. While this task is not identical to a typical meal, it allows for systematic study of various components that might affect memory of eating and in this experiment allows us to compare memory of eating to memory of similar but non-eating behaviors. Further, while the tasks of eating versus moving M&Ms are similar in a number of ways, there are a number of differences (e.g., sensory complexity, amount of motor activity, auditory, taste, and olfactory feedback, etc.) between these tasks that could presumably influence memory (but see Experiment 3 for an attempt to control for all of these limitations).

***Participants*:** A power analysis was utilized to detect a medium effect ($f = 0.25$) with 80% power (Faul, Erdfelder, Lang, & Buchner, 2007). A total of 159[†] participants (128 female) were recruited from the UCLA subject pool and were randomly assigned to each condition (n = 53). Body mass index (BMI) did not differ significantly between groups, $F(2,156) = 1.05$, $p = 0.35$. All participants were asked to refrain from eating at least two hours before their study start time and those who reported having not done this were excluded from analysis.

***Materials*:** Participants completed the experiment in individual rooms where they watched a video (a Malcom Gladwell TED Talk). Throughout the video, a 400hz tone was periodically presented for 1.0s on the same random schedule for every subject, averaging 1 tone presentation per 30 s. Concurrent with the tone, the border surrounding the video flashed

red for 1.0 s. Psychopy2 (Peirce et al., 2019) was used to create this program and the code and additional setup information for this experiment/task can be found here https://osf.io/ejtu6/.

***Procedure*:** All sessions occurred between 10am-12pm and 3-5pm. Participants were told a cover story that the objective of this study was to measure memory of verbal information while distracted, and that they would watch a video while completing a distracting task. The cover story served to prevent participants from focusing too much on their respective task. While participants watched a video, they were instructed to either eat M&Ms, move M&Ms from the bowl to the container, or move plastic beads from the bowl to the container every time a tone was sounded (*see Figure 3.1 for a depiction of the setup)*. The two moving conditions were chosen to most closely mimic the behavior of eating (but note limitations above), and given the glass container's narrow neck, a distinct rattling noise was made each time an object was deposited into it, which served as a marking stimulus to make each event more salient (Lieberman & Thomas, 1986). The tone was presented over laptop speakers and the gray video frame turned red 30 times for all participants using the same random schedule. Thus, all participants performed their respective tasks exactly 30 times under identical environmental conditions, and this was confirmed by weighing the bowls after participants had left. After watching the video, participants were moved to a separate, isolated room, and were assessed on their memory for different elements of the film. The survey began with a brief distractor task consisting of 5 basic arithmetic questions. Participants then answered multiple choice questions about verbal information presented during the film (e.g., How many pounds of armor was Goliath wearing? The rock fired from David's sling had a stopping power roughly equal to what?). Participants were also asked to estimate the duration of the film and critically, how many times they performed their respective task. Finally, participants were asked to reconstruct their task context using a bank of 10 symbols. This involved recreating the arrangement of the 7 symbols that had been placed on the cardboard frame that had stood behind the video screen.

After completing these questions, the participants' height and weight were measured and they were debriefed about the true nature of the study and compensated.

***Measures*:** Following the eating event, the post-task survey included a number of questions with the aim at measuring episodic components of the event. Episodic memories contain specific personal information about an experienced event, such as what happened, and where it happened (E Tulving, 1972). To assess the participants' episodic memory, we collected responses about "what" they ate, specifically how many items they consumed, and we also had participants recreate the task context. Memory for information presented during the video and the video's duration were included to 1) remain consistent with our cover story of measuring memory for verbal information while distracted and 2) serve as a baseline measure to compare group mnemonic performance. While we predict memory of eating to be more accurate for the eating condition relative to the moving conditions, it is also possible that the act of eating will strengthen contextual and episodic memories as well. These additional measures will allow us to evaluate this hypothesis.

Figure 3.1: *Task setup. The bowl on the left was filled with either M&MS or beads. As the video played, a 400hz tone was randomly sounded and the background of the screen filled red. When this happened, participants either ate one M&M or moved one M&M or bead to the container on the right. This occurred 30 times and all participants were later asked on how many times they performed this task.*

Items Reported: The number of M&Ms (or beads) participants reported having eaten (or moved).

Task Error: The absolute value of 30 minus the number of items reported. Thus, this measure accounts for both underestimation and overestimation and is used to assess memory accuracy.

Temporal Memory Error: The absolute value of 15 minus the duration reported. This accounts for underestimation and overestimation.

Contextual Memory Error: Error points were given for choosing the lure symbols or putting symbols in incorrect locations (max error = 10, min error = 0).

Verbal Memory Accuracy: The number of multiple-choice questions about the film that participants answered correctly (out of 5).

	Eat M&M	Move M&M	Move Bead
Items Reported	22.49 (7.50)	17.83 (5.18)	17.60 (5.51)
Task Error	9.28 (5.08)	12.17 (5.18)	12.40 (5.51)
Temporal Memory Error	4.91 (4.28)	4.14 (3.84)	4.34 (4.50)
Context Error	5.45 (3.21)	6.49 (2.58)	6.23 (2.58)
Verbal Memory Accuracy	2.60 (1.26)	2.57 (1.15)	2.72 (0.91)

Table 3.1: *Mean outcome measures and standard deviation (in parentheses) per condition from Experiment 1. Data come from a survey taken after completing the MEaT. All participants completed similar actions 30 times, the video lasted 15 minutes, the maximum context error score was 10, and the maximum verbal memory accuracy was 5.*

Results

Table 3.1 summarizes participant's memory accuracy for how many times they completed the task, their accuracy for recreating the task context, and their accuracy for information presented during the video and its duration. *Figure 3.2a* summarizes the task memory error, which was the absolute value of the difference between the actual number of times the task was performed (30) and the reported number of times the task was performed for each of the three tasks. A one-way ANOVA revealed a main effect of tasks, $F(2,156) = 5.77$, $p <$

0.01, η^2 = 0.07 with a Bayes factor of 8.31 in support of the alternative hypothesis. Planned comparisons showed that eating the M&Ms resulted in fewer errors than moving the M&Ms, $t(156) = 2.83$, $p = 0.005$, $d = 0.56$, or moving the beads, $t(156) = 3.05$, $p = 0.003$, $d = 0.59$. Thus, memory for eating was superior to the two highly similar but non-eating behaviors. To test contextual memory, participants were asked to reconstruct the task context given a bank of 10 symbols, and errors were counted for choosing the wrong symbol and/or placing the symbol in the wrong location (max error = 10). A one way ANOVA did not reveal a significant main effect of task, $F(2,156) = 1.96$, $p = 0.14$, $\eta^2 = 0.03$, Bayes Factor in favor of the null (BF_{01}) = 3.0. Planned comparisons revealed that memory for the context was numerically, though not statistically, most accurate for the M&M eating condition than the M&M moving condition, *t(156) = 1.91, p* = 0.06, *d = 0.36,* BF_{01} = 1.01, or bead moving condition, *t(156) = 1.42, p* = 0.16, *d* = 0.27, BF_{01} = 2.11. There was no difference across tasks in memory for the verbal information from the video, which was assessed by 5 questions related to the video, $F(2,156) < 1.0$, BF_{01} = 12.74, or memory for the duration of the video, $F(2,156) < 1.0$, BF_{01} = 10.64. Thus, enhanced memory for the eating behavior was specific to the actual behavioral aspect of eating and did not affect other aspects of the event.

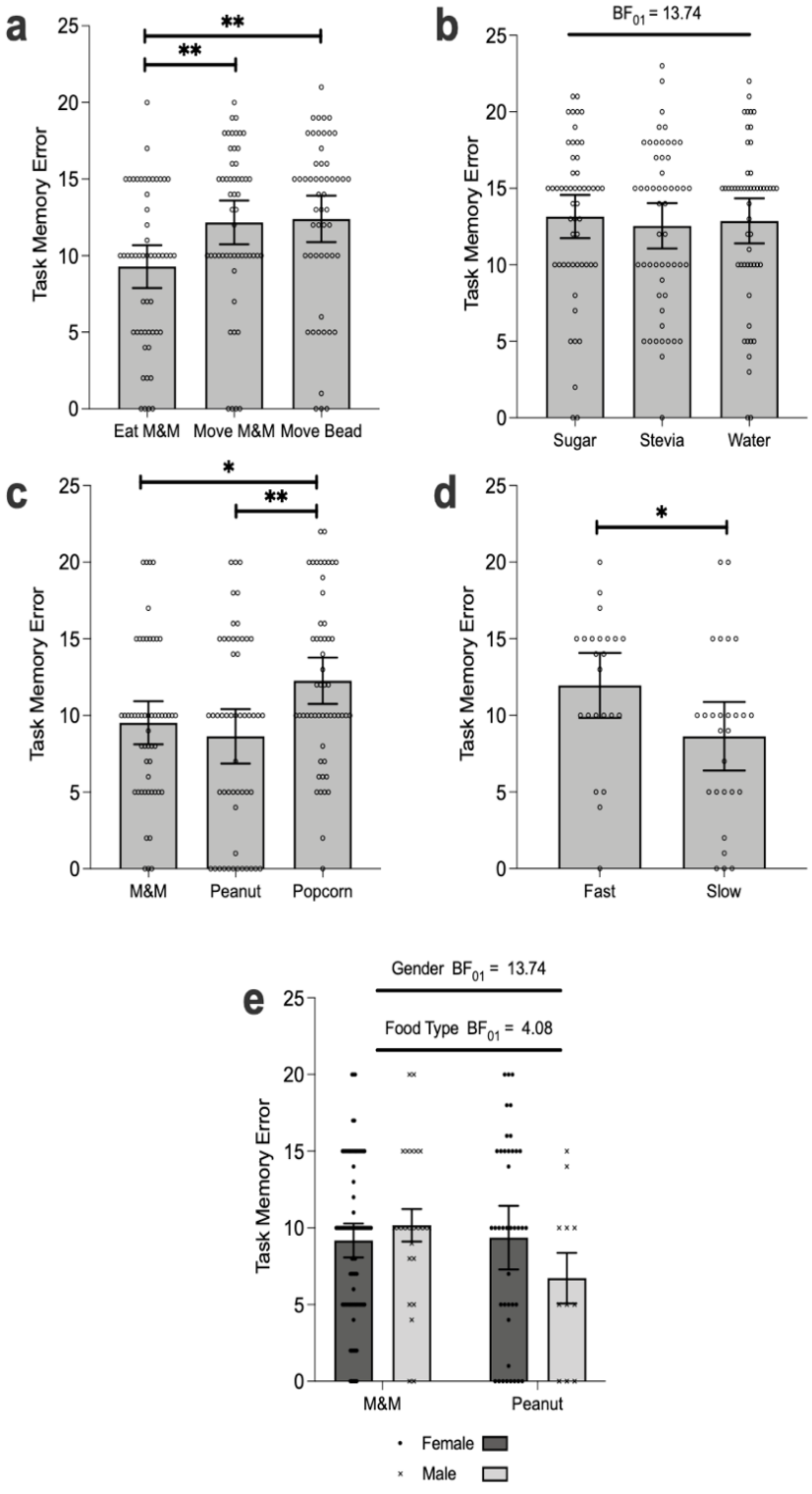

Figure 3.2*: a)** *Memory accuracy for 3 similar procedural tasks performed under identical conditions. Error scores were calculated by taking the absolute value of the difference between 30 (actual number of times the task was performed) and the reported number of times the task was performed. Planned comparisons confirmed the eating task was best remembered.* ***b) *Memory accuracy for the same bead moving task, but participants drank a liquid solution containing these additives before and after the task. No difference in memory performance despite glucose intake being equal for the Sugar and Eat M&M conditions.* ***c)*** *Memory accuracy for eating 30 pieces of different food items. Participants who ate 30 of the calorically dense items (M&Ms or Peanuts) were more accurate in remembering how much they ate compared to those who ate 30 pieces of popcorn.* ***d)*** *Memory accuracy for eating 30 M&Ms at a fast or slow eating rate. Slower eating was better remembered than fast eating.* ***e)*** *Memory accuracy by gender and food type pooled across participants who ate M&Ms or peanuts in Experiments 1 and 3. There was no effect of gender or food type on recall. * = p value < .05, ** = p value < .01, *** = p value < .001, Error bars represent 95% confidence intervals. BF_{01} indicates Bayes Factor in support for the null.*

Experiment 2

The results from Experiment 1 suggest that some elements of memory of eating are more accurately recalled than memory for similar but noneating behaviors. Even handling M&Ms did not result in the same memory benefit as did consuming the M&Ms. This suggests that food handling is qualitatively different from food consumption. However, these data do not speak to the proximate mechanisms that result in this enhanced remembrance. It is also possible that the enhanced memory was not due to the behavior of eating *per se*, and was influenced by other factors. One plausible mechanism that could have enhanced memory is the energy provided by the glucose in the M&Ms. Pre and post task glucose consumption has been shown by others to increase task memory in humans (Glenn, Minor, Vervliet, & Craske, 2014) and rats (Winocur, 1995), albeit much larger quantities of glucose were used than what participants in our study consumed (Smith, Riby, Eekelen, & Foster, 2011). To test this alternative physiological mechanism behind the results in Experiment 1, we had all participants perform the task of bead moving, but some participants consumed as much glucose as those who ate the M&Ms in Experiment 1, while others consumed Stevia (a sweetener containing no glucose) or water. If human memory is biased towards remembering the act of eating, we should not observe memory difference among the three groups. Alternatively, if the energy hypothesis is correct, that is, that energy consumption is what drove the improved memory in the eating task, then only participants drinking glucose solution should show better memory in Experiment 2.

***Participants*:** We recruited an additional 159[†] participants (119 female) based on the same power analysis for Experiment 1. There was no difference in BMI across conditions, $F(2,156) = 2.22$, $p = 0.11$.

***Materials*:** Most of the materials were the same as those used in Experiment 1 with the main exception that all participants were in the bead-moving condition, and the addition of solutions that subjects drank before and after the task. Fresh solutions were created every other

day and were stored in a standard refrigerator at 40°F. Thirty M&Ms contain approximately 17 grams of sugar; thus, we mixed a 1/2 cup of sugar (100 grams of sugar) with 10 cups of water (~2366 grams of water), which resulted in a ~4.0% sugar solution. An 8 oz (~9 grams of sugar) cup was consumed both before and after the bead moving task, resulting in roughly 18 grams of sugar consumed. The Stevia condition was created to determine the extent to which detecting sweet substances could affect memory performance in the absence of any glucose ingestion. We replaced the 1/2 cup of sugar with 12 grams of Stevia (according to the conversion chart provided at https://sweetleaf.com/stevia-conversion-chart/), and 4 blind taste testers (undergraduate assistants) confirmed the two solutions to taste equally sweet (~4% sugar vs ~0.5% Stevia).

***Procedure*:** All participants performed the same bead moving task as used in Experiment 1. Before and after completing the task, participants consumed a liquid solution. One group consumed a solution containing the same amount of glucose found in 30 M&Ms (~17 g of sugar), another drank water matched for sweetness using Stevia which is non-caloric and contains no glucose, and the third group simply drank water. The post task survey, procedure, and measures were identical to that used in Experiment 1.

Results: We measured the same dependent variables as in Experiment 1, which are summarized in Table 3.2. Recall performance for the bead moving task across the 3 groups is displayed in *Figure 3.2b*. As predicted by the eating hypothesis, no differences in task error were found across groups, $F(2,156) < 1.0$, $BF_{01} = 13.74$. There was also no difference in memory for the verbal information, $F(2,156) < 1.0$, $BF_{01} = 13.77$, or the duration of the video, $F(2,156) = 1.22$, $p = 0.30$, $BF_{01} = 5.63$. Unexpectedly, there was a significant effect of condition on memory for the task context, $F(2,156) = 4.49$, $p = 0.013$, $\eta^2 = 0.07$, Bayes Factor of 2.84 in favor of the alternative, such that participants who drank water before and after performing the bead task better remembered the context compared to those who drank Sugar Water, $t(104) = 2.40$, $p = 0.05$, $d = 0.44$ and Stevia Water, $t(104) = 2.76$, $p = 0.02$, $d = 0.53$ (note: Tukey HSD

post-hoc comparisons due to unplanned analysis). It is unclear why drinking the sweetened water attenuated memory of the task context relative to those who drank plain water. Nevertheless, the observed increase in memory performance for the M&M-eating group of Experiment 1 does not appear to be caused simply by the ingestion of glucose during the task, but instead suggests that the behavioral act of eating is better remembered than other similar procedural behaviors.

	Sugar	Stevia	Water
Items Reported	17.3 (6.18)	17.45 (5.37)	17.25 (5.61)
Task Error	13.15 (5.13)	12.55 (5.37)	12.87 (5.34)
Temporal Memory Error	5.11 (4.09)	4.91 (5.23)	3.89 (3.48)
Context Error	6.81 (2.42)	6.98 (2.17)	5.68 (2.68)
Verbal Memory Accuracy	2.60 (1.12)	2.72 (1.04)	2.62 (1.04)

Table 3.2: *Mean outcome measures and standard deviation (in parentheses) per condition from Experiment 2. Data come from a survey taken after completing the MEaT. All participants moved a bead 30 times, the video lasted 15 minutes, the maximum context error score was 10, and the maximum verbal memory accuracy was 5.*

Experiment 3

Thus far, we have shown that memory of eating is particularly strong and that this effect does not appear to be driven by the glucose provided by the M&Ms in Experiment 1. Here we ask what factors influence memory of eating. Understanding the determinants of memory of eating is important because of the moderating role that these memories have on future food consumption. Evolutionary reasoning suggests caloric density may influence memory of eating because foods with more calories are of greater evolutionary value. New et al., (2007) provided indirect evidence of this. They had participants walk through a farmer's market and sample different food items. In a later test, memory for the location of the stand was linearly related to the caloric density of the food item being sold, such that the locations of more calorically dense food stands were better remembered. Others have also found enhanced spatial memory for calorically dense food items using a modified task in which participants needed to remember the location of various imaginary food items on a map (Allan & Allan, 2013; de Vries et al., 2020).

While all of these studies showed that caloric density may affect spatial memory of where the food was consumed, they were correlational in nature, and they do not speak to the effect of caloric density on memory for how much food was actually consumed. We sought direct evidence for whether or not memory differs for *consuming* the same number of food items that differ in their caloric density. This study, therefore, will provide the first evidence of how characteristics of the food item consumed affect memory of eating.

***Participants*:** We recruited an additional 159[†] participants (117 female) based on the same power analysis for Experiment 1. There was no difference in BMI across conditions, $F(2,156) = 1.28$, $p = 0.28$.

***Materials*:** All participants performed the MEaT as in Experiment 1, but we differed the food item consumed per condition. Bowls were filled to an equivalent level (3/4 of the bowl height) with the different items, which equated to 140 grams of M&Ms, 90 grams of salted peanuts, or 15 grams of plain popcorn. These three items were selected due to that fact that they are similar in size and familiarity, because 30 of each item is not an unreasonable amount to consume per 15-minute session, and because we had previous success using M&Ms with this task. Additionally, while the popcorn is fairly flavorless and not calorically dense, the M&M and peanut are both flavorful and more densely caloric (around 5 calories per 1 piece) but differ on their specific taste (sweet versus salty) profile and sugar and fat contents. The popcorn was handmade and contained less than 1 calorie per piece (see Supplemental Material for additional nutritional information).

***Procedure*:** The procedure was identical to that used in the M&M eating condition in Experiment 1. All participants consumed 30 of their respective food items on the same randomized schedule averaging to one item every 30 seconds. Our hypotheses and data analysis plan were pre-registered prior to data collection.

***Results*:** We measured the same dependent variables as in the previous two experiments, see Table 3.3. *Figure 3.2c* shows recall performance for eating the three different food items. As predicted, there was a significant effect of food item consumed on memory accuracy, $F(2,156) = 5.82$, $p < 0.01$, $\eta^2 = 0.07$ with a Bayes factor of 8.68 in support of the alternative hypothesis. Pre-registered planned comparisons revealed more accurate memory for eating the 30 M&Ms compared to the 30 pieces of popcorn, $t(156) = 2.47$, $p = 0.015$, $d = 0.52$, and for eating the 30 peanuts compared to the 30 pieces of popcorn, $t(156) = 3.27$, $p = 0.001$, $d = 0.61$. Similar to the findings from Experiment 1, there was no effect of food item consumed on memory for the duration of the film $F(2,156) = 2.00$, $p = 0.14$, $BF_{01} = 2.89$, or verbal information presented during the film $F(2,156) = 1.39$, $p = 0.25$, $BF_{01} = 4.90$. There was also no effect of food item on memory of the context, $F(2,156) < 1.0$, $BF_{01} = 8.21$. Thus, the caloric density of the food item consumed appears to specifically influence the memory of how many times that food item was eaten, not other elements of the task. Finally, there was no difference in memory for eating the M&Ms from Experiment 1 and Experiment 3, $t(104) < 1.0$, $BF_{01} = 4.73$, which suggests the MEaT to be a reliable measure for studying memory of eating. At the same time, there was also no difference between the eat Popcorn condition and the move M&M condition from Experiment 1, $t(104) < 1.0$, $BF_{01} = 4.85$, which suggests memory of eating is not always superior to memory for noneating behaviors. Rather, and congruent with evolutionary reasoning,

	M&Ms	Peanuts	Popcorn
Items Reported	21.83 (7.10)	22.30 (7.57)	20.00 (9.02)
Task Error	9.53 (5.09)	8.64 (6.45)	12.26 (5.47)
Temporal Memory Error	4.34 (4.80)	5.66 (6.48)	3.74 (3.45)
Context Error	6.38 (2.71)	6.30 (2.76)	6.89 (2.41)
Verbal Memory Accuracy	2.75 (0.96)	2.60 (1.13)	2.94 (1.06)

Table 3.3: *Mean outcome measures and standard deviation (in parentheses) per condition from Experiment 3. Data come from a survey taken after completing the MEaT. All participants ate 30 of their respective food items, the video lasted 15 minutes, the maximum context error score was 10, and the maximum verbal memory accuracy was 5.*

the human memory system appears to prioritize memory specifically for the consumption of high calorie or palatable foods.

Experiment 4

The results above suggest that memory of eating can be influenced by aspects of the consumed food item, specifically its caloric density. That said, holding the food item constant, there may be behavioral aspects of how food is consumed that affects memory for eating it. The rate of eating is likely to be one such factor, as distributed compared to massed encoding of information has long been known to facilitate retention (Underwood, 1961). Slower and more distributed eating should therefore result in better memory of eating than eating at a faster rate. Because memory of eating is thought to moderate future eating, better memory for slower eating might partially explain why a slower pace of eating is associated with lower rates of obesity (Robinson, Almiron-Roig, et al., 2014).

To our knowledge, only two studies have to date examined how rate of eating influences memory of eating. Ferriday et al. (2015) controlled the rate of tomato soup delivery using a modified feeding tube. Participants who consumed the soup slowly were more accurate at remembering how much soup they had consumed three hours later. One limitation of this study is that consuming soup via a pump is a highly contrived eating scenario which may influence memory performance and have limited applicability to actual eating events. Additionally, having participants pour soup into a bowl based on their memory for how much they consumed is confounded by one's ability to accurately pour liquids into bowls. Because in the MEaT participants are picking up the food item and placing it in their mouths as opposed to food being pumped into their mouths, and the memory test simply involves recall of how many M&Ms were consumed, it provides a better test of how eating rate influences memory of eating.

Similar to the procedure used in the MEaT, Hawton et al., (2018) had participants consume a pasta dish either quickly (n=11) or slowly (n=10) and they controlled eating pace using an auditory cue. Two-hours later, participants who ate slowly were more accurate in

recognizing the correct portion size of their pasta dish in an array of images. In addition to the small sample size, one potential confounding factor of this design, and that used by Ferriday et al., is that the memory test occurs several hours after consuming the food, and so responses may be influenced by participant hunger levels. That is, just as memory of eating influences subsequent hunger levels (Brunstrom et al., 2012), hunger levels might also influence reported memory of eating. In the MEaT, however, participants are asked to remember how much food they consumed just minutes after consuming it, which speaks more specifically to the strength of the encoded memory of eating before it may be influenced by other factors (e.g., hunger, retroactive interference, etc.). Therefore, in a pre-registered study, we used the MEaT to investigate the role of eating rate in immediate memory of eating.

Materials: All participants performed the MEaT as in Experiment 1 and 3, but the bowl was always filled with 140 grams of M&Ms. The 15-minute video was changed to a 22.5 minute video about the history of Los Angeles freeways.

Participants: We planned to recruit 128 participants to detect a medium sized effect (d = 0.5) with 88% power. However, after reaching 50 participants, our data collection was halted due to the COVID-19 pandemic. This number of participants affords 54% power to detect a medium (d = 0.5) effect and 87% power to detect a large effect (d = 0.8).

