Neural Circuits That Mediate Selective Attention – A Comparative Perspective

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Abstract

Selective attention is central to cognition. Dramatic advances have been made in understanding the neural circuits that mediate selective attention. Forebrain networks, most elaborated in primates, control all forms of attention based on task demands and the physical salience of stimuli. These networks contain circuits that distribute top-down signals to sensory processing areas and enhance information processing in those areas. A midbrain network, most elaborated in birds, controls spatial attention. It contains circuits that continuously compute the highest priority stimulus location and route sensory information from the selected location to forebrain networks that make cognitive decisions. The identification of these circuits, their functions and mechanisms represent a major advance in our understanding of how the vertebrate brain mediates selective attention.

Keywords

Mechanisms of attention; Visual attention; Cognition

Networks that mediate information selection

Since the beginning of vertebrate evolution, neural mechanisms of attention have selected the information that gains access to networks that make cognitive decisions. When an animal, be it fish or primate, is engaged in complex behavior, such as social interactions, navigation or foraging, information selection is based on the task and goals of the animal [1–3]. During such periods, the mechanisms of attention are controlled by forebrain networks [3–7]. However, when an unexpected or highly salient stimulus occurs, information selection is dominated by the physical properties of the stimulus. When the stimulus has a location, a midbrain network acts with speed to direct spatial attention to that location and, when appropriate, also the gaze of the animal [1, 8–10]. Following capture of spatial attention by a physically salient stimulus, forebrain networks identify and evaluate the risks and benefits of the stimulus.

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The forebrain and midbrain networks that mediate these complementary aspects of attention-control each contain specialized circuits that compute the highest priority information at each moment for decision-making (Fig. 1, Key Figure). Forebrain networks select information, based on task demands or the physical salience of stimuli, from all available sources, including sensory input, plans for action, and memory stores. They direct attention either to locations, sensory modalities, stimulus features, objects or memory stores [4]. In contrast, the midbrain network is concerned only with the relative priorities of locations (Fig. 1A, purple box), based on the physical salience of stimuli and their behavioral relevance, and directs spatial attention to the highest priority location [1, 8, 11, 12].

This review summarizes the contributions made by specific midbrain and forebrain circuits to the selection or enhancement of information used for cognitive decisions. The data come from a variety of vertebrate species. The modular architecture of these selection networks provides a substrate for evolution to improve their performance. Hence, differences across species are to be expected. Nevertheless, some basic circuits have been conserved through evolution, demonstrating their adaptive value. Detailed exploration of both conserved and specialized circuits in diverse species will lead to a deeper understanding of how the vertebrate brain enables the amazing capacities of selective attention.

Selection circuits in the midbrain

The midbrain selection network

The midbrain stimulus selection network, which monitors the environment continuously for behaviorally relevant stimuli, appeared already well differentiated at the beginning of vertebrate evolution (Fig. 1B) [1, 8, 13]. The hub of the network is the optic tectum (OT), also referred to as the superior colliculus in mammals, a conspicuously laminated structure even in the earliest vertebrate species [13, 14]. The OT interconnects with the isthmic nuclei in the **midbrain tegmentum** (see Glossary); in mammals, these nuclei are named the parabigeminal nucleus and the peri-parabigeminal lateral tegmental nucleus [15]. The isthmic nuclei mediate the specialized computations carried out by the midbrain network that are essential to stimulus-driven selection across space [16]. They receive direct, topographic input from the OT, and they project back to the OT, as well as to the thalamus and basal ganglia [17]. Together, these structures constitute the midbrain selection network.

Information in each component structure of the network is organized as a topographic map of space in a retinocentric frame of reference. The OT itself is divided into two functional subdivisions. The superficial subdivision, referred to as the visual OT (OTv), is concerned primarily with visual information: it receives input directly from the retina (retinotectal tract) and indirectly from the visual forebrain, and it sends output to brainstem and thalamic nuclei involved in visual processing (including the dorsal lateral geniculate nucleus; dLGN [18]) or reflexive responses of the eye [13, 16, 19, 20]. The deep subdivision, referred to as the multimodal OT (OTm), receives visual input from the retina, but also input from all other sensory modalities that provide an animal with spatial information, as well as input from the forebrain indicating the spatial goal of impending orienting movements and the behavioral relevance of stimuli [19, 21]. The OTm sends descending output to premotor nuclei in the brainstem and spinal cord that orchestrate rapid, ballistic movements and, more importantly

for the purposes of this review, it sends ascending output to thalamic nuclei involved in sensory information processing and voluntary control of behavior (Fig. 1A) [8, 9, 22].

In monitoring the environment for behaviorally relevant stimuli, the midbrain network combines information about the physical salience of stimuli with information about the relevance of particular stimuli and locations to an animal's current task. By integrating and processing this information, the midbrain network generates a representation of the "priorities" of stimuli (Box 1) [8, 11, 23]. The network selects the highest priority location, enhances the processing of sensory information from that location (Fig. 1A, arrows 2 and 5), and if the stimulus is of sufficient priority, directs immediate ballistic orientation, attack, or defensive responses to the stimulus [8, 24].

A circuit for competitive selection. The midbrain network selects the highest priority stimulus by implementing powerful competitive inhibition that acts globally across the entire space map. The effects of global competition are demonstrated experimentally by presenting an animal with two or more stimuli at different locations. Under these conditions, the responses of a neuron to the weaker stimulus are suppressed by responses to a stronger stimulus located anywhere else in the visual field. Such "global competitive surrounds" are a distinctive property of OTm neurons that have been documented in a wide range of vertebrate species [25–28].

A neural circuit that mediates global competitive surrounds is formed by specialized inhibitory neurons in the midbrain tegmentum. Although this circuit was first recognized anatomically in reptiles [29], its structural and functional properties have been fully explored only in birds (Box 2), in which the specialized inhibitory neurons cluster in the nucleus isthmi pars magnocellularis (Imc; Fig. 2A).

When the relative priorities of competing stimuli change and neural activity representing one location exceeds the activity at all other locations in the midbrain space map (Box 1), this competitive inhibitory circuit powerfully suppresses responses at all other locations (Box 2) [30, 31]. This property causes the population activity in the OT to represent categorically the winning stimulus as the location in the space map with the highest activity, a code easily read-out by downstream neurons. Response adaptation allows the network to select, across time, different stimuli as highest priority [8, 19].

Long distance, reciprocal inhibition acting within the Imc [32] enables the competition circuit to compare relative activity levels with high precision. Computational studies show that this microcircuit motif of 'lateral inhibition of feedforward inhibition' (Fig. 2 B) is an extremely efficient mechanism for rapid adjustment of the categorization boundary for "highest priority" in response to changing stimulus strengths [33]. In addition, this mechanism sharpens the categorization boundary, enabling improved discrimination of the highest priority location by a decoding network.

