Behavioural Brain Research 199 (2009) 32–42

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Review

Basal ganglia contributions to adaptive navigation

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ARTICLE INFO

Article history:
Received 10 June 2008
Received in revised form 6 November 2008
Accepted 8 November 2008
Available online 14 November 2008

Keywords:
Spatial learning
Striatum
Hippocampus
Context
Reinforcement Learning
Dopamine
Adaptive navigation

ABSTRACT

The striatum has long been considered to be selectively important for nondeclarative, procedural types of memory. This stands in contrast with spatial context processing that is typically attributed to hippocampus. Neurophysiological evidence from studies of the neural mechanisms of adaptive navigation reveals that distinct neural systems such as the striatum and hippocampus continuously process task relevant information regardless of the current cognitive strategy. For example, both striatal and hippocampal neural representations reflect spatial location, directional heading, reward, and egocentric movement features of a test situation in an experience-dependent way, and independent of task demands. Thus, continual parallel processing across memory systems may be the norm rather than the exception. It is suggested that neuromodulators, such as dopamine, may serve to differentially regulate learning-induced neural plasticity mechanisms within these memory systems such that the most successful form of neural processing exerts the strongest control over response selection functions. In this way, dopamine may serve to optimize behavioral choices in the face of changing environmental demands during navigation.

Contents

1. Introduction

Basal ganglia structures are commonly viewed in terms of their contributions to the control or selection of voluntary behavioral acts. The profound motor impairments following its clinical or experimental disruption likely masked for many years the possibility that a critical basal ganglia function is to facilitate learning and memory. In fact, in the 1960s and 1970s, basal ganglia lesions were often included as an experimental control group to demonstrate the selective effects of limbic system lesions. While limbic system lesions produced selective memory impairments, striatal (STR) lesions produced a qualitatively different type of memory dysfunction. Emerging evidence from human clinical and animal work, as well as computational models, suggested that in contrast to limbic mediation of episodic, declarative, contextual and/or spatial memories, STR is essential for habit or response learning [39,57,94].

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0166-4328/$ – see front matter. Published by Elsevier B.V.
doi:10.1016/j.bbr.2008.11.014

More specifically, hippocampus (HPC) is critical for rapidly creating flexible memory-guided stimulus associations. In contrast, STR appears specialized for a slower form of learning that is ideally suited for linking reinforcement outcomes with specific stimuli or responses. This seemingly straightforward distinction, however, proved to be an oversimplification. Re-evaluations of the behavioral deficits of patients with basal ganglia dysfunction reveal significant and striking cognitive deficits of the sort expected from not only STR damage, but also frontal cortex lesions [15,16]. Such findings have led to the suggestion that the frontal cortex and STR work together to subserve 'executive' functions [41]. STR may also work in conjunction with HPC since a number of rodent studies show spatial learning deficits following STR lesions [22] and primate and rodent neurophysiological data show context-dependent firing of STR neurons [24,33,48,49,56,78,106,116]. The basal ganglia, then, likely contribute in complex ways to different types of memory functions. As a result, a significant challenge is to understand not only specific memory-related computations supported by intrastriatal circuitry, but also how such computations inform and influence connected memory systems of the brain.

2. Both STR and HPC contribute to experience-dependent navigation

Our approach to understanding a basal ganglia contribution to learning and memory is based on the premise that the flexible memory functions of especially mammals reflect the coadaptation of multiple brains areas across evolutionary time. Thus our goal has been to evaluate STR contributions to learning by using a complex behavioral paradigm (goal-directed spatial navigation) that allows one to assess not only egocentric movement responses of neurons, but also neural codes not directly related to an animal's movement per se, such as reward, spatial context, or working memory. This approach is appealing not only because it reflects real world learning challenges, but it also provides opportunities to examine dynamic features of neural function that are otherwise not afforded by more simple behavioral paradigms. Fig. 1 presents a neural systems architecture that may underlie adaptive, vision-based, rodent navigation [40,73,75,76,82]. This model reflects the findings of an extensive body of neurobiological and behavioral research on the neural codes across cortical, limbic and basal ganglia systems as animals explore and learn about their environment. These neural systems weave together important components of adaptive navigation such as: (1) input of the relevant external and internal sensory information, (2) modulation of sensory processing by internal state information (i.e. motivational factors, memory), (3) translation of the integrated sensory contextual and motivational information into behavioral strategies that guide subsequent behavior, and (4) an evaluation of the outcome of actions that in turn updates memory systems. Note that these do not necessarily follow in linear fashion. Rather, each component can impact the function of other components via a number of processing loops. Detailed discussion of the relationship between HPC and neocortex during spatial context analysis for the purpose of updating/retrieving remote memories can be found in Mizumori et al. [80]. What follows is an account of STR contributions to experience-dependent navigation, and how this influence may be impacted by HPC context analysis.

2.1. STR and adaptive navigation

It was hypothesized that STR assists the navigational system by helping to define future actions that are appropriate for the current context, regardless of whether the specific task to be learned is stimulus–response in nature or involves the more flexible processing of context learning [77,78]. The STR does so by engaging Reinforcement Learning algorithms (e.g. [52,104,127]) within a response reference system that compares the expected success of a learned behavior with the actual success experienced by the animal. In principle, such a function is important for many forms of learning. Stimulus–response learning, in particular, requires that an association be made between a well-defined, current external stimulus (or motor act) and its immediate consequence. Since, in theory, response flexibility is not required, and is in fact detrimental, for good performance in stimulus–response tasks, the most parsimonious way to accomplish such learning is via direct, somatotopically organized lateral dorsal STR connections with motor and somatosensory cortex [18]. As a result, learned responses seem relatively inflexible, habitual in appearance (because responses can be elicited with short latency), and slow to learn (because erroneous responses are slow to correct).

