**COGNITIVE CONTROL OF MEAL ONSET AND MEAL SIZE: ROLE OF
DORSAL HIPPOCAMPAL-DEPENDENT EPISODIC MEMORY**

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Abstract

There is a large gap in our understanding of how top-down cognitive processes, such as memory, influence energy intake. Similarly, there is limited knowledge regarding how the brain controls the timing of meals and meal frequency.

Understanding how cognition influences ingestive behavior and how the brain controls meal frequency will provide a more complete explanation of the neural mechanisms that regulate energy intake and may also increase our knowledge of the factors that contribute to diet-induced obesity. We hypothesize that dorsal hippocampal neurons, which are critical for memory of personal experiences (i.e., episodic memory), form a memory of a meal, inhibit meal onset during the period following a meal, and limit the amount ingested at the next meal. In support, we describe evidence from human research suggesting that episodic memory of a meal inhibits intake and review data from human and non-human animals showing that impaired hippocampal function is associated with increased intake. We then describe evidence from our laboratory showing that inactivation of dorsal hippocampal neurons decreases the interval between sucrose meals and increases intake at the next meal. We also describe our evidence suggesting that sweet orosensation is sufficient to induce synaptic plasticity in dorsal hippocampal neurons and raise the possibility that impaired dorsal hippocampal function and episodic memory deficits contribute to the development and/or maintenance of diet-induced obesity. Finally, we raise some critical questions that need to be addressed in future research.

Keywords: activity-regulated cytoskeleton-associated protein, meal frequency, postprandial, sucrose, saccharin,

Introduction

It is well established that hippocampal neurons are critical for encoding, storing and retrieving memories of personal experiences¹⁻³. These episodic memories represent what, where, and when something occurred in an animal's life and guide goal-directed behavior⁴⁻⁷. If one did not know that the hippocampus is vital for memory, one might think based on its organization and chemoanatomy that its principal function is to regulate energy homeostasis: Hippocampal neurons express high concentrations of receptors for virtually every food-related signal, receive neural impulses regarding energy status (e.g., taste, stomach distention), and project to most brain areas critical for energy regulation (described in detail below; see⁸ for review). These distinctive features led us to contemplate why one brain area would be poised to control two apparently disparate functions and to question whether hippocampal involvement in episodic memory and energy homeostasis are interrelated.

This paper will review evidence supporting our hypothesis that hippocampal neurons provide a mechanism through which top-down cognitive processes such as memory influence meal initiation and meal size. More specifically, we will review evidence that is consistent with our hypothesis that hippocampal-dependent episodic memory of a recently eaten meal influences the timing of the next meal and the amount consumed at that next meal^{9,10}. That is, we propose that answers to questions such as, "Should I eat now?" and "How much should I eat?" are influenced, in part, by episodic memories of what, when and/or how much was eaten in the preceding meal.

Eating bouts: starting versus stopping a meal

Across the animal kingdom, numerous invertebrate and vertebrate species ingest energy in bouts, which are commonly referred to as meals^{11,12}. Episodic intake is advantageous because it protects organisms against continuous exposure to predators and harsh climates and allows for the expression of other behaviors that may be more adaptive in a given situation. Decades of research suggest that different mechanisms regulate meal *initiation* (when to start eating) versus meal *termination* (how much to eat in a meal; satiety). Compared to our understanding of the factors that influence satiety, there is relatively very limited knowledge of the neural controls of meal onset and the duration of the postprandial intermeal interval. The postprandial intermeal interval is the time spanning from the end of one meal to the beginning of the next meal. Its duration influences meal frequency and thus can impact total intake. To date, evidence suggests that internal signals generated by a previous meal, environmental stimuli, and conditioned drives interact to influence meal onset and the duration of the postprandial intermeal interval (¹³⁻²²; reviewed in⁹).

Understanding the controls of meal frequency will not only provide a more complete explanation of the neural mechanisms that regulate energy intake, but may also increase our knowledge of the factors that contribute to diet-induced obesity. The increased prevalence of obesity coincides with an increase in meal frequency i.e., snacking²³⁻²⁵. Children and adults are eating more snacks per day and are deriving more of their daily calories from snacks (>24% of daily

calories)^{23,26,27}. Increased snacking is correlated positively with obesity²⁸, and obese individuals snack more frequently than their non-obese counterparts²⁹.

Episodic memory influences ingestive behavior

Interestingly, when scientists describe episodic memory, they often use recall of a recently eaten meal as an example (e.g.,³⁰). In human participants, disrupting the encoding of the memory of a meal (e.g., by watching television) increases the amount that is consumed at the next eating bout³¹⁻³⁴; whereas, recalling and enhancing the memory of a recently consumed meal decreases the amount that is ingested subsequently^{33,35}. Episodic memory of the hedonic aspects (i.e., enjoyment) of a recently eaten food also affects the amount of that food that is eaten at a subsequent meal³⁶. The hypothesis that episodic memory controls intake during the postprandial intermeal interval is supported by the finding that increasing memory encoding during eating has a bigger effect on intake at the next eating episode than on current food intake³⁷, and by the finding that episodic memory of the size of a previous meal rather than the actual amount ingested predicts hunger hours after the end of a meal³⁸. The latter finding also suggests that episodic memory can influence intake independent of gastric feedback.

Memory deficits and hippocampal damage increase intake

The famous patient H.M. and other humans with episodic memory deficits have difficulties determining whether they are sated, do not remember eating and will eat an additional meal when presented with food, even if they have just eaten to satiety³⁹⁻⁴¹. In rodents, hippocampal lesions increase food intake, promote

weight gain⁴², and increase meal frequency⁴³⁻⁴⁵. Collectively, these findings suggest that enhancing episodic memories of a meal could be a therapeutic strategy for controlling future intake³⁷. This is supported by the finding that, in overweight and obese participants, paying attention to food that is being eaten decreases the amount that is consumed in the next eating episode⁴⁶. Moreover, increasing attention and promoting recall of the most recently eaten food prior to eating appears to promote weight loss in overweight and obese participants³³.

Hippocampal neurons are positioned to influence ingestive behavior

Although the hippocampus is traditionally associated with episodic memory, one striking feature of hippocampal neurons is that they are anatomically poised to monitor energy status and influence energy intake. Hippocampal neurons receive neural signals regarding food stimuli from several brain areas critical for energy intake, including the arcuate nucleus of the hypothalamus, insula, and orbitofrontal cortex⁴⁷⁻⁵¹. Hippocampal neurons contain high concentrations of receptors for virtually every peripheral and central food-related signal (reviewed in^{8,52}), and are also influenced by other indicators of ingestion, such as gastric distention⁵³⁻⁵⁶ and vagal stimulation^{57,58}. Hippocampal neurons, in turn, send extensive efferent projections to brain areas critical for ingestive behavior, including the hypothalamus, nucleus accumbens, bed nucleus of the stria terminalis, and lateral septum⁵⁹⁻⁶².

Dorsal hippocampal neurons inhibit meal initiation and meal size

In rodents, the hippocampus is functionally divided into dorsal and ventral regions along the longitudinal septo-temporal axis. Dorsal hippocampal neurons

(posterior in primates⁴⁸) are critical for episodic memory,^{2,63-69}, whereas, ventral hippocampal neurons (anterior in primates) are implicated in motivational, emotional and affective processes⁷⁰⁻⁷⁶. Based on their role in episodic memory, we hypothesized that dorsal hippocampal neurons inhibit meal initiation during the postprandial intermeal interval and tested the prediction that inactivation of these neurons at the end of a meal would accelerate initiation of the next meal¹⁰. Male rats were trained to consume a 32% sucrose solution at the same time and place daily in order to minimize the contributions of novelty, time, and context. We used the sucrose solution as the meal because it is very palatable/rewarding to rats^{77,78}, its stimulus qualities are more specific than meals that include fats and proteins, many of its peripheral and central processing sites and mechanisms have been identified^{78,79}, its concentration can be varied to manipulate postingestive consequences⁸⁰⁻⁸², its effects can be compared to those of non-caloric sweeteners such as saccharin, and it cannot be hoarded. Importantly, it **may** also be relevant to the study of meal frequency, snacking and obesity because most calories from snacks are derived from desserts and sweetened beverages^{23,26,27}.

