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Contextual Modulation of Behavioral Choice

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Abstract

We review the influence of context on behavioral choice. Context can refer to external (environmental) factors such as the season or presence of predators and it can also refer to the internal or behavioral state of an animal. Usually, animals make decisions in the midst of other ongoing behaviors. We discuss recent findings on the impact of both types of context, focusing on how context gets encoded at the intersection between the sensory and motor systems, emphasizing the role of neuromodulators. We also review recent technological advances that have made feasible the exploration of neural correlates of decision making in freely moving, behaving animals.

Introduction

Repeating the same input to a nervous system can elicit different behavioral responses, depending on the context. When faced with the decision between ordering an iced tea or a hot chocolate, for instance, not only does the choice depend on taste preference but also on whether it is mid-July or mid-December. Context matters. One obvious source of context that can influence behavioral choice is the external environment. Factors such as season, physical environment, and the presence of food/predators/competitors/potential mates all bias behavioral choice. In addition, behavioral choices are influenced by internal states (such as hunger, thirst, reproductive status, and emotional state) and ongoing behavioral states (such as running and flying). Much of the prior research on behavioral choice has used animals either at rest or responding to external stimuli while passively performing simple tasks. However, most decisions in everyday life are made in the context of ongoing, often complex, behaviors. More and more, researchers have been studying behavioral choice in animals engaged in active, ethologically relevant behaviors and finding that behavioral state can modulate the perception of incoming stimuli in a way that affects behavioral choices.

This review will summarize recent findings about the effect of external and internal context on behavioral choice (Figure 1). We emphasize studies that investigated the neural mechanisms for encoding context, and focus on the role of neuromodulators.

Environmental context modulates behavioral choice

Some stimuli, especially when weak or ambiguous, can variably induce one of two or more distinct behaviors. Neural activity in sensory and sensorimotor areas correlated to behavioral choices has been found in a wide variety of nervous systems from primates to invertebrates

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[1,2]. We first review recent studies that addressed how environmental contexts affect behavioral choice.

Seasonal context

As the seasons change, so do such variables as the availability of receptive mates, various types of food, and the presence of migrating or hibernating predators. Seasonal changes are often accompanied by changes in behavior (such as communicative calls) in a variety of species that may be brought on by changes in brain area volume [3-5], neurohormone and neuromodulator levels [6], and even neural wiring of fiber tracts [7].

The activity of individual neurons can also be affected by season. One such example involves the movement detector neurons in the optic lobe of the crab (*Chasmagnathus granulatus*). The activity of these neurons correlates with the strength of escape responses, which is modulated not only by the apparent size of a predator-like stimulus presented to the crab but also by the season; escape responses are weaker in winter when there is a lower risk of predation and when the animal is in a generally lower metabolic state [8].

Physical environment

The physical environment provides strong contextual cues that can influence a variety of behavioral choices. Place cells in the hippocampus of rats (*Rattus norvegicus*) respond differentially to being placed in different rooms, despite occupying the same arena in each room [9], making circuits in the hippocampus potential candidates for encoding contextual cues about place.

Neuromodulators can encode the context of environmental substrate texture/composition and directly impact behavioral choice. The value of alternative egg-laying substrates for female fruit flies (*Drosophila melanogaster*), which appears to be communicated by the neuropeptide ILP7, depends on the relative concentration of, and the physical distance between, the alternative substrates [10•]. Both the nematode worm (*Caenorhabditis elegans*) [11] and the medicinal leech (*Hirudo sp.*) [12] decide whether to swim or to crawl based, in part, on the level of water they are in. *C. elegans* may encode water level using a class of dopamine-releasing mechanoreceptors with sensitivity to substrate texture (useful for distinguishing immersion in water versus laying on a solid surface) [13,14]. In the medicinal leech, dopamine biases the behavioral choice toward crawling [15], whereas serotonin makes swimming more likely [16]. *C. elegans* may also use dopamine and serotonin to set the balance between these two locomotory behaviors (JT Pierce-Shimomura *et al.*, abstract 287.16, Society for Neuroscience, San Diego 2010).