Procedure: In Experiments 1 and 3, participants were cued to eat on a random schedule that averaged out to one food item every 30s. In this experiment, half of participants were assigned to a fast eating schedule (n = 23) that were cued to eat an M&M on average every 15s, and half (n = 27) to a slow eating schedule that were cued to eat on average every 45s. A longer video was chosen to allow participants in the slow condition to eat 30 M&Ms over the course of the entire video. Participants in the fast eating condition did not have their first tone presented until after 15 minutes of the video had passed. This was chosen so to equate the retention interval between both conditions. This should also protect against recency effects (i.e. better memory for the beginning of an event), hold the amount of time spent in the encoding

environment and video content constant, and avoid having participants eat 30 M&Ms and then wait for a prolonged period of time. Following the eating task, all participants completed the same measures as in the previous experiments.

Results: *Figure 3.2d* shows recall performance for eating 30 M&Ms at the two different eating rates. As predicted, and according to our pre-registered analysis plan, a one-tailed independent *t* test revealed memory for eating the 30 M&Ms to be more accurate for slow compared to fast eating, $t(48) = 2.21$, $p = 0.016$, $d = 0.63$, with a Bayes Factor of 3.86 in favor of the alternative hypothesis. However, there was no effect of eating rate on memory for the duration of the film $t(48) < 1.0$, $BF_{01} = 2.68$, verbal information presented during the film, $t(48) < 1.0$, $BF_{01} = 3.26$, or the task context, $t(48) < 1.0$, $BF_{01} = 2.66$. These results suggest that a slower eating rate immediately increases memory of eating relative to a faster eating rate.

General Discussion

We sought to evaluate the strength and determinants of memory of eating. While some nutritional scientists (e.g., Archer et al., 2018; Schoeller et al., 2013; Wansink, 2006) claim memory of eating to be unreliably poor and inaccurate it remains unclear if memory of eating differs from memory of other similar behaviors. On the contrary, given the evolutionary significance of eating and the role that memory of eating has on moderating future food consumption, it may be the case that the act of eating is relatively well-remembered. We created a novel behavioral task to assess this question and demonstrated that memory of eating is more accurately recalled than memory of similar but noneating behaviors. We then ruled out glucose as a potential confound of this effect and finally, we showed that the caloric density of a consumed food item and the rate at which it is eaten influences its ability to be remembered.

One possible explanation of our results in Experiments 1 and 3 is that they were driven primarily by the demographic characteristics of our participants. That is, given our recruiting participants via the UCLA psychology subject pool, our participants were predominantly women. Restrained eating, the tendency to limit daily food consumption, and various eating disorders are far more common among women than men (Johnson, Pratt, & Wardle, 2012; Mangweth-Matzek et al., 2014; Savage, Hoffman, & Birch, 2009). Thus, participants who ate M&Ms and/or peanuts in Experiments 1 and 3 might have better remembered that eating behavior not because of some inherently unique property of eating, but rather because of their concerns with the calories being consumed which would be salient to restrained women. This alternative account predicts that women should preferentially remember eating high calorie foods compared to men. We pooled all participants who ate either M&Ms (Exp 1 & 3) or peanuts (Exp 3) at the same eating rate and analyzed their recall data for the number of items consumed (see *Figure 3.2e)*. There was no effect of gender on task error, $F(1,155) < 1.0$, $BF_{01} = 4.65$, or of food type on task error $F(1,155) = 2.95$, $p = 0.09$, $BF_{01} = 4.08$, and a medium sized, but not statistically significant, interaction between gender and food type, $F(1,155) = 3.54$, $p = 0.06$, $\eta^2 = 0.07$. The interaction was due to men better remembering peanuts (less task error). In Experiment 4, there was no effect of gender on task error, $F(1,46) < 1.0$, or gender by eating rate interaction, $F(1,46) < 1.0$ (see Table 3.4). In any event, it is clear that women did not significantly remember

	Fast	Slow
Items Reported	19.17 (7.13)	22.11 (6.68)
Task Error	11.96 (4.89)	8.63 (5.65)
Temporal Memory Error	5.67 (4.10)	4.80 (3.32)
Context Error	6.30 (3.42)	5.56 (2.97)
Verbal Memory Accuracy	3.39 (1.08)	3.52 (0.98)
Male Task Error	12.50 (4.89)	7.50 (5.56)
Female Task Error	11.77 (5.03)	9.29 (5.76)

Table 3.4**:** *Mean outcome measures and standard deviation (in parentheses) per condition from Experiment 4. Data come from a survey taken after completing the MEaT. All participants ate 30 of their respective food items, the video lasted 22.5 minutes, the maximum context error score was 10, and the maximum verbal memory accuracy was 5.*

the act of eating high calorie foods better than men, which obviates the concern that participant gender explains our results.

One possible limitation of Experiment 3 is that we cannot be certain that it was the caloric density of the food items that drove differences in memory performance. That is, M&Ms, peanuts, and plain popcorn differ on a number of characteristics, not just caloric density. For example, they may vary on liking, familiarity, chewing effort, or palatability (but see '*Future Directions'* section for a potential solution*)*. After running the first 15 participants, we decided to ask each participant how much they liked the food item they were given, as well as how often they consumed that item using a 5-point Likert scale. An ANCOVA with task memory as the dependent variable, condition as the independent variable, and how much participants liked the food they were given as a covariate still yielded a significant effect of condition, $F(2,140) = 4.94$, $p = 0.008$, $\eta^2 = 0.07$, and the covariate was not significant, $F(2,140) < 1.0$. An ANCOVA with how often participants consumed the food item also yielded a significant effect of condition, $F(2,140) = 5.73$, $p = 0.004$, $\eta^2 = 0.08$, and the covariate was not significant, $F(2,140) = 1.83$, $p = 0.18$, $\eta^2 = 0.01$. All three items are crunchy, but peanuts and M&Ms require more effort to chew, so it is possible that effortful chewing influences meal memories. Higgs and Jones (2013) however, manipulated chewing effort by making some participants chew for 30 seconds per bite, and found no difference on memory for that meal, though prolonged chewers did eat less food at a subsequent snack. Finally, M&Ms and peanuts are more palatable than the plain popcorn, so it is possible that food palatability influences meal memories. Of course, for evolutionary reasons, foods high in calories tend to be perceived as palatable, and so it would be difficult to dissociate the two without using artificial substances. In fact, palatability could be an evolutionary proxy for a food's caloric value.

Throughout these experiments, we have been primarily concerned with memory accuracy—which can be contrasted with memory of quantity (Koriat & Goldsmith, 1996). All participants performed similar tasks the same number of times, and then we calculated the

difference between participants' memory for how many times they performed the task and the actual number of times they performed the task (30 for participants in all conditions). One interesting finding was a heavy bias in underestimating the number of times participants completed their respective tasks. Of the 527 participants who completed the MEaT, only 21 reported having performed their respective action (eating or moving a food item or beads) more than 30 times, whereas 470 reported less than 30, and 36 reported exactly 30 (*see Table 3.5)*. Note that we took several measures to ensure participants performed their respective tasks exactly 30 times[†] and know of no theoretical reasons that would predict such drastic underestimation. Clearly, investigation into whether this underestimation bias exists for other procedural behaviors is warranted.

Related to this discussion of memory accuracy is also that of memory of quantity and the prevalence of false memories (Koriat & Goldsmith, 1996). While we have shown memory of eating to be more accurately recalled than memory for similar non-eating behaviors, it remains unclear whether or not memory of eating is more or less susceptible to false memories than similar non-eating behaviors. The closest data we have related to this, is the number of "lure" symbols participants chose when recreating the task context. The number of lures chosen

Exp.	Condition	n	reported < 30	reported = 30	reported > 30
1	Eat M&M	53	42	4	7
1	Move M&M	53	49	4	0
1	Move Bead	53	50	3	0
2	Sugar	53	49	2	2
2	Stevia	53	52	1	0
2	Water	53	50	2	1
3	M&Ms	53	46	3	4
3	Peanuts	53	39	12	2
3	Popcorn	53	49	1	3
4	Fast	23	21	1	1
4	Slow	27	23	3	1

Table 3.5**:** *Number of participants who reported performing their respective tasks less than, equal to, or greater than, 30 times. Note, all participants performed their respective tasks exactly 30 times*

ranged from 0-3 but did not significantly differ between condition for any of the experiments (lowest *p* value > 0.072). Nevertheless, the MEaT could be modified to test this, by having participants eat or move a variety of different food items, and then asking participants to recall all of the different items that they ate/moved.

Finally, it is important to acknowledge that not all measures of memory were enhanced in the eating condition in Experiment 1, the peanut and M&M condition in Experiment 3, or the slow eating condition in Experiment 4 relative to the respective controls. Specifically, in all three of those experiments, it was only memory for the number of times the task was performed that was more accurately recalled (the "what" aspect of the event) and not memory for the task context (the "where" aspect). We can only speculate that from an evolutionary perspective, it would be advantageous for a foraging animal to remember the number of items or the amount of food that they consumed during an eating event. For example, there is important information gained by an animal remembering they consumed 20 ripe berries from a bush versus 2 ripe berries. Further, it is now clear that in both humans (Brunstrom et al., 2012; Higgs, 2002; Higgs & Spetter, 2018) and non-human animals (Hannapel et al., 2019), memory for the amount of food consumed at a recent meal moderates future hunger and eating—so it is not surprising this information is prioritized by our memory systems, at least immediately after eating.

It is surprising that memory for the task context was not enhanced by any of these tasks. In our bush with 20 versus 2 berries example above, one would imagine it's important both to remember the number of berries in the bush but also, and critically, where that bush is located. One explanation for our null effects was that our test of contextual memory was not sensitive enough to detect this effect, as it is true that in all conditions where task memory was enhanced contextual memory was also nominally, though not significantly, enhanced relative to the respective controls. Similarly, it could be that the cues surrounding the computer screen were not particularly informative in terms of signaling the location of food. Perhaps, if we had participants eat different meals in different rooms, each containing different contextual details,

the details would become more relevant signals of location and therefore be connected more strongly to the eating event, and better remembered for higher calorie than lower calorie meals. That said, the few demonstrations that have more specifically examined memory for the location of various food items have shown that the caloric density of the food item does correlate with improved memory performance, such that the location of higher calorie food items are better remembered (Allan & Allan, 2013; de Vries et al., 2020; New, Krasnow, Truxaw, & Gaulin, 2007). Thus, we would encourage those who wish to use the MEaT to experimentally study memory of eating to explore different measures for assessing contextual memory.

Future Directions

These four experiments represent early investigations into the strength of, and the factors that influence meal memories. That said, and as alluded to above, there is still much to learn. The procedure used in the studies reported here lends itself nicely to systematically studying the characteristics of food items that affect their memorability and we have made the materials necessary for the MEaT freely available (https://osf.io/ejtu6/). For instance, time of day, meal size, and eating with others are all factors that might contribute to memory of eating. The MEaT, with some modifications, could be used to interrogate these potential influences. Additionally, whereas we performed the recall tests immediately after eating—to prevent potential interference and effects of hunger—one could delay the retention interval to several hours after eating. This may speak more closely to how memory of eating influences subsequent eating. Because eating involves input from all five senses, inexpensive knock-out procedures (e.g., a nose-clip, or blindfold) might be paired with the MEaT to determine sensory aspects that influence memory of eating. Further, the MEaT could be modified so as to explore differences in memory for olfactory cues—without having participants eat anything at all. For instance, are scents that reliably signal calories (e.g., freshly baked cookies) better remembered than scents that do signal fewer calories or none at all (e.g., rose water—c.f. de Vries et al., 2020)?

Whereas in Experiment 3 we report enhanced memory for high calorie foods, one could test the proximate mechanisms behind this effect by having all participants consume popcorn but some of which has been made more caloric with fat or sugar additives. Additionally, artificial sweeteners could be used to make some items (e.g., yogurt or brownies) sweet and calorically dense and others sweet but non-calorically dense. That said, if memory is simply tracking the sweetness of an item, that does not negate the evolutionary argument that memory has been shaped by selective pressures, as sweetness has historically been a highly reliable signal of, and therefore proxy for incoming calories (Seitz, Flaim, & Blaisdell, 2020). Finally, instead of using foods that can be easily itemized (e.g., M&Ms, peanuts, and popcorn), entire meals could be presented to participants who are then cued to take a "bite" with every presentation of the tone. While this approach suffers from the lack of standard "bite" size, it would increase the ecological validity of the task and could be used to study memory for the current task compared to semantic memory for one's average meal size. Along these lines, we could allow participants to eat as many food items as they think matches their prototypical meal, and then compare this remembered amount to some objective measure of average participant meal size.

We encourage these and other investigations because understanding the determinants of memory of eating could inform intervention strategies to enhance memory of eating in an effort to reduce overconsumption. This seems especially important given increased concerns over global overweight and obesity phenotypes. Even a small reduction in daily caloric consumption (e.g., 100 calories) is thought to prevent weight gain in most of the US population (Hill et al., 2003). Extant studies that ask participants to mindfully eat (e.g., Seguias & Tapper, 2018) or that prime participants to remember their most recent meal before snacking (e.g., Higgs, 2002; Szypula et al., 2020) report reductions of snacking of about 50-130 calories, so it is possible that we can use these simple manipulations to enhance memory of eating to our advantage. In short, we feel the time is ripe for studying memory of eating.

Conclusion

The results reported here are, to our knowledge, the first demonstrations of superior memory for an evolutionarily-important task compared to an appropriately matched task with lesser fitness relevance, using an actual behavior rather than an imagined scenario. The results from Experiment 3, in particular, are the first to demonstrate differences in memory for eating the same number of different food items. This has important implications for the literature on "adaptive memory", which has primarily been studied using various imagined scenarios and how they affect recall of neutral words. While demonstrations such as the 'survival processing effect' are suggestive of evolutionary pressures on human memory, there are a number of proximate mechanisms (e.g., elaborative encoding) that some (e.g., Howe & Otgaar, 2013; Kroneisen, Erdfelder, & Buchner, 2013) suggest to underscore this theoretical position (but see Nairne & Pandeirada, 2016 for an important discussion of proximate versus ultimate explanations of this research). While there are certainly other proximate explanations that may explain our findings of enhanced memory of eating high calorie foods, those typically used to argue against the survival processing effect (elaborative processing, self-referential processing) likely do not apply. Demonstrating memory biases for real behaviors highlights the value of a functional approach to provide insights into human memory systems. As demonstrations of mnemonic biases towards fitness relevant information continue to mount (Seitz et al., 2019), they should be considered in revisions of memory models by replacing assumptions of equipotentiality of encoded information with evolutionarily-informed assumptions about *a priori* potentiation of information memorability based on perceived fitness relevance.

Chapter 4: Learning in reverse: Dopamine errors drive excitatory and inhibitory components of backward conditioning in an outcome-specific manner

Inhibition of VTA_{DA} transients during backward conditioning prevents backward cues from exerting control over instrumental behavior

Early on, studies of associative learning were primarily concerned with understanding the basic mechanisms by which two events—broadly defined—become linked in the brain (R. Bolles, 1993; Ivan P. Pavlov, 1927). It is only recently that a shift has occurred such that major emphasis has been placed on the very specific temporal scenario in which a cue precedes a motivationally-significant outcome (e.g., reward or pain) (Kamin, 1969; Mackintosh, 1975; Pearce & Hall, 1980; Rescorla & Wagner, 1972; Sutton & Barto, 1981). Focusing on anticipatory cue→reward learning is advantageous in terms of computational modelling (Clark, 2013; Daw, Niv, & Dayan, 2005; Schultz & Dickinson, 2003; Sutton & Barto, 1981) but it leaves many learning phenomena that do not involve this specific temporal order unexplained (Miller, Barnet, & Grahame, 1995).

An example of this trend relates to discovery of the dopamine prediction error. Shortly after it was revealed that dopamine neurons in the midbrain exhibit phasic signals to unexpected rewards(Schultz, Dayan, & Montague, 1997), this error signal was interpreted as being governed by computational rules that calculate scalar values in the context of anticipatory cue-reward learning (Glimcher, 2011; Schultz et al., 1997; 2016; Waelti, Dickinson, & Schultz, 2001). Consequently, the study of the dopamine prediction error was almost exclusively focused on procedures involving anticipatory cue-reward associations that manipulate scalar value (C. Y. Chang et al., 2015; Cohen, Haesler, Vong, Lowell, & Uchida, 2012; Fiorillo, 2013; Hollerman & Schultz, 1998; Lak, Stauffer, & Schultz, 2014; Saunders, Richard, Margolis, & Janak, 2018; Steinberg et al., 2013; Tobler, Fiorillo, & Schultz, 2005; Tsai et al., 2009). Only recently have we begun to explore the role of dopamine neurons in more complex paradigms outside of simple

cue→reward learning. This work has uncovered that the prediction-error signal is capable of driving anticipatory learning of sensory events that transcend scalar value inherent in rewards, such as an association between two neutral cues (Chang, Gardner, Di Tillio, & Schoenbaum, 2017; Engelhard et al., 2019; Howard & Kahnt, 2018; Keiflin, Pribut, Shah, & Janak, 2019; Sadacca, Jones, & Schoenbaum, 2016; Sharpe et al., 2020; Sharpe, Chang, et al., 2017; Stalnaker et al., 2019; Takahashi et al., 2017). Such findings question the assumption that dopamine neurons are "specialized" for anticipatory reward learning specifically, and whether anticipatory reward learning is "special" more generally.

Backward conditioning—when a reward is *followed* by a cue (reward→cue)—breaks this temporal mold and provides a serious challenge to current computational hypotheses of dopamine function. Backward conditioning can result in both excitatory and inhibitory associations (Barnet & Miller, 1996; Chang, Blaisdell, & Miller, 2003; R. P. Cole & Miller, 1999; Prével, Rivière, Darcheville, Urcelay, & Miller, 2019; Urushihara, 2004). That is, a backward cue is capable of exciting or inhibiting representation of associated rewards, which motivates the animal towards or away from that specific reward. Here, we tested the necessity of dopamine transients in backward conditioning using an established procedure that combines backward conditioning with Pavlovian-to-Instrumental Transfer (PIT) (Laurent & Balleine, 2015; Laurent, Wong, & Balleine, 2015, 2017), which probes for both the specific excitatory and inhibitory components of the association (see Figure 4.S1). This allows us to test whether dopamine neurons are exclusively involved in anticipatory learning, or whether they function as a teaching signal to drive the formation of associations in a broader sense, regardless of whether those associations are anticipatory, inhibitory, or excitatory, and in a manner that transcends scalar value.

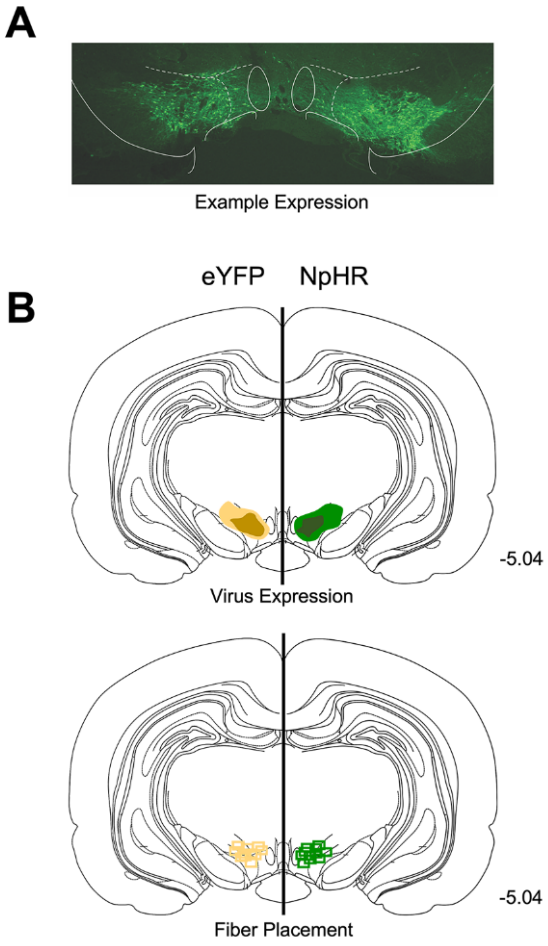

Figure 4.1. **Histological representation of virus expression and fiber placement in TH-Cre rats.** A) Neurons in VTA expressing eYFP. B) Unilateral representation of the bilateral virus expression (upper) and fiber placements (lower). Fiber implants (green and yellow squares) were localized in the vicinity of NpHR (green) and eYFP (yellow) expression in VTA.

Rats expressing Cre-recombinase under the control of the tyrosine hydroxylase (TH) promoter (Witten et al., 2011) received bilateral injections of either inhibitory halorhodopsin (NpHR, AAV5-Ef1a-DIO eNpHR3.0-eYFP, *n* = 9) or control virus that lacks the inhibitory opsin (eYFP, AAV5-Ef1a-DIO-eYFP, *n* = 9) in VTA (see Figure 4.1). Optic fibers were also implanted bilaterally over VTA. After recovery, rats were food restricted and then received backward training, where two distinct rewards (pellets and maltodextrin solution) were each followed by one of two auditory cues [white noise and clicker (counterbalanced); 8 days, 24 presentations per day]. The pairing of the reward and cue were arranged such that the cue would be presented 10s after the rat entered the magazine to consume the reward. This ensured the cue would be delivered shortly after the rats had consumed the reward. We delivered green light (532nm, 16–18 mW output) into the VTA 500ms before the onset of the cue and continuing for 2s, as we have done previously (Maes et al., 2020; Sharpe, Chang, et al., 2017). We used these parameters to prevent phasic firing at the onset of the backward cue, which would suppress a potential prediction error to the backward cue, without producing a negative prediction error [27].

Responding to the cues decreased over the course of conditioning, in line with other backward conditioning reports (Laurent & Balleine, 2015; Laurent et al., 2015, 2017), and this was similar across groups (Figure 4.2A; day: $F_{7, 112}$= 4.593, p = 0.005; group: $F_{1, 16}$ = 0.218, p = 0.647; day x group: $F_{7, 112}$= 0.445, p = 0.741; Figure 4.2A). Rats then learned to press different levers for the distinct rewards (e.g., left lever→pellets; right lever→solution, counterbalanced), on an increasingly lean random-ratio schedule (CRF, RR5, RR10). All rats acquired the lever-pressing responses with no between-

group differences (Figure 4.2B; day: $F_{7, 112} = 650.415$, $p < 0.001$; group: $F_{1, 16} = 0.016$, $p = 0.901$; day x group: $F_{7, 112} = 1.521$, $p = 0.227$; Figure 4.2B).

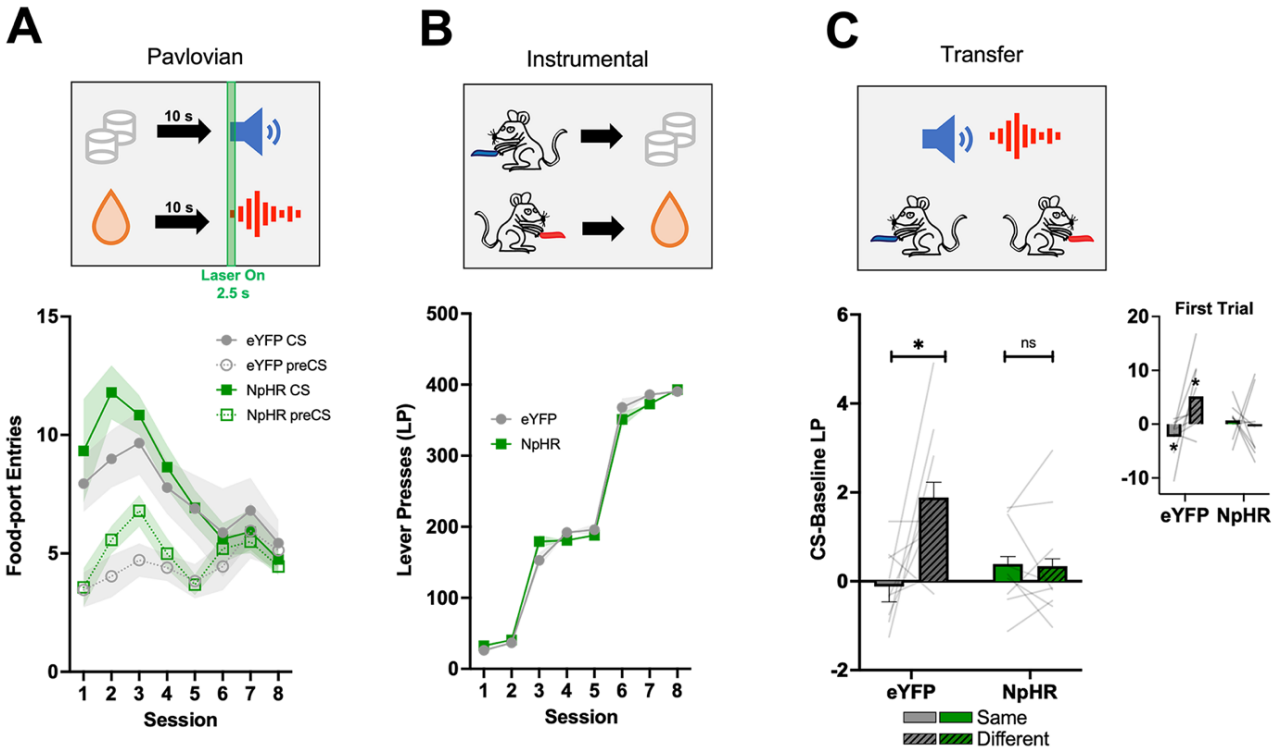

Figure 4.2. **Inhibition of VTA_{DA} transients during backward conditioning prevents backward cues from exerting excitatory and inhibitory control over instrumental behavior.** Rates of responding are represented as the number of entries into the food port or lever presses during cue presentation (±SEM), with lines indicating individual data points. **A)** Rats first learned backward relationships between two distinct rewards and two auditory cues (Conditioned stimuli: CSs). The backward cue was presented 10s after the rats entered the magazine to consume the rewards. Here, green light was delivered into VTA at the onset of the backward cue for 2.5s to suppress phasic firing of dopamine neurons without producing a negative prediction error [27]. Responding during cues decreased over the course of conditioning with no difference between groups. **B)** Rats then learned to make a left lever press to obtain one reward, and a right lever press to obtain the other. All rats acquired the instrumental responses for the rewards, with no difference between groups. **C)** Finally, during the unrewarded PIT test, both levers were made available and the cues were individually presented without rewards (right). During the PIT test, the backward cues biased our eYFP group's responding away from the associated reward, and towards the lever associated with the different reward. However, our NpHR group showed no change in responding from baseline during cue presentation or bias between the levers. * Indicates significance at $p < 0.05$.