On experimental days, the rats were given access to the sucrose solution and then given a dorsal hippocampal infusion of vehicle or the GABA agonist muscimol after they had finished their first sucrose meal. We operationally defined the end of a sucrose meal as 5 consecutive minutes without any licking. We used this criterion because once a rat has stopped eating for 5 minutes there is a very low probability that the rat will initiate eating; the longer the criterion the

greater the probability of eating^{83,84}. Moreover, this 5-minute interval is associated with the expression of the behavioral satiety sequence in rats, which is an increase in grooming and locomotor activity (e.g., sniffing & rearing) following a meal that eventually terminates with resting behavior^{83,85,86}. We elected to infuse the muscimol *after* the end of a meal in order to restrict the inactivation to the postprandial intermeal interval, thereby allowing us to study meal initiation without affecting ingestive behavior during the preceding meal. Moreover, the inactivation occurred during the period when the memory of the meal would be expected to be undergoing consolidation. Measures of meal onset included the latency to eat since the end of the first sucrose meal (i.e., postprandial intermeal interval duration), the satiety ratio, which is the duration of the postprandial intermeal interval divided by the size of the preceding meal⁸⁷, and the postprandial correlation, which describes the positive association between the size of a meal and the length of time that passes before the next meal is initiated^{88,89}.

To the best of our knowledge, we are the first to show that dorsal hippocampal neurons delay meal initiation and also inhibit the amount eaten at that next meal¹⁰. Specifically, we found that postmeal inactivation of dorsal hippocampal neurons decreased the A) postprandial intermeal interval (ppIMI) and B) satiety ratio and C) abolished the postprandial correlation (see Figure 1). Post meal inactivation also increased A) the size of the first postinfusion meal and the B) duration of that meal (see Figure 2).

<Insert Figures 1 and 2 about here>

Our findings support the hypothesis that dorsal hippocampal neurons encode an episodic memory of a meal and inhibit intake during the period following a meal. This interpretation is consistent with evidence showing that posttraining reversible inactivation of dorsal hippocampal neurons impairs consolidation of other types of memory, including a conditioned place preference for food⁹⁰, contextual fear conditioning^{91,92}, object-place recognition⁹³, place avoidance^{94,95}, and spatial water maze^{96,97}, **albeit these examples are all spatial and mostly nonappetitive**. Our interpretation is also in line with evidence suggesting that these neurons are important for memory of where food is located^{90,98,99} and when food is available¹⁰⁰⁻¹⁰³.

Ingestion increases synaptic plasticity in dorsal hippocampal neurons

If dorsal hippocampal neurons form a memory of a meal, then consuming a meal should induce synaptic plasticity in these neurons. We tested this by using a highly sensitive fluorescent *in situ* hybridization (FISH) technique to measure expression of the immediate early gene activity-regulated cytoskeleton-associated protein (*Arc*) in dorsal hippocampal neurons following a sucrose meal¹⁰⁴. We focused on dorsal CA1 because this subfield is critical for episodic memory^{64,105,106}, and we measured *Arc* expression because it is a marker of synaptic plasticity necessary for memory consolidation¹⁰⁷⁻¹¹². Behavioral stimulation initiates a brief period of *Arc* transcription that is observed in the nucleus for up to 16 min; subsequently, *Arc* mRNA becomes perinuclear and accumulates in the cytoplasm and dendrites where it can be detected for approximately 45 min after induction¹⁰⁹. Importantly, unlike other immediate early

genes such as *zif* and *fos*, *Arc* expression is a measure of synaptic plasticity rather than neural activity: *Arc* expression can be dissociated from neural activity¹¹³, and the amount of learning-induced *Arc* expression is correlated with electrophysiological measures of plasticity rather than with neuronal firing rate¹¹⁴. Thus, measuring the *Arc* mRNA in the nuclei of dorsal hippocampal CA1 neurons following a sucrose meal is a powerful strategy for detecting synaptic plasticity associated with that meal.

As in our previous experiment, rats were trained to consume a sucrose solution at the same time and place daily. We also tested the effects of an isopreferred concentration of saccharin, which produces similar orosensory stimulation to sucrose but does not result in any significant postingestive effects¹¹⁵⁻¹¹⁹. On the experimental day, the rats were given a solution for 7 min, euthanized, and then FISH procedures were used to measure *Arc* mRNA expression. The meal was terminated after 7 min in order to maximize the ability to detect intra-nuclear *Arc* foci that were specifically activated from consuming the solution¹⁰⁹. Our results indicated that *Arc* expression in dorsal hippocampal CA1 neurons was significantly higher in rats that consumed sucrose than in cage control rats that had been given comparable handling and transportation (see Figure 3).

<Insert Figure 3 about here>

Interestingly, we also observed that rats given additional experience with sucrose prior to the experimental day had less *Arc* expression than rats with less previous sucrose experience, even though both groups consumed similar

amounts on the experimental day. These findings are consistent with previous evidence showing that repeated training in a hippocampal-dependent memory task decreases hippocampal involvement in that task¹²⁰, and with evidence showing that extensive training or repeated exposure to an environment decreases behavior-induced *Arc* expression in CA1 neurons¹²¹⁻¹²³. **Extensive evidence suggests that repeated practice in a task decreases hippocampal involvement in that task and shifts the control to a more habit-based memory system¹²⁴. Based on these combined findings, we speculate that additional exposure to the sucrose solution decreased dorsal hippocampal involvement in the memory of that solution, thereby producing sparse *Arc* expression in dorsal hippocampal CA1 neurons.** It is possible that a portion of the *Arc* expression that was observed was due to variables other than orosensory stimulation, such as licking and ingesting a solution. However, the difference in *Arc* expression between the two sucrose groups that differed in terms of previous experience cannot be due to such variables because they ingested similar amounts of sucrose on the experimental day.

Surprisingly, our findings also showed that ingesting saccharin induced significantly more *Arc* expression than did sucrose (see Figure 4A). This increase cannot be due to novelty or differences in the amount of **recent** experience with the solutions because both groups had comparable exposure to sucrose and saccharin **for the 10 days** prior to the experimental day, ingested a similar volume on the experimental day (see Figure 4B), and preferred both solutions comparably during training (see Figure 4C). **It is unlikely that the animals had**

a similar lifetime experience with the two solutions, however, because they presumably encountered caloric, but not non-caloric sweet tastes prior to the experiment in their chow and before weaning. This raises the possibility that the greater *Arc* expression in response to saccharin could be due to a larger expectancy violation (sweet taste not followed by caloric consequences). **Nonetheless**, these findings suggest that, in addition to orosensation, the caloric value of the food influences *Arc* expression.

<Insert Figure 4 about here>

Collectively, our findings appear to be the first to suggest that sweet orosensory stimulation is sufficient to induce synaptic plasticity in neurons critical for episodic memory in an experience-dependent manner. Previous findings indicate that hippocampal *Arc* expression is NMDA-receptor dependent¹²⁵⁻¹²⁷. Thus, the present results are consistent with recent findings indicating that NMDA receptor-dependent plasticity in dorsal CA1 neurons is required to form an associative memory between a taste and illness¹²⁸. Combined with our previous finding showing that inactivation of dorsal hippocampal neurons induced after rats had stopped consuming a sucrose solution accelerates the onset of the next sucrose bout and increases the amount consumed¹⁰, our findings support the hypothesis that dorsal hippocampal neurons form a memory of a meal and inhibit meal onset during the postprandial period^{9,10}.