A response reference system function is also useful for context learning. Indeed, behavioral studies also show an important role for STR in adaptive navigation. STR lesions produce selective spatial deficits, especially during new learning [2,27,32,98], and this may reflect a specialization for spatial processing by ventral and the dorsomedial subareas of STR. The anatomical separation of what appears as different STR learning functions is likely related to the different patterns of afferent and efferent connections found in these areas, rather than differences in local neurocomputations. For example, the ventral and dorsomedial STR receives extensive convergent input from multiple sensory and association areas of neocortex and the limbic system [67], while lateral STR has a distinct topographic pattern of connections with sensory and motor areas of neocortex [26]. Computationally speaking, the topographically constrained pattern of inputs into lateral STR places a restriction on the number of combinatorial patterns that can be produced, resulting in well-defined stimulus–response relationships. In contrast, the highly convergent input to ventral and dorsomedial STR results in a high degree of combinatorial power to produce the flexible (or contextual) processing needed to evaluate the reinforcement outcomes of behavior in ever changing spatial contexts [77]. Although there is a clear and distinct regionally specific organization to the STR afferent patterns, intrastriatal computations appear relatively consistent across the structure. That is, the distribution of STR GABAergic medium spiny projection neurons and cholinergic interneurons is rather homogeneous across the lateral and medial STR. Further, all medium spiny neurons possess a bistable membrane property that permits selective filtering of incoming information [123,132]. The synaptic efficiency of spiny neurons is modulated by dopamine signals that are thought to reflect current reinforcement conditions [52,110,113,114]. Thus, the different regions within STR may perform similar response reference system computations, but on distinct types of information.

The response reference theory of STR function requires that a variety of types of information is represented in STR. Indeed, in behaving animals, dorsal and ventral STR neurons exhibit changes in firing relative to specific egocentric movements (e.g. right turns, forward movement, etc.), reward acquisition, as well as an animal's location and directional heading within an environment (for examples, see Fig. 2; refs. [58,77,78,130]). STR place fields tend to be larger than those of HPC place cells, yet their fields are similar in terms of reliability and in-field firing rates when tested in a familiar environment. As observed for head direction cells recorded in other brain areas, STR head direction cells increase firing (by as much as ten times the baseline rate) when a rat's head is aligned with certain orientations in space, regardless of the location of the animal in a fixed environment. STR head direction cells show many of the same features as place cells in that the preferred orientations can be shown to shift by an amount that corresponds with a shift in the visual environment, or the preference can shift randomly if