Social context

Many animals base important behavioral choices on the presence of potential mates and their current social status. Dopaminergic neurons in the output of the basal ganglia-forebrain circuit of a male zebra finch (*Taeniopygia guttata*) modulate the male's song variability depending on whether he sings to females (directed) or in isolation (undirected) [17,18]. Neurons expressing D1 dopamine receptors in both zebra finches [19,20] and European starlings [21] also may help to determine which songs are sung in different social contexts. In addition, female zebra finches strongly prefer directed songs (a preference that is enhanced with experience) and express an immediate early gene (*ZENK*) associated with memory formation in telencephalic auditory areas if they listen to a recording of a directed (but not undirected) male song [22].

Serotonin may also signal social context, especially social status. Serotonin modulates the crayfish (*Procambarus clarkii*) escape circuitry differently depending on social status:

serotonin is excitatory in dominant crayfish and inhibitory in subordinates [23,24]. In addition, serotonin increases the activity of leg motor neurons that make crayfish stand taller when confronting other crayfish [25]. Serotonergic modulation may also increase the intensity of Mauthner cell-evoked escape responses when the African cichlid fish (*Astatotilapia burtoni*) transitions from a subordinate social position (having drab coloring that attracts neither mates nor predators) to a dominant social position (with bright coloring that attracts both mates and predators) [26•]. Finally, locusts (*Schistocerca gregaria*) sense their population density by increases in hindleg mechanosensory activity or by visual/odor cues. These sensory cues trigger a switch from solitary to gregarious (swarming) states [27•], bringing about extensive changes in morphology, physiology, and behavior. Serotonin is both necessary and sufficient to induce this switch.

Availability of food

The prospect of a meal can influence an animal's response to threatening stimuli. In fish, the perceived speed of a predator's attack – as well as such variables as predator type and size, and distance to refuge – determines how it avoids predation [28]. Similarly, crayfish produce a large tail flip to avoid a slowly moving predator, but will freeze in response to a swiftly moving predator. These two behaviors are activated by different subsets of interneurons [29•]. The presence of food can bias the choice of behavioral response: the likelihood of large tail flips (which move the animal further from the food) decreases when food is present, as does the activity of medial giant interneurons (which receive tactile and visual inputs) that drive the tail flip response. Medicinal leeches ignore mechanosensory stimulation that would normally elicit locomotion behaviors in the presence of artificial blood [30]. Pinching the tail of a marine slug (*Aplysia californica*) can elicit either feeding or locomotory behavior, and serotonergic neurons sensitive to food modulate the choice between these two behaviors [31]. The presence of high quality food causes *C. elegans* worms to spend less time roaming [32] and to crawl more slowly, a behavioral change mediated by dopamine [14]. This slowing is enhanced when the worm is starved, a response mediated by serotonin.

Monkeys (*Macaca mulatta*) bias their decisions in a discrimination task towards targets with larger rewards [33]. In sensory accumulator models of area LIP (which is thought to be an important site of sensory-motor integration), asymmetric reward payoffs affect the starting point of the neural accumulator, pushing it closer to a decision threshold, whereas task-related sensory information instead affects the rate of accumulation. Hence, in monkeys, too, food can influence the outcome of behavioral trials.

Task-related contexts

When performing one of two types of directional discrimination tasks using the exact same stimuli (one that promotes cooperative interactions between neurons or one that promotes competitive interactions), the level of correlated “noise” between two medial temporal (MT) neurons in monkeys depends on which task (cooperative or competitive) is to be performed [34•]. For example, the correlated noise between two MT neurons (e.g. two neurons with preference for motion direction at 45° and 135°, respectively) was higher in one context that facilitated cooperation between the two neurons (discriminating upward vs. downward motion), and lower in another context (discriminating leftward vs. rightward motion) that facilitated competition between the two neurons.