Does impaired dorsal hippocampal function and impaired episodic memory contribute to diet-induced obesity?

Others and we have shown that excess intake of fats and/or sugars and

obesity impair dorsal hippocampal-dependent memory in rodents¹²⁹⁻¹³⁴. Similarly, in humans obesity is associated with episodic memory deficits¹³⁵ and hippocampal atrophy¹³⁶. Moreover, human participants with higher self-reported intake of fat and sugar have impaired episodic memory, are less able to accurately recall what they most recently ate, and eat more than subjects who report lower intake of fat and sugar¹³⁷. Collectively, the evidence reviewed here indicates that excess intake of fat and sugar impairs dorsal hippocampal function and, in turn, that impairing dorsal hippocampal function increases intake. Combined, these findings are consistent with the possibility that diet-induced obesity is caused and maintained, at least in part, by a vicious cycle wherein excess intake disrupts dorsal hippocampal-dependent episodic memory, which further increases intake¹³⁸⁻¹⁴⁰. Importantly, a myriad of illnesses and stressors impair dorsal hippocampal function (reviewed in⁹) and thus may also contribute to overeating and diet-induced obesity, at least in part, through their effects on dorsal hippocampal neurons.

Critical questions and future challenges

Collectively, the evidence reviewed above is consistent with our hypothesis that dorsal hippocampal-dependent episodic memory of a meal inhibits initiation of the next meal and limits the amount ingested at that subsequent meal. This hypothesis provides an experimental approach for studying the neural mechanisms through which top-down higher-level cognitive processes modulate basic functions such as ingestive behavior. In the future it will be critical to determine whether dorsal hippocampal neurons also control

intake of nutritionally balanced liquid or solid diets that contain protein, fat, and carbohydrates, whether consumption of these foods elevates dorsal hippocampal *Arc* expression, and whether manipulations that prevent increases in dorsal hippocampal *Arc* expression influence meal timing and amount ingested. Moreover, it will be essential to test the likelihood that there are sex differences in the contributions of dorsal hippocampal neurons to energy intake¹⁴¹⁻¹⁴³.

Although the results described in this review provide converging evidence in support of the hypothesis that dorsal hippocampus controls future intake through a process involving episodic memory, additional research is needed to address the necessity and specificity of episodic memory. For instance, evidence from human studies suggests that episodic memory deficits are associated with reduced sensitivity to interoceptive cues^{39-41,137} and large hippocampal lesions that include dorsal and ventral hippocampus also produce a similar effect⁴². This leaves open the question of whether dorsal hippocampal inactivation increases meal initiation and frequency by interfering with episodic memory directly or by reducing the ability to detect interoceptive satiety signals, which presumably would be needed to form a memory of a meal. Also, dorsal hippocampal neurons are involved in interval timing, which raises the possibility that dorsal hippocampal neurons could also control meal initiation by tracking elapsed time since the last meal^{102,144}. Dorsal hippocampal neurons are also involved in occasion setting¹⁴⁵ and could thus decrease ingestion by suppressing the memories of the reinforcing

aspects of eating in sated animals¹⁴⁶. Indeed, it is possible that dorsal hippocampal neurons control intake through multiple mechanisms that are not necessarily mutually exclusive.

An important question is how dorsal hippocampal modulation of ingestive behavior intersects with homeostatic and hedonic controls of intake, with other cognitive processes that influence ingestion, and with other controls of meal initiation. This question may be addressed, in part, by identifying critical hippocampal subfields (i.e., dentate gyrus, CA1-CA3) and the neural circuit through which dorsal hippocampal neurons inhibit intake. This will include determining whether dorsal hippocampal neurons influence intake through a process that involves an interaction with ventral hippocampal neurons given the extensive evidence implicating ventral hippocampal neurons in ingestive behavior. For instance, permanent ventral hippocampal lesion impair performance in a task that involves learning to associate internal energy states with shocks¹⁴⁷, and increase food consumption and body mass⁴². Also, activation of ventral hippocampal receptors for the gut hormones glucagon-like peptide-1 (GLP-1) and leptin reduces food intake and enhances food-related memory^{148,149}; whereas activation of ventral hippocampal receptors for the orexigenic hormone ghrelin increase food intake¹⁵⁰. Importantly, our preliminary findings suggest that ventral hippocampal neurons also inhibit meal initiation. Specifically, reversible inactivation of these neurons during the period following a sucrose meal (i.e., during the postprandial intermeal interval) accelerates the onset of the next sucrose meal and increases meal frequency¹⁵¹. **These findings**

raise the question of whether dorsal and ventral hippocampus control intake through similar or different underlying processes. For instance, although both regions are involved in memory, dorsal hippocampus is more critical for memory of what, where and when, whereas ventral hippocampus is more important for affective/emotional memory.

Presumably the memory of a meal could contain both components, raising the possibility that both inhibit intake via their distinct contributions to the memory of a meal. Ventral hippocampus could also influence intake through non-mnemonic motivational processes. Another possibility that is not mutually exclusive is that dorsal hippocampal neurons mediate their effects via longitudinal projections to ventral hippocampus¹⁵²⁻¹⁵⁵, which in turn, are the primary source of hippocampal projections to brain regions critically involved in energy regulation, such as the lateral hypothalamus, bed nucleus of the stria terminalis, lateral septum, and nucleus accumbens^{61,156,157}.

Ingestive behavior is adaptive in some situations, but not in others. Cognitive processes such as dorsal hippocampal-dependent episodic memory may contribute to the ability to modulate ingestive behavior in a flexible manner⁴⁻⁶. One implication is that there may be some circumstances wherein episodic memory promotes rather than inhibits ingestive behavior. In support, research from humans has shown that promoting episodic memories of the hedonic qualities of a recently consumed food increases subsequent intake of that food³⁶. Although it is known that ventral hippocampal neurons can influence intake in a

bidirectional manner¹⁴⁸⁻¹⁵⁰, the evidence to date has only demonstrated an inhibitory role for dorsal hippocampal neurons^{10,149,150}. Accordingly, research is needed to determine whether there are conditions under which dorsal hippocampal neurons *promote* intake.

In summary, we propose that dorsal hippocampal-dependent episodic memory of a meal (where, when, what and how much was eaten) influences the timing of the next meal and the amount ingested at that meal. We have shown that dorsal hippocampal dysfunction accelerates meal initiation and increases meal size, meal frequency and total intake. Given that a host of life events impair dorsal hippocampal function, including excess intake of fats and sugars, it is possible that impaired dorsal hippocampal inhibition of intake contributes to the development and/or maintenance diet-induce obesity.

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Figure captions

Figure 1. Reversible inactivation of dorsal hippocampal neurons with muscimol (Mus) during the postprandial period A) decreases the duration of the postprandial intermeal interval (ppIMI), B) decreases the satiety ratio (duration of the ppIMI/size of the preceding meal), and C) prevents the postprandial correlation (positive association between the size of a meal and the length of time before the next meal is initiated; $*P < 0.05$ and $** P < 0.01$ vs. vehicle [Veh] infusions). Adapted with permission from¹⁰.

Figure 2. Reversible inactivation of dorsal hippocampal neurons with muscimol during the postprandial period A) increases the postinfusion meal size B) and increases the duration of the postinfusion meal ($*P < 0.05$ vs. vehicle infusions). Adapted with permission from¹⁰.