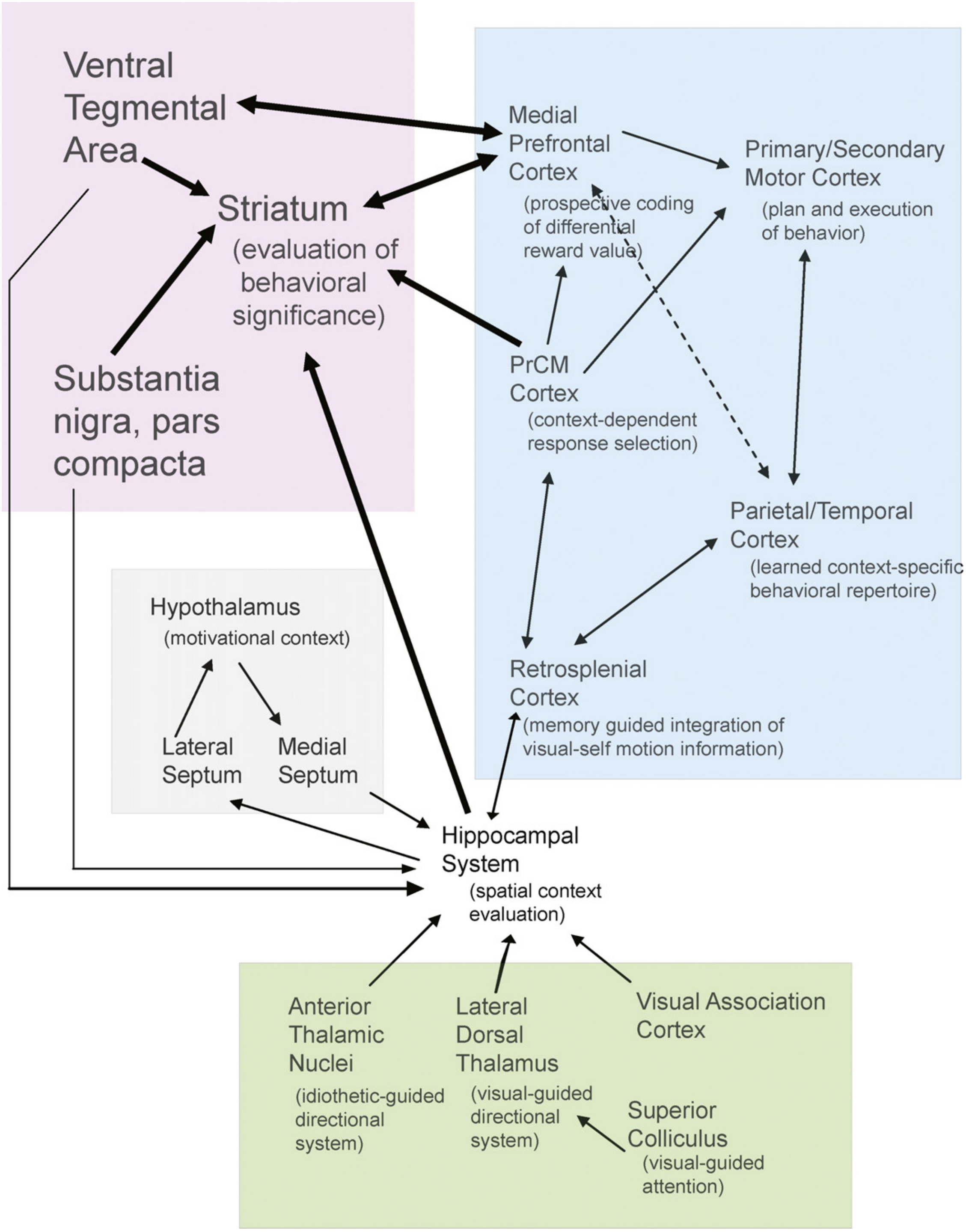

Fig. 1. Schematic illustration of the neural circuitry underlying an animal's ability to navigate effectively in familiar and changing environmental conditions. Using visual navigation as a model, it can be seen that both geniculo-striatal and tecto-cortical visual streams are in a position to inform multimodal association areas of the brain (e.g. hippocampus) about salient spatial stimuli. As explained in more detail in text, hippocampus is postulated to then determine the extent to which the spatial context is different from what is expected based on past memories (via retrosplenial cortex input). Also the input about the current motivational state derives from hypothalamo-septohippocampal circuitry, and this may bias the result of the context comparison. When context changes are detected by hippocampus, output (ultimately) to parietal and frontal cortices prepare an animal to execute the appropriate behavioral responses. There are many opportunities for striatum to be informed of changes in context (e.g. via ventral subicular, PrCM (medial precentral cortex), and prefrontal output to striatum). Neural signals that reflect a context change may increase the precision with which striatal circuitry evaluates whether the expected consequences of specific behavioral responses are achieved. Detected errors in behavior (i.e. unexpected absence of reward) may differentially impact subsequent striatal and hippocampal processing in such a way that one type of processing is strengthened in its control over behavior, while the other form of processing is weakened. In this way, with repeated trials, animals learn to adopt a preferred (i.e. most effective) cognitive strategy to solve tasks.

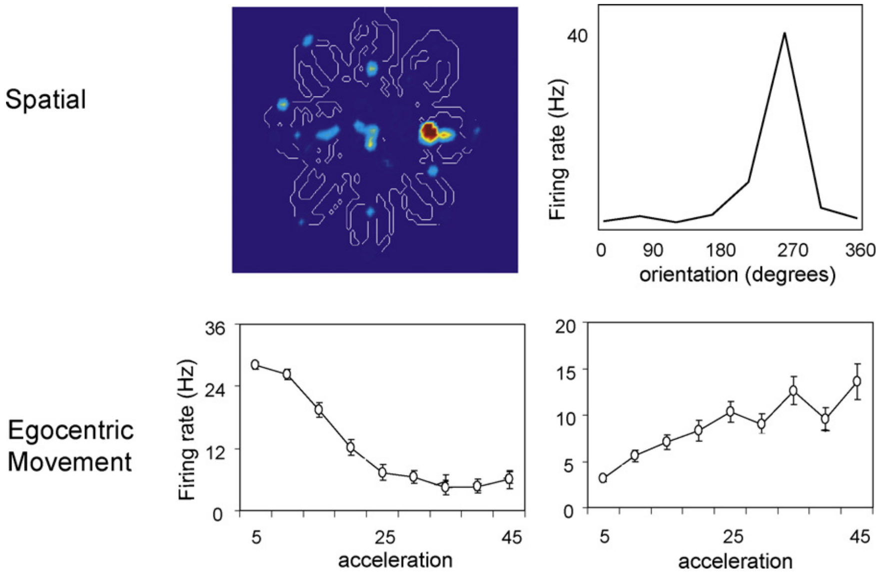

Fig. 2. (Top) Examples of spatial correlates of striatal neural discharge. On the left, a color density plot illustrates location selectivity activity that has been observed for many striatal neurons (white lines outline the area of the maze sampled by the rat). The right panel illustrates a tuning curve for a cell that selectively fired when an animal faced one direction in space. Such head direction cells tend to be located in the dorsomedial sector of dorsal striatum. (Bottom) Examples of striatal neurons whose firing was negatively (left) or positively (right) correlated with the acceleration of the rat performing a plus maze task.

the visual cues are changed sufficiently [78]. Thus, these cells are thought to signal context-dependent directional orientation, and not orientation relative to geomagnetic conditions or to a specific visual cue.

Strikingly similar to HPC recordings from animals tested in the same behavioral conditions (described below), all of the behaviorally (i.e. egocentric movement) correlated STR neuron types exhibit *partial reorganization* after a change in spatial context. That is, only a portion of the movement-correlated cells shows a change in the relationship between cell firing and movement after alterations in environmental context. This implies that a portion of STR representations is driven by active memory circuitry, i.e. they reflect behavioral conditions that have been associated with specific sensory environments. Other STR movement-correlated cells seem guided by the ongoing behaviors regardless of context. In sum, then, the particular combination of neural representations found in STR (movement, reward, place, orientation, etc.), the finding that all of these representation types appear context-dependent [77,78,136], and the finding of partial reorganization after context changes are consistent with the view that STR evaluates the consequences of behaviors in a context-dependent way.