Finally, rats received a probe test in which both levers were available with no rewards delivered, and the backward cues were presented individually (i.e., the PIT test). The PIT test

allows us to examine the nature of the associations that have developed during Pavlovian training. In our eYFP group, backward cues biased lever-pressing away from the associated reward, and towards the alternate reward (Figure 4.2C; lever x group: $F_{1, 16} = 7.054$, $p = 0.017$; simple main effect of lever: $F_{1, 16} = 8.318$, $p = 0.020$; see Figure 4.S2 for baseline responding and food-port entries). That is, the pellet-associated backward cue led to rats pressing more for solution, and the solution-associated backward cue led rats to press more for the pellet, in line with previous studies (Laurent & Balleine, 2015; Laurent et al., 2015, 2017). This shows that the backward cues excite one behavior (lever press for different reward), while also inhibiting the other (lever press for same reward), in a sensory-specific manner. Indeed, on the first trial, responding in our eYFP group to the different lever was significantly elevated from baseline ($t_8 = 2.474$, $p = 0.038$) whereas analyses suggested responding on the same lever was lower than baseline ($t_8 = 5.500$, $p = 0.050$). However, rats in our NpHR group showed no bias on lever responding and were not *elevated or decreased* from baseline lever-press responses (simple main effect of lever: $F_{1, 16} = 0.021$, $p = 0.889$; different lever versus baseline on first trial: $t_8 = 0.202$, $p = 0.845$; same lever versus baseline on first trial: $t_8 = 0.669$, $p = 0.504$). Finally, baseline lever press responding did not statistically differ between the two groups, $t_{16} = 0.946$, $p = 0.358$ (Figure S2A). Similarly, head entries into the food-port did not differ between groups, $t_{16} = 0.480$, $p = 0.638$ (Figure 4.S2B). These findings suggest that inhibition of VTA_{DA} neurons at cue onset prevent the backward cues from exerting any effect over instrumental responding for the paired rewards, in an inhibitory or excitatory manner.

Inhibition of VTA_{DA} Neurons Prevents Acquisition of the Specific and General Inhibitory Components of Backward Conditioning

There are multiple interpretations that could be made from the failure of our NpHR group to use the backward cues to modulate instrumental performance. We suggest that VTA_{DA} inhibition prevented learning about the excitatory and inhibitory relationships between the rewards and backward cues. However, it is also possible that the NpHR rats still learned the inhibitory

associations, but that the cues lacked some aspect of motivational significance that would allow them to exert control over an instrumental response. A second interpretation of the PIT data is that the NpHR rats may have learned the backwards cues were generally inhibitory of rewards. Thus, the performance of the NpHR rats during the PIT test could be interpreted as blanket inhibition of both lever-press responses during the PIT test—though this is unlikely as these rats did not reduce lever-pressing from baseline in the PIT test (see Figure 4.2C).

To dissociate these accounts, we next taught the same rats two new forward associations with visual cues (e.g., house light→pellets; flashing light→maltodextrin solution; Figure 4.S2). Training these new associations allowed us to investigate the impact of the backward cues on Pavlovian responding when presented in compound with the visual cues in an un-rewarded test session (i.e., a summation test). That is, when presented by themselves the visual cues should elicit high levels of responding because they signal the occurrence of a rewarding outcome. However, when each visual cue is presented in compound with the backward cue that signals the absence of the same outcome (i.e., a congruent compound), responding should be considerably reduced if the auditory cues are inhibitory. As predicted, responding in group eYFP was high when the visual cue was presented individually, while pairing it with the congruent backward cue significantly attenuated responding (Figure 4.3: Summation test; cue type x group: $F_{1, 9} = 11.893$, $p = 0.007$; simple main effect of cue type: $F_{1, 9} = 16.975$, $p = 0.009$). However, in the NpHR group, the presence of the backward cue had no impact on responding to the visual cue (simple main effect of cue type: $F_{1, 9} = 0.375$, $p = 0.573$). This confirmed that the backward cues possessed inhibitory properties that could influence Pavlovian responding, and that inhibition of VTA_{DA} neurons prevented backward cues from acquiring inhibitory properties.

While the summation test above shows that VTA_{DA} inhibition prevents animals from learning the inhibitory component of backward cues in a Pavlovian procedure, they cannot speak to whether the backward cues generally or specifically inhibit Pavlovian responding in either the NpHR or eYFP rats. This is because we only presented a compound where both cues were

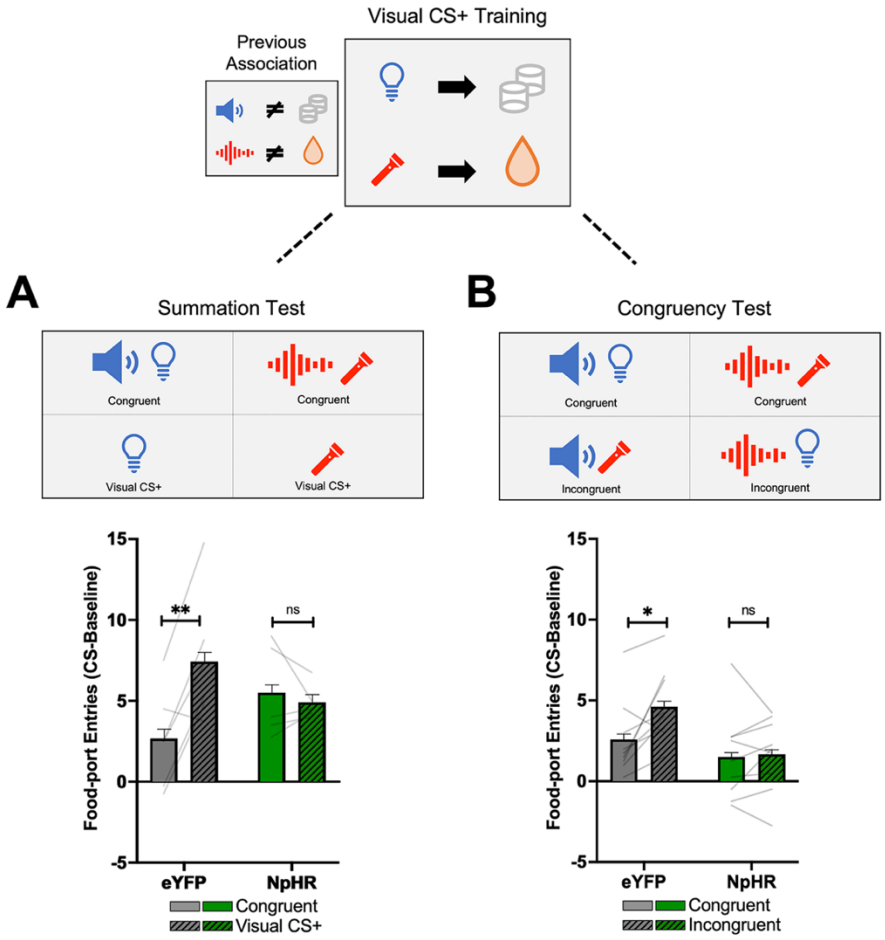

Figure 4.3. **Inhibition of VTA_{DA} transients prevents backward cues from generally and specifically inhibiting Pavlovian responses.** Responding is represented as number of entries into the food port during cue presentation (±SEM), with lines indicating individual data points. **Top)** *visual forward training*: To assess the nature of the deficit in the instrumental PIT test, we trained rats with two new forward cue-reward associations with visual stimuli (Figure 4.S3). This allowed us to perform a number of tests with novel audiovisual compounds to investigate the source of the deficit in our NpHR group. **A)** *Summation test:* we tested responding to the visual cue by itself, relative to when it was presented in compound with the backward cue associated with the same outcome (i.e., congruent compound). If the backward cue is inhibitory, responding should be reduced on congruent trials relative to trials with the visual cue alone. Indeed, this is what we observed in the eYFP group. In contrast, the NpHR group showed the same high levels of responding to the visual cue whether or not it was presented in compound with the backward cue. **B)** *Congruency test:* The previous test indicates the backward cues are inhibitory when paired with the same outcome, but did not test whether those cues possess specific or general inhibitory properties. To test this, we presented the visual cues in compound with the auditory cue predicting the same (congruent) or different (incongruent) reward. In the eYFP group, rats responded less on congruent relative to incongruent trials, suggesting the backward cues were specifically inhibitory. Again, there was no effect of the backwards cues on responding to the visual cues in the NpHR group. *Indicates significance at $p < 0.05$, **Indicates significance at $p < 0.01$.

associated with the same outcome and thus do not know if a backward cue presented in compound with a visual cue associated with the different outcome would similarly inhibit responding in a general fashion. A congruency test was used to tease apart the general versus specific nature of the inhibitory relationship that our NpHR group failed to learn. Specifically, just as we had previously presented in compound backward and forward cues associated with the same outcome (i.e., congruent compound), we could also present in compound backward and forward cues associated with different outcomes (i.e., incongruent). If the inhibitory relationship is specific, congruent compounds should show reduced responding relative to incongruent compounds. However, if the inhibitory relationship is general, there should be no difference between congruent and incongruent compounds. In our eYFP group, we observed a reduction in responding on congruent relative to incongruent compound trials (Figure 3: Congruency Test; compound x group: $F_{1, 16} = 4.571$, $p = 0.048$; simple main effect of compound: $F_{1,16} = 8.790$, $p = 0.018$). In contrast, rats in group NpHR showed no difference in Pavlovian responding during congruent versus incongruent trials (simple main effect of compound: $F_{1,16} = 0.096$, $p = 0.765$), confirming they had not learned the specific inhibitory associations with the backwards cue, and it was not a more general deficit in using the Pavlovian cues to exert control over instrumental behavior.

Inhibition of VTA_{DA} Neurons at Cue Onset in Forward Conditioning Does Not Prevent Learning or Make Cues Aversive

Our prior results showed that brief optogenetic inhibition of VTA_{DA} neurons at cue onset in backward conditioning prevented rats from learning the excitatory and inhibitory components in backward conditioning, which we would interpret as indicating the dopamine prediction error is a broad teaching signal that transcends both scalar value and anticipatory associative structures. However, it is possible that inhibiting VTA_{DA} neurons at cue onset somehow made these cues

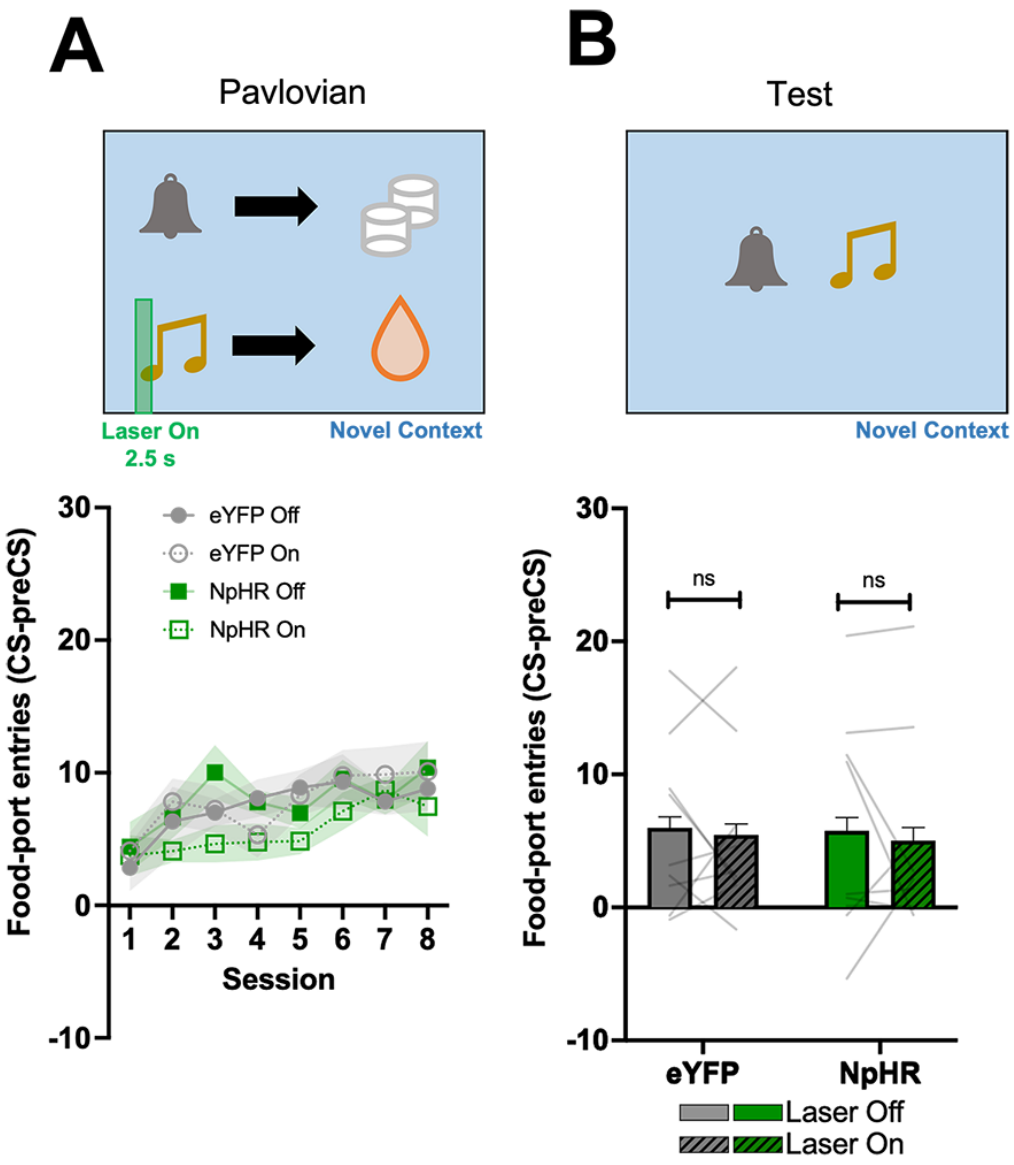

Figure 4.4. **Inhibition of VTA_{DA} transients at cue onset in forward conditioning does not impair learning.** Responding is represented as number of entries into the food port during cue presentation (±SEM). To ensure our findings could not be the result of VTA_{DA} inhibition at cue onset causing the backward cues to become aversive or reducing their salience, we taught rats novel auditory cue-reward associations with VTA_{DA} inhibition at cue onset. **A)** Rats learned forward relationships with two novel auditory cues, one of which received light delivery into VTA at cue onset. Pavlovian training progressed normally for both cues in group eYFP, with a non-significant reduction in responding to the NpHR group at the beginning of training. **B)** We then tested responding to the auditory cues by themselves without laser inhibition. There were no differences in responding between groups, or between cues. These results suggest VTA_{DA} inhibition at cue onset does not prevent learning.

aversive, or simply reduced their salience so that they could not be learned about. To test this, we taught all rats new forward relationships between two novel auditory cues (siren and tone) and two distinct food rewards in a novel context. We delivered green light (532 nm, 16–18 mW output) to VTA_{DA} neurons at cue onset for one of the auditory cues but not the other (counterbalanced), using the same inhibition parameters as backward conditioning (i.e. 2.5s inhibition at cue onset). We observed no difference in acquisition between the cue with laser on versus the cue with the laser off in either group (Figure 4.4A; day: $F_{7, 112} = 2.741$, $p = 0.060$; laser: $F_{1, 16} = 0.947$, $p = 0.345$; group: $F_{1, 16} = 0.079$, $p = 0.782$; day x group: $F_{7, 112} = 0.246$, $p = 0.845$; day x laser: $F_{7, 112} = 1.266$, $p = 0.291$; laser x group: $F_{1, 16} = 2.051$, $p = 0.171$; day x laser x group: $F_{7, 112} = 0.522$, $p = 0.734$). However, in the NpHR group, the cue with the laser on showed a small, but statistically non-significant, retardation of acquisition, approximately replicating the results of Morrens et al. (2020) (simple main effect of laser status: $F_{1,16} = 3.940$, $p = 0.082$; Figure 4.4A). Despite this, responding during the two cues was virtually indistinguishable after the initial sessions, and an extinction test after the completion of training revealed no between-group or within-group differences in responding (Figure 4.4B; laser status: $F_{1, 16} = 0.236$, $p = 0.634$; group: $F_{1, 16} = 0.011$, $p = 0.916$, laser status x group: $F_{1, 16} = 0.006$, $p = 0.937$). These results suggest that VTA_{DA} inhibition at cue onset does not prevent learning about the cue-reward association. Thus, the results from the previous studies cannot be explained by VTA_{DA} neuronal inhibition reducing the salience of the cues to the extent that they cannot be learned about or making them in some way aversive.

Discussion

These data show that backward reward→cue associations can modulate instrumental behavior in an excitatory, inhibitory, and outcome specific manner. Further, inhibition of VTA_{DA} neurons at the onset of the backward cue to suppress phasic firing of dopamine neurons prevents learning of these backward associations. We also ruled out the possibility that inhibiting VTA_{DA} neurons at cue onset simply prevents learning by reducing cue salience. These data are

consistent with recent work implicating phasic activity in VTA_{DA} neurons in learning outside the context of scalar values (Chang et al., 2017; Engelhard et al., 2019; Howard & Kahnt, 2018; Keiflin et al., 2019; Sadacca et al., 2016; Sharpe et al., 2020; Sharpe, Chang, et al., 2017; Stalnaker et al., 2019; Takahashi et al., 2017), and extend this research in critical ways.

Canonical models (Glimcher, 2011; Schultz et al., 1997; Schultz, 1998, 2016; Schultz & Dickinson, 2003; Waelti et al., 2001) of the dopamine prediction error has restricted these neurons to anticipatory cue-reward learning, via the backpropagation of scalar value to a reward-predictive cue. However, our data show that VTA_{DA} transients are necessary for the excitatory and inhibitory components of backward conditioning in a manner that entails specific knowledge of the identity of the events. This comes at a time when there is mounting evidence that the dopamine error facilitates far more complex learning than that afforded by the backpropagation of scalar value (Langdon, Sharpe, Schoenbaum, & Niv, 2018; Sharpe & Schoenbaum, 2018). For example, VTA_{DA} transients are necessary and sufficient for learning associations between two neutral cues (e.g., tone→light), and VTA_{DA} neurons achieve this without making the neutral cues valuable in and of themselves (Sadacca et al., 2016; Sharpe et al., 2020; Sharpe et al., 2017). Similarly, artificially inducing dopamine prediction errors during cue-reward learning allows the cue to evoke a detailed representation of the reward (Keiflin, Pribut, Shah, & Janak, 2019b). Results like these and others (Chang et al., 2017; Howard & Kahnt, 2018; Sadacca et al., 2016; Sharpe et al., 2020; Stalnaker et al., 2019; Takahashi et al., 2017) suggest VTA_{DA} neurons are capable of producing an error that facilitates "model-based" learning, which refers to an ability to associate (and predict) sensory representations of events. However, even an error signal that facilitates model-based learning cannot fully explain our results with backward conditioning. This is because model-based accounts still ultimately rely on value back propagating to earlier predictors of reward, albeit in the context of more complex associative structures, whether inferred or directly experienced (Daw et al., 2005; Gardner, Schoenbaum, & Gershman, 2018).

How should we interpret the necessity of VTA_{DA} neurons in backward conditioning? The most parsimonious explanation of our data and other recent findings is that VTA_{DA} neurons are computing prediction errors between contiguously-occurring events. Thus, regardless of if the events are two contiguously-occurring cues (as in sensory preconditioning (Sharpe et al., 2017) and second-order conditioning (Maes et al., 2020)) or other sensory events, VTA_{DA} neurons might be sending errors that reflect a mismatch between sensory expectations and events. That is, it could be considered a more general sensory prediction error, that serves to reduce the presence of prediction errors in our everyday sensory experience, which sometimes involves events that possess value (like rewards). Indeed, the original Rescorla-Wagner model (Rescorla & Wagner, 1972), which serves as the basis for Temporal Difference Reinforcement Learning (TDRL) algorithms, is agnostic towards whether prediction errors are value-based or more cognitive like we are now suggesting. Such a stance would argue that VTA_{DA} neurons are contributing to learning in ways more closely aligned with historical interpretations of associative learning (R. Bolles, 1993) and less with modern TDRL-centric interpretations.

The implications of dopamine acting as a more universal teaching signal are profound. First, if dopamine contributes to mentally linking contiguously-occurring events, rather than for predicting rewards (either proximally or distally), it would explain why it has been found to be necessary for higher-order conditioning (Maes et al., 2020; Sharpe et al., 2017), and also places dopamine at the center of many complex forms of cognition (e.g., spatial and causal reasoning) (Seitz, Blaisdell, & Sharpe, 2021). Ultimately, this may have important implications in pathologies characterized by abnormal dopaminergic functioning (e.g., schizophrenia and addiction). Indeed, an excess of subcortical dopamine (a trademark of schizophrenia) would be expected to be correlated with an excess in learning relationships between potentially irrelevant events—which could result in hallucinogenic or delusional experiences (Corlett et al., 2007; Corlett, Taylor, Wang, Fletcher, & Krystal, 2010; Jensen et al., 2007; Millard, Bearden, Karlsgodt, & Sharpe, 2021; Morris, Griffiths, Le Pelley, & Weickert, 2013; Morris et al., 2012). To expand, not all co-

occurring events need be associated, and there are also regions (e.g., lateral hypothalamus) whose function appears to be opposing the learning of relationships that do not immediately predict rewards (Hoang & Sharpe, 2021; Sharpe, Batchelor, Mueller, Gardner, & Schoenbaum, 2021). Such findings situate the VTA_{DA} prediction error at the center of a dynamic system whose main function is to direct learning in one way or another via distinct circuits, depending on current context or motivational state, and past experience. Future research will tell how far we can push the boundaries of dopamine's involvement in learning and cognition.

Experimental Model and Subject Details

Subjects

18 transgenic Long-Evans rats (8 Female, 10 Male) expressing Cre-recombinase under the control of the tyrosine hydroxylase promoter were used in this study. Rats were randomly allocated to groups and matched for age and sex. Rats were maintained on a 12-h light–dark cycle, where all behavioral experiments took place during the light cycle. Rats had ad libitum access to food and water unless undergoing the behavioral experiment during which they received sufficient chow to maintain them at ~85% of their free-feeding body weight. All experimental procedures were conducted in accordance with the UCLA Institutional Animal Care and Use Committee.

Surgeries

Surgical procedures have been described elsewhere(Sharpe, Chang, et al., 2017). Briefly, rats received bilateral infusions of 1.0-2.0 μL of AAV5-EF1α-DIO-eYFP (n = 9) or eNpHR3.0-eYFP (n = 9) into the VTA at the following coordinates relative to bregma: AP: −5.3 mm; ML: ± 0.7 mm; DV: −6.5 mm and −7.7 (females) or −7.0 mm and −8.2 mm (males). Virus was obtained from Addgene. During surgery, optic fibers were implanted bilaterally (200-μm diameter, Thorlabs, CA) at the following coordinates relative to bregma: AP: −5.3 mm; ML: ± 2.61 mm and DV: −7.05 mm (female) or −7.55 mm (male) at an angle of 15° pointed toward the midline.

Apparatus

Behavioral sessions were conducted in identical sound-attenuated conditioning chambers (Med Associates, St. Albans, VT). The chambers contained 2 retractable levers that could be inserted to the left and right of a recessed food delivery port in the front wall when triggered. A photobeam entry detector was positioned at the entry to the food port. The chambers were also equipped with syringe pumps to deliver 15% maltodextrin solution in 0.1 ml increments through a stainless steel tube into a custom-designed well in the food port and a pellet dispenser to deliver a single 45-mg sucrose pellet (Bio-Serv, Frenchtown, NJ). Both a tone and white noise generator

were attached to individual speakers on the wall opposite the lever and magazine. A 3-watt, 24-volt house light mounted on the top of the back wall opposite the food cup and two white lights were mounted above the levers and served as visual cues.