Figure 3. (A) The percentage of neurons expressing nuclear *Arc* expression in dorsal hippocampal CA1 neurons is significantly higher in rats that just consumed a 32% sucrose solution (SUC) than in caged control rats (CTRL). Sample images from the dorsal hippocampal CA1 region of a (B) CTRL and (C) SUC rat. Each image is a stack of six 1.5 μm -thick optical sections from the center of a 20 μm -thick stack. *Arc* mRNA is in red and nuclei stained with DAPI in blue. Hue and brightness were adjusted in Adobe Photoshop® CS6. $*p < 0.05$ vs. CTRL.

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Figure 4. (A) 0.2% saccharin (SACCH) produced larger increases in nuclear *Arc* expression in dCA1 neurons than 4% sucrose (SUC), and both SUC and SACCH produced more *Arc* expression than caged control rats (CTRL). The rats (B)

consumed similar amounts of the test solution on the experimental day and (C) preferred the 4% sucrose and the 0.2% saccharin solutions comparably during training. * $p < 0.05$ vs. CTRL, # $p < 0.05$ vs. SUC. Reprinted with permission from¹⁰⁴.

Figure 1

Figure 2

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References

1. Tulving, E., W. Donaldson, G.H. Bower, and United States Office of Naval Research., *Organization of memory*. 1972, New York,: Academic Press. xiii, 423 p.
2. Shapiro, M.L., P.J. Kennedy, and J. Ferbinteanu, *Representing episodes in the mammalian brain*. Curr Opin Neurobiol, 2006. **16**(6): p. 701-9.
3. Dickerson, B.C. and H. Eichenbaum, *The episodic memory system: neurocircuitry and disorders*. Neuropsychopharmacology, 2010. **35**(1): p. 86-104.
4. Crystal, J.D., *Remembering the past and planning for the future in rats*. Behav Processes, 2013. **93**: p. 39-49.
5. Numan, R., *A Prefrontal-Hippocampal Comparator for Goal-Directed Behavior: The Intentional Self and Episodic Memory*. Front Behav Neurosci, 2015. **9**: p. 323.
6. Veyrac, A., M. Allerborn, A. Gros, F. Michon, L. Raguette, J. Kenney, F. Godinot, M. Thevenet, S. Garcia, B. Messaoudi, S. Laroche, and N. Ravel, *Memory of occasional events in rats: individual episodic memory profiles, flexibility, and neural substrate*. J Neurosci, 2015. **35**(19): p. 7575-86.
7. Shapiro, M., *A limited positioning system for memory*. Hippocampus, 2015. **25**(6): p. 690-6.
8. Kanoski, S.E. and H.J. Grill, *Hippocampus Contributions to Food Intake Control: Mnemonic, Neuroanatomical, and Endocrine Mechanisms*. Biol Psychiatry, 2015.
9. Parent, M.B., J.N. Darling, and Y.O. Henderson, *Remembering to eat: hippocampal regulation of meal onset*. Am J Physiol Regul Integr Comp Physiol, 2014. **306**(10): p. R701-13.
10. Henderson, Y.O., G.P. Smith, and M.B. Parent, *Hippocampal neurons inhibit meal onset*. Hippocampus, 2013. **23**(1): p. 100-7.
11. Simpson, S.J. and E.A. Bernays, *The regulation of feeding: locusts and blowflies are not so different from mammals*. Appetite, 1983. **4**(4): p. 313-46.
12. Smith, G.P., *The controls of eating: a shift from nutritional homeostasis to behavioral neuroscience*. Nutrition, 2000. **16**(10): p. 814-20.
13. Cornell, C.E., J. Rodin, and H. Weingarten, *Stimulus-induced eating when satiated*. Physiol Behav, 1989. **45**(4): p. 695-704.
14. Weingarten, H.P., *Conditioned cues elicit feeding in sated rats: a role for learning in meal initiation*. Science, 1983. **220**(4595): p. 431-3.
15. Sclafani, A. and A. Rendel, *Food deprivation-induced activity in dietary obese, dietary lean, and normal-weight rats*. Behav Biol, 1978. **24**(2): p. 220-8.
16. Reppucci, C.J. and G.D. Petrovich, *Learned food-cue stimulates persistent feeding in sated rats*. Appetite, 2012. **59**(2): p. 437-47.
17. Weingarten, H.P., *Meal initiation controlled by learned cues: basic behavioral properties*. Appetite, 1984. **5**(2): p. 147-58.

18. Petrovich, G.D., C.A. Ross, P.C. Holland, and M. Gallagher, *Medial prefrontal cortex is necessary for an appetitive contextual conditioned stimulus to promote eating in sated rats*. J Neurosci, 2007. **27**(24): p. 6436-41.
19. Strubbe, J.H. and G. van Dijk, *The temporal organization of ingestive behaviour and its interaction with regulation of energy balance*. Neurosci Biobehav Rev, 2002. **26**(4): p. 485-98.
20. Collier, G., D.F. Johnson, and C. Mitchell, *The relation between meal size and the time between meals: effects of cage complexity and food cost*. Physiol Behav, 1999. **67**(3): p. 339-46.
21. Kraly, F.S., W.J. Carty, and G.P. Smith, *Effect of pregastric food stimuli on meal size and internal intermeal in the rat*. Physiol Behav, 1978. **20**(6): p. 779-84.
22. Strubbe, J.H., J. Keyser, T. Dijkstra, and A.J. Prins, *Interaction between circadian and caloric control of feeding behavior in the rat*. Physiol Behav, 1986. **36**(3): p. 489-93.
23. Cutler, D.M., E.L. Glaeser, and J.M. Shapiro, *Why have Americans become more obese?* Journal of Economic Perspectives, 2003. **17**(3): p. 93-118.
24. Nicklas, T.A., S.J. Yang, T. Baranowski, I. Zakeri, and G. Berenson, *Eating patterns and obesity in children. The Bogalusa Heart Study*. Am J Prev Med, 2003. **25**(1): p. 9-16.
25. Nielsen, S.J., A.M. Siega-Riz, and B.M. Popkin, *Trends in energy intake in U.S. between 1977 and 1996: similar shifts seen across age groups*. Obes Res, 2002. **10**(5): p. 370-8.
26. Piernas, C. and B.M. Popkin, *Snacking increased among U.S. adults between 1977 and 2006*. J Nutr, 2010. **140**(2): p. 325-32.
27. Piernas, C. and B.M. Popkin, *Trends in snacking among U.S. children*. Health Aff (Millwood), 2010. **29**(3): p. 398-404.
28. Howarth, N.C., T.T. Huang, S.B. Roberts, B.H. Lin, and M.A. McCrory, *Eating patterns and dietary composition in relation to BMI in younger and older adults*. Int J Obes (Lond), 2007. **31**(4): p. 675-84.
29. Berteus Forslund, H., J.S. Torgerson, L. Sjostrom, and A.K. Lindroos, *Snacking frequency in relation to energy intake and food choices in obese men and women compared to a reference population*. Int J Obes (Lond), 2005. **29**(6): p. 711-9.
30. Tromp, D., A. Dufour, S. Lithfous, T. Pebayle, and O. Despres, *Episodic memory in normal aging and Alzheimer disease: Insights from imaging and behavioral studies*. Ageing Res Rev, 2015. **24**(Pt B): p. 232-62.
31. Oldham-Cooper, R.E., C.A. Hardman, C.E. Nicoll, P.J. Rogers, and J.M. Brunstrom, *Playing a computer game during lunch affects fullness, memory for lunch, and later snack intake*. Am J Clin Nutr, 2011. **93**(2): p. 308-13.
32. Higgs, S. and M. Woodward, *Television watching during lunch increases afternoon snack intake of young women*. Appetite, 2009. **52**(1): p. 39-43.