For an animal to compare two successive stimuli, it must process each stimulus in the context of which stimulus came first. For instance, monkeys trained to discriminate the frequency of a succession of two vibrating stimuli, the information about the first stimulus must be interpreted, then compared to the second stimulus in the opposite manner. A model

using data from secondary somatosensory cortex (S2) and the prefrontal cortex (PFC) suggests that a simple sign inversion in the connection between S2 and PFC could produce the context-dependent processing, with no change in the functional circuitry that codes for the frequencies of the individual stimuli [35].

Current internal or behavioral state modulates sensorimotor processing which can affect upcoming behavioral choices

Reproductive state

An animal's reproductive state can influence its receptivity to some stimuli, leading to alterations in behavior. For instance, neurons in the antennal lobes of recently mated male moths (*Agrotis ipsilon*) [36] are less sensitive to pheromones, contributing to a refractory period for subsequent mating behavior. Neurons in olfactory bulbs of recently mated female mice (*Mus musculus*) [37] are also less sensitive to pheromones, contributing to maintenance of pregnancy. Recently mated female green treefrogs (*Hyla cinerea*) approach vocalizing males less often than non-mated females, in part due to shifts in the representation of auditory information in an area homologous to the inferior colliculus [38]. Recently mated female fruit flies display a variety of post-mating behaviors that are partly driven by a handful of neurons in the reproductive tract that are modulated by Sex peptide [39,40]. In addition, these flies change their dietary preference upon mating, choosing yeast over sucrose, a change mediated by S6 kinase and serotonin [41,42].

Current behavioral state

Another important influence on behavioral choice is the animal's current behavioral state (Figure 2). How will an animal's engagement in one behavior affect its response to incoming stimuli? The medicinal leech has a clear behavioral hierarchy, with feeding taking precedence over all other behaviors [43]. Following up the earlier study by Brodfuehrer et al., (2006) [30] showing decreased responsiveness to touch in the presence of artificial blood, Gaudry and Kristan [44••] found that when a leech is actively engaged in feeding on blood, serotonin presynaptically inhibits the connections between mechanosensory neurons and interneurons that mediate other behaviors such as swimming, crawling, shortening and bending (Figure 2A). This inhibition, which makes the leech able to maintain feeding and be unresponsive to even intense mechanosensory sensation, was observed behaviorally in sanguivorous (bloodsucking) species, but not carnivorous species [45]. Similarly, when *C. elegans* crawls backward in response to anterior touch [46], it is less responsive to stimuli that would otherwise induce head movements and forward locomotion [47]. In this case, anterior touch activates tyramine-gated chloride channels that inhibit neck muscle motor neurons as well as a command neuron that controls forward locomotion and head movements, presumably to aid in escape after encountering constricting ring traps made by fungi [47,48••].

Ongoing flight in insects provides another powerful context that influences behavioral choice via modulation of sensory processing. The act of flying by locusts [49] and fruit flies [50••], or walking fast by fruit flies [51], modulates responses of visual neurons (Figure 2C,D) so that they can shift into a highly energy intensive processing state that could facilitate precise course stabilization [52]. This modulation may be regulated by octopamine [53], the invertebrate equivalent of norepinephrine, which regulates many aspects of flight physiology [54], including, possibly, the changes in amplitude and direction of optomotor head pitch movements during flight in blowflies (*Calliphora vicina*) [55,56]. The underlying responses of neck motor neurons to optomotor stimuli appear to be gated by the activity of gyroscopic sensory appendages that are synchronized (in antiphase) to wing beat during flight [57]. A similar modulation of perception occurs in running rats [58] and mice (Figure

2B) [59•], which have stronger responses in their visual cortices. Responses in the lateral geniculate nuclei of mice were not elevated, suggesting a cortical source of visual modulation, possibly cholinergic.

As we have seen, many aspects of the environment and the animal's current behavioral state can be encoded by neuromodulators (Figure 1), which are thought to play a much larger role in motor neuron excitability than ionotropic inputs [60]. Serotonin and dopamine in general are implicated in behavioral switching [61] by perhaps indicating shifts in environmental context [62-64].