Backward Pavlovian Training

Rats received 8 consecutive days of Pavlovian conditioning. Outcomes (sucrose pellet or maltodextrin solution) were delivered into the food port, and auditory cues (clicker or white noise) were played 10 s following the first entry into the magazine. Outcome-cue relationships were fully counterbalanced. Cue duration varied from 2-58 s with an average of 30 s. Data are presented as average entries per minute. Variable cue duration was chosen to stay consistent with the procedure described elsewhere (Laurent & Balleine, 2015; Laurent et al., 2015, 2017) and because variable cue length helps promote instrumental responding at test by preventing the animal from timing the delivery of the outcome. Stimuli were presented 12 times each in a pseudorandom order with a variable inter-trial-interval (ITI) ranging from 80-190 s with an average of 125 s. Rats received three reminder sessions of this training; reminder 1 occurred after instrumental conditioning, reminder 2 occurred after PIT test, and reminder 3 occurred after the incongruent/congruent test.

Instrumental Training

Rats received 8 consecutive days of Instrumental conditioning. Each day consisted of two training sessions separated by at least 3 hours. In each session, left or right lever was extended for 30 minutes or until 20 outcomes had been received. Lever and outcome relationships were fully counterbalanced as was the time of day (early vs late) for each session. Lever pressing was continuously reinforced for the first 2 days of training, reinforced on a random ratio 5 schedule for days 3-5, and reinforced on a random ratio 10 schedule for days 6-8. Rats received a reminder RR10 session in between the two PIT tests. Data are presented as total number of lever presses per session/day.

Transfer Test

Rats received 2 transfer test sessions. The sessions were separated by 2 rest days and one RR10 instrumental reminder session. The data is collapsed between the two days and a 2 (Day 1 vs Day 2) x 2 (Same-Baseline vs Different-Baseline) x 2 (eYFP vs NpHR) mixed measures ANOVA revealed no significant effect of day: $F_{1, 16} = 2.373$, $p = 0.143$, no interaction between day and group: $F_{1, 16} = 0.240$, $p = 0.631$, nor interaction between day and lever: $F_{1, 16} = 0.565$, $p = 0.463$. At the start of the session, both levers were extended for 8 min to allow for extinction to the levers. All rats then received the following order of stimulus presentation: white-noise, clicker, clicker, white-noise, clicker, white-noise, white-noise, clicker, as is standard in the field (Laurent & Balleine, 2015; Laurent et al., 2015, 2017). Thus, each cue was presented 4 times for 60 s. Because cues are counterbalanced relative to the rewards they predict, the order of cue presentation is also counterbalanced in the above order. Lever pressing during the cue is subtracted from a 60 s baseline (average of lever pressing made to both levers prior to each cue presentation). This gives us a measure of how much rats increase (or decrease) responding from baseline during the cues. Data are presented as average lever presses-baseline per minute. Trials were separated by a fixed ITI of 180 s.

Forward Conditioning with Visual Cues

Rats received 3 consecutive days of Pavlovian training where a visual cue (house light or flashing white lights) predicted the occurrence of an outcome (sucrose pellet or maltodextrin solution). Visual cues were randomly presented 15 times each for a fixed duration of 30 s and immediately terminated with the delivery of the outcome. Responding during the visual cue is measured relative to the number of entries made 30 s before the cue was presented (CS-preCS). Data are presented as average entries per minute. Trials were separated by a variable ITI ranging from 130-230 s with an average of 180 s. Rats received two consecutive reminder sessions of this training after completing the congruency test session and before the summation test.

Congruency Test

Rats received a single test session responding to congruent/incongruent audiovisual compounds presented in extinction. Four unique compounds (2 congruent and 2 incongruent) were presented four times each. Compounds were presented in the following order: clicker_flash, noise_house, noise_flash, clicker_house, noise_house, clicker_flash, clicker_house, noise_flash. Compounds were presented for a total of 30 s and were measured relative to responding made 30 s prior to compound presentation. Data are presented as average entries per minute. Trials were separated by a variable ITI ranging from 130-230 s with an average of 180 s.

Summation Test

A subset of rats (N=11) received a single summation test in which the visual cues were presented by themselves or in compounds with the specific auditory cue associated with the same outcome (congruent compound). Each visual cue and audiovisual compound was presented 4 times each for a total of 16 trials. Order of presentation was pseudo-randomly counterbalanced. Cues were presented for a total of 30 s and are measured relative to responding made 30 s prior to compound presentation. Data are presented as average entries per minute. Trials were separated by a variable ITI ranging from 130-230 s with an average of 180 s.

VTA_{DA} neuronal inhibition at cue onset in forward conditioning

Rats received 8 consecutive days of Pavlovian training in a novel context where novel auditory cues (siren and pure tone) predicted the occurrence of an outcome (sucrose pellet or maltodextrin solution). Auditory cues were randomly presented 15 times each for a fixed duration of 30 s and immediately terminated with the delivery of the outcome. Laser light was delivered for 2.5s beginning 0.5s before cue onset for one of the two cues (counterbalanced). Responding during the cues was measured relative to the number of entries made 30 s before the cue was presented. Trials were separated by a variable ITI ranging from 130-230 s with an average of 180 s. After 8 days of conditioning, rats received a single test session in extinction where each stimulus was presented 8 times without laser delivery. Stimulus presentation was pseudo-randomly

ordered and fully counterbalanced. Auditory cues were presented for a total of 30 s and are measured relative to responding made 30 s prior to cue presentation. Trials were separated by a variable ITI ranging from 130-230 s with an average of 180 s. Data are presented as average entries per minute.

Histology

The rats were euthanized with an overdose of carbon dioxide and perfused with phosphate-buffered saline followed by 4% paraformaldehyde (Santa Cruz Biotechnology Inc.). Fixed brains were cut in 20-μm sections, and images of these brain slices were acquired and examined under a fluorescence microscope (Carl Zeiss Microscopy). The viral spread and optical fiber placement (Figure 2A and 2B) were verified and later analyzed and graphed using Adobe Photoshop.

Data collection and statistics

Data was collected using Med-Associates automated software and the text file output were analyzed using MPC2XL (Med Associates, St. Albans, VT). Repeated Measures Analysis of Variance (ANOVA) were used to assess training and test data in JASP (version 0.15). Simple main effects were used to follow up on significant interactions and assess the effect of lever (Same vs Diff) on each group (eYFP vs NpHR), the effect of compound type (Incongruent vs Congruent) on each group, and the effect of cue type (Visual CS+ vs Compound) on each group. One sample T-tests were used to measure responding relative to baseline (expected value = 0). All data were tested for normality and analyses that did not pass this criterion were adjusted using a Greenhouse-Geisser (Repeated Measures) or Wilcoxon (T-test) correction. For instances in which a Greenhouse-Geisser correction was used, the adjusted p value is reported but degrees of freedom are reported in their uncorrected form. Pilot data (n=11) presented in the supplementary material revealed the effect of lever on the PIT test was very large, $\eta^2 = 0.519$ or $f = 1.039$ using the formula ($f = \text{sqr}(\eta^2 / (1 - \eta^2))$. A power analysis conducted in G*power (version 3.1) revealed 8 participants would be necessary to discover a similarly sized effect with 90%

power (between measurement $r = 0.074$). Thus, we were well powered to detect a main effect of lever in our initial PIT test with 9 participants per group.

Pilot Study

A pilot study was conducted in wild-type rats (n=11) to confirm successful influence of backward conditioning on PIT and to replicate the procedure described elsewhere (Laurent & Balleine, 2015; Laurent et al., 2015, 2017). The procedure was identical to that described in the Pavlovian, Instrumental, and Transfer Test sections in those manuscripts (Figure 4.S2A). Responding to both the pellet and maltodextrin cue decreased over the course of conditioning and there was no difference between cues (day: $F_{7, 70} = 3.531$, $p = 0.003$; reward: $F_{1, 10} = 0.008$, $p = 0.931$; day x reward: $F_{7, 70} = 0.821$, $p = 0.573$; Figure 4.S1A). Rats then learned to press different levers for the distinct rewards on an increasingly lean random-ratio schedule (Figure S1B). All rats acquired the lever-pressing responses with no differences between the rewards (day: $F_{7, 70} = 1321.052$, $p < 0.001$; reward: $F_{1, 10} = 1.051$, $p = 0.329$; day X reward: $F_{7, 70} = 0.992$, $p = 0.444$; Figure 4.S1B). Finally at test, both levers were extended and the backward cues were presented sequentially. Backward cues biased lever pressing towards making the opposite lever press relative to baseline (lever: $F_{1, 10} = 10.809$, $p = 0.008$, $\eta^2 = 0.519$; Figure 4.S1C).

Forward Conditioning with Visual Cues

All rats readily learned forward relationships between visual cues and rewards (described in detail in Methods) with no difference between groups (day: $F_{4,64} = 30.989$, $p < 0.001$; group $F_{1,16} = 0.466$; $p = 0.504$, day X group: $F_{4, 64} = 0.221$, $p = 0.926$; Figure 4.S3).

Supplementary Materials

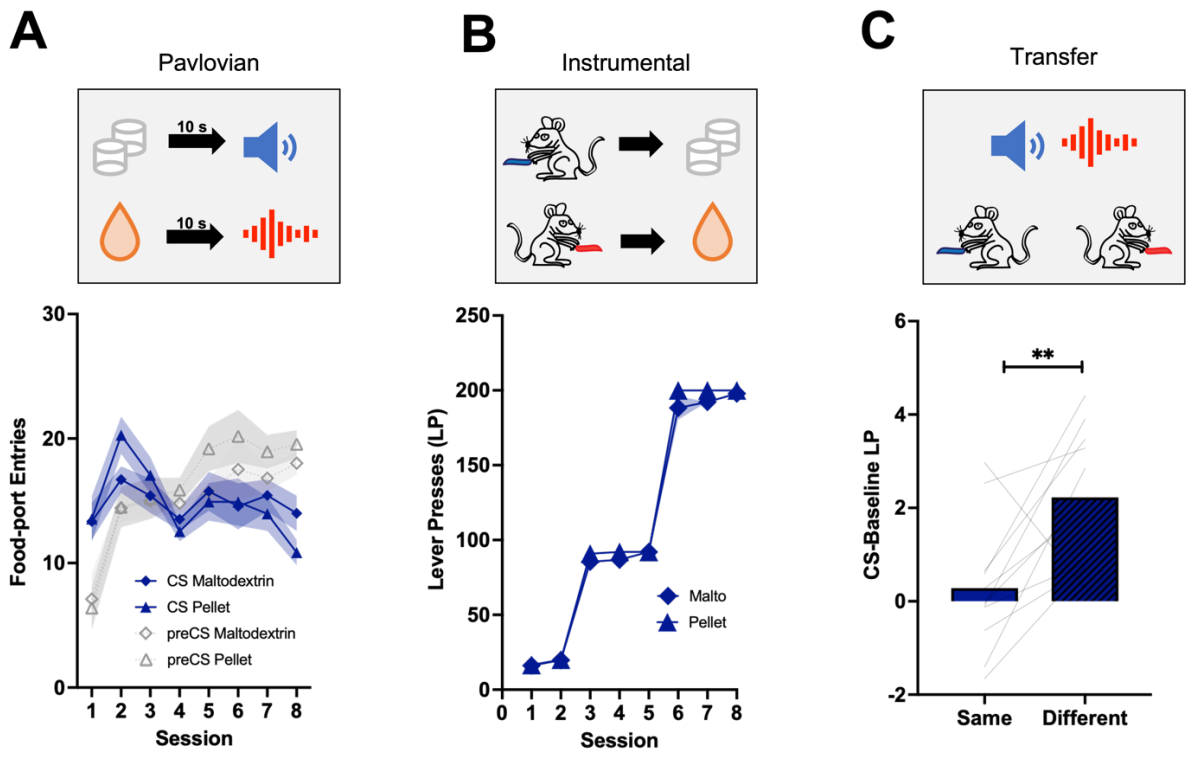

Figure 4.S1. ***Backward conditioning Pavlovian to Instrumental Transfer Test Pilot study.*** ***A)*** *Backward Pavlovian training.* ***B)*** *Instrumental conditioning.* ***C)*** *Transfer test.*

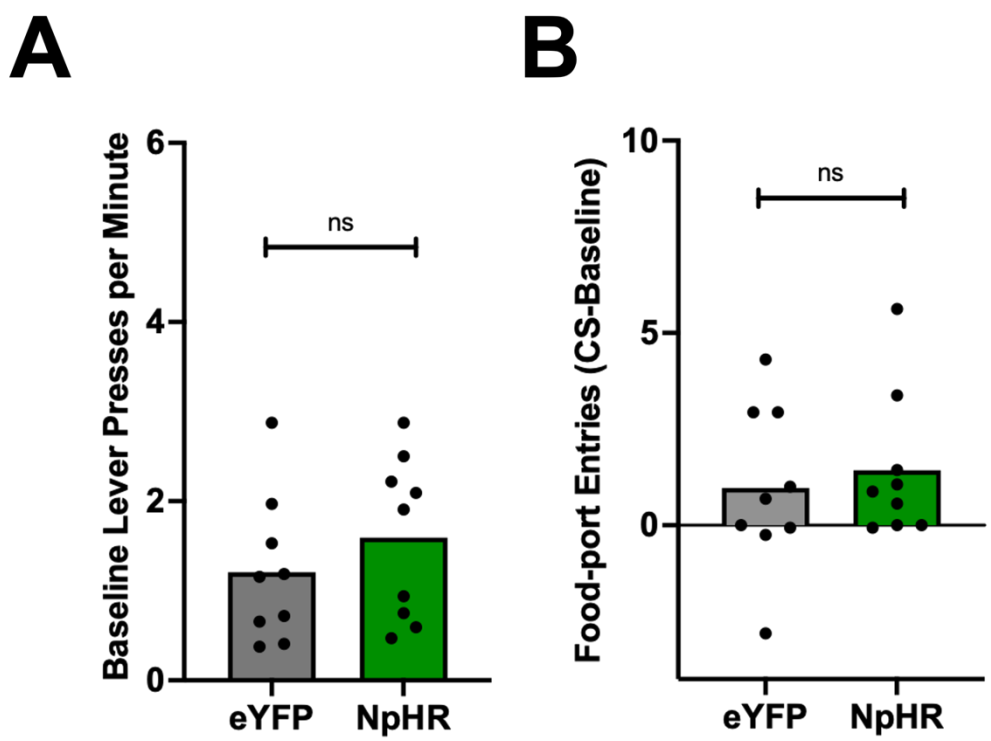

Figure 4.S2. ***No difference in baseline lever pressing or head entry responses during transfer test.*** ***A)*** *Transfer test data are displayed in Figure 2C as lever presses made relative to baseline responding. Those baseline levels are shown here and do not differ between groups,* $t_{16} = 0.946$, $p = 0.358$. ***B)*** *During the transfer test rats also had the ability to enter the food port as well as lever press. We find the backward cues have little effect on head entries into the food port in both groups,* $t_{16} = 0.946$, $p = 0.358$.

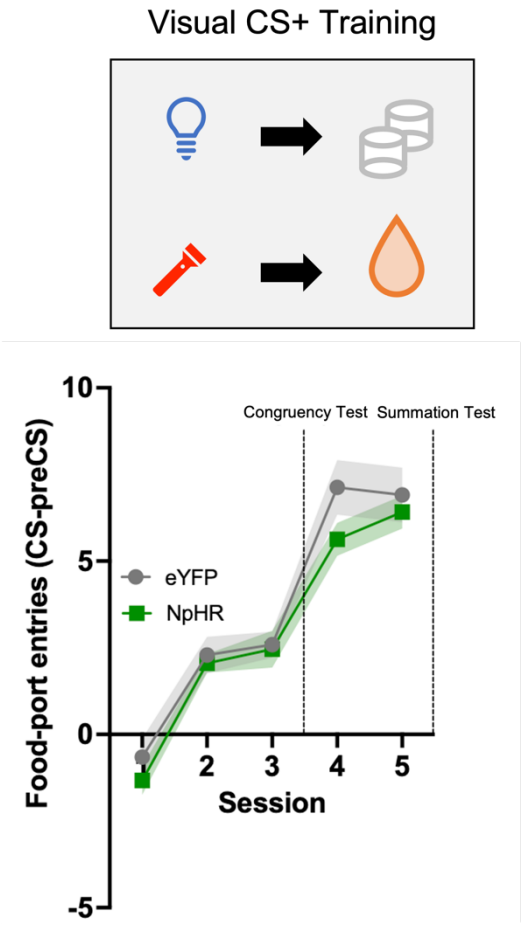

Figure 4.S3*. Forward conditioning with visual cues.* *Rats learned relationships between two visual cues (house light and flashing-light) and two rewards (sucrose pellet and maltodextrin solution). Rats received 3 days of this training before completing the Congruency test and then two more days of training before the Summation test.*

Chapter 5: Conclusion

The experiments reported on in this dissertation have sought to demonstrate foraging related biases to learning and memory systems in both human and non-human animals. In brief, I have shown that flavors appear to elucidate unconditioned metabolic responses that are fairly resistant to habituation. Rats given daily access to a small amount of flavored water failed to gain weight relative to rats given unflavored water or flavored-sugar water over a three-week period. As flavors have historically been reliable predictors of calories and nutrients, and because failing to metabolize novel food items could be consequential, I suggest animals have evolved unconditioned metabolic responses to novel flavors that can then be "calibrated" through further learning of flavor-calorie associations. I next created a novel behavioral procedure to show how the human memory system is biased towards remembering the behavior of eating relative to similar noneating behaviors. Using the same procedure, I also showed eating high-calorie foods is better remembered than eating low-calorie foods and that slower eating also enhances memory of eating. That memory is biased towards remembering the act of eating and eating high-calorie foods suggests evolution has shaped memory systems to prioritize the remembering of food relevant information. Finally, I showed that rats are capable of learning detail-rich backward relationships between food rewards and environmental cues and that learning these associations is dependent on VTA_{DA} activity. That these dopamine neurons are capable of facilitating backward associations suggests their contribution to learning is far more complex than previously conceptualized (Glimcher, 2011; W. Schultz et al., 1997; Wolfram Schultz, 2016; Waelti et al., 2001). It also highlights the sophisticated ways that learning processes can aid in foraging. Not only were rats able to learn a complicated backward relationship between food reward and cue and use that information to guide their behavior, but their behavior indicated they associated the cue with a detail rich memory of the specific food reward and not just a general value association. In addition to the experiments reported here,

there are several other lines of evidence that converge upon a similar thesis that learning and memory systems appear highly specialized for foraging.

Evolutionary and comparative evidence

Comparative analyses in non-human animals demonstrate the important role that foraging and eating behavior has had on shaping memory processes. For instance, some species of birds (e.g., Clark's Nutcrackers and Black-Capped Chickadees) have evolved remarkable mnemonic capabilities (via hippocampal enlargement and specialization) allowing them to remember the location of cached food over several months (Balda & Kamil, 1992; Feeney, Roberts, & Sherry, 2009; Sherry et al., 1992; Shettleworth, 1990). Scrub jays distinguish between the location of perishable (worms) and non-perishable (peanuts) food items depending on the time between caching and retrieval (Clayton & Dickinson, 1998) which is suggestive of episodic memory (Crystal, 2010; Tulving, 2002). Evidence of episodic memory in rodents is also found when rats are tasked with remembering the location of distinct food flavors, some of which are experimentally devalued (Babb & Crystal, 2006). While comparative studies often use appetitive food outcomes to motivate animal behavior, the fact that nearly all evidence of episodic-like memory comes from animals remembering specific details about food (e.g., Babb & Crystal, 2006; Clayton & Dickinson, 1998; de Kort, Dickinson, & Clayton, 2005; Feeney et al., 2009; Roberts et al., 2008; Zhou & Crystal, 2009), as opposed to an aversive outcome like shock (but see, Iordanova, Good, & Honey, 2008), raises the possibility that episodic memory evolved to facilitate learning about how to obtain food. Under this assumption, memory is expected to be best for eating behaviors, because it is precisely what the memory system was "designed" to do.

While we can certainly use our learning and memory capabilities for a whole host of tasks (e.g., list-learning, remembering where one left their keys, etc.), I feel there is a case to be made that these are exaptations—that is, tasks that have shifted from their original evolutionary function and may or may not be currently relevant to evolutionary fitness (Buss, Haselton,

Shackelford, Bleske, & Wakefield, 1998; Gould & Vrba, 1982). There are several design features that suggest this. As mentioned earlier, though conditioned taste aversion and fear conditioning can both occur with a single pairing of the CS and US, conditioned taste aversion can occur even with extended gaps between the CS and US, is more resistant to extinction, and occurs earlier in development than fear conditioning (Garcia et al., 1955; Garcia & Koelling, 1966; Gruest et al., 2004). Similarly, under states of hunger and resource scarcity, drosophila were shown to down regulate specific dopaminergic neurons responsible for fear conditioning—rending this learning severely reduced while leaving appetitive conditioning intact. When these neurons were artificially activated, fear learning resumed but at a cost to the overall survival of these flies (Plaçais & Preat, 2013). Similar patterns have been found in mice who, when briefly fasted before learning, show impaired fear conditioning, and when briefly fasted before extinction, exhibit facilitated extinction (Verma et al., 2016). This suggests the resource-heavy process of fear conditioning can be temporarily "shut off" in times of starvation and that this is an evolutionarily conserved trait. The facilitated extinction by hunger suggests a trade-off between expressing fear states as well as being concerned by fearful stimuli and searching for food. Finally the types of animals that serve to benefit the most from fear conditioning, prey animals, paradoxically consume significantly more food than predators (who presumably gain less from fear conditioning) (Raubenheimer & Simpson, 1997). Thus, prey animals are likely to be highly reliant on using learning and memory mechanisms to obtain food and may even prioritize this learning over learning to avoid prey in times of hunger. Taken together, these patterns are suggestive of learning and memory capabilities having evolved, at least primarily, to aid animals in foraging.

Functionality evidence

As reviewed earlier, memory of recent eating plays an important role in moderating future food consumption. A popular stance among memory researchers is that the key adaptive feature of memory is its ability to generate predictions about future events (Josselyn &

Tonegawa, 2020; Mullally & Maguire, 2014; Schacter et al., 2012). And yet, memory for everyday behaviors and events is generally poor (Misra et al., 2018). This may be because at the time of encoding, it is difficult to gauge the importance or future relevance of any given event/behavior. As an example, when standing in line next to an individual, one may not strongly encode aspects of their physical characteristics. As a result, if that person is later accused of committing a crime, it may be difficult to accurately report details of that person to the authorities. Memory of eating, however, is different, assuming there is some recognition (conscious or not) that encoding this eating event is of particular importance given a recollection of its details will later be used to moderate future food intake. While only speculative, this reasoning makes the same prediction as the evolutionary argument—that memory of eating should be better remembered than similar noneating behaviors. With that said, the effect of memory of recent eating on regulating future eating has been reported to wane over 3-hours (Higgs, 2002). On one hand, this might be taken as evidence that the meal memory is not particularly strong, but on the other hand, may be evidence that temporal information regarding when the meal took place is also strongly integrated in the memory. That is, in "deciding" whether to consume a meal one might integrate information about the content, quantity, and timing of their last meal. Thus, even if one consumed a large portion of a high-quality food, if this meal occurred 5 hours ago, this temporal information should be used to no longer inhibit future eating.

Evidence of superior memory for eating behavior

Seitz et al. (2021) (Chapter 3) directly tested how memory differs for eating compared to a similar non-eating behavior. Participants watched a film in front of a bowl of M&Ms and an opaque container. As they watched, a tone was randomly sounded 30 times, which cued some participants to eat an M&M and others to move an M&M from the bowl to the container. Participants who ate the M&Ms were significantly better at remembering how many times they performed this task (reduced task memory error), despite all participants performing nearly

identical procedural behaviors under identical conditions. A follow up experiment ruled out glucose provided by consuming the M&Ms as a potential physiological explanation behind this effect (c.f. Glenn, Minor, Vervliet, & Craske, 2014; Smith, Riby, Eekelen, & Foster, 2011). These results support the prediction that memory of eating is particularly strong, although it remains unclear if this is due to their importance in moderating future eating behavior, their evolutionary significance, or some combination of the two.

More specific mechanisms by which eating a meal becomes so well remembered is similarly, at this point, unknown. For instance, it is possible that eating is more strongly encoded than other actions—potentially via enhanced attention. It is also possible that memory of eating is more easily retrieved or less prone to interference. At present, we simply know that eating a meal is especially well remembered, and what accounts for this special status has yet to be identified. The neurological underpinnings responsible for this enhanced memory might inform on this matter and is in its own right an interesting research pursuit. The neural underpinnings responsible for calorically dense food items being better remembered than consuming the same number of a low-calorie food items is similarly intriguing (Seitz et al., 2021). These questions are especially compelling in light of the various sensory inputs that could moderate the enhanced memory of eating—because eating involves input from all five senses (Delwiche, 2012; Fantino, 1984; Havermans, Hermanns, & Jansen, 2010; Spence, 2015). Additionally, many foods are associated with rich memory networks (Allen, 2012). Even the smell of certain foods can bring back memories of childhood and special events. This richness in associations may enhance memory from a connectionist perspective. The diversity and complexity of different flavor and food combinations also makes memory of eating some foods less susceptible to retroactive interference. Alternatively, from an evolutionary perspective, there might be pressures to enhance the memory of eating novel compared to previously consumed food items, because novel foods could serve as pathogen vectors and cause other bodily harms (c.f., Seligman, 1970). Sensory knockouts, whole-brain imaging, and controlled behavioral studies are needed

to elucidate what leads to enhanced memory of eating and enhanced memory of eating high calorie foods.