2.2. HPC and adaptive navigation

HPC may serve as a *spatial context discriminator* that determines the extent to which the expected definition of a context matches the one currently being experienced [64,72,73,129]. There is now strong evidence that HPC processes contextual information (e.g. refs. [7,50]) and that it is particularly responsive to a variety of changes in contextual-defining features (reviewed in ref. [72]). This is consistent with hypotheses that HPC is necessary for the flexible use of conjunctive, sequential, relational, and spatial information since each of these functions is fundamentally important for the detection of changes in context. Such a novelty detection function is vital for accurate performance of a variety of learning tasks (i.e., navigation-based learning, instrumental conditioning, classical conditioning). For example, Smith and Mizumori [120] showed that HPC neurons develop context-specific responses, but only when rats were required to discriminate contexts. Differential neural responses were not observed when rats were allowed to randomly forage for the same amount of time. Also Manns et al. [65] showed that relative to match trials in an odor cue or object recognition task, CA1 neurons preferentially discharged when animals experienced a nonmatch situation in these same tasks. Cell firing tended to occur during the 'encoding phase' and not 'retrieval phase' of the ongoing theta rhythm (see review in ref. [47]). Thus, detection of a nonmatch situation changes the relationship between cell discharge and the local theta rhythm such that encoding functions are enhanced. Detection of matches, on the other hand, does not cause changes in the HPC neural activity profile, resulting in efferent messages that continue to retrieve/utilize the currently active memory network [73]. Consistent with these findings, the detection of novelty engages exploratory activity, which in turn is thought to trigger cellular processes that facilitate new learning at potentially important times [97].

Considering the multidimensional and complex nature of HPC neural responses to context changes [72,80], it appears that there are (at least) three qualitatively distinct types of influences on HPC neural codes that occur automatically regardless of the specific task demands: memory (i.e. past experience), spatial, and temporal. This proposal is based in part on suggestions that HPC-dependent memory involves associations of spatial and temporal features (e.g. [9,10,23,79,84,92,93,100]). At slight variance with these proposals, however, Mizumori et al. [80] suggest that the default mode of HPC processing is to continually integrate memory-guided perceptions of sensory, movement, and motivational information, or memory (M), within a spatial (S) reference framework as a function of time (T). Continual processing is essential in order for HPC to rapidly detect potentially important novel or changed events. Specifically, we emphasize that HPC receives highly preprocessed M information that becomes spatially and temporally organized. This type of integration is proposed to occur according to a hierarchically organized scheme that considers M, S, and T information as fundamental inputs to place cells which in turn combine to form networks that distinguish expected and actual contextual information. As a result, during unrestrained navigation, place fields appear as neural representations of salient sensory, behavioral, and internal context-defining information that have strong spatial and temporal features.

The present context discrimination model of HPC processing [80] considers S information as a form of organization rather than specific environmental features that individual cells discriminate. The preponderance of place fields regardless of the cognitive strategy required (e.g. ref. [24]) suggests that HPC is naturally predisposed to automatically organize contextual information spatially during active navigation. Since place cell experiments require (usually voluntary) movement through an environment, translocation signals may be directed through the medial entorhinal cortex such that networks of spatial *grid cells* become activated [44,60,108]. Grid cells selectively discharge when rats traverse positions that coincide with the vertices of a regularly tessellating grid of environmental space. The *grid fields* appear to represent conjunctions of location, direction, and movement information within a two-dimensional coordinate representation of the environment. The path integration based coordinate system of the entorhinal cortex may pass on to HPC a spatial framework [68] within which context-specific M and T information is organized. This can account for the common finding of location-selective, context-dependent firing by HPC neurons.

The notion of exploration-induced spatial organization of HPC representations is consistent with the finding that HPC place fields are observed upon first exposure to a new environment [30,46,66,86,90,133]. Also, compared to passive movement conditions in which rats are made to go through a place field either by being held by the experimenter or by being placed on a moveable robotic device, active and unrestrained movement seems to generate more selective and reliable place fields [29,37,122]. Furthermore, place cells fire more robustly when rats run faster in a given location (i.e. running in a running wheel; ref. [19]). Thus, a computational framework that incorporates the conjunction of movement and spatial information should have the effect of producing sharper neural images of spatial context representations, at least in dorsal HPC and likely in other brain areas as well. A sharper code should relay more specific spatial information to intrinsic and extrinsic computational circuits. The finding that unrestrained movement produced sharper codes than passive movement suggests that purposeful behavioral responses have more meaning for, and impact on, place fields than random movement of the animal. This may be one way in which learned M information (in particular information about the learned relevance of specific behavioral responses) helps to define a spatial context code. Accordingly, we have recently demonstrated that more specific place fields predict better spatial memory abilities [99].

2.3. *Optimal navigation benefits from combined HPC and STR processing*

Evidence supports the view, then, that both STR and HPC normally contribute to spatial context learning. Presumably HPC updates or transforms cortical representations according to detected changes in the expected spatial context, while STR updates cortical representations based on the most recent reinforcement consequences of previously learned (and at least initially context-dependent) sensory/motor associations. In this way HPC allows animals to continuously, and automatically, organize sensory information in different ways, while (medial) STR allows animals to quickly update behavioral strategies as environmental demands change.

The above conceptualization of STR and HPC functions is consistent with theoretical accounts that suggest learning is error (or mismatch) driven [45,52,63,72,104,115]. Detection of mismatches between expected and experienced reinforcements (for STR) or mismatches between expected and experienced sensory environments (for HPC) results in neural signals that are different from signals that occur when matches are found. As a result, the nature of the output signal can either strengthen existing patterns of memory-related neural activity, or cause a shift in the stable state, resulting in a different but related activity landscape [52,93]. These STR and HPC evaluations should occur continuously (even during asymptotic performance) in order to allow rapid adaptation to unexpected changes in environmental conditions [72,73].