33. Robinson, E., S. Higgs, A.J. Daley, K. Jolly, D. Lycett, A. Lewis, and P. Aveyard, *Development and feasibility testing of a smart phone based attentive eating intervention*. BMC Public Health, 2013. **13**: p. 639.
34. Mittal, D., R. Stevenson, M. Oaten, and L. Miller, *Snacking while watching TV impairs food recall and promotes food intake on a later TV free test meal*. Applied Cognitive Psychology, 2011. **25**(6): p. 871-877.
35. Higgs, S., *Memory for recent eating and its influence on subsequent food intake*. Appetite, 2002. **39**(2): p. 159-66.
36. Robinson, E., J. Blissett, and S. Higgs, *Changing memory of food enjoyment to increase food liking, choice and intake*. Br J Nutr, 2012. **108**(8): p. 1505-10.
37. Robinson, E., P. Aveyard, A. Daley, K. Jolly, A. Lewis, D. Lycett, and S. Higgs, *Eating attentively: a systematic review and meta-analysis of the effect of food intake memory and awareness on eating*. Am J Clin Nutr, 2013. **97**(4): p. 728-42.
38. Brunstrom, J.M., J.F. Burn, N.R. Sell, J.M. Collingwood, P.J. Rogers, L.L. Wilkinson, E.C. Hinton, O.M. Maynard, and D. Ferriday, *Episodic memory and appetite regulation in humans*. PLoS One, 2012. **7**(12): p. e50707.
39. Hebden, N., S. Corkin, H. Eichenbaum, and K. Shedlack, *Diminished ability to interpret and report internal states after bilateral medial temporal resection: case H.M.* Behav Neurosci, 1985. **99**(6): p. 1031-9.
40. Higgs, S., A.C. Williamson, P. Rotshtein, and G.W. Humphreys, *Sensory-specific satiety is intact in amnesics who eat multiple meals*. Psychol Sci, 2008. **19**(7): p. 623-8.
41. Rozin, P., S. Dow, M. Moscovitch, and S. Rajaram, *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*. Psychol Sci, 1998. **9**(5): p. 392-96.
42. Davidson, T.L., K. Chan, L.E. Jarrard, S.E. Kanoski, D.J. Clegg, and S.C. Benoit, *Contributions of the hippocampus and medial prefrontal cortex to energy and body weight regulation*. Hippocampus, 2009. **19**(3): p. 235-52.
43. Davidson, T.L. and L.E. Jarrard, *A role for hippocampus in the utilization of hunger signals*. Behav Neural Biol, 1993. **59**(2): p. 167-71.
44. Osborne, B. and A.B. Dodek, *Disrupted patterns of consummatory behavior in rats with fornix transections*. Behav Neural Biol, 1986. **45**(2): p. 212-22.
45. Clifton, P.G., S.P. Vickers, and E.M. Somerville, *Little and often: ingestive behavior patterns following hippocampal lesions in rats*. Behav Neurosci, 1998. **112**(3): p. 502-11.
46. Robinson, E., I. Kersbergen, and S. Higgs, *Eating 'attentively' reduces later energy consumption in overweight and obese females*. Br J Nutr, 2014. **112**(4): p. 657-61.
47. Amaral, D.G., R. Insausti, and W.M. Cowan, *The entorhinal cortex of the monkey: I. Cytoarchitectonic organization*. J Comp Neurol, 1987. **264**(3): p. 326-55.

48. Insausti, R., D.G. Amaral, and W.M. Cowan, *The entorhinal cortex of the monkey: II. Cortical afferents*. J Comp Neurol, 1987. **264**(3): p. 356-95.
49. Rolls, E.T., *Functions of the orbitofrontal and pregenual cingulate cortex in taste, olfaction, appetite and emotion*. Acta Physiol Hung, 2008. **95**(2): p. 131-64.
50. Wang, G.J., D. Tomasi, W. Backus, R. Wang, F. Telang, A. Geliebter, J. Korner, A. Bauman, J.S. Fowler, P.K. Thanos, and N.D. Volkow, *Gastric distention activates satiety circuitry in the human brain*. Neuroimage, 2008. **39**(4): p. 1824-31.
51. Kondo, H. and M.P. Witter, *Topographic organization of orbitofrontal projections to the parahippocampal region in rats*. J Comp Neurol, 2014. **522**(4): p. 772-93.
52. Lathe, R., *Hormones and the hippocampus*. J Endocrinol, 2001. **169**(2): p. 205-31.
53. Min, D.K., U.I. Tuor, and P.K. Chelikani, *Gastric distention induced functional magnetic resonance signal changes in the rodent brain*. Neuroscience, 2011. **179**: p. 151-8.
54. Spetter, M.S., C. de Graaf, M. Mars, M.A. Viergever, and P.A. Smeets, *The sum of its parts--effects of gastric distention, nutrient content and sensory stimulation on brain activation*. PLoS One, 2014. **9**(3): p. e90872.
55. Xu, L., Y. Gong, H. Wang, X. Sun, F. Guo, S. Gao, and F. Gu, *The stimulating effect of ghrelin on gastric motility and firing activity of gastric-distension-sensitive hippocampal neurons and its underlying regulation by the hypothalamus*. Exp Physiol, 2014. **99**(1): p. 123-35.
56. Xu, L., X. Sun, J. Lu, M. Tang, and J.D. Chen, *Effects of gastric electric stimulation on gastric distention responsive neurons and expressions of CCK in rodent hippocampus*. Obesity (Silver Spring), 2008. **16**(5): p. 951-7.
57. Wang, G.J., J. Yang, N.D. Volkow, F. Telang, Y. Ma, W. Zhu, C.T. Wong, D. Tomasi, P.K. Thanos, and J.S. Fowler, *Gastric stimulation in obese subjects activates the hippocampus and other regions involved in brain reward circuitry*. Proc Natl Acad Sci U S A, 2006. **103**(42): p. 15641-5.
58. Uematsu, A., T. Tsurugizawa, H. Uneyama, and K. Torii, *Brain-gut communication via vagus nerve modulates conditioned flavor preference*. Eur J Neurosci, 2010. **31**(6): p. 1136-43.
59. Groenewegen, H.J., E. Vermeulen-Van der Zee, A. te Kortschot, and M.P. Witter, *Organization of the projections from the subiculum to the ventral striatum in the rat. A study using anterograde transport of Phaseolus vulgaris leucoagglutinin*. Neuroscience, 1987. **23**(1): p. 103-20.
60. Brog, J.S., A. Salyapongse, A.Y. Deutch, and D.S. Zahm, *The patterns of afferent innervation of the core and shell in the "accumbens" part of the rat ventral striatum: immunohistochemical detection of retrogradely transported fluoro-gold*. J Comp Neurol, 1993. **338**(2): p. 255-78.
61. Cenquizca, L.A. and L.W. Swanson, *Analysis of direct hippocampal cortical field CA1 axonal projections to diencephalon in the rat*. J Comp Neurol, 2006. **497**(1): p. 101-14.