Memory of eating: Superior but still imperfect

Although the literature and experiments reviewed above indicate that meal memories are more accurate relative to non-meal memories, there is also evidence of systematic underestimation of the amount of food consumed. Studies have shown a similar bias towards underestimating the amount of food consumed immediately (~30% in Seitz et al., 2021, Chapter 3) and 24 hours after consumption (Armstrong et al., 2000; Baxter et al., 2002; Fries et al., 1995). These data should inform an ongoing debate within nutritional and medical communities regarding the validity of self-reported dietary assessment techniques. That there is a discrepancy between self-reported and actual eating, particularly among individuals with higher BMI, has long been a concern in nutritional research (Dao et al., 2019; Lichtman et al., 1992; Macdiarmid & Blundell, 1998; Schoeller et al., 2013) but some have recently argued that self-reported energy intakes are entirely inadequate measures that should not be used in scientific studies (Archer et al., 2018; Schoeller et al., 2013). If participants are so inaccurate in recalling how much food they consumed just minutes earlier (Seitz et al., 2021, Chapter 3), relying on memory-based measures of dietary intake is likely to result in highly unreliable findings. As memory researchers have been instrumental in advising detectives and police officers on proper techniques for interviewing witnesses and victims (Geiselman, Fisher, MacKinnon, & Holland, 1986), I suggest they might also be useful in informing more reliable measures of reporting dietary intake by dietitians and in the study of human nutrition (e.g., Martin et al., 2012).

Manipulating memory of eating to better understand learning

Dopaminergic neurons have long been implicated in the computation of prediction errors—the difference between expected and experienced rewards or events (Glimcher, 2011; Niv & Schoenbaum, 2008; Schultz et al., 1997; 2016). In order to compute a prediction error, a prediction needs to be derived (Rescorla & Wagner, 1972). While the notion of prediction error

has captured the attention of many researchers, surprisingly little is known about where/how these predictions arrive nor do we know much of their contents. One possibility is that dopaminergic neurons receive an expectation of the reward outcome from GABAergic neurons which synapse on the dopaminergic neurons (Cohen et al., 2012; Sharpe et al., 2017). While dopaminergic neurons would typically fire during reward presentation, the inhibitory input from the GABA neurons may cancel out this action potential—thus resulting in no phasic activity in these neurons which is typically observed over the course of conditioning (Schultz et al., 1997). In this sense, during conditioning with an appetitive food outcome, the GABA neurons may actually be delivering the expectation of future food reward—which requires some mnemonic representation of that food reward. However, the content of this expectation is not clear and could either be a specific representation of the outcome or a more general representation of reward value. That is, after presentation of a reward-predictive cue, the GABA neurons may be carrying an expectation of the exact contents of the reward (a sweet crunchy sugar pellet) or more simply, a scalar value of reward associated with consuming the sweet pellet. This of course, could be tested experimentally by silencing GABAergic neuron projections to VTA_{DA} and observing the effect on learning. If these neurons do in fact carry this expectation signal and that signal is outcome-specific, it would beg the question of how they are able to "tap into" the food memory and if this same memory is used to dictate other elements of behavior (i.e., modulating future consummatory behavior).

Another way the neurological underpinnings of memory of eating could be studied is through advances in memory engram capture and manipulation techniques. In brief, an engram is the physical instantiation of a memory and refers to the enduring changes to a cellular network as the result of a specific experience (Josselyn, Köhler, & Frankland, 2015; Josselyn & Tonegawa, 2020). During encoding, cells compete to become part of the engram and cells in a more excitable state are more likely to be recruited. Using neurotropic viruses, cells can be made artificially more excitable, allowing researchers to dictate which cells become part of an

engram and later manipulate or record them (Josselyn et al., 2015; A. Park et al., 2019; Rashid et al., 2016). While this method has primarily been used in capturing memory of fear events, it could theoretically also be used to capture memory of eating. Successfully doing so could answer a number of interesting questions related to the mnemonic control of eating. First, amnesiac patients exhibit willingness to eat food despite recent eating (Higgs, Williamson, Rotshtein, et al., 2008; Rozin et al., 1998) and reducing memory of eating results in humans (Higgs & Woodward, 2009; Oldham-Cooper et al., 2011) and rats (Hannapel et al., 2019) eating more at subsequent meals. Some evidence suggests enhancing memory of eating reduces future eating, but this has only been shown in humans (Allirot et al., 2018; Robinson, et al., 2014) using techniques that may be highly confounded (i.e., asking participants to mindfully eat) (Seitz, Tomiyama, & Blaisdell, 2021). If memory of eating does dictate future eating, and a meal memory can be successfully captured and manipulated, reactivation of this memory would be expected to significantly reduce consumption, even in a nutrient deprived or hungry animal. Similarly, engram network complexity, not size, has been shown to correlate with memory strength (Josselyn & Tonegawa, 2020), and so this metric may be able to support our findings high-calorie foods being better remembered than low-calorie foods (Seitz et al., 2021, Chapter 3).

Final Remarks

The study of memory is at the heart of cognitive science. While many might associate the study of memory as having connections with aging, education, neuroscience, and/or eyewitness testimony reliability, this dissertation has shown that memory and eating are also highly intertwined. Both memory processes and eating behavior appear heavily reliant on hippocampal functions (Stevenson & Francis, 2017; Swithers et al., 2009) and are also influenced by similar neuroendocrine signals (e.g., leptin and ghrelin) (Hsu, Suarez, & Kanoski, 2016; Kanoski & Grill, 2017; Suarez et al., 2019). Interestingly, whereas the hippocampus has predominantly been implicated in memory and only recently implicated in regulating eating

behavior and being impacted by obesity, the lateral hypothalamus has long been implicated in eating behavior and only very recently been found to be critical in learning cue-food associations (i.e., Pavlovian Conditioning) (Sharpe, Marchant, et al., 2017) and altered by obesity (Rossi et al., 2019). Associative learning processes have long been implicated in influencing eating behavior, particularly as it relates to taste preference and avoidance (Sclafani, 2001). More recent studies now show episodic memory processes influence eating behavior, in that episodic memory of recent eating moderates future intake (Higgs & Spetter, 2018). In animal models, dietary-induced obesity causes memory impairments (Beilharz et al., 2015) and conversely, inducing memory impairments in rodents causes obesity (Davidson et al., 2009). Similar patterns are shown in humans (Attuquayefio et al., 2017; Cheke et al., 2016; Prickett et al., 2015). While enhancing memory of eating may be a potential intervention to reduce overconsumption, little is known about the factors that influence memory of eating. It may also be the case, that memory for eating is particularly strong relative to other behaviors (Seitz et al., 2021) and yet, still an unreliable source for nutritional studies measuring dietary intake.

This dissertation has shown the interconnected nature between memory processes and eating and advocated for the position that these two systems are deeply evolutionary rooted. There are a number of exciting opportunities for future research in this space. For instance, though much work has shown memory deficits are associated with obesity, and that memory for recent eating moderates future eating, to my knowledge, no studies have examined how participant BMI interacts with this latter pattern. Similarly, while attentional biases to food and food cues are observed in participants with obesity (Hagan, Alasmar, Exum, Chinn, & Forbush, 2020; Werthmann, Jansen, & Roefs, 2015), it remains untested whether *mnemonic* biases for these items are also observed and more or less pronounced in those with obesity. How memory of eating differs in populations with normal versus overweight and obese BMI may be particularly interesting, given serum levels of leptin and ghrelin differ in these populations (Klok, Jakobsdottir, & Drent, 2007) and are also implicated in mnemonic processes (Suarez et al.,

2019). Related, while both leptin and ghrelin influence physiological states of hunger and interact with the hippocampus to improve memory formation, there has been a considerable dearth of research on how hunger states influence general memory performance and memory of eating/food stimuli. The neural underpinnings of memory of eating as well as the factors that influence these memories are still largely unknown, as are methods to improve memory of eating. Increasing memory of eating might reduce future overconsumption and also increase the reliability of self-reported dietary intake measures. As diseases of overconsumption continue to rise and as methods to study and understand mnemonic processes advance, the combination of these two seemingly distant areas should result in exciting research pursuits with relevance to both clinical and basic science.

References

Abbott, K. N., Arnott, C. K., Westbrook, R. F., & Tran, D. M. D. (2019). The effect of high fat, high sugar, and combined high fat-high sugar diets on spatial learning and memory in rodents: A meta-analysis. *Neuroscience and Biobehavioral Reviews*, Vol. 107, pp. 399–421. https://doi.org/10.1016/j.neubiorev.2019.08.010

Allan, K., & Allan, J. L. (2013). An obesogenic bias in women's spatial memory for high calorie snack food. *Appetite*, *67*, 99–104. https://doi.org/10.1016/J.APPET.2013.03.011

Allen, J. (2012). *The omnivorous mind: Our evolving relationship with food*. Harvard University Press.

Allirot, X., Miragall, M., Perdices, I., Baños, R. M., Urdaneta, E., & Cebolla, A. (2018). Effects of a Brief Mindful Eating Induction on Food Choices and Energy Intake: External Eating and Mindfulness State as Moderators. *Mindfulness*, *9*(3), 750–760. https://doi.org/10.1007/s12671-017-0812-0

Anderson, J. R., & Schooler, L. J. (2000). The adaptive nature of memory. In E. Tulving & F. I. M. Craik (Eds.), *The Oxford handbook of memory* (pp. 557–570). New York, NY: Oxford University Press.

Andrade, A. M., Greene, G. W., & Melanson, K. J. (2008). Eating Slowly Led to Decreases in Energy Intake within Meals in Healthy Women. *Journal of the American Dietetic Association*, *108*(7), 1186–1191. https://doi.org/10.1016/j.jada.2008.04.026

Andrade, A. M., Kresge, D. L., Teixeira, P. J., Baptista, F., & Melanson, K. J. (2012). Does eating slowly influence appetite and energy intake when water intake is controlled? *International Journal of Behavioral Nutrition and Physical Activity*, *9*(1), 135. https://doi.org/10.1186/1479-5868-9-135

Apovian, C. M. (2016). Obesity: definition, comorbidities, causes, and burden. *The American Journal of Managed Care*, *22*(7 Suppl), s176-85.

http://www.ncbi.nlm.nih.gov/pubmed/27356115

Arch, J. J., Brown, K. W., Goodman, R. J., Della Porta, M. D., Kiken, L. G., & Tillman, S. (2016). Enjoying food without caloric cost: The impact of brief mindfulness on laboratory eating outcomes. *Behaviour Research and Therapy*, *79*, 23–34. https://doi.org/10.1016/j.brat.2016.02.002

Archer, E., Marlow, M. L., & Lavie, C. J. (2018). Controversy and debate: Memory-Based Methods Paper 1: the fatal flaws of food frequency questionnaires and other memory-based dietary assessment methods. *Journal of Clinical Epidemiology*, *104*, 113–124. https://doi.org/10.1016/j.jclinepi.2018.08.003

Armstrong, A. M., MacDonald, A., Booth, I. W., Platts, R. G., Knibb, R. C., & Booth, D. A. (2000). Errors in memory for dietary intake and their reduction. *Applied Cognitive Psychology*, *14*, 183–191. https://doi.org/10.1002/(SICI)1099-0720(200003/04)14:2<183::AID-ACP645>3.0.CO;2-

Atkinson, R. C., & Shiffrin, R. M. (1968). *Human Memory: A Proposed System and its Control Processes*. https://doi.org/10.1016/S0079-7421(08)60422-3

Attuquayefio, T., Stevenson, R. J., Oaten, M. J., & Francis, H. M. (2017). A four-day Western-style dietary intervention causes reductions in hippocampal-dependent learning and memory and interoceptive sensitivity. *PLoS ONE*, *12*(2), e0172645. https://doi.org/10.1371/journal.pone.0172645

Babb, S. J., & Crystal, J. D. (2006). Episodic-like Memory in the Rat. *Current Biology*, *16*(13), 1317–1321. https://doi.org/10.1016/j.cub.2006.05.025

Baddeley, A. D., Eysenck, M. W., & Anderson, M. C. (Michael C. (2014). *Memory* (2nd ed.).

Baddeley, A. (1992). Working memory. *Science (New York, N.Y.)*, *255*(5044), 556–559. https://doi.org/10.1126/SCIENCE.1736359

Baddeley, Alan. (2000). The episodic buffer: A new component of working memory? *Trends in Cognitive Sciences*, Vol. 4, pp. 417–423. https://doi.org/10.1016/S1364-6613(00)01538-2

Balda, R. P., & Kamil, A. C. (1992). Long-term spatial memory in clark's nutcracker, Nucifraga columbiana. *Animal Behaviour*, *44*(4), 761–769. https://doi.org/10.1016/S0003-3472(05)80302-1

Barnet, R. C., & Miller, R. R. (1996). Scond-order excitation mediated by a backward conditioned inhibitor. *Journal of Experimental Psychology: Animal Behavior Processes*, *22*(3), 279–296. https://doi.org/10.1037/0097-7403.22.3.279

Bartoshuk, L. M., & Beauchamp, G. K. (1994). Chemical Senses. *Annual Review of Psychology*, *45*(1), 419–449. https://doi.org/10.1146/annurev.ps.45.020194.002223

Baxter, S. D., Hardin, J. W., Royer, J. A., Guinn, C. H., & Smith, A. F. (2008). Insight into the Origins of Intrusions (Reports of Uneaten Food Items) in Children's Dietary Recalls, Based on Data from a Validation Study of Reporting Accuracy over Multiple Recalls and School Foodservice Production Records. *Journal of the American Dietetic Association*, *108*(8), 1305–1314. https://doi.org/10.1016/j.jada.2008.05.012

Baxter, S. D., Thompson, W. O., Litaker, M. S., Frye, F. H. A., & Guinn, C. H. (2002). Low accuracy and low consistency of fourth-graders' school breakfast and school lunch recalls. *Journal of the American Dietetic Association*, *102*(3), 386–395. https://doi.org/10.1016/S0002-8223(02)90089-1

Beilharz, J. E., Maniam, J., & Morris, M. J. (2014). Short exposure to a diet rich in both fat and sugar or sugar alone impairs place, but not object recognition memory in rats. *Brain, Behavior, and Immunity*, *37*, 134–141. https://doi.org/10.1016/j.bbi.2013.11.016

Beilharz, J. E., Maniam, J., & Morris, M. J. (2015, August 12). Diet-induced cognitive deficits: The role of fat and sugar, potential mechanisms and nutritional interventions. *Nutrients*, Vol. 7, pp. 6719–6738. https://doi.org/10.3390/nu7085307

Bekinschtein, P., Weisstaub, N. V., Gallo, F., Renner, M., & Anderson, M. C. (2018). A retrieval-specific mechanism of adaptive forgetting in the mammalian brain. *Nature Communications*, *9*(1), 1–12. https://doi.org/10.1038/s41467-018-07128-7

Bentham, J., Di Cesare, M., Bilano, V., Bixby, H., Zhou, B., Stevens, G. A., … Cisneros, J. Z. (2017). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. *The Lancet*, *390*(10113), 2627–2642. https://doi.org/10.1016/S0140-6736(17)32129-3

Berridge, K. C., Ho, C.-Y., Richard, J. M., & DiFeliceantonio, A. G. (2010). The tempted brain eats: pleasure and desire circuits in obesity and eating disorders. *Brain Research*, *1350*, 43–64. https://doi.org/10.1016/j.brainres.2010.04.003

Berriman, J., Stevenson, R. J., Thayer, Z. C., Thompson, E., Mohamed, A., Watson, J. D. G., & Miller, L. A. (2016). Testing the importance of the Medial Temporal Lobes in human interoception: Does it matter if there is a memory component to the task? *Neuropsychologia*, *91*, 371–379. https://doi.org/10.1016/j.neuropsychologia.2016.09.005

Birch, L L, McPhee, L., Steinberg, L., & Sullivan, S. (1990). Conditioned flavor preferences in young children. *Physiology & Behavior*, *47*(3), 501–505. http://www.ncbi.nlm.nih.gov/pubmed/2359760

Birch, Leann L. (1999). Development of Food Preferences. *Annual Review of Nutrition*, *19*(1), 41–62. https://doi.org/10.1146/annurev.nutr.19.1.41

Bird, C. M., & Burgess, N. (2008, March). The hippocampus and memory: Insights from spatial processing. *Nature Reviews Neuroscience*, Vol. 9, pp. 182–194. https://doi.org/10.1038/nrn2335

Bjork, R. A., & Bjork, E. L. (1992). A new theory of disuse and an old theory of stimulus fluctuation. In A. F. Healy, S. M. Kosslyn, & R. M. Shiffrin (Eds.), *Essays in honor of William K. Estes, Vol. 1. From learning theory to connectionist theory; Vol. 2. From learning processes to cognitive processes* (pp. 35–67).

Blaisdell, A. P., Biedermann, T., Sosa, E., Abuchaei, A., Youssef, N., & Bradesi, S. (2017). An obesogenic refined low-fat diet disrupts attentional and behavioral control processes in a

vigilance task in rats. *Behavioural Processes*, *138*, 142–151. https://doi.org/10.1016/j.beproc.2017.03.007

Blaisdell, A. P., Lau, Y. L. M., Telminova, E., Lim, H. C., Fan, B., Fast, C. D., … Pendergrass, D. C. (2014). Food quality and motivation: A refined low-fat diet induces obesity and impairs performance on a progressive ratio schedule of instrumental lever pressing in rats. *Physiology and Behavior*, *128*, 220–225. https://doi.org/10.1016/j.physbeh.2014.02.025

Bolhuis, D. P., Lakemond, C. M. M., de Wijk, R. A., Luning, P. A., & de Graaf, C. (2011). Both Longer Oral Sensory Exposure to and Higher Intensity of Saltiness Decrease Ad Libitum Food Intake in Healthy Normal-Weight Men. *The Journal of Nutrition*, *141*(12), 2242–2248. https://doi.org/10.3945/jn.111.143867

Bolles, R. (1993). The story of psychology: a thematic history. In *Choice Reviews Online* (Vol. 31). https://doi.org/10.5860/choice.31-5147

Bolles, R. C., Hayward, L., & Crandall, C. (1981). Conditioned taste preferences based on caloric density. *Journal of Experimental Psychology. Animal Behavior Processes*, *7*(1), 59–69. http://www.ncbi.nlm.nih.gov/pubmed/7229574

Bonin, P., Thiebaut, G., Witt, A., & Méot, A. (2019). Contamination Is “Good” for Your Memory! Further Evidence for the Adaptive View of Memory. *Evolutionary Psychological Science*, 1–17. https://doi.org/10.1007/s40806-019-00188-y

Boutelle, K. N., & Bouton, M. E. (2015). Implications of learning theory for developing programs to decrease overeating. *Appetite*, *93*, 62–74. https://doi.org/10.1016/j.appet.2015.05.013

Bouton, M. E. (2004). Context and Behavioral Processes in Extinction. *Learning & Memory*, *11*(5), 485–494. https://doi.org/10.1101/LM.78804

Bower, G. H. (2000). *The Oxford handbook of memory* (E Tulving & F. I. M. Craik, Eds.). Oxford University Press.

Bradburn, N. M., Rips, L. J., & Shevell, S. K. (1987, April 10). Answering autobiographical questions: The impact of memory and inference on surveys. *Science*, Vol. 236, pp. 157–

161. https://doi.org/10.1126/science.3563494

Brunstrom, J. M., Burn, J. F., Sell, N. R., Collingwood, J. M., Rogers, P. J., Wilkinson, L. L., … Ferriday, D. (2012). Episodic Memory and Appetite Regulation in Humans. *PLoS ONE*, *7*(12). https://doi.org/10.1371/journal.pone.0050707

Brunstrom, J. M., & Mitchell, G. L. (2007). Flavor–nutrient learning in restrained and unrestrained eaters. *Physiology & Behavior*, *90*(1), 133–141. https://doi.org/10.1016/j.physbeh.2006.09.016

Burgess, N., & Hitch, G. (2005). Computational models of working memory: Putting long-term memory into context. *Trends in Cognitive Sciences*, Vol. 9, pp. 535–541. https://doi.org/10.1016/j.tics.2005.09.011

Buss, D. M., Haselton, M. G., Shackelford, T. K., Bleske, A. L., & Wakefield, J. C. (1998). Adaptations, exaptations, and spandrels. *American Psychologist*, *53*(5), 533–548. https://doi.org/10.1037//0003-066x.53.5.533

Cahill, S. P., Hatchard, T., Abizaid, A., & Holahan, M. R. (2014). An examination of early neural and cognitive alterations in hippocampal-spatial function of ghrelin receptor-deficient rats. *Behavioural Brain Research*, *264*, 105–115. https://doi.org/10.1016/j.bbr.2014.02.004

Capaldi, E. D. (1996). Conditioned food preferences. In *Why we eat what we eat: The psychology of eating.* (pp. 53–80). https://doi.org/10.1037/10291-003

Capaldi, E. D., Hunter, M. J., & Lyn, S. A. (1997). Conditioning with taste as the CS in conditioned flavor preference learning. *Animal Learning & Behavior*, *25*(4), 427–436. https://doi.org/10.3758/BF03209849

Carlini, V. P., Monzón, M. E., Varas, M. M., Cragnolini, A. B., Schiöth, H. B., Scimonelli, T. N., & De Barioglio, S. R. (2002). Ghrelin increases anxiety-like behavior and memory retention in rats. *Biochemical and Biophysical Research Communications*, *299*(5), 739–743. https://doi.org/10.1016/S0006-291X(02)02740-7

Carlini, V. P., Varas, M. M., Cragnolini, A. B., Schiöth, H. B., Scimonelli, T. N., & De Barioglio, S.