The proposed functional distinction between STR and HPC is consistent with findings that only STR lesions produce impairments in stimulus–response or egocentric learning. Both forms of response learning require an association between a well-defined motor act, or current external stimulus, and the immediate consequence. Response learning can take advantage of the direct connections of lateral STR with motor and somatosensory cortices. Since HPC does not have such direct connections with motor or somatosensory cortex, it, is not normally a central contributor to response learning. It is possible however that with extend time after STR damage, HPC systems may be recruited to mediate previously STR functions since Parkinson's patients initially show normal probabilistic learning that is correlated with medial temporal lobe activation [83].

Goal-directed navigation, on the other hand, can take place quickly because *both* STR and HPC reference systems are engaged. To explain findings that HPC lesions, but not STR lesions, result in context learning deficits, the following should be noted. First, STR lesions in rodents that do not impact context learning tend to be in either central or lateral dorsal STR, leaving the medial STR essentially intact. Selective medial STR lesions produce spatial learning deficits [22], and medial STR preferentially receives limbic input [55]. Medial and lateral STR also possess different NMDA systems, suggesting different mechanisms of neuroplasticity. Second, there are two routes by which HPC information may impact behavior in an experience-dependent way [75], one initially involving STR circuitry and another passing through cortical circuitry. Thus, even if the STR route is compromised, spatial performance can improve by utilizing HPC-cortical pathways. Since the spatial context comparator function of HPC uniquely contributes to spatial or context learning, one often finds deficits in such learning following lesions of only HPC.

Consistent with the working theory described above, context-sensitive place [89,91] – and movement [73,74]-specific representations are found in both HPC and STR regardless of task strategy, and the qualitative nature of STR and HPC responses to changes in strategy is essentially indistinguishable. The findings that similar information is represented by these brain structures, and that as a population, these cells were sensitive to the same environmental manipulations, presented an initial challenge for the view that STR and HPC mediate different forms of learning. However, the functional specializations attributed to these areas may reflect intrinsic local circuits that use similar types of information for different neurocomputational objectives. An analogous explanation was used to account for differential processing by HPC and neocortex [93]: It was concluded that distinct processing systems of the brain vary by learning rate and level of overall activity, and not solely the nature of the information coded. Indeed, although STR and HPC place and movement cells are found regardless of task strategy, HPC place cells respond similarly to context change *regardless of cognitive strategy*, while egocentric movement correlates of STR and HPC neurons are context-dependent during place, but not response, task performance. In addition, when making comparisons between HPC and STR contributions to learning, it is important to consider the strong likelihood that learning results from the differential regulation of temporally coordinated neural activity: local field potential evidence shows that theta oscillations in especially medial STR circuits are entrained to the HPC theta rhythm during spatial task performance [5] and during procedural learning [20].

2.4. *HPC–Neocortical–STR interactions during navigation*

HPC output to posterior neocortical regions may facilitate the selection of specific appropriate cognitive and behavioral strategies to be used by an animal (e.g. refs. [43,68,126]). Retrosplenial cortex, in particular, seems important for integrating current self motion and sensory information within existing memory networks that in turn determine the appropriate adaptive strategy [17]. From retrosplenial cortex, updated information may be passed on to STR [105], or to premotor areas of cortex [102]. An important relay in the latter pathway may include the medial precentral nucleus, or PrCm (also referred to as medial agranular cortex; refs. [101,103]). Indeed, reversible inactivation of the retrosplenial cortex produces significant alteration of PrCm neural correlates [76].

The direct projection from PrCm to STR [137] could provide HPC spatial context information to STR circuitry for use in its evaluation of the reinforcement outcomes of current behaviors (e.g. refs. [77,115,127]). Such an analysis should ultimately facilitate new learning as well as maintain asymptotic performance. In order for this to happen, there should be continual feedback from STR to cortex regarding the effectiveness of the current behavioral/cognitive strategy. If the PrCm signal to STR is one that indicates that the context has changed (or is not as expected), STR may become primed for maximal sensitivity to impending input about the consequences of behaviors to allow animals to quickly and maximally respond to changes in a familiar environment, or to adapt in new situations. This may be reflected in greater dopamine cell responsiveness (a topic discussed in more detail below). For situations in which the strategy remains constant (i.e. during asymptotic performance in a static environment), behaviors can be implemented relatively quickly via direct PrCm efferent connection to motor cortex. The PrCm, then, may allow organisms to quickly respond to changes in familiar situations as well as to appear to 'automate' their responses in well-learned, stable situations. Given that dopamine importantly regulates synaptic efficiency in not only STR, but also HPC and frontal cortex, dopamine neurons may play a critical role in orchestrating the relative efficiencies of the many memory-related brain structures discussed thus far such that response selection is optimized for a given context [82].

3. A role for mesolimbic dopamine during goal-directed navigation

3.1. *Dopamine projections to STR and HPC*

VTA (ventral tegmental area) dopamine neurons project to subiculum, CA1 and CA3 regions of both dorsal and ventral HPC, whereas SNc (substantia nigra pars compacta) projects mainly to ventral HPC (Fig. 1) [35,109]. Also, VTA afferents show a paucity of collateralization in its projection patterns, while the SNc afferents are extensively collateralized [1,25]. Thus, VTA may have more specific impact on HPC processing than SNc. VTA or SNc lesions result in a significant reduction in HPC dopamine content [109], and HPC is perhaps the only brain structure known to express mRNA for five types of dopamine receptors [69,128]. VTA projects mainly to ventral STR while SNc projects mainly to dorsal STR [34]. Thus, VTA and SNc are anatomically situated to differentially control STR and HPC output in accordance, perhaps, with task demands (Fig. 3).