The beneficial effects of the global competitive inhibitory circuit are apparent only when an animal must select among multiple competing stimuli. When an animal confronts only a single stimulus (which occurs rarely in nature, but often in the laboratory), the advantage gained from suppressing responses at all other locations is minimized. This can account for

the observation that, in monkeys trained to perform attention-demanding tasks, OT inactivation has devastating effects on target selection only when competing stimuli are present [9, 34].

A circuit for space-specific amplification. In addition to suppressing neural responses to lower priority stimuli, the midbrain selection network amplifies and, at least in birds, causes periodic (25–60 Hz; " low **gamma-band**") synchronization of neural responses to the selected stimulus [16]. Response amplification is mediated by a different specialized circuit, which is established in parallel with the global competition circuit and includes cholinergic neurons in the isthmic nuclei (Fig. 2C, green). The circuit involves precise, reciprocal, topographic connections between the OT and isthmic cholinergic neurons. This circuit was first described in mammals, in which the cholinergic isthmic neurons are referred to as the parabigeminal nucleus [35]. However, the structural and functional properties of these neurons have been explored primarily in birds (Box 3), in which they are called the nucleus isthmi pars parvocellularis (Ipc) and pars semilunaris (SLu) (Fig. 2C) [36].

Activity in this circuit controls the sensitivity and gain of visual responses in the OT [37]. Cholinergic isthmic neurons project heavily to the retino-recipient layers of the OT. In these layers, the release of ACh facilitates the release of glutamate from the afferent terminals of retinal ganglion cells, thereby enhancing their effects [38, 39]. ACh release also drives local OT inhibitory neurons, which, in turn, inhibit other inhibitory neurons [40], an "inhibition-of-inhibition" motif that could increase the response gain of OT output neurons. In addition, ACh release increases the amplitude of the synchronizing, gamma-band **oscillations** (Box 3) [40, 41].

The space-specific amplification circuit provides a critical node where top-down information from the forebrain can bias the competition that takes place within the midbrain network. In birds, space-specific top-down signals, by facilitating sensory responses to a particular location, shift the balance of competition to favor the location signaled by the forebrain [42]. Conversely, focal inactivation of the Ipc or OT prevents any stimulus at the represented location from being selected as "highest priority," even when there are no competing stimuli [43].

In birds, the periodic synchronization of activity in the midbrain network provides a physiological tag of neural responses that correspond to the stimulus at the "highest priority" location [44]. Ascending projections from the SLu and OT transmit this distinctively periodic activity to the thalamus (specifically, the nucleus Rotundus, ROT; pulvinar in mammals) which, in turn, transmits it to high-order areas in the forebrain **pallium** (Fig. 2D, Entopallium) [45]. Although visual and multimodal neurons in the ROT have large receptive fields and exhibit little evidence of topographic RF organization [46], their responses, when periodic at low gamma frequencies, represent stimuli at the highest priority location, and the location itself is signaled by the site of synchronized activity in the midbrain space maps. Periodic ascending activity from the midbrain could influence how the forebrain selects both the visual information it receives from the OT as well as simultaneous information that converges in the forebrain via OT-independent pathways [47].

Two major roles of the activity that ascends from the OT to the forebrain are 1) to provide the forebrain with visual information to analyze the identity of a stimulus (Fig. 1A, arrow 5), critically important for non-mammalian vertebrate species (Box 4), and 2) to alert the forebrain to the location of the highest priority stimulus and filter forebrain sensory information for that location (Fig. 1A, arrow 2). The importance of OT activity in both of these roles has changed dramatically across vertebrate evolution (Box 4).

It is important to underscore the specific effects that the amplification circuit have on activity in the midbrain network. The mechanisms engaged by this circuit, including presynaptic afferent facilitation, amplification of inhibition, disinhibition, and oscillation gain-control, do not alone drive the activity of OT output neurons. Instead, they modulate their responses and regulate the balance of competition across the space map. Specifically, these mechanisms (1) increase the sensitivity, gain and resolution of the system (and, thereby, provide a means for task-related signals to influence the competitive selection of a particular location), (2) increase the persistence of responses, thereby retaining information for short periods and stabilizing the dynamics of the system, and (3) impose a temporal signature and windowing of the visual activity that passes through the OT. It will be important to determine which of the mechanisms that operate in birds (Boxes 2 and 3) are also found in species from other vertebrate Classes, and which may be specializations to meet the particularly high demands that flight places on decision-making.

Selection circuits in the forebrain

Forebrain selection networks

Forebrain selection networks have been studied almost exclusively in mammals, particularly in primates and rodents. The mammalian networks comprise mutually connected areas of the prefrontal and posterior parietal cortex (frontoprietal network), sensory cortices, and subcortical structures in the thalamus, basal ganglia and brainstem [4, 7, 48].

Unlike the midbrain network described above, the forebrain networks are thought to encode information less topographically, with more mixed and distributed representations, and with heterogeneous dynamics [49–52]. Computations for the identification of stimuli or the accumulation of information toward cognitive decisions are readout from the trajectory of activity (**population vector**) across the population of neurons [53]. The information that is selected for decision-making may influence the recurrent dynamics of the network as well as drive the trajectory of the population vector toward a decision [51].

Forebrain networks in the earliest vertebrate species probably operated in a fashion similar to the one discussed above. In turtles (Fig. 1B) for example, even the primary visual cortex (V1) acts as a distributed, **dynamical system**, with neurons exhibiting **mixed selectivities**, extremely large visual receptive fields, and sustained oscillatory activity that develops over time [54]. In fish, amphibians and reptiles, various forebrain areas process sensory, motor, or high-order information [2, 3, 45, 55, 56]. These areas are likely to be organized hierarchically, in a **layered control architecture** [57], as they are in birds and mammals, but the number of hierarchical levels is extremely limited, and there is as yet no evidence that

the features of stimuli, such as visual contour orientation or motion, are analyzed in separate specialized areas.

Distributed dynamical networks, although slower to categorize information than feedforward hierarchies, are far more versatile and efficient for small populations of neurons to convert high dimensional information into low dimensional adaptive decisions [58]. This versatile neural architecture, which presumably evolved first in the vertebrate forebrain to analyze olfactory information, eventually led to the distributed, dynamical processing networks of the prefrontal, parietal and inferotemporal cortices [55, 59].

Most research on forebrain attention networks focuses not on the mechanisms that generate selection signals, but rather on pathways that distribute selection signals and the mechanisms by which these signals regulate the quality of the selected information [4, 7, 60, 61]. Effects on neural activity that correlate with attention include increases in neuronal sensitivity, gain, decorrelation of activity with neighboring neurons, periodic synchronization of activity both within a cortical area and across areas and, at high levels of processing, dynamic shifts or sharpening of receptive field tuning (e.g., for location or feature values), resulting in the preferential representation of the attended stimulus [62–65]. At the same time, neuronal responses to distracting stimuli tend to be suppressed [66, 67]. In addition to enhancing the representation of information, forebrain networks may also improve decisions by adjusting the criteria used in making cognitive decisions [68]. The influence of these effects on neuronal responses increases at progressively higher levels in hierarchies of forebrain information processing.