Outlook

Many laboratories are poised to study the impact of ongoing behavior on upcoming behavioral choices. A prerequisite for this type of study is a freely moving animal. Though single neuron electrophysiological recordings in freely moving animals have been possible for decades [65,66], the increasing miniaturization of electronics, coupled with the flexibility of fiber optic devices, has enabled researchers to implant imaging [67,68], multi-channel neural amplifier [58], and whole-cell electrophysiological [69] recording devices directly onto the heads of mice and rats that move about freely in mazes and in the wild. The neural activity of flying (tethered) flies [50••] can be assessed in a virtual reality apparatus. Locomotory behavior can also be monitored in head fixed mice [70,71] and fruit flies [51,72] that are positioned on a rotating track ball, that – coupled with an immersive video screen and neural recordings – provide a virtual environment allowing the exploration of the neural basis of behavioral choice within the context of an ongoing running behavior. Finally, genetically encoded optical probes have enabled simultaneous real time recordings of neural activity and behavior in freely moving *C. elegans* [73,74]. These technical advances should facilitate finding the cellular and network mechanisms responsible for how animals make choices between alternative behaviors, and how internal and external context influences these choices.

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Highlights for Contextual Modulation of Behavioral Choice

- > Behavioral choice can be modulated by both external and internal context.
- > Ongoing activity provides an important context for decision making.
- > Neuromodulators are important for encoding context.
- > New tools allow neural correlates of choice to be studied in freely moving animals.

Figure 1. Summary of contextual modulation of behavioral choice

Stimuli are processed by the nervous system in a manner that elicits a behavioral response. External (left column) and internal (right column) contexts can have a significant impact on the choice of behavior. Context can be encoded through functional circuitry or through the modulation of specific neuromodulators (represented here by color; see key). Context can affect (1) the encoding or decoding of stimuli (represented here by arrows extending to the “sensory” compartment); (2) the activity of the motor system (represented here by arrows extending to the “motor” compartment); or (3) have a more systemic affect on the nervous system (represented here by arrows extending to the “nervous system” compartment). Numbers next to contexts indicate reference number. For example, when leeches are engaged in feeding (an internal context) [ref 44], serotonin (represented by red arrow) presynaptically inhibits connections between sensory cells (represented by arrow extending to the “sensory” compartment) and interneurons that mediate other behaviors, leading to a noticeable modulation of behavioral choice.

Figure 2. Behavioral state influences processing of sensory information

(a) Feeding in the medicinal leech decreases the excitatory post-synaptic potential (EPSP) amplitude of a local bend interneuron (cell 212) elicited by spikes in a pressure sensitive mechanosensory cell (P cell). Cell 212 is involved in the production of a local bending behavior in the leech. The inset shows three overlaid traces from cell 212 illustrating the responses to P cell stimulation in pre-feeding, feeding, and post-feeding time periods (scale bars = 20 mV and 100 ms). Modified from [44••]. (b) Average power spectrum of local field potential (LFP) response in mouse primary visual cortex to drifting, oriented bars while the head fixed mouse was stationary (red trace) or running on a floating track ball (blue trace). The amplitudes of the signals at different frequencies change significantly when the animal was moving. Reprinted with permission from [59•]. (c) Membrane voltage, measured with patch clamp, of one motion sensitive VS (vertical-system) interneuron in *Drosophila* before (red), during (blue), and after (black) flight. The synaptic inputs onto VS interneurons increased during flight. Directions (L – left; R – right; D – down; DL – down left; DR – down right; U – up; UL – up left; UR – up right) refer to motion of drifting grating visual stimulus. Reprinted with permission from [50••]. (d) Two-photon calcium imaging of a single motion sensitive HS (horizontal-system) interneuron in *Drosophila* during walking (red trace) or at rest (blue trace). The visual responses of the HS cell increased dramatically in response to gratings drifting in the cell's preferred direction (PD), but not in the null direction (ND). Reprinted with permission from [51].