3.2. *Dopamine and spatial memory*

Although dopamine has been largely considered to be a central component of the brain's reward system, several lines of evidence indicate that dopamine is also important for detecting either the presence of novel information, or changes in familiar information [63]. Exposure to a novel context has been shown to increase HPC dopamine release [53] which in turn facilitates LTP induction [59,62]. In addition, intraHPC injections of D1 agonists and D2 antagonists improve memory [95,96,131], while 6-OHDA lesions of dopamine input to HPC result in spatial working memory deficits [36]. However, other studies have shown that dopamine manipulations can have effects opposite to those just described [8]. The discrepancy could be due to the fact that some studies focused

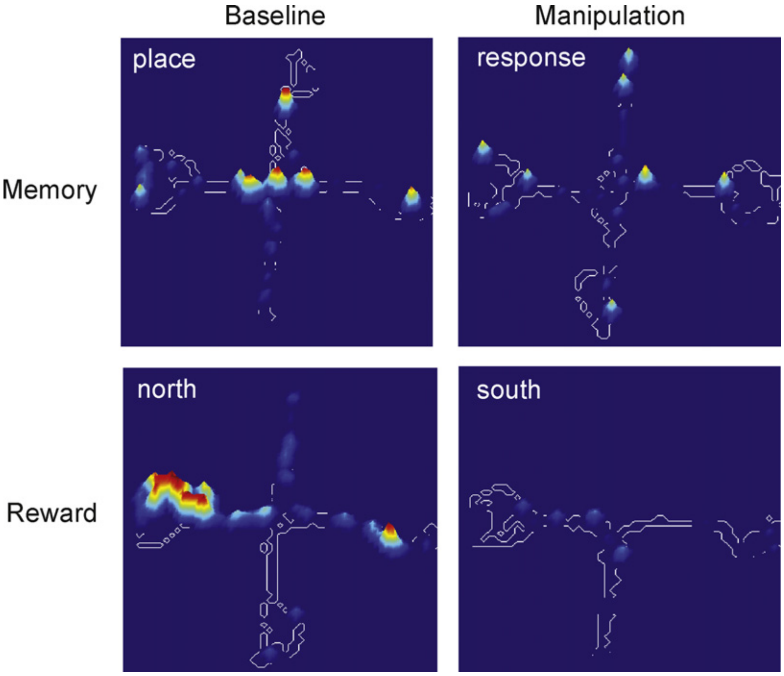

Fig. 3. (Top) An example of a striatal cell that changed its location selective firing when the rat switched from the use of a place strategy to a response strategy to find food reward on a plus maze. Importantly, this cell was recorded in both conditions within a single recording session in which the behavioral, motivational, and sensory conditions were identical. Such a change in strategy presumably reflects changes in the active memory. (Bottom) Another striatal place field, recorded from a different rat, shows changes in location selective firing when the single available reward was moved from the north to the south maze arm.

on the function of dorsal HPC while others focused exclusively on ventral HPC. Indeed, dorsal and ventral HPC are thought to make distinct contributions to learning [77,85].

3.3. *VTA/SNc modulation of HPC and STR neural activity*

VTA stimulation results in either inhibition or facilitation of ventral STR neural activity that had been driven by HPC stimulation [134,135], suggesting that VTA can importantly modulate HPC efferent (NMDA) signals to STR. Dopamine released in STR enhances activation of NMDA receptors [118] which, in turn, increases the likelihood that STR firing will transform from a slow, irregular pattern to a high frequency burst pattern, the latter of which may be important for precise STR-mediated learning or cognitive processing. Since dopamine signaling is slow (i.e. G protein mediated [117]), the altered neural function can persist beyond the period of NMDA activation. Depending upon the receptor subtype activated, increases or decreases in adenylate cyclase are found. Therefore, dopamine could result in increases [31] or decreases in neuronal firing [4], as well as changes in the oscillatory pattern of STR discharge [4,21,107]. As a result, it is the overall temporal pattern and spatial distribution of elevated and reduced cell responses that determine the nature of the population code received by efferent structures. Dopamine may contribute to reinforcement evaluation by stabilizing STR neural representations such that a reliable signal is passed on to downstream brain areas. Consistent with this hypothesis, the stability of the directional selectivity of STR head direction signals has been shown to be disrupted following injection of a D1 receptor antagonist [38].

Dopamine effects in HPC are multifaceted: they may determine the duration of plasticity in HPC [119] since application of D1 and D2 receptor agonists produces long lasting activation and inhibition, respectively, of CA1 pyramidal neuron firing rate. *In vitro* dopamine application to HPC tissue initially reduces CA1 population responses [3]; this is followed by a potentiated response [6], suggesting short- and long-term effects. One mechanism for dopamine's effects on HPC plasticity is via increased acetylcholine release [70], which in turn may stabilize place representations in new environments [61]. Although dopamine increases the stability of neural representations in both HPC and STR [38], it may have differential effects in terms of its impact on the spatial extent, magnitude, and timing (e.g. onset, duration and conditional control) of the representation relative to behavioral output systems.