Mechanisms have been identified in rodents and primates that can account for many of these neural correlates of attention [60, 69, 70]. In a few cases, specific circuits have been shown to be causally involved in attending animals. These include (1) feedback circuits from higher order to lower order cortical areas [71, 72], (2) thalamic circuits that include inhibitory neurons in the thalamic reticular nucleus (TRN) [73]; and (3) circuits formed by broadly projecting cholinergic neurons in the basal forebrain (BF) [74, 75]. These circuits act cooperatively, with different degrees of anatomical and functional precision, to enhance the representation of selected information. However, all of these circuits act with high temporal precision, enabling the rapid modulation of information processing that is required for selective attention in a rapidly changing world.

Corticocortical feedback circuits

In birds and mammals, selection signals computed in high-order forebrain areas propagate to progressively lower order areas, modulating the processing and representation of selected information [76–78]. These circuits have the anatomical precision to differentially modulate the responses of specific functional subgroups of neurons within an area (Fig. 3A), as occurs in the context of space-, feature-, object-specific attention. Although these circuits may contribute to all forms of selective attention, they have been studied primarily in the context of visual spatial attention.

In primates, selection signals for visual spatial attention often originate in high-order areas of the PFC [52, 79–81], where task demands and multiple sources of information are

integrated in non-retinocentric frames of reference (space representations that do not move with the eyes [82, 83]). These selection signals are translated into retinocentric signals, perhaps in the lateral intraparietal area (LIP) [4, 84, 85], and are conveyed to the frontal eye field (FEF), a gaze control area in the PFC. The FEF encodes spatial information in retinocentric coordinates [61, 86] and communicates topographically with retinocentric visual areas in the posterior cortex, as well as with the OTm. Under most conditions, the FEF is not likely to be the site where selection signals are initially generated. However, when a behavioral task does not require the translation of information across spatial frames of reference (for example, during explicit spatial cueing or selection based on the physical salience of a stimulus), the FEF, like the midbrain OTm, may itself generate the selection signal for the highest priority location [61, 87].

The FEF broadcasts retinocentric selection signals to the visual cortex [88, 89]. In monkeys, these signals produce the neurophysiological correlates and behavioral effects of voluntary spatial attention [61]. Focal electrical microstimulation of the FEF improves behavioral discrimination of target stimuli and increases the responses of high-order visual neurons in area V4, specifically for targets at the microstimulated location [61, 72]. During attention-demanding tasks, visual responses of FEF neurons are strongly enhanced when a receptive field stimulus is of highest priority, either because of its physical salience (sensory-driven) or its relevance to a current task (task-driven). Activity from the FEF, in turn, increases the strength and synchronization of neuronal responses in V4 in a space-specific, attention-dependent manner [90]. Attention also increases the periodic synchronization of visual responses both within the FEF and between the FEF and V4 [91]. These effects can cascade to progressively lower order visual areas via corticocortical projections [78].

In mice, the cingulate region (Cg) of the PFC, like the FEF in monkeys, has been shown to transmit selection signals to the visual cortex (mouse V1; Fig. 3A) [71]. Optogenetic activation of Cg axons in V1 improves the ability of behaving mice to discriminate visual contour orientations at the corresponding location. Neurophysiologically, Cg axon activation increases the gain and orientation discriminability of nearby V1 neurons and decreases the responses of more distant neurons.

The visual cortex provides specific examples of circuits that enhance the representation of selected information. For instance in the mouse V1, Cg axons connect directly with several classes of inhibitory interneurons as well as directly with pyramidal output neurons (Fig. 3A) [71]. One class of interneuron (VIP+), which in mice receives the strongest input from Cg axons, inhibits locally acting inhibitory interneurons, thereby releasing pyramidal neurons from inhibition (disinhibition). This circuit increases the responses of cortical output neurons to the selected stimulus. In addition, the direct Cg input to pyramidal neurons could act cooperatively to increase the responsiveness of pyramidal neurons, possibly via activation of NMDA receptors. As a comparative side note, in contrast to the circuitry in the mouse, in the monkey the dominant connection of FEF axons with V4 pyramidal neurons is direct [94], even though the monkey neocortex contains similar chemically and anatomically distinct classes of neurons [92, 93]. Returning to the mouse V1, Cg input to two other classes of interneurons (PV+ and SOM+) causes inhibition of more distant pyramidal neurons. Activation of PV+ interneurons sharpens pyramidal neuron tuning for stimulus

orientation [95]. These same classes of interneurons are also driven by sensory input, and their activity normalizes responses across the cortex [96, 97]. In addition, these classes of interneurons generate and regulate the periodic synchronization of visual responses at beta (5–30 Hz; SOM) and low gamma (30–80 Hz; PV) frequencies [98–100]. Thus, these circuits in mice can account for many of the neurophysiological effects of selection signals in the visual cortex.

In birds, the forebrain area analogous to the primate FEF is called the arcopallial gaze field (AGF) [101]. Like the FEF and Cg, the AGF projects to the OTm, which in birds is a major pathway for transmitting visual information to the forebrain (Box 4) [46]. Focal microstimulation of the AGF in owls increases the gain and sensitivity of OTm visual neurons, and it sharpens and shifts their spatial tuning toward the location encoded at the AGF stimulation site [102]. These effects (Fig. 1A, arrow 3) reflect, at least in part, the action of the midbrain cholinergic amplification circuit (Fig. 2C), which receives direct input from the AGF [37]. At the same time, AGF microstimulation increases the inhibition of visual responses at surrounding locations in the space map [30], an effect that is mediated by the GABAergic Imc circuit (Fig. 2A,B). Thus, midbrain circuits that participate in the generation of selection signals are also engaged by top-down feedback circuits to regulate the processing of ascending visual information (Fig. 1A, arrow 5), at least in birds.

Thalamic circuits

The thalamus controls the access of information to the forebrain pallium (cortex, in mammals [45]) as well as regulates the transmission of information between pallial areas [103]. The thalamus is an ancestral structure that receives ascending information from the brainstem and spinal cord and descending information from pallial areas [104, 105]. Discrete thalamic nuclei interconnect with functional sectors of the pallium such that the functional topography of the thalamus reflects the topography of the pallium (Fig. 3B).

The thalamus is a key node in the forebrain selection network [103]. In primates, deactivation of the thalamic nuclei that connect with the posterior parietal cortex or high-order visual cortex results in severe attention deficits [106]. Thalamic circuits modulate the amplitude of periodic synchronization of cortical responses to attended targets [107]. Attentive viewing synchronizes oscillations of **local field potentials** (LFPs) in connected sectors of the thalamic LGN and V1 in cats [108]. It also increases the mutual coherence of LFPs in high-order visual areas, such as V4 and TEO in monkeys [107]. This coupling of oscillations across brain structures, mediated by the thalamus, could provide a mechanism for selectively routing task-relevant information for decision-making.