62. Hahn, J.D. and L.W. Swanson, *Connections of the lateral hypothalamic area juxtadorsomedial region in the male rat*. J Comp Neurol, 2012. **520**(9): p. 1831-90.
63. Kennedy, P.J. and M.L. Shapiro, *Motivational states activate distinct hippocampal representations to guide goal-directed behaviors*. Proc Natl Acad Sci U S A, 2009. **106**(26): p. 10805-10.
64. Barbosa, F.F., I.M. Pontes, S. Ribeiro, A.M. Ribeiro, and R.H. Silva, *Differential roles of the dorsal hippocampal regions in the acquisition of spatial and temporal aspects of episodic-like memory*. Behav Brain Res, 2012. **232**(1): p. 269-77.
65. Hoge, J. and R.P. Kesner, *Role of CA3 and CA1 subregions of the dorsal hippocampus on temporal processing of objects*. Neurobiol Learn Mem, 2007. **88**(2): p. 225-31.
66. Kesner, R.P., M.R. Hunsaker, and M.W. Warthen, *The CA3 subregion of the hippocampus is critical for episodic memory processing by means of relational encoding in rats*. Behav Neurosci, 2008. **122**(6): p. 1217-25.
67. Li, J.S. and Y.S. Chao, *Electrolytic lesions of dorsal CA3 impair episodic-like memory in rats*. Neurobiol Learn Mem, 2008. **89**(2): p. 192-8.
68. Manns, J.R., M.W. Howard, and H. Eichenbaum, *Gradual changes in hippocampal activity support remembering the order of events*. Neuron, 2007. **56**(3): p. 530-40.
69. Quinn, J.J., H.M. Wied, Q.D. Ma, M.R. Tinsley, and M.S. Fanselow, *Dorsal hippocampus involvement in delay fear conditioning depends upon the strength of the tone-footshock association*. Hippocampus, 2008. **18**(7): p. 640-54.
70. Bannerman, D.M., J.N. Rawlins, S.B. McHugh, R.M. Deacon, B.K. Yee, T. Bast, W.N. Zhang, H.H. Pothuizen, and J. Feldon, *Regional dissociations within the hippocampus--memory and anxiety*. Neurosci Biobehav Rev, 2004. **28**(3): p. 273-83.
71. Fanselow, M.S. and H.W. Dong, *Are the dorsal and ventral hippocampus functionally distinct structures?* Neuron, 2010. **65**(1): p. 7-19.
72. Moser, M.B. and E.I. Moser, *Functional differentiation in the hippocampus*. Hippocampus, 1998. **8**(6): p. 608-19.
73. O'Mara, S.M., M.V. Sanchez-Vives, J.R. Brotons-Mas, and E. O'Hare, *Roles for the subiculum in spatial information processing, memory, motivation and the temporal control of behaviour*. Prog Neuropsychopharmacol Biol Psychiatry, 2009. **33**(5): p. 782-90.
74. Kesner, R.P., *Role of the hippocampus in mediating interference as measured by pattern separation processes*. Behav Processes, 2013. **93**: p. 148-54.
75. Barkus, C., S.B. McHugh, R. Sprengel, P.H. Seeburg, J.N. Rawlins, and D.M. Bannerman, *Hippocampal NMDA receptors and anxiety: at the interface between cognition and emotion*. Eur J Pharmacol, 2010. **626**(1): p. 49-56.

76. Strange, B.A., M.P. Witter, E.S. Lein, and E.I. Moser, *Functional organization of the hippocampal longitudinal axis*. Nat Rev Neurosci, 2014. **15**(10): p. 655-69.
77. Hajnal, A., G.P. Smith, and R. Norgren, *Oral sucrose stimulation increases accumbens dopamine in the rat*. Am J Physiol Regul Integr Comp Physiol, 2004. **286**(1): p. R31-7.
78. Smith, G.P., *Accumbens dopamine mediates the rewarding effect of orosensory stimulation by sucrose*. Appetite, 2004. **43**(1): p. 11-3.
79. Levine, A.S., C.M. Kotz, and B.A. Gosnell, *Sugars: hedonic aspects, neuroregulation, and energy balance*. Am J Clin Nutr, 2003. **78**(4): p. 834S-842S.
80. Davis, J.D., G.P. Smith, and B. Singh, *Type of negative feedback controlling sucrose ingestion depends on sucrose concentration*. Am J Physiol Regul Integr Comp Physiol, 2000. **278**(2): p. R383-9.
81. Kirkham, T.C. and S.J. Cooper, *Naloxone attenuation of sham feeding is modified by manipulation of sucrose concentration*. Physiol Behav, 1988. **44**(4-5): p. 491-4.
82. Waldbillig, R.J. and T.J. Bartness, *The suppression of sucrose intake by cholecystokinin is scaled according to the magnitude of the orosensory control over feeding*. Physiol Behav, 1982. **28**(4): p. 591-5.
83. Zorrilla, E.P., K. Inoue, E.M. Fekete, A. Tabarin, G.R. Valdez, and G.F. Koob, *Measuring meals: structure of prandial food and water intake of rats*. Am J Physiol Regul Integr Comp Physiol, 2005. **288**(6): p. R1450-67.
84. Fekete, E.M., K. Inoue, Y. Zhao, J.E. Rivier, W.W. Vale, A. Szucs, G.F. Koob, and E.P. Zorrilla, *Delayed satiety-like actions and altered feeding microstructure by a selective type 2 corticotropin-releasing factor agonist in rats: intra-hypothalamic urocortin 3 administration reduces food intake by prolonging the post-meal interval*. Neuropsychopharmacology, 2007. **32**(5): p. 1052-68.
85. Antin, J., J. Gibbs, J. Holt, R.C. Young, and G.P. Smith, *Cholecystokinin elicits the complete behavioral sequence of satiety in rats*. J Comp Physiol Psychol, 1975. **89**(7): p. 784-90.
86. Kushner, L.R. and D.G. Mook, *Behavioral correlates of oral and postingestive satiety in the rat*. Physiol Behav, 1984. **33**(5): p. 713-8.
87. Panksepp, J., *Reanalysis of feeding patterns in the rat*. J Comp Physiol Psychol, 1973. **82**(1): p. 78-94.
88. Le Magnen, J. and S. Tallon, *[Recording and preliminary analysis of "spontaneous nutritional periodicity" in the white rat]*. J Physiol (Paris), 1963. **55**: p. 286-7.
89. Le Magnen, J. and S. Tallon, *[The spontaneous periodicity of ad libitum food intake in white rats]*. J Physiol (Paris), 1966. **58**(3): p. 323-49.
90. Holahan, M.R., *Complementary roles for the amygdala and hippocampus during different phases of appetitive information processing*. Neurobiol Learn Mem, 2005. **84**(2): p. 124-31.
91. Chang, S.D., D.Y. Chen, and K.C. Liang, *Infusion of lidocaine into the dorsal hippocampus before or after the shock training phase impaired*

- conditioned freezing in a two-phase training task of contextual fear conditioning.* Neurobiol Learn Mem, 2008. **89**(2): p. 95-105.
92. Chang, S.D. and K.C. Liang, *Roles of hippocampal GABA(A) and muscarinic receptors in consolidation of context memory and context-shock association in contextual fear conditioning: a double dissociation study.* Neurobiol Learn Mem, 2012. **98**(1): p. 17-24.
 93. Oliveira, A.M., J.D. Hawk, T. Abel, and R. Havekes, *Post-training reversible inactivation of the hippocampus enhances novel object recognition memory.* Learn Mem, 2010. **17**(3): p. 155-60.
 94. Cimadevilla, J.M., M. Wesierska, A.A. Fenton, and J. Bures, *Inactivating one hippocampus impairs avoidance of a stable room-defined place during dissociation of arena cues from room cues by rotation of the arena.* Proc Natl Acad Sci U S A, 2001. **98**(6): p. 3531-6.
 95. Lorenzini, C.A., E. Baldi, C. Bucherelli, B. Sacchetti, and G. Tassoni, *Role of dorsal hippocampus in acquisition, consolidation and retrieval of rat's passive avoidance response: a tetrodotoxin functional inactivation study.* Brain Res, 1996. **730**(1-2): p. 32-9.
 96. Cimadevilla, J.M., R. Miranda, L. Lopez, and J.L. Arias, *Bilateral and unilateral hippocampal inactivation did not differ in their effect on consolidation processes in the Morris water maze.* Int J Neurosci, 2008. **118**(5): p. 619-26.
 97. Holahan, M.R. and A. Routtenberg, *Lidocaine injections targeting CA3 hippocampus impair long-term spatial memory and prevent learning-induced mossy fiber remodeling.* Hippocampus, 2011. **21**(5): p. 532-40.
 98. Gaskin, S. and N.M. White, *Parallel processing of information about location in the amygdala, entorhinal cortex and hippocampus.* Hippocampus, 2013. **23**(11): p. 1075-83.
 99. Yamada, K., M. Shimizu, K. Kawabe, and Y. Ichitani, *Hippocampal AP5 treatment impairs both spatial working and reference memory in radial maze performance in rats.* Eur J Pharmacol, 2015. **758**: p. 137-41.
 100. Tam, S.K. and C. Bonardi, *Dorsal hippocampal lesions disrupt Pavlovian delay conditioning and conditioned-response timing.* Behav Brain Res, 2012. **230**(1): p. 259-67.
 101. Tam, S.K. and C. Bonardi, *Dorsal hippocampal involvement in appetitive trace conditioning and interval timing.* Behav Neurosci, 2012. **126**(2): p. 258-69.
 102. Tam, S.K., D.J. Jennings, and C. Bonardi, *Effects of dorsal hippocampal damage on conditioning and conditioned-response timing: A pooled analysis.* Hippocampus, 2015. **25**(4): p. 444-59.
 103. Meck, W.H., R.M. Church, and M.S. Matell, *Hippocampus, time, and memory--a retrospective analysis.* Behav Neurosci, 2013. **127**(5): p. 642-54.
 104. Henderson, Y.O., R. Nalloor, A. Vazdarjanova, and M.B. Parent, *Sweet orosensation induces Arc expression in dorsal hippocampal CA1 neurons in an Experience-dependent manner.* Hippocampus, 2016. **26**(3): p. 405-13.