3.4. *Behavioral correlates of VTA–SNc neurons*

Recently we found evidence that: (1) putative dopamine cell firing is context-dependent under conditions that result in context-dependent firing by HPC and STR neurons ([81], Gill and Mizumori, submitted), and (2) there is differential regulation of neural function in HPC and STR by dopaminergic systems (e.g. refs. [38,40]). Recent efforts have been aimed at understanding the functional and cellular regulation of dopamine cell firing during learning. Our finding that dopamine neurons are regulated by contextual information during navigation tasks ([38], Puryear and Mizumori, submitted), suggests that dopamine cells are part of a larger context processing loop that allows iterative behavioral adaptation [64].

3.5. *Relevance to STR functions*

Numerous studies show that dopamine neurons increase discharge either during new learning, or when reward contingencies change from what was expected based on past experience [111], leading to the view that dopamine functions as a teacher within the striato-cortical network [52]. Relatedly, dopamine may serve as an enabling device that regulates postsynaptic responses to afferent input [42]. The behavioral similarities observed after PFC and STR lesions, or dopamine manipulation, suggest that basal ganglia and cortex function as an integrated unit that considers reinforcement outcomes within the context of behaviors [11,41,87]. Our model of navigation applies Reinforcement Learning principles to evaluate the outcome of behavioral acts. The temporal difference (TD) learning algorithm [127] has been used to calculate probabilities of reinforcement based on a comparison of past experience with current behavioral responses and subsequent success. The TD model predicts specific changes in neural responses to stimuli during learning. For example, dopamine neural activation should gradually shift to earlier predictors of subsequent reinforcement ([125]; reviewed in ref. [124]). Indeed it was shown that presentation of reward when it was not expected induced robust dopamine firing in monkey performing an operant task. After learning, unexpected reward omission results in significant reduction in dopamine neural activity [51,71,112], indicating a prediction error. New evidence from our laboratory shows for the first time comparable evidence for prediction error signals by putative dopamine cells that were recorded as rats freely navigate a maze to known goal locations (Puryear and Mizumori, submitted; Fig. 4).

Consistent with (and extending) recent propositions by Lisman and Grace [63] and Foster et al. [28], changes in dopamine neural activity should inform STR computational networks of the results of comparisons between expected and current reinforcement contingencies. This computation may be biased by a HPC evaluation of the extent to which the spatial context has changed [82] via a subicular–pedunculopontine–VTA pathway [88]. Indeed, electrophysiological recordings from both HPC and dorsal STR demonstrate that neurons in these regions alter their behavioral correlates in response to changes in the expected, or familiar, reinforcement conditions as well as changes in the surrounding test environment [38,73,82,120,121]. A mismatch detected by STR in terms of expected and experienced rewards during *new* learning should signal animals to engage an alternative behavior or cognitive strategy (i.e. activate a different map) until expectations match current reinforcement conditions. A mismatch detected by STR during performance in a *familiar* environment could signal, the need to adjust, or optimize, the most recent behavior or cognitive strategy (i.e. map) to maintain accurate performance [24,73,82]. In either case, active exploration should be engaged or maintained, respectively. If the outcome of the comparison is that the expected and actual rewards match, then the output message should strengthen currently active memory circuits of the brain.

3.6. *Relevance to HPC functions*

Detection of a context change by HPC can be used to update memory systems, which in turn may signal dopamine neurons to increase phasic dopamine release upon subsequent encounters with reward. The consequent increase in dopamine release (in HPC) seems to increase the duration of neural responses to glutamatergic input [119]. Such an effect could contribute to the increased stabilization of place fields typically observed as rats become accustomed to new environmental conditions [30]. Greater stability of place fields after multiple exposures to a novel environment might be considered to reflect the successful consolidation of new learning about the learned significance of specific locations or environments. In the presence of prediction error signals, the related inhibition of dopamine cell firing could serve to signal cortical memory systems of the unexpected omission of reward, which in turn would update memory systems (resulting in the activation of new maps) that increase new exploratory behaviors. The subsequent activation of the entorhinal grid cell system could make place cells more sensitive to current (rather than expected) sensory