Distributed among the thalamic nuclei are GABAergic inhibitory neurons that receive ascending input from thalamo-pallial neurons as well as feedback input from the pallium (Fig. 3B). In reptiles, birds and mammals, these inhibitory neurons are referred to as the thalamic reticular nucleus (TRN) [104]. Based on its unique anatomical position and functional properties, Crick proposed that the TRN controls the "searchlight of attention" [109]. In mammals, the TRN exerts powerful inhibitory control over thalamo-cortical transmission. The TRN surrounds the other thalamic nuclei, and its functional topography

reflects their functional topography [110]. Although the PFC in monkeys connects most strongly with the anterior TRN, it projects widely across the TRN [111].

TRN neurons inhibit thalamocortical neurons and also each other [110, 112]. They discharge at high rates, and their discharge rates are modulated selectively by the task relevance of a stimulus during attention-demanding behaviors [113]. TRN activity suppresses thalamic responses to non-selected information. One example comes from experiments in mice in which animals were cued to select either a visual target or a simultaneously presented auditory target for making a perceptual decision. In this study, optogenetic inhibition of the TRN neurons that connect with the LGN (TRNLGN; Fig. 3B) eliminated the cue-dependent modulation of both LGN neuronal responses and behavioral discrimination in the task [73]. In addition, lesions of the TRN eliminate faster behavioral responses to cued stimuli, a hallmark of attention [114].

In mammals, thalamocortical inputs to the PFC are regulated by the anterior portion of the TRN (Fig. 3B). Hence, the TRNANT is likely to play a key role in the generation of task-related selection signals. The functional precision of the signals from the PFC to the thalamus is sufficient to differentially select a location or a sensory modality for enhanced processing and decision-making [73, 113, 115]. The limit of the functional precision of this circuit and the degree to which analogous circuits and mechanisms operate in other Classes of vertebrates remain to be determined.

Cholinergic circuits in the basal forebrain

The ancestral vertebrate brain also contained diffusely projecting systems capable of modulating information processing in the forebrain [116]. The systems are identified by the distinguishing neurotransmitter that mediates their respective effects: acetylcholine (ACh), dopamine (DA), noradrenaline and serotonin. In mammals, each of these neuromodulatory systems can influence behavioral performance in attention-demanding tasks. Many of these influences can be attributed to general effects on brain state, working memory, reinforcement learning, action selection or inhibitory control [60]. The cholinergic system, however, has recently been shown to have an anatomical precision that enables selective modulation of functional systems and the capacity to modulate neural activity with a temporal precision that enables trial-by-trial modulation of sensory processing [75, 117]. Although others of the neuromodulatory systems (particularly the DA system [60, 118]) may be shown, by future experiments, to contribute specifically to selective attention, the evidence that the cholinergic system does so is already compelling.

The cholinergic neurons that establish this circuit are located in the basal forebrain (BF) of all vertebrate species [74, 116, 117, 119]. The cholinergic BF is the major source of ACh in the forebrain (Fig. 3C). In mammals, these neurons receive strong inputs from the PFC, amygdala, and nucleus accumbens, and they project broadly to the thalamus and to the cortex, particularly to the PFC [120].

Definitive evidence from multiple lines of inquiry, links the cholinergic BF in mammals to the control of selective attention. Lesions of the cholinergic BF in mice impair the behavioral identification of target stimuli [74, 121]. The activity of cholinergic BF neurons

correlates with attentional demand in these behavioral tasks. Neurons in the BF are activated by high priority sensory stimuli and are spatially selective for stimuli that predict reward [122, 123]. They are activated top-down, when distractors must be identified or when task conditions change. Electrical or optogenetic stimulation of cholinergic BF neurons increases the gain and reliability of neuronal responses in mouse V1 and decreases the mutual correlation of those responses [75]. And in the monkey V1, local application ACh receptor antagonists reduces attentional modulations of neuronal responses [124].

Cholinergic mechanisms in the forebrain that enhance information processing are similar to those that operate in the midbrain network, discussed previously. In the cortex, ACh release increases sensory drive by presynaptic facilitation of glutamate release from thalamic afferent terminals [125, 126]; it drives inhibitory neurons that increase the gain of output neurons by inhibiting local inhibitory neurons (disinhibition) [127]; it drives other inhibitory neurons that provide surround inhibition at distant locations [128]; and it increases the periodic synchrony of sensory responses, by acting on local oscillatory circuits [98, 129].

Although cholinergic BF neurons project broadly, they project to functionally related regions of the cortex [117, 120]. The coarseness of their projections implies that they are unlikely to contribute to the precision of space-or feature-specific attention (but see [60]). On the other hand, the modulation of responses in the cortex by cholinergic BF neurons is fast: their temporal resolution in mice is <1 s [75]. The functional selectivity and temporal resolution of cholinergic BF neurons, together with the effects of BF lesions, suggest that this circuit contributes to selective attention.

Coordination of forebrain and midbrain selection signals

The forebrain and midbrain networks carry out computations in parallel to determine the information that has the highest priority for access to forebrain networks that make cognitive decisions (Fig. 1A). Our understanding of how the networks coordinate their computations is at an early stage. Coordination depends on communication between the networks and the relative dominance of their effects (Box 5). Descending inputs from the forebrain bias the competition that takes place in the midbrain [11, 24]. However, they do not dictate the winner: when a stimulus at a location different from the location signaled by the forebrain network is sufficiently more salient, it wins the midbrain competition for "highest priority," overriding the top-down signals [42].

The influence of forebrain networks in controlling attention has increased across vertebrate evolution, reflecting the increasing computational capacities of the forebrain. Conversely, the role of the OT as a site of spatial selection of sensory information (Fig. 1A, arrow 5) has decreased (Box 4). In addition, the relative dominance of the forebrain and midbrain networks is likely to vary across prey versus predatory species within a taxonomic group: to avoid predation, there is an intuitive advantage for the midbrain network (Fig. 1A, purple box), which monitors the environment for unexpected stimuli, to dominate information selection; conversely, in the context of hunting, there is an intuitive advantage for forebrain networks to dominate (Fig. 1A, red box). Moreover, the relative influence of the networks probably varies dynamically within individuals, with the midbrain network becoming more

dominant in times of stress or increased likelihood of unexpected stimuli, and forebrain networks becoming more dominant in times of focused, voluntary behavior.

Concluding remarks

We have begun to identify some of the circuits and mechanisms in the vertebrate brain that mediate selective attention. This progress notwithstanding, much remains unknown (see Outstanding Questions). In particular, further research is needed to understand how forebrain networks generate and transform task-related selection signals, and the mechanisms by which selection signals generated in the midbrain network control the access of information to forebrain networks involved in making cognitive decisions.