105. Hunsaker, M.R., B. Lee, and R.P. Kesner, *Evaluating the temporal context of episodic memory: the role of CA3 and CA1*. Behav Brain Res, 2008. **188**(2): p. 310-5.
106. Farovik, A., L.M. Dupont, and H. Eichenbaum, *Distinct roles for dorsal CA3 and CA1 in memory for sequential nonspatial events*. Learn Mem, 2010. **17**(1): p. 12-17.
107. Miyashita, T., S. Kubik, N. Haghighi, O. Steward, and J.F. Guzowski, *Rapid activation of plasticity-associated gene transcription in hippocampal neurons provides a mechanism for encoding of one-trial experience*. J Neurosci, 2009. **29**(4): p. 898-906.
108. Plath, N., O. Ohana, B. Dammermann, M.L. Errington, D. Schmitz, C. Gross, X. Mao, A. Engelsberg, C. Mahlke, H. Welzl, U. Kobalz, A. Stawrakakis, E. Fernandez, R. Waltereit, A. Bick-Sander, E. Therstappen, S.F. Cooke, V. Blanquet, W. Wurst, B. Salmen, M.R. Bosl, H.P. Lipp, S.G. Grant, T.V. Bliss, D.P. Wolfer, and D. Kuhl, *Arc/Arg3.1 is essential for the consolidation of synaptic plasticity and memories*. Neuron, 2006. **52**(3): p. 437-44.
109. Vazdarjanova, A., B.L. McNaughton, C.A. Barnes, P.F. Worley, and J.F. Guzowski, *Experience-dependent coincident expression of the effector immediate-early genes arc and Homer 1a in hippocampal and neocortical neuronal networks*. J Neurosci, 2002. **22**(23): p. 10067-71.
110. McIntyre, C.K., T. Miyashita, B. Setlow, K.D. Marjon, O. Steward, J.F. Guzowski, and J.L. McGaugh, *Memory-influencing intra-basolateral amygdala drug infusions modulate expression of Arc protein in the hippocampus*. Proc Natl Acad Sci U S A, 2005. **102**(30): p. 10718-23.
111. Guzowski, J.F., G.L. Lyford, G.D. Stevenson, F.P. Houston, J.L. McGaugh, P.F. Worley, and C.A. Barnes, *Inhibition of activity-dependent arc protein expression in the rat hippocampus impairs the maintenance of long-term potentiation and the consolidation of long-term memory*. J Neurosci, 2000. **20**(11): p. 3993-4001.
112. Messaoudi, E., T. Kanhema, J. Soule, A. Tiron, G. Dagyte, B. da Silva, and C.R. Bramham, *Sustained Arc/Arg3.1 synthesis controls long-term potentiation consolidation through regulation of local actin polymerization in the dentate gyrus in vivo*. J Neurosci, 2007. **27**(39): p. 10445-55.
113. Guzowski, J.F., T. Miyashita, M.K. Chawla, J. Sanderson, L.I. Maes, F.P. Houston, P. Lipa, B.L. McNaughton, P.F. Worley, and C.A. Barnes, *Recent behavioral history modifies coupling between cell activity and Arc gene transcription in hippocampal CA1 neurons*. Proc Natl Acad Sci U S A, 2006. **103**(4): p. 1077-82.
114. Carpenter-Hyland, E.P., T.K. Plummer, A. Vazdarjanova, and D.T. Blake, *Arc expression and neuroplasticity in primary auditory cortex during initial learning are inversely related to neural activity*. Proc Natl Acad Sci U S A, 2010. **107**(33): p. 14828-32.
115. Renwick, A.G., *The disposition of saccharin in animals and man--a review*. Food Chem Toxicol, 1985. **23**(4-5): p. 429-35.

116. Renwick, A.G., *The metabolism of intense sweeteners*. Xenobiotica, 1986. **16**(10-11): p. 1057-71.
117. Sclafani, A. and J.W. Nissenbaum, *On the role of the mouth and gut in the control of saccharin and sugar intake: a reexamination of the sham-feeding preparation*. Brain Res Bull, 1985. **14**(6): p. 569-76.
118. Mook, D.G., C.A. Bryner, D.L. Rainey, and C.L. Wall, *Release of feeding by the sweet tasted in rats: oropharyngeal satiety*. Appetite, 1980. **1**: p. 299-315.
119. Byard, J.L. and L. Goldberg, *The metabolism of saccharin in laboratory animals*. Food Cosmet Toxicol, 1973. **11**(3): p. 391-402.
120. Packard, M.G. and J.L. McGaugh, *Inactivation of hippocampus or caudate nucleus with lidocaine differentially affects expression of place and response learning*. Neurobiol Learn Mem, 1996. **65**(1): p. 65-72.
121. Guzowski, J.F., B. Setlow, E.K. Wagner, and J.L. McGaugh, *Experience-dependent gene expression in the rat hippocampus after spatial learning: a comparison of the immediate-early genes Arc, c-fos, and zif268*. J Neurosci, 2001. **21**(14): p. 5089-98.
122. Kelly, M.P. and S.A. Deadwyler, *Acquisition of a novel behavior induces higher levels of Arc mRNA than does overtrained performance*. Neuroscience, 2002. **110**(4): p. 617-26.
123. Kelly, M.P. and S.A. Deadwyler, *Experience-dependent regulation of the immediate-early gene arc differs across brain regions*. J Neurosci, 2003. **23**(16): p. 6443-51.
124. Gasbarri, A., A. Pompili, M.G. Packard, and C. Tomaz, *Habit learning and memory in mammals: behavioral and neural characteristics*. Neurobiol Learn Mem, 2014. **114**: p. 198-208.
125. Bloomer, W.A., H.M. VanDongen, and A.M. VanDongen, *Arc/Arg3.1 translation is controlled by convergent N-methyl-D-aspartate and Gs-coupled receptor signaling pathways*. J Biol Chem, 2008. **283**(1): p. 582-92.
126. Chia, C. and T. Otto, *Hippocampal Arc (Arg3.1) expression is induced by memory recall and required for memory reconsolidation in trace fear conditioning*. Neurobiol Learn Mem, 2013. **106**: p. 48-55.
127. Czerniawski, J., F. Ree, C. Chia, K. Ramamoorthi, Y. Kumata, and T.A. Otto, *The importance of having Arc: expression of the immediate-early gene Arc is required for hippocampus-dependent fear conditioning and blocked by NMDA receptor antagonism*. J Neurosci, 2011. **31**(31): p. 11200-7.
128. Chinnakkaruppan, A., M.E. Wintzer, T.J. McHugh, and K. Rosenblum, *Differential contribution of hippocampal subfields to components of associative taste learning*. J Neurosci, 2014. **34**(33): p. 11007-15.
129. Darling, J.N., A.P. Ross, T.J. Bartness, and M.B. Parent, *Predicting the effects of a high-energy diet on fatty liver and hippocampal-dependent memory in male rats*. Obesity (Silver Spring), 2013. **21**(5): p. 910-7.