R. (2004). Differential role of the hippocampus, amygdala, and dorsal raphe nucleus in regulating feeding, memory, and anxiety-like behavioral responses to ghrelin. *Biochemical and Biophysical Research Communications*, *313*(3), 635–641. https://doi.org/10.1016/j.bbrc.2003.11.150

Castel, A. D., Farb, N. A. S., & Craik, F. I. M. (2007). Memory for general and specific value information in younger and older adults: Measuring the limits of strategic control. *Memory and Cognition*, *35*(4), 689–700. https://doi.org/10.3758/BF03193307

Cepeda, N. J., Pashler, H., Vul, E., Rohrer, D., & Wixted, J. (2006). Distributed Practice in Verbal Recall Tasks: A Review and Quantitative Synthesis. *Psychological Bulletin*, *132*(3). https://escholarship.org/content/qt3rr6q10c/qt3rr6q10c.pdf?t=lnr1h0

Chang, C. Y., Esber, G. R., Marrero-Garcia, Y., Yau, H. J., Bonci, A., & Schoenbaum, G. (2015). Brief optogenetic inhibition of dopamine neurons mimics endogenous negative reward prediction errors. *Nature Neuroscience 2016 19:1*, *19*(1), 111–116. https://doi.org/10.1038/nn.4191

Chang, C. Y., Gardner, M., Di Tillio, M. G., & Schoenbaum, G. (2017). Optogenetic Blockade of Dopamine Transients Prevents Learning Induced by Changes in Reward Features. *Current Biology*, *27*(22), 3480-3486.e3. https://doi.org/10.1016/j.cub.2017.09.049

Chang, R. C., Blaisdell, A. P., & Miller, R. R. (2003, July). Backward Conditioning: Mediation by the Context. *Journal of Experimental Psychology: Animal Behavior Processes*, Vol. 29, pp. 171–183. https://doi.org/10.1037/0097-7403.29.3.171

Cheke, L. G., Simons, J. S., & Clayton, N. S. (2016). Higher body mass index is associated with episodic memory deficits in young adults. *Quarterly Journal of Experimental Psychology (2006)*, *69*(11), 2305. https://doi.org/10.1080/17470218.2015.1099163

Chuang, J. C., Perello, M., Sakata, I., Osborne-Lawrence, S., Savitt, J. M., Lutter, M., & Zigman, J. M. (2011). Ghrelin mediates stress-induced food-reward behavior in mice. *Journal of Clinical Investigation*, *121*(7), 2684–2692. https://doi.org/10.1172/JCI57660

Clark, A. (2013). Whatever next? Predictive brains, situated agents, and the future of cognitive science. *Behavioral and Brain Sciences*, *36*(3), 181–204. https://doi.org/10.1017/S0140525X12000477

Clayton, N. S., & Dickinson, A. (1998). Episodic-like memory during cache recovery by scrub jays. *Nature*, *395*(6699), 272–274. https://doi.org/10.1038/26216

Cohen, J. Y., Haesler, S., Vong, L., Lowell, B. B., & Uchida, N. (2012, February 2). Neuron-type-specific signals for reward and punishment in the ventral tegmental area. *Nature*, Vol. 482, pp. 85–88. https://doi.org/10.1038/nature10754

Cole, R. P., & Miller, R. R. (1999). Conditioned Excitation and Conditioned Inhibition Acquired through Backward Conditioning. *Learning and Motivation*, *30*(2), 129–156. https://doi.org/10.1006/lmot.1998.1027

Cole, S. N., & Pauly-Takacs, K. (2017, March 4). Is obesity linked with episodic memory impairment? A commentary on Cheke, Simons, and Clayton (2016). *Quarterly Journal of Experimental Psychology*, Vol. 70, pp. 590–591. https://doi.org/10.1080/17470218.2016.1173075

Cook, R. L., O'Dwyer, N. J., Donges, C. E., Parker, H. M., Cheng, H. L., Steinbeck, K. S., … O'Connor, H. T. (2017). Relationship between Obesity and Cognitive Function in Young Women: The Food, Mood and Mind Study. *Journal of Obesity*, *2017*, 5923862. https://doi.org/10.1155/2017/5923862

Cordner, Z. A., & Tamashiro, K. L. K. (2015, December 1). Effects of high-fat diet exposure on learning & memory. *Physiology and Behavior*, Vol. 152, pp. 363–371. https://doi.org/10.1016/j.physbeh.2015.06.008

Corlett, P. R., Murray, G. K., Honey, G. D., Aitken, M. R. F., Shanks, D. R., Robbins, T. W., … Fletcher, P. C. (2007). Disrupted prediction-error signal in psychosis: evidence for an associative account of delusions. *Brain : A Journal of Neurology*, *130*(Pt 9), 2387–2400. https://doi.org/10.1093/BRAIN/AWM173

Corlett, P. R., Taylor, J. R., Wang, X. J., Fletcher, P. C., & Krystal, J. H. (2010). Toward a Neurobiology of Delusions. *Progress in Neurobiology*, *92*(3), 345. https://doi.org/10.1016/J.PNEUROBIO.2010.06.007

Cournot, M., Marquié, J. C., Ansiau, D., Martinaud, C., Fonds, H., Ferrières, J., & Ruidavets, J. B. (2006). Relation between body mass index and cognitive function in healthy middle-aged men and women. *Neurology*, *67*(7), 1208–1214. https://doi.org/10.1212/01.wnl.0000238082.13860.50

Craik, F. I. M., & Lockhart, R. S. (1972). Levels of processing: A framework for memory research. *Journal of Verbal Learning and Verbal Behavior*, *11*(6), 671–684. https://doi.org/10.1016/S0022-5371(72)80001-X

Crystal, J. D. (2010, December). Episodic-like memory in animals. *Behavioural Brain Research*, Vol. 215, pp. 235–243. https://doi.org/10.1016/j.bbr.2010.03.005

Dao, M. C., Subar, A. F., Warthon-Medina, M., Cade, J. E., Burrows, T., Golley, R. K., … Holmes, B. A. (2019). Dietary assessment toolkits: An overview. *Public Health Nutrition*, *22*(3), 404–418. https://doi.org/10.1017/S1368980018002951

Davidson, T. L., Kanoski, S. E., Walls, E. K., & Jarrard, L. E. (2005). Memory inhibition and energy regulation. *Physiology and Behavior*, *86*(5), 731–746. https://doi.org/10.1016/j.physbeh.2005.09.004

Davidson, T.L., Sample, C. H., & Swithers, S. E. (2014). An application of Pavlovian principles to the problems of obesity and cognitive decline. *Neurobiology of Learning and Memory*, *108*, 172–184. https://doi.org/10.1016/J.NLM.2013.07.014

Davidson, T L, & Swithers, S. E. (2004). A Pavlovian approach to the problem of obesity. *International Journal of Obesity*, *28*(7), 933–935. https://doi.org/10.1038/sj.ijo.0802660

Davidson, Terry L., Chan, K., Jarrard, L. E., Kanoski, S. E., Clegg, D. J., & Benoit, S. C. (2009). Contributions of the hippocampus and medial prefrontal cortex to energy and body weight regulation. *Hippocampus*, *19*(3), 235–252. https://doi.org/10.1002/hipo.20499

Davidson, Terry L., Jones, S., Roy, M., & Stevenson, R. J. (2019). The Cognitive Control of Eating and Body Weight: It's More Than What You "Think." *Frontiers in Psychology*, *10*, 62. https://doi.org/10.3389/fpsyg.2019.00062

Davidson, Terry L., Kanoski, S. E., Chan, K., Clegg, D. J., Benoit, S. C., & Jarrard, L. E. (2010). Hippocampal Lesions Impair Retention of Discriminative Responding Based on Energy State Cues. *Behavioral Neuroscience*, *124*(1), 97–105. https://doi.org/10.1037/a0018402

Davidson, Terry L., Monnot, A., Neal, A. U., Martin, A. A., Horton, J. J., & Zheng, W. (2012). The effects of a high-energy diet on hippocampal-dependent discrimination performance and blood-brain barrier integrity differ for diet-induced obese and diet-resistant rats. *Physiology and Behavior*, *107*(1), 26–33. https://doi.org/10.1016/j.physbeh.2012.05.015

Davidson, Terry L, Jones, S., Roy, M., & Stevenson, R. J. (2019). The Cognitive Control of Eating and Body Weight: It's More Than What You "Think". *Frontiers in Psychology*, *10*, 62. https://doi.org/10.3389/fpsyg.2019.00062

Davis, J. F., Choi, D. L., Schurdak, J. D., Fitzgerald, M. F., Clegg, D. J., Lipton, J. W., … Benoit, S. C. (2011). Leptin regulates energy balance and motivation through action at distinct neural circuits. *Biological Psychiatry*, *69*(7), 668–674. https://doi.org/10.1016/j.biopsych.2010.08.028

Daw, N. D., Niv, Y., & Dayan, P. (2005). Uncertainty-based competition between prefrontal and dorsolateral striatal systems for behavioral control. *Nature Neuroscience 2005 8:12*, *8*(12), 1704–1711. https://doi.org/10.1038/nn1560

de Kort, S. R., Dickinson, A., & Clayton, N. S. (2005). Retrospective cognition by food-caching western scrub-jays. *Learning and Motivation*, *36*(2 SPEC. ISS.), 159–176. https://doi.org/10.1016/j.lmot.2005.02.008

de Vries, R., de Vet, E., de Graaf, K., & Boesveldt, S. (2020). Foraging minds in modern environments: High-calorie and savory-taste biases in human food spatial memory. *Appetite*, *152*, 104718. https://doi.org/10.1016/j.appet.2020.104718

Delwiche, J. F. (2012). You eat with your eyes first. *Physiology and Behavior*, *107*(4), 502–504. https://doi.org/10.1016/j.physbeh.2012.07.007

Dhillon, J., Lee, J. Y., & Mattes, R. D. (2017). The cephalic phase insulin response to nutritive and low-calorie sweeteners in solid and beverage form. *Physiology & Behavior*, *181*, 100–109. https://doi.org/10.1016/J.PHYSBEH.2017.09.009

Diano, S., Farr, S. A., Benoit, S. C., McNay, E. C., Da Silva, I., Horvath, B., … Horvath, T. L. (2006). Ghrelin controls hippocampal spine synapse density and memory performance. *Nature Neuroscience*, *9*(3), 381–388. https://doi.org/10.1038/nn1656

Domingos, A. I., Vaynshteyn, J., Voss, H. U., Ren, X., Gradinaru, V., Zang, F., … Friedman, J. (2011). Leptin regulates the reward value of nutrient. *Nature Neuroscience*, *14*(12), 1562–1568. https://doi.org/10.1038/nn.2977

Engelhard, B., Finkelstein, J., Cox, J., Fleming, W., Jang, H. J., Ornelas, S., … Witten, I. B. (2019). Specialized coding of sensory, motor and cognitive variables in VTA dopamine neurons. *Nature 2019 570:7762*, *570*(7762), 509–513. https://doi.org/10.1038/s41586-019-1261-9

Engelkamp, J. (1998). *Memory for Actions*. East Sussex, England: Psychology Press.

Erskine, H. E., Whiteford, H. A., & Pike, K. M. (2016, October 1). The global burden of eating disorders. *Current Opinion in Psychiatry*, Vol. 29, pp. 346–353. https://doi.org/10.1097/YCO.0000000000000276

Escobar, M., & Miller, R. R. (2004). A Review of the Empirical Laws of Basic Learning in Pavlovian Conditioning. *International Journal of Comparative Psychology*, *17*, 279–303.

Fantino, M. (1984). Role of sensory input in the control of food intake. *Journal of the Autonomic Nervous System*, *10*(3–4), 347–358. https://doi.org/10.1016/0165-1838(84)90032-8

Farooqi, I. S., Jebb, S. A., Langmack, G., Lawrence, E., Cheetham, C. H., Prentice, A. M., … O'Rahilly, S. (1999). Effects of recombinant leptin therapy in a child with congenital leptin deficiency. *New England Journal of Medicine*, *341*(12), 879–884.

https://doi.org/10.1056/NEJM199909163411204

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*(2), 175–191. http://www.ncbi.nlm.nih.gov/pubmed/17695343

Feeney, M. C., Roberts, W. A., & Sherry, D. F. (2009). Memory for what, where, and when in the black-capped chickadee (Poecile atricapillus). *Animal Cognition*, *12*(6), 767–777. https://doi.org/10.1007/s10071-009-0236-x

Fenwick, N., Griffin, G., & Gauthier, C. (2009). The welfare of animals used in science: how the "Three Rs" ethic guides improvements. *The Canadian Veterinary Journal = La Revue Veterinaire Canadienne*, *50*(5), 523–530. http://www.ncbi.nlm.nih.gov/pubmed/19436640

Fernandes, N. L., Pandeirada, J. N. S., Soares, S. C., & Nairne, J. S. (2017). Adaptive memory: The mnemonic value of contamination. *Evolution and Human Behavior*. https://doi.org/10.1016/j.evolhumbehav.2017.04.003

Ferriday, D., Bosworth, M. L., Lai, S., Godinot, N., Martin, N., Martin, A. A., … Brunstrom, J. M. (2015). Effects of eating rate on satiety: A role for episodic memory? *Physiology & Behavior*, *152*(Pt B), 389–396. https://doi.org/10.1016/j.physbeh.2015.06.038

Figlewicz, D. P., Sipols, A. J., Bennett, J., Evans, S. B., Kaiyala, K., & Benoit, S. C. (2004). Intraventricular insulin and leptin reverse place preference conditioned with high-fat diet in rats. *Behavioral Neuroscience*, *118*(3), 479–487. https://doi.org/10.1037/0735-7044.118.3.479

Finlayson, G., King, N., & Blundell, J. E. (2007). Liking vs. wanting food: Importance for human appetite control and weight regulation. *Neuroscience and Biobehavioral Reviews*, Vol. 31, pp. 987–1002. https://doi.org/10.1016/j.neubiorev.2007.03.004

Fiorillo, C. D. (2013). Two dimensions of value: dopamine neurons represent reward but not aversiveness. *Science (New York, N.Y.)*, *341*(6145), 546–549.

https://doi.org/10.1126/SCIENCE.1238699

Foerde, K., & Steinglass, J. E. (2017). Decreased feedback learning in anorexia nervosa persists after weight restoration. *International Journal of Eating Disorders*, *50*(4), 415–423. https://doi.org/10.1002/eat.22709

Forloni, G., Fisone, G., Guaitani, A., Ladinsky, H., & Consolo, S. (1986). Role of the hippocampus in the sex-dependent regulation of eating behavior: Studies with kainic acid. *Physiology and Behavior*, *38*(3), 321–326. https://doi.org/10.1016/0031-9384(86)90101-0

Francis, H. M., Stevenson, R. J., Oaten, M. J., Mahmut, M. K., & Yeomans, M. R. (2017). The immediate and delayed effects of TV: Impacts of gender and processed-food intake history. *Frontiers in Psychology*, *8*(SEP). https://doi.org/10.3389/fpsyg.2017.01616

Francisco, V., Pino, J., Campos-Cabaleiro, V., Ruiz-Fernández, C., Mera, A., Gonzalez-Gay, M. A., … Gualillo, O. (2018, June 1). Obesity, fat mass and immune system: Role for leptin. *Frontiers in Physiology*, Vol. 9. https://doi.org/10.3389/fphys.2018.00640

Freeman, L. R., Haley-Zitlin, V., Rosenberger, D. S., & Granholm, A. C. (2014, November 1). Damaging effects of a high-fat diet to the brain and cognition: A review of proposed mechanisms. *Nutritional Neuroscience*, Vol. 17, pp. 241–251. https://doi.org/10.1179/1476830513Y.0000000092

Fries, E., Green, P., & Bowen, D. J. (1995). What did I eat yesterday? Determinants of accuracy in 24-hour food memories. *Applied Cognitive Psychology*, *9*(2), 143–155. https://doi.org/10.1002/acp.2350090204

García-García, I., Michaud, A., Dadar, M., Zeighami, Y., Neseliler, S., Collins, D. L., … Dagher, A. (2019, May 1). Neuroanatomical differences in obesity: meta-analytic findings and their validation in an independent dataset. *International Journal of Obesity*, Vol. 43, pp. 943–951. https://doi.org/10.1038/s41366-018-0164-4

Garcia, J, Kimeldorf, D. J., & Koelling, R. A. (1955). Conditioned aversion to saccharin resulting from exposure to gamma radiation. *Science (New York, N.Y.)*, *122*(3160), 157–158.

https://doi.org/10.1126/SCIENCE.122.3160.157

Garcia, J, & Koelling, R. A. (1966). Relation of cue to consequence in avoidance learning. *Psychonomic Science*, *4*(1), 123–124. https://doi.org/10.3758/BF03342209

Gardner, M. P. H., Schoenbaum, G., & Gershman, S. J. (2018). Rethinking dopamine as generalized prediction error. *Proceedings of the Royal Society B*, *285*(1891). https://doi.org/10.1098/RSPB.2018.1645

Gearhardt, A. N., Corbin, W. R., & Brownell, K. D. (2009). Preliminary validation of the Yale Food Addiction Scale. *Appetite*, *52*(2), 430–436. https://doi.org/10.1016/j.appet.2008.12.003

Geiselman, R. E., Fisher, R. P., MacKinnon, D. P., & Holland, H. L. (1986). Enhancement of Eyewitness Memory with the Cognitive Interview. *The American Journal of Psychology*, *99*(3), 385. https://doi.org/10.2307/1422492

Glenn, D. E., Minor, T. R., Vervliet, B., & Craske, M. G. (2014). The Effect of Glucose on Hippocampal-Dependent Contextual Fear Conditioning. *Biological Psychiatry*, *75*(11), 847–854. https://doi.org/10.1016/J.BIOPSYCH.2013.09.022

Glimcher, P. W. (2011). Understanding dopamine and reinforcement learning: The dopamine reward prediction error hypothesis. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(SUPPL. 3), 15647–15654. https://doi.org/10.1073/pnas.1014269108

Gould, S. J., & Vrba, E. S. (1982). Exaptation—a Missing Term in the Science of Form. *Paleobiology*, *8*(1), 4–15. https://doi.org/10.1017/S0094837300004310

Grob, S., Pizzagalli, D. A., Dutra, S. J., Stern, J., Mörgeli, H., Milos, G., … Hasler, G. (2012). Dopamine-related deficit in reward learning after catecholamine depletion in unmedicated, remitted subjects with bulimia nervosa. *Neuropsychopharmacology*, *37*(8), 1945–1952. https://doi.org/10.1038/npp.2012.41

Groppe, K., & Elsner, B. (2017). Executive function and weight status in children: A one-year

longitudinal perspective. *Child Neuropsychology*, *23*(2), 129–147. https://doi.org/10.1080/09297049.2015.1089981

Grosshans, M., Vollmert, C., Dt-Klein, S. V., Tost, H., Leber, S., Bach, P., … Kiefer, F. (2012). Association of leptin with food cue-induced activation in human reward pathways. *Archives of General Psychiatry*, *69*(5), 529–537. https://doi.org/10.1001/archgenpsychiatry.2011.1586

Gruest, N., Richer, P., & Hars, B. (2004). Emergence of long-term memory for conditioned aversion in the rat fetus. *Developmental Psychobiology*, *44*(3), 189–198. https://doi.org/10.1002/dev.20004

Gunstad, J., Paul, R. H., Cohen, R. A., Tate, D. F., & Gordon, E. (2006). Obesity is associated with memory deficits in young and middle-aged adults. *Eating and Weight Disorders*, *11*(1), e15–e19. https://doi.org/10.1007/BF03327747

Hagan, K. E., Alasmar, A., Exum, A., Chinn, B., & Forbush, K. T. (2020). A systematic review and meta-analysis of attentional bias toward food in individuals with overweight and obesity. *Appetite*, 104710. https://doi.org/10.1016/j.appet.2020.104710

Hall, K. D., Sacks, G., Chandramohan, D., Chow, C. C., Wang, Y. C., Gortmaker, S. L., & Swinburn, B. A. (2011). Quantification of the effect of energy imbalance on bodyweight. *The Lancet*, Vol. 378, pp. 826–837. https://doi.org/10.1016/S0140-6736(11)60812-X

Han, J. E., Frasnelli, J., Zeighami, Y., Larcher, K., Boyle, J., McConnell, T., … Dagher, A. (2018). Ghrelin Enhances Food Odor Conditioning in Healthy Humans: An fMRI Study. *Cell Reports*, *25*(10), 2643-2652.e4. https://doi.org/10.1016/j.celrep.2018.11.026

Hannapel, R., Ramesh, J., Ross, A., LaLumiere, R. T., Roseberry, A. G., & Parent, M. B. (2019). Postmeal optogenetic inhibition of dorsal or ventral hippocampal pyramidal neurons increases future intake. *Eneuro*, ENEURO.0457-18.2018. https://doi.org/10.1523/ENEURO.0457-18.2018

Hargrave, S. L., Davidson, T. L., Zheng, W., & Kinzig, K. P. (2016). Western Diets Induce

Blood-Brain Barrier Leakage and Alter Spatial Strategies in Rats. *Behavioral Neuroscience*, *130*(1), 123–135. https://doi.org/10.1037/bne0000110

Havermans, R. C., Hermanns, J., & Jansen, A. (2010). Eating Without a Nose: Olfactory Dysfunction and Sensory-Specific Satiety. *Chemical Senses*, *35*(8), 735–741. https://doi.org/10.1093/chemse/bjq074

Hawton, K., Ferriday, D., Rogers, P., Toner, P., Brooks, J., Holly, J., … Hinton, E. (2018). Slow Down: Behavioural and Physiological Effects of Reducing Eating Rate. *Nutrients*, *11*(1), 50. https://doi.org/10.3390/nu11010050

Hebben, N., Corkin, S., Eichenbaum, H., & Shedlack, K. (1985). Diminished ability to interpret and report internal states after bilateral medial temporal resection: Case H.M. *Behavioral Neuroscience*, *99*(6), 1031–1039. https://doi.org/10.1037//0735-7044.99.6.1031

Herrmann, M. J., Tesar, A., Beier, J., Berg, M., & Warrings, B. (2019). Grey matter alterations in obesity: A meta-analysis of whole-brain studies. *Obesity Reviews*, *20*(3), 464–471. https://doi.org/10.1111/obr.12799

Hess, T. M. (2005). Memory and aging in context. *Psychological Bulletin*, *131*(3), 383–406. https://doi.org/10.1037/0033-2909.131.3.383

Higgs, S. (2002). Memory for recent eating and its influence on subsequent food intake. *Appetite*, *39*(2), 159–166. https://doi.org/10.1006/APPE.2002.0500

Higgs, S. (2015). Manipulations of attention during eating and their effects on later snack intake. *Appetite*, *92*, 287–294. https://doi.org/10.1016/j.appet.2015.05.033

Higgs, S., & Donohoe, J. E. (2011). Focusing on food during lunch enhances lunch memory and decreases later snack intake. *Appetite*, *57*(1), 202–206. https://doi.org/10.1016/J.APPET.2011.04.016

Higgs, S., & Jones, A. (2013). Prolonged chewing at lunch decreases later snack intake. *Appetite*, *62*, 91–95. https://doi.org/10.1016/j.appet.2012.11.019

Higgs, S., & Spetter, M. S. (2018). Cognitive Control of Eating: the Role of Memory in Appetite

and Weight Gain. *Current Obesity Reports*, *7*(1), 50–59. https://doi.org/10.1007/s13679-018-0296-9

Higgs, S., Williamson, A. C., & Attwood, A. S. (2008). Recall of recent lunch and its effect on subsequent snack intake. *Physiology & Behavior*, *94*(3), 454–462. https://doi.org/10.1016/j.physbeh.2008.02.011

Higgs, S., Williamson, A. C., Rotshtein, P., & Humphreys, G. W. (2008). Sensory-specific satiety is intact in amnesics who eat multiple meals. *Psychological Science*, *19*(7), 623–628. https://doi.org/10.1111/j.1467-9280.2008.02132.x

Higgs, S., & Woodward, M. (2009). Television watching during lunch increases afternoon snack intake of young women. *Appetite*, *52*(1), 39–43. https://doi.org/10.1016/J.APPET.2008.07.007

Hill, J. O., Wyatt, H. R., Reed, G. W., & Peters, J. C. (2003, February 7). Obesity and the environment: Where do we go from here? *Science*, Vol. 299, pp. 853–855. https://doi.org/10.1126/science.1079857

Hisashi Kuribara, Tetsu Hayashi, Alam, M. R., Sakutaro Tadokoro, & Toyohiko Miura. (1978). Automatic measurement of drinking in rats: Effects of hypophysectomy. *Pharmacology Biochemistry and Behavior*, *9*(5), 697–702. https://doi.org/10.1016/0091-3057(78)90224-1

Hoang, I. B., & Sharpe, M. J. (2021). The basolateral amygdala and lateral hypothalamus bias learning towards motivationally significant events. *Current Opinion in Behavioral Sciences*, *41*, 92–97. https://doi.org/10.1016/J.COBEHA.2021.04.014

Hoek, H. W. (2016, October 1). Review of the worldwide epidemiology of eating disorders. *Current Opinion in Psychiatry*, Vol. 29, pp. 336–339. https://doi.org/10.1097/YCO.0000000000000282

Hollerman, J. R., & Schultz, W. (1998). Dopamine neurons report an error in the temporal prediction of reward during learning. *Nature Neuroscience*, *1*(4), 304–309. https://doi.org/10.1038/1124

Hommel, J. D., Trinko, R., Sears, R. M., Georgescu, D., Liu, Z. W., Gao, X. B., … DiLeone, R. J. (2006). Leptin Receptor Signaling in Midbrain Dopamine Neurons Regulates Feeding. *Neuron*, *51*(6), 801–810. https://doi.org/10.1016/j.neuron.2006.08.023

Hou, C., & Liu, Z. (2019). The Survival Processing Advantage of Face: The Memorization of the (Un)Trustworthy Face Contributes More to Survival Adaptation. *Evolutionary Psychology*, *17*(2), 147470491983972. https://doi.org/10.1177/1474704919839726

Howard, J. D., & Kahnt, T. (2018). Identity prediction errors in the human midbrain update reward-identity expectations in the orbitofrontal cortex. *Nature Communications 2018 9:1*, *9*(1), 1–11. https://doi.org/10.1038/s41467-018-04055-5

Howe, M. L., & Otgaar, H. (2013). Proximate Mechanisms and the Development of Adaptive Memory. *Current Directions in Psychological Science*, *22*(1), 16–22. https://doi.org/10.1177/0963721412469397

Hsu, T. M., Suarez, A. N., & Kanoski, S. E. (2016, January 13). Ghrelin: A link between memory and ingestive behavior. *Physiology and Behavior*, Vol. 162, pp. 10–17. https://doi.org/10.1016/j.physbeh.2016.03.039

Iordanova, M. D., Good, M. A., & Honey, R. C. (2008). Configural Learning without Reinforcement: Integrated Memories for Correlates of What, Where, and When. *Quarterly Journal of Experimental Psychology*, *61*(12), 1785–1792. https://doi.org/10.1080/17470210802194324

Jastreboff, A. M., Lacadie, C., Seo, D., Kubat, J., Van Name, M. A., Giannini, C., … Sinha, R. (2014). Leptin is associated with exaggerated brain reward and emotion responses to food images in adolescent obesity. *Diabetes Care*, *37*(11), 3061–3068. https://doi.org/10.2337/dc14-0525

Jensen, J., Willeit, M., Zipursky, R. B., Savina, I., Smith, A. J., Menon, M., … Kapur, S. (2007). The Formation of Abnormal Associations in Schizophrenia: Neural and Behavioral Evidence. *Neuropsychopharmacology 2008 33:3*, *33*(3), 473–479.

https://doi.org/10.1038/sj.npp.1301437

Johnson, F., Pratt, M., & Wardle, J. (2012, May 9). Dietary restraint and self-regulation in eating behavior. *International Journal of Obesity*, Vol. 36, pp. 665–674. https://doi.org/10.1038/ijo.2011.156

Josselyn, S. A., Köhler, S., & Frankland, P. W. (2015). Finding the engram. *Nature Reviews Neuroscience 2015 16:9*, *16*(9), 521–534. https://doi.org/10.1038/nrn4000

Josselyn, S. A., & Tonegawa, S. (2020, January 3). Memory engrams: Recalling the past and imagining the future. *Science*, Vol. 367. https://doi.org/10.1126/science.aaw4325

Kahana, M. J. (2020). Computational Models of Memory Search. *Annual Review of Psychology*, *71*(1), 107–138. https://doi.org/10.1146/annurev-psych-010418-103358

Kamin, L. J. (1969). Predictability, Surprise, Attention, and Conditioning. In B. A. Campbell & R.M. Church (Eds.), *Punishment Aversive Behavior* (pp. 279–296).