It is important to remember that each of the circuits discussed in this review has been explored thoroughly only in one or a few species. Studies in a wide range of species, from all Classes of vertebrates, are required in order to determine which of these circuits and mechanisms are shared universally and which are specializations that reflect specific demands or novel brain architectures of species. The answer to this comparative question will lead to a deeper understanding of how selective attention is achieved in vertebrate brains and how the capacities and mechanisms of attention have evolved over time.

Acknowledgements

Glossary

Dynamical system
In the context of the brain, a population of neurons that encodes information as time-dependent patterns of activity across the population.

Gamma-band oscillations
Rhythmic fluctuations in the local field potential that contain spectral power in the frequency range of 25–140 Hz.

Layered control architecture
An architecture consisting of multiple brain areas, organized in a functional hierarchy of layers. Within a layer are modules mediating sensory, planning and motor functions. Higher layers support progressively more sophisticated tasks. Higher layers often operate by modulating the activity of lower layers to generate more complex behaviors. Higher levels can subsume the roles of lower levels by suppressing the outputs of lower layers and substituting their own.

Local field potential (LFP)
The electrical potential that is generated by the summed electrical currents of nearby neurons and glia, as measured extracellularly using a low-impedance electrode and processed to remove action potentials.

Midbrain tegmentum

The ventral portion of the midbrain, located beneath the cerebral aqueduct or tectal ventricle.

Mixed selectivity

Neuronal activity that correlates with multiple stimulus modalities, conditions, or components of a task.

Oscillations

In the context of the brain, fluctuations in neural activity that are periodic. The frequency of the oscillations indicates the periodicity of the neural activity.

Pallium

The portion of the telencephalon in all Classes of vertebrate species that, in mammals, gives rise to cortical structures.

Population vector

A decoding approach to identify the information represented in the pattern of activity in a population of neurons, derived as the sum of the preferred tuning properties of each neuron weighted by its spike rate, and summed across all neurons in the population.

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Highlights

- Cognitive decisions rely on neuronal circuits that select or differentially process information. Such circuits have been identified in mammalian and bird species. For many of these circuits, anatomical precursors exist also in earlier Classes of vertebrate species.

- Circuits in the mammalian forebrain include: feedback circuits from the prefrontal to sensory cortex that distribute top-down selection signals; circuits within sensory cortex; thalamic circuits; and cholinergic circuits in the basal forebrain.

- A midbrain network continuously monitors the world for behaviorally relevant stimuli and controls spatial attention. Specific circuits in the bird midbrain network signal the highest priority stimulus location by implementing global competitive inhibition across all of space, space-specific amplification, and periodic synchronization of activity at low gamma-band frequencies.

Box 1

Computation of the highest priority location by the OT

To compute the highest priority stimulus, the OT is provided with sensory information that represents the physical salience of stimuli [8, 9, 20, 23]. Topographic visual input originates from the entire contralateral retina (except in primates, in which the representation extends to just past the vertical meridian) as well as from those portions of the ipsilateral retina that represent corresponding locations [130]. OT neurons exhibit a strong preference for small stimuli, due in part to lateral inhibition in the OTv [131]. The activity of OT neurons increases with increasing luminance or motion speed, and decreases when the same stimulus is presented repeatedly, largely due to adaptation mechanisms that operate within the OT [8, 19]. The OT also receives information about stimulus properties from the forebrain. The forebrain indicates, for instance, when a particular stimulus feature value (for example, a color) occurs rarely across space, referred to as "popout," (Fig. 1A, arrow 4) [23, 34, 132, 133]. Afferent inputs from other sensory modalities, including auditory and somatosensory, encode the strength, motion, and novelty of a stimulus, but not its identity [21]. By combining these inputs, a population of neurons in the OT space map encodes the physical salience and novelty of a stimulus.

The OT generates a representation of stimulus priority by combining information about physical salience with activity that represents the immediate behavioral relevance of particular locations or stimuli [11]. Information about the relevance of a location or stimulus to an animal's current task originates in the forebrain, and is conveyed to the OT via descending pathways (Fig. 1A, arrow 3) [6, 11]. Neural activity from voluntary gaze control areas in the forebrain, indicating a plan to orient toward a location and the learned benefits of a stimulus, facilitate sensory responses at corresponding locations in the OT space map [61]. The resulting relevance-modulated sensory responses compete for supremacy (highest priority) in the OT space map.

Box 2

The midbrain circuit in birds that mediates global competitive inhibition

The circuit that mediates stimulus competition across space in the midbrain network of birds, begins with anatomically and biophysically specialized neurons located in the OT (Fig. 2A, orange) [134]. These neurons have radial, bipolar dendrites that extend into the OTv and OTm [36]. They receive direct retinal input as well as direct multimodal and behavioral relevance input, and they project topographically to specialized inhibitory neurons located in the midbrain tegmentum in the nucleus isthmi pars magnocellularis (Imc). Imc neurons, in turn, project broadly back to the OT, to the cholinergic isthmic nuclei, and to each other (Fig. 2A, black) [32, 135]. Because the inhibitory influence of Imc neurons acts globally across the maps in each of these structures, the activity evoked by any stimulus in each of these structures competes with the activities evoked by stimuli at all other locations (Fig. 2B). The stimulus that evokes the highest level of Imc activity wins this competition and suppresses sensory responses at all other locations [136].

The OT neurons that project to the Imc exhibit an unusual biophysical property that enables their function [134]. They transform transient afferent drive into persistent, stochastic, exceptionally high firing rates (>100 spikes/s). This activity drives Imc neurons at similarly high rates, allowing them to powerfully suppress network responses to competing stimuli (Fig. 2B).

Box 3

The midbrain circuit in birds for space-specific amplification and synchronization

The circuit that amplifies and synchronizes sensory responses in the midbrain network of birds (Fig. 2C), begins with specialized OT neurons with bipolar dendrites that sample inputs to both the OTv and OTm, in parallel with the OT neurons that project to the Imc [36, 134]. The specialized OT neurons send axons topographically to the Ipc and SLu, creating space maps in both nuclei [36]. The Ipc and SLu send topographic projections back to the OTv and OTm, precisely to the location that provides their input. SLu neurons also send cholinergic projections to the thalamus and to the source of basal ganglia input to the OT in the brainstem [17].