130. Beilharz, J.E., J. Maniam, and M.J. Morris, *Short exposure to a diet rich in both fat and sugar or sugar alone impairs place, but not object recognition memory in rats*. Brain Behav Immun, 2014. **37**: p. 134-41.
131. Erion, J.R., M. Wosiski-Kuhn, A. Dey, S. Hao, C.L. Davis, N.K. Pollock, and A.M. Stranahan, *Obesity elicits interleukin 1-mediated deficits in hippocampal synaptic plasticity*. J Neurosci, 2014. **34**(7): p. 2618-31.
132. Pathan, A.R., A.B. Gaikwad, B. Viswanad, and P. Ramarao, *Rosiglitazone attenuates the cognitive deficits induced by high fat diet feeding in rats*. Eur J Pharmacol, 2008. **589**(1-3): p. 176-9.
133. Ross, A.P., T.J. Bartness, J.G. Mielke, and M.B. Parent, *A high fructose diet impairs spatial memory in male rats*. Neurobiol Learn Mem, 2009. **92**(3): p. 410-6.
134. Ross, A.P., E.C. Bruggeman, A.W. Kasumu, J.G. Mielke, and M.B. Parent, *Non-alcoholic fatty liver disease impairs hippocampal-dependent memory in male rats*. Physiol Behav, 2012. **106**(2): p. 133-41.
135. Cheke, L.G., J.S. Simons, and N.S. Clayton, *Higher BMI is Associated with Episodic Memory Deficits in Young Adults*. Q J Exp Psychol (Hove), 2015: p. 1-25.
136. Cherbuin, N., K. Sargent-Cox, M. Fraser, P. Sachdev, and K.J. Anstey, *Being overweight is associated with hippocampal atrophy: the PATH Through Life Study*. Int J Obes (Lond), 2015. **39**(10): p. 1509-14.
137. Francis, H.M. and R.J. Stevenson, *Higher reported saturated fat and refined sugar intake is associated with reduced hippocampal-dependent memory and sensitivity to interoceptive signals*. Behav Neurosci, 2011. **125**(6): p. 943-55.
138. Davidson, T.L., S.E. Kanoski, E.K. Walls, and L.E. Jarrard, *Memory inhibition and energy regulation*. Physiol Behav, 2005. **86**(5): p. 731-46.
139. Davidson, T.L., C.H. Sample, and S.E. Swithers, *An application of Pavlovian principles to the problems of obesity and cognitive decline*. Neurobiol Learn Mem, 2014. **108**: p. 172-84.
140. Kanoski, S.E. and T.L. Davidson, *Western diet consumption and cognitive impairment: links to hippocampal dysfunction and obesity*. Physiol Behav, 2011. **103**(1): p. 59-68.
141. Benedict, C., W. Kern, B. Schultes, J. Born, and M. Hallschmid, *Differential sensitivity of men and women to anorexigenic and memory-improving effects of intranasal insulin*. J Clin Endocrinol Metab, 2008. **93**(4): p. 1339-44.
142. Forloni, G., G. Fisone, A. Guaitani, H. Ladinsky, and S. Consolo, *Role of the hippocampus in the sex-dependent regulation of eating behavior: studies with kainic acid*. Physiol Behav, 1986. **38**(3): p. 321-6.
143. Hwang, L.L., C.H. Wang, T.L. Li, S.D. Chang, L.C. Lin, C.P. Chen, C.T. Chen, K.C. Liang, I.K. Ho, W.S. Yang, and L.C. Chiou, *Sex differences in high-fat diet-induced obesity, metabolic alterations and learning, and synaptic plasticity deficits in mice*. Obesity (Silver Spring), 2010. **18**(3): p. 463-9.

144. Yin, B. and W.H. Meck, *Comparison of interval timing behaviour in mice following dorsal or ventral hippocampal lesions with mice having delta-opioid receptor gene deletion*. Philos Trans R Soc Lond B Biol Sci, 2014. **369**(1637): p. 20120466.
145. Yoon, T., L.K. Graham, and J.J. Kim, *Hippocampal lesion effects on occasion setting by contextual and discrete stimuli*. Neurobiol Learn Mem, 2011. **95**(2): p. 176-84.
146. Hargrave, S.L., S. Jones, and T.L. Davidson, *The Outward Spiral: A vicious cycle model of obesity and cognitive dysfunction*. Curr Opin Behav Sci, 2016. **9**: p. 40-46.
147. Hock, B.J., Jr. and M.D. Bunsey, *Differential effects of dorsal and ventral hippocampal lesions*. J Neurosci, 1998. **18**(17): p. 7027-32.
148. Hsu, T.M., J.D. Hahn, V.R. Konanur, A. Lam, and S.E. Kanoski, *Hippocampal GLP-1 receptors influence food intake, meal size, and effort-based responding for food through volume transmission*. Neuropsychopharmacology, 2015. **40**(2): p. 327-37.
149. Kanoski, S.E., M.R. Hayes, H.S. Greenwald, S.M. Fortin, C.A. Gianessi, J.R. Gilbert, and H.J. Grill, *Hippocampal leptin signaling reduces food intake and modulates food-related memory processing*. Neuropsychopharmacology, 2011. **36**(9): p. 1859-70.
150. Kanoski, S.E., S.M. Fortin, K.M. Ricks, and H.J. Grill, *Ghrelin signaling in the ventral hippocampus stimulates learned and motivational aspects of feeding via PI3K-Akt signaling*. Biol Psychiatry, 2013. **73**(9): p. 915-23.
151. Hannapel, R.C. and M.B. Parent, *Ventral hippocampal neurons influence meal onset and meal frequency*, in *Annual Meeting of the Society for Neuroscience*. 2014: Washington, DC.
152. Amaral, D.G. and M.P. Witter, *The three-dimensional organization of the hippocampal formation: a review of anatomical data*. Neuroscience, 1989. **31**(3): p. 571-91.
153. Ishizuka, N., J. Weber, and D.G. Amaral, *Organization of intrahippocampal projections originating from CA3 pyramidal cells in the rat*. J Comp Neurol, 1990. **295**(4): p. 580-623.
154. Tamamaki, N., K. Abe, and Y. Nojyo, *Three-dimensional analysis of the whole axonal arbors originating from single CA2 pyramidal neurons in the rat hippocampus with the aid of a computer graphic technique*. Brain Res, 1988. **452**(1-2): p. 255-72.
155. Tamamaki, N., K. Watanabe, and Y. Nojyo, *A whole image of the hippocampal pyramidal neuron revealed by intracellular pressure-injection of horseradish peroxidase*. Brain Res, 1984. **307**(1-2): p. 336-40.
156. Kishi, T., T. Tsumori, K. Ono, S. Yokota, H. Ishino, and Y. Yasui, *Topographical organization of projections from the subiculum to the hypothalamus in the rat*. J Comp Neurol, 2000. **419**(2): p. 205-22.
157. Walaas, I. and F. Fonnum, *Biochemical evidence for glutamate as a transmitter in hippocampal efferents to the basal forebrain and hypothalamus in the rat brain*. Neuroscience, 1980. **5**(10): p. 1691-8.