Kandel, E. R., Dudai, Y., & Mayford, M. R. (2014, March 27). The molecular and systems biology of memory. *Cell*, Vol. 157, pp. 163–186. https://doi.org/10.1016/j.cell.2014.03.001

Kanoski, S. E., & Davidson, T. L. (2010). Different patterns of memory impairments accompany short- and longer-term maintenance on a high-energy diet. *Journal of Experimental Psychology: Animal Behavior Processes*, *36*(2), 313–319. https://doi.org/10.1037/a0017228

Kanoski, S. E., & Davidson, T. L. (2011). Western diet consumption and cognitive impairment: Links to hippocampal dysfunction and obesity. *Physiology and Behavior*, *103*(1), 59–68. https://doi.org/10.1016/j.physbeh.2010.12.003

Kanoski, S. E., & Grill, H. J. (2017). Hippocampus Contributions to Food Intake Control: Mnemonic, Neuroanatomical, and Endocrine Mechanisms. *Biological Psychiatry*, *81*(9), 748–756. https://doi.org/10.1016/j.biopsych.2015.09.011

Kanoski, S. E., Hayes, M. R., Greenwald, H. S., Fortin, S. M., Gianessi, C. A., Gilbert, J. R., & Grill, H. J. (2011). Hippocampal leptin signaling reduces food intake and modulates food-

related memory processing. *Neuropsychopharmacology*, *36*(9), 1859–1870. https://doi.org/10.1038/npp.2011.70

Kanoski, S. E., Zhang, Y., Zheng, W., & Davidson, T. L. (2010). The effects of a high-energy diet on hippocampal function and blood-brain barrier integrity in the rat. *Journal of Alzheimer's Disease*, *21*(1), 207–219. https://doi.org/10.3233/JAD-2010-091414

Keating, C. (2010, January). Theoretical perspective on anorexia nervosa: The conflict of reward. *Neuroscience and Biobehavioral Reviews*, Vol. 34, pp. 73–79. https://doi.org/10.1016/j.neubiorev.2009.07.004

Keiflin, R., Pribut, H. J., Shah, N. B., & Janak, P. H. (2019). Ventral Tegmental Dopamine Neurons Participate in Reward Identity Predictions. *Current Biology*, *29*(1), 93-103.e3. https://doi.org/10.1016/j.cub.2018.11.050

Kennedy, P. J., & Shapiro, M. L. (2004). Retrieving memories via internal context requires the hippocampus. *Journal of Neuroscience*, *24*(31), 6979–6985. https://doi.org/10.1523/JNEUROSCI.1388-04.2004

Kharabian Masouleh, S., Arélin, K., Horstmann, A., Lampe, L., Kipping, J. A., Luck, T., … Witte, A. V. (2016). Higher body mass index in older adults is associated with lower gray matter volume: Implications for memory performance. *Neurobiology of Aging*, *40*, 1–10. https://doi.org/10.1016/j.neurobiolaging.2015.12.020

King, B. M., Kass, J. M., Cadieux, N. L., Sam, H., Neville, K. L., & Arceneaux, E. R. (1993). Hyperphagia and obesity in female rats with temporal lobe lesions. *Physiology & Behavior*, *54*(4), 759–765. https://doi.org/10.1016/0031-9384(93)90088-w

Klok, M. D., Jakobsdottir, S., & Drent, M. L. (2007, January). The role of leptin and ghrelin in the regulation of food intake and body weight in humans: A review. *Obesity Reviews*, Vol. 8, pp. 21–34. https://doi.org/10.1111/j.1467-789X.2006.00270.x

Koriat, A., & Goldsmith, M. (1996). Monitoring and Control Processes in the Strategic Regulation of Memory Accuracy. *Psychological Review*, *103*(3), 490–517.

https://doi.org/10.1037/0033-295X.103.3.490

Kroneisen, M. (2018). Is he important to me? Source memory advantage for personally relevant cheaters. *Psychonomic Bulletin and Review*, *25*(3), 1129–1137. https://doi.org/10.3758/s13423-017-1345-1

Kroneisen, M., Erdfelder, E., & Buchner, A. (2013). The proximate memory mechanism underlying the survival-processing effect: Richness of encoding or interactive imagery? *Memory*, *21*(4), 494–502. https://doi.org/10.1080/09658211.2012.741603

Kuhl, B. A., Dudukovic, N. M., Kahn, I., & Wagner, A. D. (2007). Decreased demands on cognitive control reveal the neural processing benefits of forgetting. *Nature Neuroscience*, *10*(7), 908–914. https://doi.org/10.1038/nn1918

Lak, A., Stauffer, W. R., & Schultz, W. (2014). Dopamine prediction error responses integrate subjective value from different reward dimensions. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(6), 2343–2348. https://doi.org/10.1073/PNAS.1321596111/-/DCSUPPLEMENTAL

Langdon, A. J., Sharpe, M. J., Schoenbaum, G., & Niv, Y. (2018). Model-based predictions for dopamine. *Current Opinion in Neurobiology*, *49*, 1–7. https://doi.org/10.1016/J.CONB.2017.10.006

Lathe, R. (2001). Hormones and the hippocampus. *Journal of Endocrinology*, Vol. 169, pp. 205–231. https://doi.org/10.1677/joe.0.1690205

Laurent, J. S., Watts, R., Adise, S., Allgaier, N., Chaarani, B., Garavan, H., … Mackey, S. (2020). Associations among Body Mass Index, Cortical Thickness, and Executive Function in Children. *JAMA Pediatrics*, *174*(2), 170–177. https://doi.org/10.1001/jamapediatrics.2019.4708

Laurent, V., & Balleine, B. W. (2015). Factual and counterfactual action-outcome mappings control choice between goal-directed actions in rats. *Current Biology*, *25*(8), 1074–1079. https://doi.org/10.1016/j.cub.2015.02.044

Laurent, V., Wong, F. L., & Balleine, B. W. (2015). δ-Opioid receptors in the accumbens shell mediate the influence of both excitatory and inhibitory predictions on choice. *British Journal of Pharmacology*, *172*(2), 562–570. https://doi.org/10.1111/bph.12731

Laurent, V., Wong, F. L., & Balleine, B. W. (2017). The lateral habenula and its input to the rostromedial tegmental nucleus mediates outcome-specific conditioned inhibition. *Journal of Neuroscience*, *37*(45), 10932–10942. https://doi.org/10.1523/JNEUROSCI.3415-16.2017

Lee, S. (2018, February 25). Here's How Cornell Scientist Brian Wansink Turned Shoddy Data Into Viral Studies About How We Eat. *Buzzfeednews.Com*.

Lichtman, S. W., Pisarska, K., Berman, E. R., Pestone, M., Dowling, H., Offenbacher, E., … Heymsfield, S. B. (1992). Discrepancy between Self-Reported and Actual Caloric Intake and Exercise in Obese Subjects. *New England Journal of Medicine*, *327*(27), 1893–1898. https://doi.org/10.1056/NEJM199212313272701

Lieberman, D. A., & Thomas, G. V. (1986). The Quarterly Journal of Experimental Psychology Marking, memory and superstition in the pigeon Marking, Memory and Superstition in the Pigeon. *The Quarterly Journal of Experimental PsychoZogy*, *38*, 449–459. https://doi.org/10.1080/14640748608402245

Loftus, E. F. (1975). Leading questions and the eyewitness report. *Cognitive Psychology*, *7*(4), 560–572. https://doi.org/10.1016/0010-0285(75)90023-7

Loftus, E. F., & Hoffman, H. G. (1989). Misinformation and Memory: The Creation of New Memories. *Journal of Experimental Psychology: General*, *118*(1), 100–104. https://doi.org/10.1037/0096-3445.118.1.100

Loprinzi, P. D., & Frith, E. (2018, July 1). Obesity and episodic memory function. *Journal of Physiological Sciences*, Vol. 68, pp. 321–331. https://doi.org/10.1007/s12576-018-0612-x

Macdiarmid, J., & Blundell, J. (1998). Assessing dietary intake: Who, what and why of under-reporting. *Nutrition Research Reviews*, *11*(2), 231–253. https://doi.org/10.1079/nrr19980017

Mackintosh, N. J. (1975). A theory of attention: Variations in the associability of stimuli with reinforcement. *Psychological Review*, *82*(4), 276–298. https://doi.org/10.1037/H0076778

Maes, E. J. P., Sharpe, M. J., Usypchuk, A. A., Lozzi, M., Chang, C. Y., Gardner, M. P. H., … Iordanova, M. D. (2020). Causal evidence supporting the proposal that dopamine transients function as temporal difference prediction errors. *Nature Neuroscience*, *23*(2), 176–178. https://doi.org/10.1038/s41593-019-0574-1

Malekizadeh, Y., Holiday, A., Redfearn, D., Ainge, J. A., Doherty, G., & Harvey, J. (2017). A Leptin Fragment Mirrors the Cognitive Enhancing and Neuroprotective Actions of Leptin. *Cerebral Cortex*, *27*(10), 4769–4782. https://doi.org/10.1093/cercor/bhw272

Malik, S., McGlone, F., Bedrossian, D., & Dagher, A. (2008). Ghrelin Modulates Brain Activity in Areas that Control Appetitive Behavior. *Cell Metabolism*, *7*(5), 400–409. https://doi.org/10.1016/j.cmet.2008.03.007

Mangweth-Matzek, B., Hoek, H. W., Rupp, C. I., Lackner-Seifert, K., Frey, N., Whitworth, A. B., … Kinzl, J. (2014). Prevalence of eating disorders in middle-aged women. *International Journal of Eating Disorders*, *47*(3), 320–324. https://doi.org/10.1002/eat.22232

Martin, C. K., Anton, S. D., Walden, H., Arnett, C., Greenway, F. L., & Williamson, D. A. (2007). Slower eating rate reduces the food intake of men, but not women: Implications for behavioral weight control. *Behaviour Research and Therapy*, *45*(10), 2349–2359. https://doi.org/10.1016/j.brat.2007.03.016

Martin, C. K., Correa, J. B., Han, H., Allen, H. R., Rood, J. C., Champagne, C. M., … Bray, G. A. (2012). Validity of the Remote Food Photography Method (RFPM) for Estimating Energy and Nutrient Intake in Near Real-Time. *Obesity*, *20*(4), 891–899. https://doi.org/10.1038/oby.2011.344

McLean, F. H., Grant, C., Morris, A. C., Horgan, G. W., Polanski, A. J., Allan, K., … Williams, L. M. (2018). Rapid and reversible impairment of episodic memory by a high-fat diet in mice. *Scientific Reports*, *8*(1), 1–9. https://doi.org/10.1038/s41598-018-30265-4

Medic, N., Ziauddeen, H., Ersche, K. D., Farooqi, I. S., Bullmore, E. T., Nathan, P. J., … Fletcher, P. C. (2016). Increased body mass index is associated with specific regional alterations in brain structure. *International Journal of Obesity*, *40*(7), 1177–1182. https://doi.org/10.1038/ijo.2016.42

Mehiel, R., & Bolles, R. C. (1984). Learned flavor preferences based on caloric outcome. *Animal Learning & Behavior*, *12*(4), 421–427. https://doi.org/10.3758/BF03199989

Mennella, J. A., Griffin, C. E., & Beauchamp, G. K. (2004). Flavor programming during infancy. *Pediatrics*, *113*(4), 840–845. http://www.ncbi.nlm.nih.gov/pubmed/15060236

Millard, S. J., Bearden, C. E., Karlsgodt, K. H., & Sharpe, M. J. (2021). The prediction-error hypothesis of schizophrenia: new data point to circuit-specific changes in dopamine activity. *Neuropsychopharmacology 2021*, 1–13. https://doi.org/10.1038/s41386-021-01188-y

Miller, R. R., Barnet, R. C., & Grahame, N. J. (1995). Assessment of the Rescorla-Wagner model. *Psychological Bulletin*, *117*(3), 363–386. https://doi.org/10.1037/0033-2909.117.3.363

Miller, R. R., & Escobar, M. (2002). Learning: Laws and models of basic conditioning. In *Stevens' handbook of experimental psychology* (pp. 47–102).

Misra, P., Marconi, A., Peterson, M., & Kreiman, G. (2018). Minimal memory for details in real life events. *Scientific Reports*, *8*(1), 16701. https://doi.org/10.1038/s41598-018-33792-2

Mittal, D., Stevenson, R. J., Oaten, M. J., & Miller, L. A. (2011). Snacking while watching TV impairs food recall and promotes food intake on a later TV free test meal. *Applied Cognitive Psychology*, *25*(6), 871–877. https://doi.org/10.1002/acp.1760

Morales, I., & Berridge, K. C. (2020). 'Liking' and 'wanting' in eating and food reward: Brain mechanisms and clinical implications. *Physiology & Behavior*, *227*, 113152. https://doi.org/10.1016/j.physbeh.2020.113152

Morewedge, C. K., Huh, Y. E., & Vosgerau, J. (2010). Thought for food: Imagined consumption

reduces actual consumption. *Science*, *330*(6010), 1530–1533. https://doi.org/10.1126/science.1195701

Morin, J. P., Rodríguez-Durán, L. F., Guzmán-Ramos, K., Perez-Cruz, C., Ferreira, G., Diaz-Cintra, S., & Pacheco-López, G. (2017, February 14). Palatable hyper-caloric foods impact on neuronal plasticity. *Frontiers in Behavioral Neuroscience*, Vol. 11. https://doi.org/10.3389/fnbeh.2017.00019

Morrens, J., Aydin, Ç., Janse van Rensburg, A., Esquivelzeta Rabell, J., & Haesler, S. (2020). Cue-Evoked Dopamine Promotes Conditioned Responding during Learning. *Neuron*, *106*(1), 142-153.e7. https://doi.org/10.1016/J.NEURON.2020.01.012

Morris, R., Griffiths, O., Le Pelley, M. E., & Weickert, T. W. (2013). Attention to irrelevant cues is related to positive symptoms in schizophrenia. *Schizophrenia Bulletin*, *39*(3), 575–582. https://doi.org/10.1093/SCHBUL/SBR192

Morris, R. W., Vercammen, A., Lenroot, R., Moore, L., Langton, J. M., Short, B., … Weickert, T. W. (2012). Disambiguating ventral striatum fMRI-related BOLD signal during reward prediction in schizophrenia. *Molecular Psychiatry*, *17*(3), 280–289. https://doi.org/10.1038/MP.2011.75

Mullally, S. L., & Maguire, E. A. (2014). Memory, imagination, and predicting the future: A common brain mechanism? *Neuroscientist*, Vol. 20, pp. 220–234. https://doi.org/10.1177/1073858413495091

Müller, T. D., Nogueiras, R., Andermann, M. L., Andrews, Z. B., Anker, S. D., Argente, J., … Tschöp, M. H. (2015, June 1). Ghrelin. *Molecular Metabolism*, Vol. 4, pp. 437–460. https://doi.org/10.1016/j.molmet.2015.03.005

Münzberg, H., Björnholm, M., Bates, S. H., & Myers, M. G. (2005, March). Leptin receptor action and mechanisms of leptin resistance. *Cellular and Molecular Life Sciences*, Vol. 62, pp. 642–652. https://doi.org/10.1007/s00018-004-4432-1

Myers, K P, & Hall, W. G. (1998). Evidence that oral and nutrient reinforcers differentially

condition appetitive and consummatory responses to flavors. *Physiology & Behavior*, *64*(4), 493–500. https://doi.org/10.1016/s0031-9384(98)00106-1

Myers, Kevin P. (2018). The convergence of psychology and neurobiology in flavor-nutrient learning. *Appetite*, *122*, 36–43. https://doi.org/10.1016/j.appet.2017.03.048

Myers, Kevin P., & Sclafani, A. (2006). Development of learned flavor preferences. *Developmental Psychobiology*, *48*(5), 380–388. https://doi.org/10.1002/dev.20147

Myers, M. G., Leibel, R. L., Seeley, R. J., & Schwartz, M. W. (2010, November). Obesity and leptin resistance: Distinguishing cause from effect. *Trends in Endocrinology and Metabolism*, Vol. 21, pp. 643–651. https://doi.org/10.1016/j.tem.2010.08.002

Nairne, J. S., & Pandeirada, J. N. S. (2016). Adaptive Memory: The Evolutionary Significance of Survival Processing. *Perspectives on Psychological Science*, *11*(4), 496–511. https://doi.org/10.1177/1745691616635613

Nairne, J. S., Thompson, S. R., & Pandeirada, J. N. S. (2007). Adaptive memory: Survival processing enhances retention. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *33*(2), 263–273. https://doi.org/10.1037/0278-7393.33.2.263

New, J., Krasnow, M. M., Truxaw, D., & Gaulin, S. J. . (2007). Spatial adaptations for plant foraging: women excel and calories count. *Proceedings of the Royal Society B: Biological Sciences*, *274*(1626), 2679–2684. https://doi.org/10.1098/rspb.2007.0826

Niv, Y., & Schoenbaum, G. (2008, July 1). Dialogues on prediction errors. *Trends in Cognitive Sciences*, Vol. 12, pp. 265–272. https://doi.org/10.1016/j.tics.2008.03.006

Öhman, A., Eriksson, A., & Olofsson, C. (1975). One-Trial Learning and Superior Resistance to Extinction of Autonomic Responses Conditioned to Potentially Phobic Stimuli. *Journal of Comparative and Physiological Psychology*, *88*(2), 619–627. https://doi.org/10.1037/h0078388

Öhman, A., Fredrikson, M., Hugdahl, K., & Rimmö, P. A. (1976). The premise of equipotentiality in human classical conditioning: conditioned electrodermal responses to potentially phobic

stimuli. *Journal of Experimental Psychology. General*, *105*(4), 313–337. http://www.ncbi.nlm.nih.gov/pubmed/1003120

Öhman, A., & Mineka, S. (2001). Fears, phobias, and preparedness: Toward an evolved module of fear and fear learning. *Psychological Review*, *108*(3), 483–522. https://doi.org/10.1037/0033-295X.108.3.483

Oldham-Cooper, R. E., Hardman, C. A., Nicoll, C. E., Rogers, P. J., & Brunstrom, J. M. (2011a). Playing a computer game during lunch affects fullness, memory for lunch, and later snack intake. *The American Journal of Clinical Nutrition*, *93*(2), 308–313. https://doi.org/10.3945/ajcn.110.004580

Oomura, Y., Hori, N., Shiraishi, T., Fukunaga, K., Takeda, H., Tsuji, M., … Sasaki, K. (2006). Leptin facilitates learning and memory performance and enhances hippocampal CA1 long-term potentiation and CaMK II phosphorylation in rats. *Peptides*, *27*(11), 2738–2749. https://doi.org/10.1016/j.peptides.2006.07.001

Pandeirada, J. N. S., Fernandes, N. L., Vasconcelos, M., & Nairne, J. S. (2017). Adaptive Memory: Remembering Potential Mates. *Evolutionary Psychology*, *15*(4), 147470491774280. https://doi.org/10.1177/1474704917742807

Park, A., Jacob, A. D., Walters, B. J., Park, S., Rashid, A. J., Jung, J. H., … Josselyn, S. A. (2019). A time-dependent role for the transcription factor CREB in neuronal allocation to an engram underlying a fear memory revealed using a novel in vivo optogenetic tool to modulate CREB function. *Neuropsychopharmacology 2020 45:6*, *45*(6), 916–924. https://doi.org/10.1038/s41386-019-0588-0

Park, D. C., & Festini, S. B. (2017). Theories of Memory and Aging: A Look at the Past and a Glimpse of the Future. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*, *72*(1), 82–90. https://doi.org/10.1093/geronb/gbw066

Pavlov, Ivan P. (1927). *Conditioned reflexes: An investigation of the physiological activity of the cerebral cortex*. https://doi.org/10.5214/ans.0972-7531.1017309

Pavlov, Ivan Petrovich. (1910). *The work of the digestive glands* (2nd. English Edition). https://archive.org/details/workofdigestiveg00pavlrich/page/n17

Pearce, J. M., & Hall, G. (1980). A model for Pavlovian learning: Variations in the effectiveness of conditioned but not of unconditioned stimuli. *Psychological Review*, *87*(6), 532–552. https://doi.org/10.1037/0033-295X.87.6.532

Peirce, J., Gray, J. R., Simpson, S., MacAskill, M., Höchenberger, R., Sogo, H., … Lindeløv, J. K. (2019). PsychoPy2: Experiments in behavior made easy. *Behavior Research Methods*, *51*(1), 195–203. https://doi.org/10.3758/s13428-018-01193-y

Perello, M., Sakata, I., Birnbaum, S., Chuang, J. C., Osborne-Lawrence, S., Rovinsky, S. A., … Zigman, J. M. (2010). Ghrelin Increases the Rewarding Value of High-Fat Diet in an Orexin-Dependent Manner. *Biological Psychiatry*, *67*(9), 880–886. https://doi.org/10.1016/j.biopsych.2009.10.030

Plaçais, P. Y., & Preat, T. (2013). To favor survival under food shortage, the brain disables costly memory. *Science*, *339*(6118), 440–442. https://doi.org/10.1126/science.1226018

Prével, A., Rivière, V., Darcheville, J. C., Urcelay, G. P., & Miller, R. R. (2019). Excitatory second-order conditioning using a backward first-order conditioned stimulus: A challenge for prediction error reduction. *Quarterly Journal of Experimental Psychology*, *72*(6), 1453–1465. https://doi.org/10.1177/1747021818793376

Prickett, C., Brennan, L., & Stolwyk, R. (2015). Examining the relationship between obesity and cognitive function: A systematic literature review. *Obesity Research & Clinical Practice*, *9*(2), 93–113. https://doi.org/10.1016/j.orcp.2014.05.001

Prickett, C., Stolwyk, R., O'Brien, P., & Brennan, L. (2018). Neuropsychological Functioning in Mid-life Treatment-Seeking Adults with Obesity: a Cross-sectional Study. *Obesity Surgery*, *28*(2), 532–540. https://doi.org/10.1007/s11695-017-2894-0

Raji, C. A., Ho, A. J., Parikshak, N. N., Becker, J. T., Lopez, O. L., Kuller, L. H., … Thompson, P. M. (2010). Brain structure and obesity. *Human Brain Mapping*, *31*(3), 353–364.

https://doi.org/10.1002/hbm.20870

Rashid, A. J., Yan, C., Mercaldo, V., Hsiang, H. L., Park, S., Cole, C. J., … Josselyn, S. A. (2016). Competition between engrams influences fear memory formation and recall. *Science*, *353*(6297), 383–387. https://doi.org/10.1126/SCIENCE.AAF0594/SUPPL_FILE/RASHID.SM.PDF

Raubenheimer, D., & Simpson, S. J. (1997). Integrative models of nutrient balancing: application to insects and vertebrates. *Nutrition Research Reviews*, *10*(1), 151–179. https://doi.org/DOI: 10.1079/NRR19970009

Rescorla, R. A. (1993). Inhibitory associations between S and R in extinction. *Animal Learning & Behavior*, *21*(4), 327–336. https://doi.org/10.3758/BF03197998

Rescorla, R. A., & Wagner, A. R. (1972). A Theory of Pavlovian Conditioning: Variations in the Effectiveness of Reinforcement and Nonreinforcement. In A. . Black & W. . Prokasy (Eds.), *Classical conditioning II: current research and theory* (pp. 64–99).

Rhinehart-Doty, J. A., Schumm, J., Smith, J. C., & Smith, G. P. (1994). A non-taste cue of sucrose in short-term taste tests in rats. *Chemical Senses*, *19*(5), 425–431. https://doi.org/10.1093/chemse/19.5.425

Roberts, S. (2004). Self-experimentation as a source of new ideas: Ten examples about sleep, mood, health, and weight. *Behavioral and Brain Sciences*, *27*(02). https://doi.org/10.1017/s0140525x04000068

Roberts, S. (2006). *The Shangri-La diet: The no hunger eat anything weight-loss plan*. Penguin.