In addition to amplifying OT responses, these cholinergic circuits also cause network responses to synchronize at a periodicity of 25–60 Hz (low gamma frequencies). The oscillatory activity originates in the OT: the Ipc-projecting neurons receive periodic inhibition from local inhibitory neurons (Fig. 2C, black) [41]. The periodicity of this inhibitory microcircuit is regulated by the strength of γ-aminobutyric acid $(GABA)_A$ – receptor currents, and the amplitude of the resulting periodic inhibition is regulated by the activation of non-alpha 7 nicotinic acetylcholine (ACh) receptors on a subset of these interneurons [40]. As a result, Ipc-projecting neurons in the OT respond to sensory input with periodic spikes at low gamma frequencies (Fig. 2C, red lines). Neurons in the Ipc transform these periodic spikes into spike bursts (Fig. 2C, black lines), which are transmitted to neurons in most layers of the OT [137]. These bursts also entrain the discharges of SLu neurons [44]. The resulting synchronization of activity across OT layers can enhance the transmission of visual responses within the OT, specifically for this location in the space map (Fig. 2D) [47]. The persistence of responses that is caused by this circuit retains information for a brief period and momentarily stabilizes the activity of the network in an attractor state [41]. Response adaptation of the inputs to this circuit would enable the network to select different attractor states across time.

Box 4

Evolution of midbrain network functions

The role of the midbrain as a site where information is selected for processing in the forebrain has decreased dramatically across vertebrate evolution. Early in vertebrate evolution, as represented by fish, amphibians and reptiles (Fig. 1B), the vast majority of visual information passed through the OT on its way to the forebrain, where complex behaviors were planned [1, 8, 45]. In these species, visual information used by the forebrain for stimulus identification is filtered in the OT for physical salience and, presumably, for priority through top-down modulation. Such spatial filtering (Fig. 1A, arrow 5) would cause visual information from one location at a time to dominate the information that the OT transmits to the forebrain (Fig. 1A, black ascending arrow). This dimension-reduction strategy enables the anatomically limited resources of the early vertebrate forebrain [45] to analyze one, selected stimulus in detail. Thus, in these species, the OT serves as the primary site where visual information for cognitive decisions is filtered, based on both exogenous and endogenous information.

The retino-geniculate pathway and the architecture of the forebrain are more elaborated in birds and are far more elaborated in mammals [138–140]. Correspondingly, the importance of the midbrain selection signal in filtering visual information that passes through the OT is reduced (Fig. 1A, arrow 5), while its importance in filtering information that passes through the dLGN is increased (Fig. 1A, arrow 2).

In primates, the role of the OT as a site of visual information filtering decreases further. Primates have foveae, and the retinogeniculate pathway and the forebrain (frontoparietal) selection networks are uniquely well differentiated [4, 141]. Conversely, only ~10% of retinal afferents project to the OT, in contrast to the massive projection of retinal afferents to the OT that exists in all non-primate species [139]. Nevertheless, focal electrical microstimulation of the OT in monkeys mimics the behavioral effects of spatial attention: it improves the detection and discrimination of visual stimuli specifically for target stimuli at the microstimulated location [142, 143]. As in other vertebrate species, the primate OT monitors the environment for physically salient stimuli, its ascending signal can override task-related spatial selection and direct attention to a particular location, and it contributes to space selection for cognitive decisions, especially when distracting stimuli are present [9, 12, 24, 144].

The midbrain network achieves its highest degree of anatomical differentiation in birds, the Class of vertebrates that, due to flight, must make extremely rapid, reliable decisions about approaching objects [8]. In birds, specialized circuits in the midbrain generate a conspicuously rhythmic, categorical selection signal indicating the location of the highest priority stimulus [41, 136]. This selection signal spatially filters visual information within the OT as well as in the forebrain (Fig. 2D) [43].

Box 5

Resolution of forebrain-midbrain selection conflicts

Conflicting forebrain and midbrain signals have been induced experimentally by focal inactivation of the OT in trained monkeys [145]. When a cued target and a task-relevant distractor are presented simultaneously, and the cued target is positioned at an OT-inactivated location, monkeys fail to report the feature properties of a cued stimulus and, instead, report the properties of the distractor. Enhanced processing of information about the cued stimulus persists in the visual cortex. Nevertheless, the midbrain network selects information from the distractor stimulus location (not inactivated) for decision-making. This implies that a midbrain influence on information selection in the forebrain (Fig. 1A, arrow 2) acts downstream from task-related influences on cortical sensory processing (Fig. 1A, arrow 1).

Computational studies that employed a multidimensional, signal detection framework to analyze behavioral results from OT inactivation experiments in monkeys concluded that the OT exerts its effects on perceptual decisions primarily by altering an animal's spatial choice bias for selecting information, rather than by altering the quality of the sensory information itself [146]. Spatial choice bias could be implemented by gating forebrain sensory information based on spatial location (Fig. 1A, arrow 2). Results from electrophysiological and microstimulation experiments are consistent with this conclusion [12, 24, 144]. The mechanisms by which the midbrain network exerts its effects on information processing in the forebrain remain unknown. A likely possibility, however, is that they involve the engagement of gating circuits in the thalamus (Fig. 3B).

Outstanding Questions

- How do forebrain networks generate selection signals based on task demands or on the relative priorities of stimuli? How do these networks translate selection signals into representations that can modulate the processing of information that is encoded in different formats and coordinate spaces in various parts of the brain?

- Do the circuits that have been shown to regulate information processing in the neocortex of mice or monkeys exist also in other mammalian species? Do similar circuits exist in other Classes of vertebrates that do not have a neocortex?

- Do the forebrains of fish, amphibians and reptiles contain feedback circuits from high-order to low-order pallial areas? Given the limited differentiation of their pallial areas and the likelihood that these areas act as distributed, dynamical systems, it is possible that interpallial feedback circuits (and, indeed, the capacity to attend to specific feature values) do not exist in these species.

- Do the circuits of the midbrain selection network in other Classes of vertebrate species perform the same computations and employ the same mechanisms as in birds, in which the network is so highly differentiated?

- What is the functional role of low gamma-band activity synchronization in attention? The mechanisms that generate and shape gamma-band oscillations are strikingly similar in the mammalian neocortex and the bird midbrain. The presence of these oscillations in widely different structures and species suggests that the periodic synchronization of activity at gamma frequencies plays a critical role in the processing of attended information.

- How do selection signals from the midbrain network control information processing in the forebrain? The midbrain network projects heavily to the thalamus in all Classes of vertebrates, and the thalamus contains circuits capable of gating information in the cortex. The thalamus is, therefore, an excellent site to begin such studies.