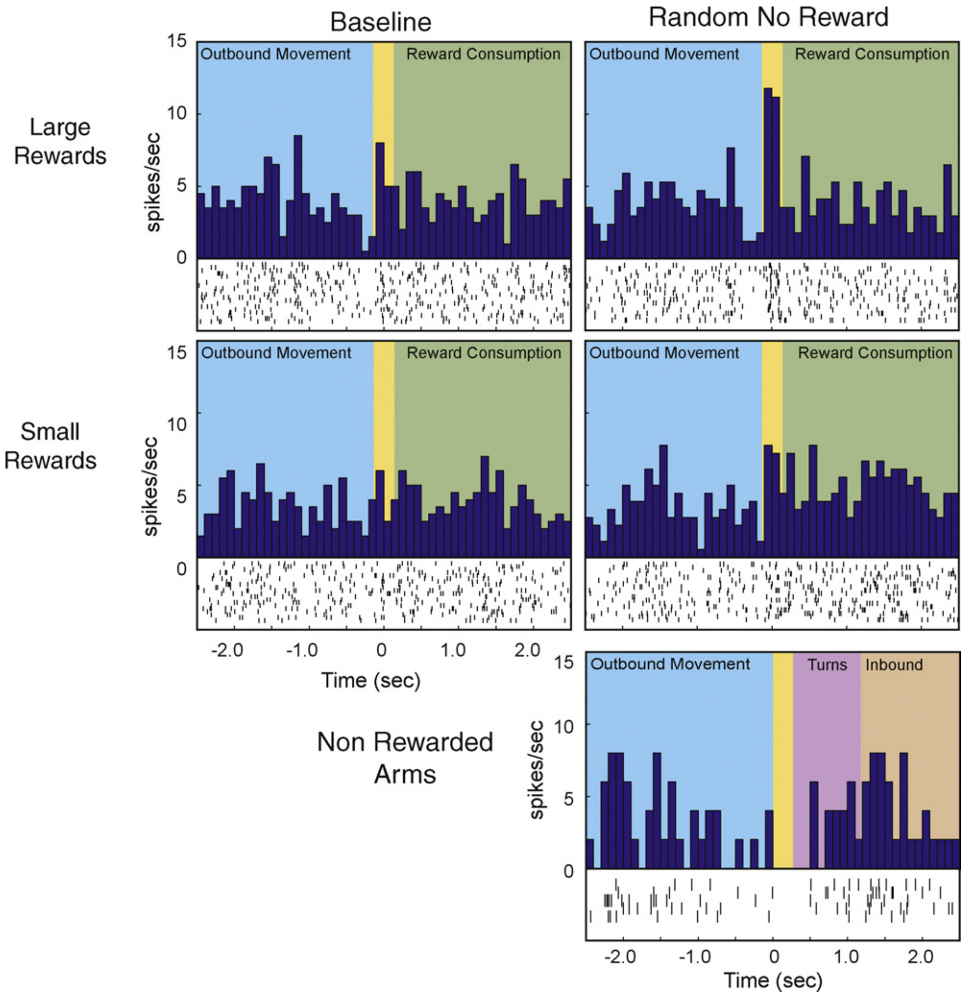

Fig. 4. (Baseline) Illustration of fairly nondiscriminate firing by a VTA neuron when a rat retrieved large or small rewards from consistent locations on a radial maze. During subsequent probe trials in the same recording session, a set of two rewards (one large and one small) was randomly selected (for each trial) to be omitted from locations in which the rat expected rewards. During these RANDOM NO REWARD trials, the same cell developed discriminative firing: it exhibited higher firing when large rewards were encountered. Significant *inhibition* of cell firing was observed when the rat arrived at locations at which the reward was unexpectedly omitted (bottom panel in the right column). This overall pattern is consistent with temporal difference models of dopamine neural function (see text for more details).

input. Such an effect may be facilitated by the decrease in dopamine release in HPC following negative prediction error signals; indeed place fields become less stable in the absence of dopamine (e.g. refs. [38,54]).

4. Concluding remarks

The study of basal ganglia mnemonic function within the context of adaptive navigation has revealed that this neural system is likely an essential part of an extended neural network that underlies this evolutionarily conserved, natural behavior. Observation of similar types of representations across many brain structures and neural systems suggests that there may be a broad, but well orchestrated, level of systems organization that ultimately serves to integrate different types of processing in the service of successful goal-directed navigation. The differences in neural codes across brain areas give clear indications of the computational uniqueness of each neural structure. As an example, one striking type of neural code found in most (if not all) of the brain structures recorded in rats during investigations of navigation is one that reflects some aspect of egocentric movement. Furthermore, within each neural system, movement-correlated cells represent one of the largest categories of functionally correlated cells.

Different interpretations could be offered to account for the parallel coding of egocentric movement. One scenario is that information about the current behavioral state forms an informational base on which to build the local neurocomputational architecture. In this way, the behaviors relevant to a particular association (stimulus–stimulus, or stimulus–reward) or a specific stimulus can not only be encoded, but they can guide the nature of associations in the future. Another scenario relates to the finding that HPC and STR egocentric movement correlates often change if the expected spatial context is changed [136]. This result suggests that the egocentric code is not necessarily a mere reflection of ongoing behavior. It may also reflect a learned association between expected contextual information and the relevant behavior (or aspect of behavior such as velocity). Such an integrated representation could be useful to provide information to the local computational network about the expected behavioral context of a task, a variable known to impact movement-related responses of parietal cortex neurons in primates [12,13,14]). The fact that many brain structures contain such movement codes that are sensitive to changes in the sensory environment suggests that the behavioral context (i.e., the behaviors appropriate to a given situation) in which learning occurs is a fundamental unit of information that is useful for multiple forms of learning.

A common observation across different categories of correlated neurons that were recorded within different neural systems is that changes in context produced only partial reorganization of firing patterns. That is, only a subset of place, movement, and reward-related cells responded to context change while others did not. If context-independent firing reflects expected information based on past experience (e.g. expected spatial contexts, learned responses, or reinforcement outcomes), and if context-dependent neural codes reflect ongoing features of a current situation, then a fundamental operating principle that applies to diverse neural systems could be the engagement in error-driven (match–mismatch) computations. Such a conclusion is consistent with the prediction of computational models of STR and HPC function (e.g. refs. [52,65]). This conclusion is also consistent with the fact that many fields in neuroscience (from hindbrain analysis of sensory information to neocortex mediated 'decision making') employ a match–mismatch rule to interpret their findings. This seems true regardless of the task, species, or brain area under investigation. Perhaps this type of computation has been conserved across evolution because it provides a neural mechanism for a key function that is necessary for survival: novelty detection, a process whereby past experience can modify processing of different forms of incoming information. Novelty detection may be a universal consequence of neural network function, one that emerges from common synaptic plasticity mechanisms that are found in numerous brain areas.

Acknowledgements

The work described in this review was supported by NIMH grant MH58755, and by the countless hours of dedicated effort and stimulating discussions by outstanding students, most recently Oxana Eschenko, Katy Gill, Wayne Pratt, and David Smith.

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