Roberts, W. A., Feeney, M. C., MacPherson, K., Petter, M., McMillan, N., & Musolino, E. (2008). Episodic-like memory in rats: Is it based on when or how long ago? *Science*, *320*(5872), 113–115. https://doi.org/10.1126/science.1152709

Robinson, E., Almiron-Roig, E., Rutters, F., de Graaf, C., Forde, C. G., Tudur Smith, C., … Jebb, S. A. (2014). A systematic review and meta-analysis examining the effect of eating rate on energy intake and hunger. *The American Journal of Clinical Nutrition*, *100*(1), 123–

151. https://doi.org/10.3945/ajcn.113.081745

Robinson, E., Aveyard, P., Daley, A., Jolly, K., Lewis, A., Lycett, D., & Higgs, S. (2013). Eating attentively: a systematic review and meta-analysis of the effect of food intake memory and awareness on eating. *The American Journal of Clinical Nutrition*, *97*(4), 728–742. https://doi.org/10.3945/ajcn.112.045245

Robinson, E., Kersbergen, I., & Higgs, S. (2014). Eating 'attentively' reduces later energy consumption in overweight and obese females. *British Journal of Nutrition*, *112*(4), 657–661. https://doi.org/10.1017/S000711451400141X

Robinson, M. J. F., Fischer, A. M., Ahuja, A., Lesser, E. N., & Maniates, H. (2015). Roles of "Wanting" and "Liking" in Motivating Behavior: Gambling, Food, and Drug Addictions. In *Current topics in behavioral neurosciences* (Vol. 27, pp. 105–136). https://doi.org/10.1007/7854_2015_387

Robinson, T. E., & Berridge, K. C. (2008). The incentive sensitization theory of addiction: Some current issues. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *363*(1507), 3137–3146. https://doi.org/10.1098/rstb.2008.0093

Rogers, P. J., Hogenkamp, P. S., De Graaf, C., Higgs, S., Lluch, A., Ness, A. R., … Mela, D. J. (2016, March 1). Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies. *International Journal of Obesity*, Vol. 40, pp. 381–394. https://doi.org/10.1038/ijo.2015.177

Rossi, M. A., Basiri, M. L., McHenry, J. A., Kosyk, O., Otis, J. M., Van Den Munkhof, H. E., … Stuber, G. D. (2019). Obesity remodels activity and transcriptional state of a lateral hypothalamic brake on feeding. *Science*, *364*(6447), 1271–1274. https://doi.org/10.1126/science.aax1184

Rozin, P., Dow, S., Moscovitch, M., & Rajaram, S. (1998). What Causes Humans to Begin and End a Meal? A Role for Memory for What Has Been Eaten, as Evidenced by a Study of

Multiple Meal Eating in Amnesic Patients. *Psychological Science*, *9*(5), 392–396. https://doi.org/10.1111/1467-9280.00073

Rumelhart, D. E., & Mcclelland, J. L. (1986). *Parallel Distributed Processing: Explorations in the Microstructure of Cognition Volume 1: Foundations*.

Sadacca, B. F., Jones, J. L., & Schoenbaum, G. (2016). Midbrain dopamine neurons compute inferred and cached value prediction errors in a common framework. *ELife*, *5*(MARCH2016). https://doi.org/10.7554/eLife.13665

Sanders, H. R., Heroux, N. A., & Stanton, M. E. (2020). Infant rats can acquire, but not retain contextual associations in object-in-context and contextual fear conditioning paradigms. *Developmental Psychobiology*, *62*(8), 1158–1164. https://doi.org/10.1002/dev.21980

Saunders, B. T., Richard, J. M., Margolis, E. B., & Janak, P. H. (2018). Dopamine neurons create Pavlovian conditioned stimuli with circuit-defined motivational properties. *Nature Neuroscience 2018 21:8*, *21*(8), 1072–1083. https://doi.org/10.1038/s41593-018-0191-4

Savage, J. S., Hoffman, L., & Birch, L. L. (2009). Dieting, restraint, and disinhibition predict women's weight change over 6 y. *American Journal of Clinical Nutrition*, *90*(1), 33–40. https://doi.org/10.3945/ajcn.2008.26558

Scarpace, P. J., & Zhang, Y. (2009, March). Leptin resistance: A prediposing factor for diet-induced obesity. *American Journal of Physiology - Regulatory Integrative and Comparative Physiology*, Vol. 296. https://doi.org/10.1152/ajpregu.90669.2008

Schacter, D. L., Addis, D. R., & Buckner, R. L. (2007, September). Remembering the past to imagine the future: The prospective brain. *Nature Reviews Neuroscience*, Vol. 8, pp. 657–661. https://doi.org/10.1038/nrn2213

Schacter, D. L., Addis, D. R., Hassabis, D., Martin, V. C., Spreng, R. N., & Szpunar, K. K. (2012, November 21). The Future of Memory: Remembering, Imagining, and the Brain. *Neuron*, Vol. 76, pp. 677–694. https://doi.org/10.1016/j.neuron.2012.11.001

Schacter, D. L., Benoit, R. G., & Szpunar, K. K. (2017, October 1). Episodic future thinking:

mechanisms and functions. *Current Opinion in Behavioral Sciences*, Vol. 17, pp. 41–50. https://doi.org/10.1016/j.cobeha.2017.06.002

Schoeller, D. A., Thomas, D., Archer, E., Heymsfield, S. B., Blair, S. N., Goran, M. I., … Allison, D. B. (2013, June 1). Self-report-based estimates of energy intake offer an inadequate basis for scientific conclusions. *American Journal of Clinical Nutrition*, Vol. 97, pp. 1413–1415. https://doi.org/10.3945/ajcn.113.062125

Schultz, W., Dayan, P., & Montague, P. R. (1997). A neural substrate of prediction and reward. *Science*, *275*(5306), 1593–1599. https://doi.org/10.1126/science.275.5306.1593

Schultz, W. (1998). Predictive reward signal of dopamine neurons. *Journal of Neurophysiology*, Vol. 80, pp. 1–27. https://doi.org/10.1152/jn.1998.80.1.1

Schultz, W. (2016, March 1). Dopamine reward prediction-error signalling: A two-component response. *Nature Reviews Neuroscience*, Vol. 17, pp. 183–195. https://doi.org/10.1038/nrn.2015.26

Schultz, W, & Dickinson, A. (2003). Neuronal Coding of Prediction Errors. *Annual Review of Neuroscience*, *23*, 473–500. https://doi.org/10.1146/ANNUREV.NEURO.23.1.473

Scisco, J. L., Muth, E. R., Dong, Y., & Hoover, A. W. (2011). Slowing Bite-Rate Reduces Energy Intake: An Application of the Bite Counter Device. *Journal of the American Dietetic Association*, *111*(8), 1231–1235. https://doi.org/10.1016/j.jada.2011.05.005

Sclafani, A. (2001). Psychobiology of food preferences. *International Journal of Obesity*, *25*(S5), S13–S16. https://doi.org/10.1038/sj.ijo.0801905

Sclafani, A. (2018). From appetite setpoint to appetition: 50 years of ingestive behavior research. *Physiology & Behavior*, *192*, 210–217. https://doi.org/10.1016/J.PHYSBEH.2018.01.001

Seguias, L., & Tapper, K. (2018). The effect of mindful eating on subsequent intake of a high calorie snack. *Appetite*, *121*, 93–100. https://doi.org/10.1016/j.appet.2017.10.041

Seitz, B.M, Blaisdell, A. P., Polack, C. W., & Miller, R. R. (2019). The Role of Biological

Significance in Human Learning and Memory. *International Journal of Comparative Psychology*, *32*.

Seitz, B.M, Blaisdell, A. P., & Sharpe, M. J. (2021). Higher-Order Conditioning and Dopamine: Charting a Path Forward. *Frontiers in Behavioral Neuroscience*, *0*, 228. https://doi.org/10.3389/FNBEH.2021.745388

Seitz, B.M, Blaisdell, A. P., & Tomiyama, A. J. (2021). Calories count: Memory of eating is evolutionarily special. *Journal of Memory and Language*, *117*, 104192. https://doi.org/10.1016/j.jml.2020.104192

Seitz, B.M, Flaim, M. E., & Blaisdell, A. P. (2020). Evidence that novel flavors unconditionally suppress weight gain in the absence of flavor-calorie associations. *Learning and Behavior*, *48*(3), 351–363. https://doi.org/10.3758/s13420-020-00419-4

Seitz, B.M, Polack, C. W., & Miller, R. R. (2018). Adaptive memory: Is there a reproduction-processing effect? *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *44*(8), 1167–1179. https://doi.org/10.1037/xlm0000513

Seitz, B.M., Tomiyama, A. J., & Blaisdell, A .P. (2021). Eating behavior as a new frontier in memory research. *Neuroscience & Biobehavioral Reviews. 127.* 795-807. https://doi.org/10.1016/j.neubiorev.2021.05.024

Seitz, B.M., Stolyarova, A., & Blaisdell, A. (n.d.). *The Modified Law of Effect Explains the Partial Reinforcement Extinction Effect*. https://doi.org/10.31234/OSF.IO/KBYMR

Seligman, M. E. (1970). On the generality of the laws of learning. *Psychological Review*, *77*(5), 406–418. https://doi.org/10.1037/h0029790

Sharpe, M. J., Batchelor, H. M., Mueller, L. E., Gardner, M. P. H., & Schoenbaum, G. (2021). Past experience shapes the neural circuits recruited for future learning. *Nature Neuroscience 2021 24:3*, *24*(3), 391–400. https://doi.org/10.1038/s41593-020-00791-4

Sharpe, M. J., Batchelor, H. M., Mueller, L. E., Yun Chang, C., Maes, E. J. P., Niv, Y., & Schoenbaum, G. (2020). Dopamine transients do not act as model-free prediction errors

during associative learning. *Nature Communications*, *11*(1), 1–10. https://doi.org/10.1038/s41467-019-13953-1

Sharpe, M. J., Batchelor, H. M., & Schoenbaum, G. (2017). Preconditioned cues have no value. *ELife*, *6*. https://doi.org/10.7554/eLife.28362

Sharpe, M. J., Chang, C. Y., Liu, M. A., Batchelor, H. M., Mueller, L. E., Jones, J. L., … Schoenbaum, G. (2017). Dopamine transients are sufficient and necessary for acquisition of model-based associations. *Nature Neuroscience*, *20*(5), 735–742. https://doi.org/10.1038/nn.4538

Sharpe, M. J., Marchant, N. J., Whitaker, L. R., Richie, C. T., Zhang, Y. J., Campbell, E. J., … Schoenbaum, G. (2017). Lateral Hypothalamic GABAergic Neurons Encode Reward Predictions that Are Relayed to the Ventral Tegmental Area to Regulate Learning. *Current Biology*, *27*(14), 2089-2100.e5. https://doi.org/10.1016/j.cub.2017.06.024

Sharpe, M. J., & Schoenbaum, G. (2018). Evaluation of the hypothesis that phasic dopamine constitutes a cached-value signal. *Neurobiology of Learning and Memory*, *153*, 131–136. https://doi.org/10.1016/j.nlm.2017.12.002

Sherry, D. F., Jacobs, L. F., & Gaulin, S. J. C. (1992). Spatial memory and adaptive specialization of the hippocampus. *Trends in Neurosciences*, *15*(8), 298–303. https://doi.org/10.1016/0166-2236(92)90080-R

Shettleworth, S. (1990). Spatial memory in food-storing birds. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *329*(1253), 143–151. https://doi.org/10.1098/rstb.1990.0159

Shimizu, Y., Son, C., Aotani, D., Nomura, H., Hikida, T., Hosoda, K., & Nakao, K. (2017). Role of leptin in conditioned place preference to high-fat diet in leptin-deficient ob/ob mice. *Neuroscience Letters*, *640*, 60–63. https://doi.org/10.1016/j.neulet.2017.01.033

Small, D. M., & Prescott, J. (2005). Odor/taste integration and the perception of flavor. *Experimental Brain Research*, *166*(3–4), 345–357. https://doi.org/10.1007/s00221-005-

2376-9

Smith, G. P. (1995). Pavlov and appetite. *Integrative Physiological and Behavioral Science*, *30*(2), 169–174. https://doi.org/10.1007/BF02691685

Smith, M. A., Riby, L. M., Eekelen, J. A. M. van, & Foster, J. K. (2011). Glucose enhancement of human memory: A comprehensive research review of the glucose memory facilitation effect. *Neuroscience & Biobehavioral Reviews*, *35*(3), 770–783. https://doi.org/10.1016/J.NEUBIOREV.2010.09.008

Speakman, J. R. (2013). Measuring energy metabolism in the mouse - theoretical, practical, and analytical considerations. *Frontiers in Physiology*, *4*, 34. https://doi.org/10.3389/fphys.2013.00034

Spence, C. (2015). Eating with our ears: assessing the importance of the sounds of consumption on our perception and enjoyment of multisensory flavour experiences. *Flavour*, *4*(1), 1–14. https://doi.org/10.1186/2044-7248-4-3

Spinelli, M., Fusco, S., Mainardi, M., Scala, F., Natale, F., Lapenta, R., … Grassi, C. (2017). Brain insulin resistance impairs hippocampal synaptic plasticity and memory by increasing GluA1 palmitoylation through. *Nature Communications*, *8*(1), 1–14. https://doi.org/10.1038/s41467-017-02221-9

Squire, L. R. (2004). Memory systems of the brain: A brief history and current perspective. *Neurobiology of Learning and Memory*, *82*(3), 171–177. https://doi.org/10.1016/j.nlm.2004.06.005

Squire, L. R., & Wixted, J. T. (2011). The Cognitive Neuroscience of Human Memory Since H.M. *Annual Review of Neuroscience*, *34*(1), 259–288. https://doi.org/10.1146/annurev-neuro-061010-113720

Stalnaker, T. A., Howard, J. D., Takahashi, Y. K., Gershman, S. J., Kahnt, T., & Schoenbaum, G. (2019). Dopamine neuron ensembles signal the content of sensory prediction errors. *ELife*, *8*. https://doi.org/10.7554/ELIFE.49315

Steinberg, E. E., Keiflin, R., Boivin, J. R., Witten, I. B., Deisseroth, K., & Janak, P. H. (2013). A causal link between prediction errors, dopamine neurons and learning. *Nature Neuroscience*, *16*(7), 966–973. https://doi.org/10.1038/NN.3413

Stevenson, R. J., & Francis, H. M. (2017). The hippocampus and the regulation of human food intake. *Psychological Bulletin*, *143*(10), 1011–1032. https://doi.org/10.1037/bul0000109

Stevenson, R. J., Francis, H. M., Attuquayefio, T., Gupta, D., Yeomans, M. R., Oaten, M. J., & Davidson, T. (2020). Hippocampal-dependent appetitive control is impaired by experimental exposure to a Western-style diet. *Royal Society Open Science*, *7*(2). https://doi.org/10.1098/rsos.191338

Stickrod, G., Kimble, D. P., & Smotherman, W. P. (1982). In utero taste/odor aversion conditioning in the rat. *Physiology and Behavior*, *28*(1), 5–7. https://doi.org/10.1016/0031-9384(82)90093-2

Suarez, A. N., Noble, E. E., & Kanoski, S. E. (2019, February 12). Regulation of memory function by feeding-relevant biological systems: Following the breadcrumbs to the hippocampus. *Frontiers in Molecular Neuroscience*, Vol. 12. https://doi.org/10.3389/fnmol.2019.00101

Suddendorf, T., & Corballis, M. C. (2007). The evolution of foresight: What is mental time travel, and is it unique to humans? *Behavioral and Brain Sciences*, *30*(3), 299–313. https://doi.org/10.1017/S0140525X07001975

Sutton, R. S., & Barto, A. G. (1981). Toward a modern theory of adaptive networks: Expectation and prediction. *Psychological Review*, *88*(2), 135–170. https://doi.org/10.1037/0033-295X.88.2.135

Swithers, S. E. (2013). Artificial sweeteners produce the counterintuitive effect of inducing metabolic derangements. *Trends in Endocrinology and Metabolism: TEM*, *24*(9), 431–441. https://doi.org/10.1016/j.tem.2013.05.005

Swithers, S. E., Baker, C. R., & Davidson, T. L. (2009). General and persistent effects of high-

intensity sweeteners on body weight gain and caloric compensation in rats. *Behavioral Neuroscience*, *123*(4), 772–780. https://doi.org/10.1037/a0016139

Swithers, S. E., & Davidson, T. L. (2008). A role for sweet taste: Calorie predictive relations in energy regulation by rats. *Behavioral Neuroscience*, *122*(1), 161–173. https://doi.org/10.1037/0735-7044.122.1.161

Swithers, S. E., Martin, A. A., & Davidson, T. L. (2010). High-intensity sweeteners and energy balance. *Physiology & Behavior*, *100*(1), 55–62. https://doi.org/10.1016/J.PHYSBEH.2009.12.021

Szypula, J., Ahern, A., & Cheke, L. (2020). The role of memory ability, depth and mode of recall in the impact of memory on later consumption. *Appetite*, 104628. https://doi.org/10.1016/j.appet.2020.104628

Takahashi, Y. K., Batchelor, H. M., Liu, B., Khanna, A., Morales, M., & Schoenbaum, G. (2017). Dopamine Neurons Respond to Errors in the Prediction of Sensory Features of Expected Rewards. *Neuron*, *95*(6), 1395-1405.e3. https://doi.org/10.1016/j.neuron.2017.08.025

Tapper, K., & Seguias, L. (2020). The effects of mindful eating on food consumption over a half-day period. *Appetite*, *145*, 104495. https://doi.org/10.1016/j.appet.2019.104495

Tobler, P. N., Fiorillo, C. D., & Schultz, W. (2005). Adaptive coding of reward value by dopamine neurons. *Science (New York, N.Y.)*, *307*(5715), 1642–1645. https://doi.org/10.1126/SCIENCE.1105370

Tran, D. M. D., & Westbrook, R. F. (2015). Rats Fed a Diet Rich in Fats and Sugars Are Impaired in the Use of Spatial Geometry. *Psychological Science*, *26*(12), 1947–1957. https://doi.org/10.1177/0956797615608240

Tremmel, M., Gerdtham, U. G., Nilsson, P. M., & Saha, S. (2017, April 19). Economic burden of obesity: A systematic literature review. *International Journal of Environmental Research and Public Health*, Vol. 14. https://doi.org/10.3390/ijerph14040435

Tsai, H. C., Zhang, F., Adamantidis, A., Stuber, G. D., Bond, A., De Lecea, L., & Deisseroth, K.

(2009). Phasic firing in dopaminergic neurons is sufficient for behavioral conditioning. *Science (New York, N.Y.)*, *324*(5930), 1080–1084. https://doi.org/10.1126/SCIENCE.1168878

Tulving, E. (1972). Episodic and semantic memory. In E Tulving & W. Davidson (Eds.), *Organization of Memory*. https://psycnet.apa.org/record/1973-08477-007

Tulving, Endel. (2002). Episodic Memory: From Mind to Brain. *Annual Review of Psychology*, *53*(1), 1–25. https://doi.org/10.1146/annurev.psych.53.100901.135114

Underwood, B. J. (1961). Ten years of massed practice on distributed practice. *Psychological Review*, *68*(4), 229–247. https://doi.org/10.1037/h0047516

Urushihara, K. (2004). Excitatory backward conditioning in an appetitive conditioned reinforcement preparation with rats. *Behavioural Processes*, *67*(3), 477–489. https://doi.org/10.1016/j.beproc.2004.08.002

van't Riet, J., Sijtsema, S. J., Dagevos, H., & de Bruijn, G. J. (2011, December 1). The importance of habits in eating behaviour. An overview and recommendations for future research. *Appetite*, Vol. 57, pp. 585–596. https://doi.org/10.1016/j.appet.2011.07.010

van der Zee, T. (2017, March 21). The Wansink Dossier: An Overview . https://doi.org/10.1111/j.1651-2227.2012.02747.x

Vartanian, L. R., Chen, W. H., Reily, N. M., & Castel, A. D. (2016). *The parallel impact of episodic memory and episodic future thinking on food intake*. https://doi.org/10.1016/j.appet.2016.02.149

Veniaminova, E., Oplatchikova, M., Bettendorff, L., Kotenkova, E., Lysko, A., Vasilevskaya, E., … Strekalova, T. (2020). Prefrontal cortex inflammation and liver pathologies accompany cognitive and motor deficits following Western diet consumption in non-obese female mice. *Life Sciences*, *241*, 117163. https://doi.org/10.1016/j.lfs.2019.117163

Verma, D., Wood, J., Lach, G., Herzog, H., Sperk, G., & Tasan, R. (2016). Hunger Promotes Fear Extinction by Activation of an Amygdala Microcircuit. *Neuropsychopharmacology*,

41(2), 431–439. https://doi.org/10.1038/npp.2015.163

Vigorito, M., & Sclafani, A. (1988). Ontogeny of polycose and sucrose appetite in neonatal rats. *Developmental Psychobiology*, *21*(5), 457–465. https://doi.org/10.1002/dev.420210505

Waelti, P., Dickinson, A., & Schultz, W. (2001). Dopamine responses comply with basic assumptions of formal learning theory. *Nature*, *412*(6842), 43–48. https://doi.org/10.1038/35083500

Wagner, A., Aizenstein, H., Venkatraman, V. K., Bischoff-Grethe, A., Fudge, J., May, J. C., … Kaye, W. H. (2010). Altered striatal response to reward in bulimia nervosa after recovery. *International Journal of Eating Disorders*, *43*(4), 289–294. https://doi.org/10.1002/eat.20699

Wagner, A., Aizenstein, H., Venkatraman, V. K., Fudge, J., May, J. C., Mazurkewicz, L., … Kaye, W. H. (2007). Altered reward processing in women recovered from anorexia nervosa. *American Journal of Psychiatry*, *164*(12), 1842–1849. https://doi.org/10.1176/appi.ajp.2007.07040575

Wansink, B. (2006). *Mindless eating : why we eat more than we think*. New York, NY: Bantam.

Watson, P., Wiers, R. W., Hommel, B., & de Wit, S. (2014). Working for food you don't desire. Cues interfere with goal-directed food-seeking. *Appetite*, *79*, 139–148. https://doi.org/10.1016/J.APPET.2014.04.005

Werthmann, J., Jansen, A., & Roefs, A. (2015). Worry or craving? A selective review of evidence for food-related attention biases in obese individuals, eating-disorder patients, restrained eaters and healthy samples. *Proceedings of the Nutrition Society*, *74*(2), 99–114. https://doi.org/10.1017/S0029665114001451

White, N. M., & McDonald, R. J. (2002, March 1). Multiple parallel memory systems in the brain of the rat. *Neurobiology of Learning and Memory*, Vol. 77, pp. 125–184. https://doi.org/10.1006/nlme.2001.4008

Whitelock, V., Gaglione, A., Davies-Owen, J., & Robinson, E. (2019). Focused attention during

eating enhanced memory for meal satiety but did not reduce later snack intake in men: A randomised within-subjects laboratory experiment. *Appetite*, *136*, 124–129. https://doi.org/10.1016/j.appet.2019.01.021

Whitelock, V., Higgs, S., Brunstrom, J. M., Halford, J. C. G., & Robinson, E. (2018). No effect of focused attention whilst eating on later snack food intake: Two laboratory experiments. *Appetite*, *128*, 188–196. https://doi.org/10.1016/j.appet.2018.06.002

Whitelock, V., Kersbergen, I., Higgs, S., Aveyard, P., Halford, J. C. G., & Robinson, E. (2019). A smartphone based attentive eating intervention for energy intake and weight loss: Results from a randomised controlled trial. *BMC Public Health*, *19*(1), 1–11. https://doi.org/10.1186/s12889-019-6923-x

Willette, A. A., & Kapogiannis, D. (2015, March 1). Does the brain shrink as the waist expands? *Ageing Research Reviews*, Vol. 20, pp. 86–97. https://doi.org/10.1016/j.arr.2014.03.007

Williams, E. P., Mesidor, M., Winters, K., Dubbert, P. M., & Wyatt, S. B. (2015, September 1). Overweight and Obesity: Prevalence, Consequences, and Causes of a Growing Public Health Problem. *Current Obesity Reports*, Vol. 4, pp. 363–370. https://doi.org/10.1007/s13679-015-0169-4

Winocur, G. (1995). Glucose-enhanced performance by aged rats on a test of conditional discrimination learning. *Psychobiology*, *23*(4), 270–276. https://doi.org/10.3758/bf03333073

Witten, I. B., Steinberg, E. E., Lee, S. Y., Davidson, T. J., Zalocusky, K. A., Brodsky, M., … Deisseroth, K. (2011). Recombinase-driver rat lines: Tools, techniques, and optogenetic application to dopamine-mediated reinforcement. *Neuron*, *72*(5), 721–733. https://doi.org/10.1016/J.NEURON.2011.10.028/ATTACHMENT/BA572C42-51D5-43EE-A265-0324D3547B47/MMC1.PDF

Wixted, J. T. (2004). The Psychology and Neuroscience of Forgetting. *Annual Review of Psychology*, *55*(1), 235–269. https://doi.org/10.1146/annurev.psych.55.090902.141555

Yeomans, M. R. (2012). Flavour–nutrient learning in humans: An elusive phenomenon?

Physiology & Behavior, *106*(3), 345–355. https://doi.org/10.1016/j.physbeh.2012.03.013

Zhou, W., & Crystal, J. D. (2009). Evidence for remembering when events occurred in a rodent model of episodic memory. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(23), 9525–9529. https://doi.org/10.1073/pnas.0904360106

Zimmet, P., Hodge, A., Nicolson, M., Staten, M., De Courten, M., Moore, J., … Dowse, G. (1996). Serum leptin concentration, obesity, and insulin resistance in Western Samoans: Cross sectional study. *British Medical Journal*, *313*(7063), 965–969. https://doi.org/10.1136/bmj.313.7063.965