- How do the forebrain and midbrain networks coordinate so that the information selected at each moment is of the highest priority to the animal? Particularly vital is the ability to shift rapidly between current task demands and attention to unexpected stimuli. How is this flexibility and coordination of information selection achieved?
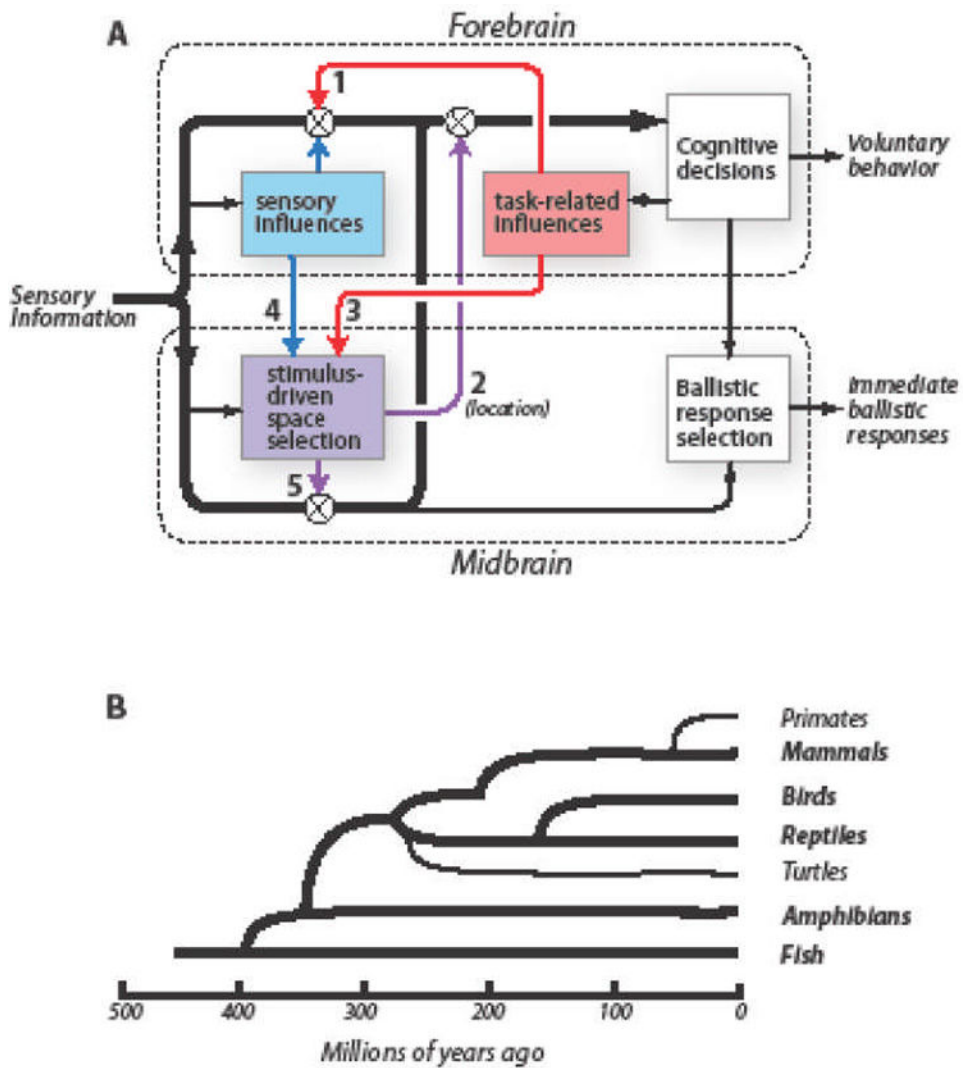
Figure 1.
Key Figure. Schemata for attention-dependent modulation of sensory information and for the evolutionary relationships of living vertebrate taxonomic groups.

A: Sensory information is processed in parallel by the forebrain (upper dashed rectangle) and the midbrain (lower dashed rectangle). Thick black arrows: information used for stimulus identification. Red rectangle: information selection based on task relevance. Blue rectangle: stimulus selection based on the physical properties of stimuli. Purple rectangle: stimulus selection based on the priority of stimulus location (stimulus-driven space selection). Symbols: circled X, regulation of sensory information by a selection signal; arrow 1, sites where task-related signals modulate sensory representations in the forebrain; arrow 2, sites where midbrain selection signals modulate forebrain sensory information processing based on stimulus location; arrow 3, sites where task-related signals bias space selection by the midbrain network; arrow 4, sites where sensory information from the forebrain biases space selection by the midbrain network; arrow 5, sites where midbrain selection signals modulate visual information in the OT.
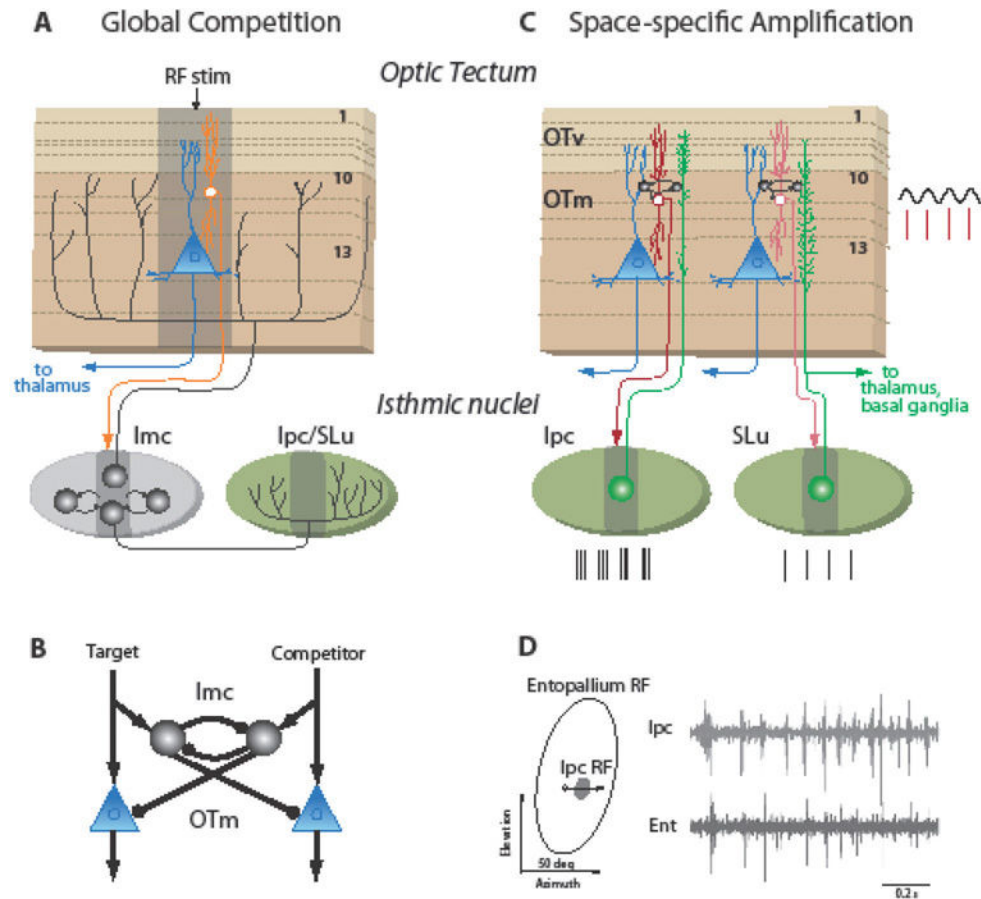
B: Diagram showing the evolutionary relationships of extant Classes and two key Orders of vertebrate animals. Based on [140].

Figure 2.
Circuits that generate selection signals in the bird midbrain selection network.

A: The circuit that mediates global competitive selection across the space map. Orange neuron: OT neurons that project to the nucleus isthmi pars magnocellularis (Imc). Blue neuron: OT neurons that project to the high-order thalamic nucleus Rotundus (Pulvinar, in mammals). Black neurons: GABAergic inhibitory neurons that project broadly to the space maps in the OT, the cholinergic isthmic nuclei (green), or to each other. Ipc: nucleus isthmi pars parvocellularis; SLu: nucleus isthmi pars semilunaris; numbers: prominent layers in the OT; RF stim: center of the region activated by a small, salient stimulus; dark gray areas: regions activated by a small stimulus. Data from [32, 36].

B: Circuit model of reciprocal lateral inhibition of feedforward inhibition that implements global competitive selection in the midbrain network. Black circles: Imc neurons; blue triangles: OTm output neurons that project to the thalamus; arrows: excitatory connections; dots: inhibitory connections. Based on [32].

C: The circuit that amplifies and rhythmically synchronizes activity in the network. Abbreviations as in **A**. GABAergic neurons (black) in layer 10a generate periodic depolarization (black oscillations) of neurons in layer 10b that project to the cholinergic Ipc or SLu [41]. Periodic spikes from layer 10b neurons (red lines) evoke periodic spike bursts in Ipc neurons (black lines) and periodic single spikes or doublets in SLu neurons (single black lines) [44]. Ipc and SLu neurons project back topographically across layers in the

visual (OTv) and multimodal OT (OTm) [36]. SLu neurons also project to the thalamus and to the basal ganglia [17].

D: Electrophysiological recordings of synchronized, periodic visual responses measured simultaneously in the pigeon Ipc (top trace) and high-order forebrain pallial area, (Entopallium; bottom trace), at sites with overlapping visual RFs, as shown on the left. The open circle and vector represent the position and trajectory, respectively, of a small bright visual stimulus that was swept across the RFs. Figure 2D is from Marin et. al. [44].
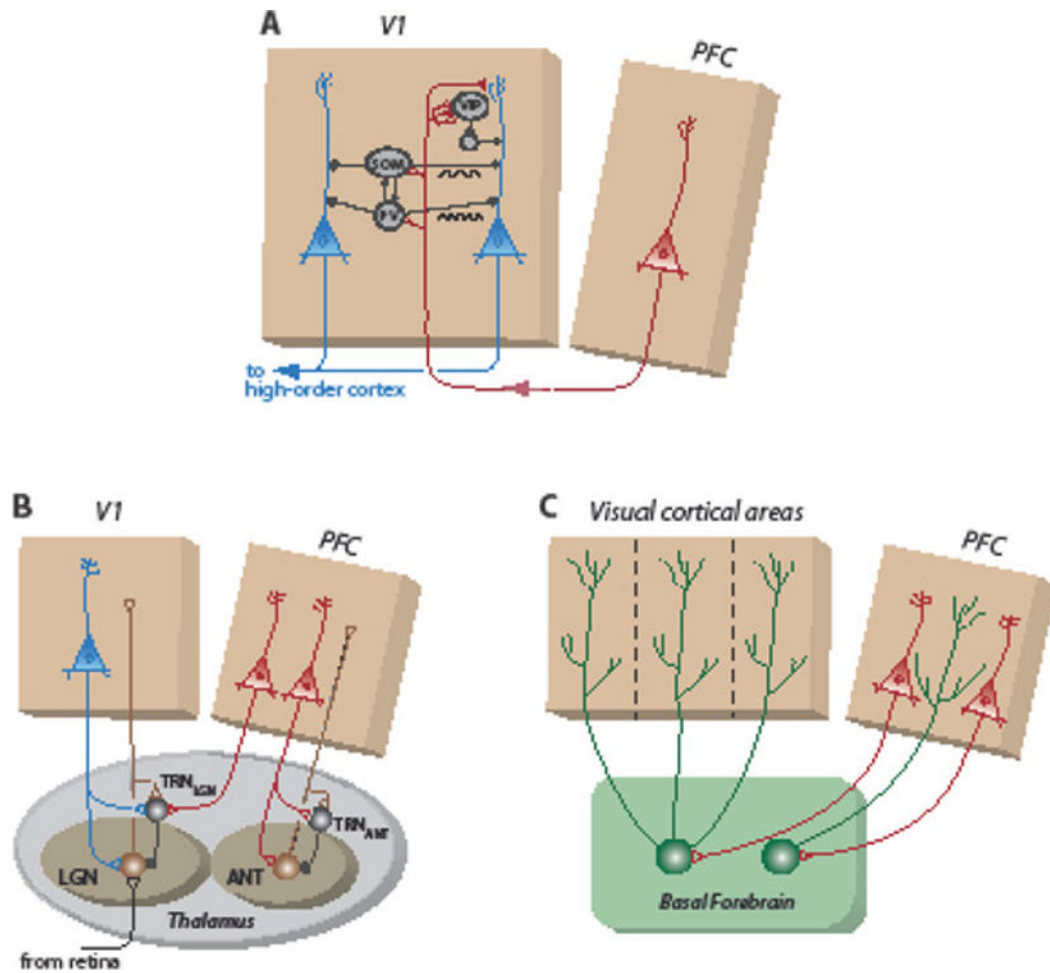
Figure 3.
Circuits that enhance or gate sensory responses in the mammalian neocortex.

A: Corticocortical feedback circuits. Red neuron: pyramidal neurons in the cingulate region of the mouse prefrontal cortex (PFC) that project to the primary visual cortex (V1). Blue neurons: layer 2/3 V1 pyramidal neurons. Black neurons: local inhibitory interneurons. PV: parvalbumin-positive; SOM: somatostatin-positive; VIP: vasoactive intestinal peptide-positive. Based on [71]. Rhythmic activation of SOM interneurons entrains resonant activity in the 5–30 Hz band, and of PV interneurons in the 20–80 Hz band (black oscillations) [98]. In monkeys, the anatomically dominant path is the direct connection from the PFC to V4 pyramidal neurons [94].

B: Thalamic circuits. Brown neurons: excitatory output neurons to the cortex. Black neurons: GABAergic inhibitory neurons in the thalamic reticular nucleus (TRN) that connect with output neurons either in the lateral geniculate nucleus (LGN) or in the anterior nuclei (ANT) [73, 111].

C: Circuits formed by cholinergic neurons in the basal forebrain (BF). Red neurons: pyramidal neurons in the PFC that project to the BF. Green neurons: cholinergic BF neurons that project to functionally related regions of the cortex or PFC.