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Bottom-up and top-down modulation of multisensory integration

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Sensory perception in the real world requires proper integration of different modality inputs. Process of multisensory integration is not uniform. It varies from individual to individual and changes at different behavioral states of the animal. What factors affect multisensory integration? How does the mammalian brain reconstruct a multisensory world at different states? Here, we summarize recent findings on bottom-up and top-down factors that can modulate sensory processing and multisensory integration. We discuss cortical circuits that are responsible for modulation of multisensory processing based on recent rodent studies. We suggest that multisensory information is not a simple, fixed signal in the brain. Multisensory processing is dynamically modulated in the mammalian brain and leads to a unique and subjective experience of perception.

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In the late 1970s, American psychologist JJ Gibson proposed an ecological approach to study visual perception [1]. One critical view he presented is researchers should consider 'moving observers', those who make active motion during visual perception. Most studies on sensory perception have been focused on animal models in unnatural conditions. Subjects must be kept immobile and receive well-controlled stimuli passively. Animals often undergo an extensive training period in this unnatural condition. In nature, however, animals 'move' around the space while rapidly processing relevant sensory information to make optimal behavioral decisions. In this natural condition, sensory processing is not just a simple representation of the stimuli in the brain. Rather, it needs to be modulated continuously for the animal to reconstruct the world in an egocentric way. To understand how this process occurs in the mammalian brain, we might need to pay more attention to Gibson's idea.

An equivalent perspective on sensory perception is 'perception is fundamentally a multisensory experience' [2,3]. Multiple sensory organs in the mammalian body simultaneously detect various physical features in the environment. Brain circuits then integrate these inputs and eventually form a multimodal percept [4]. Multisensory integration enhances neural responses to weak stimuli [5] and helps the animal to make efficient perceptual decisions by enhancing attention and increasing perceptual salience [5–7,8••]. Furthermore, multisensory integration can modify unisensory perception and even generate illusions [8••,9–11]. Where in the cortex does this multisensory processing occur? Is multisensory perception pre-determined only by bottom-up signals, or can it be modulated by changes in behavioral states, a.k.a. top-down signals?

Recently, wide-field calcium imaging in the mouse cortex has identified distinct cortical regions responding to different sensory modalities [12]. Multisensory stimuli induce rapid phase-locking of on-going network activities in the association cortex, which receives inputs across different modalities, suggesting dynamic change in the cortical population including higher-level cortices is critical for multisensory integration [13]. However, modulation of cross-modal interaction at different behavioral states of the animal is not fully demonstrated yet.

Intensities and spatiotemporal structures of the stimuli initiate neural signals in the sensory system. These are core bottom-up features that can elicit patterned activity in sensory neurons. The bottom-up sensory responses are further modulated by top-down information in the brain such as memory, attention, and motor status. In fact, top-down information is always present in the brain before the bottom-up signal arrives, as animals constantly adjust their behavior using accumulated experience. An unresolved question here is when and how does the modulation occur in the steps of multisensory integration. In this review, we summarize both bottom-up and top-down factors that can modulate multisensory integration. We first identify bottom-up features that are critical for basic construction of a multisensory percept. We next examine top-down factors that can modulate sensory processing and discuss their potential roles in multisensory integration. In each step, we examine cortical circuits that can mediate the bottom-up and top-down processing based on recently identified cortical circuits in mice [14••].

Bottom-up processing for the multisensory integration

Multisensory perception starts with modality-specific processing of unisensory inputs that have unique bottom-up features. Here, we discuss critical features in the bottom-up signal for construction of a multisensory percept and further examine cortical circuits that are responsible for delivering and integrating unisensory features (Figure 1).

Strength of the sensory stimuli

Perceptual salience is initially determined by the stimulus intensity, which is determined by physical strength of the stimulus. Stronger stimuli can recruit more attention and elicit higher responses in the sensory system [5,15]. The more salient modality in the multisensory stimulus often dominates other modalities and reduces integration effects [8••,16]. Therefore, matching the salience between modalities is important for experiencing a multisensory percept. When different modalities in a multisensory stimulus indicate the same information (a.k.a. congruency between modalities), multisensory effects become stronger during perception [8••,17]. Furthermore, an increase in perceptual salience by multisensory integration becomes higher when the stimulus intensity becomes weaker. This effect is known as the 'inverse effectiveness' [5]. Inverse effectiveness has been explained by the non-linear characteristics of multisensory response in neurons receiving multiple unisensory inputs [5,18]. Overall, multisensory perception is largely modulated by the strength of unisensory inputs constructing a multisensory stimulus. It is degraded when salience is not matching between modalities and becomes stronger when the stimulus intensity becomes weaker across modalities (Figure 3).

Spatial location of the sensory stimuli

Sensory stimuli are localized in space. Understanding location of stimuli is critical for an animal to find where objects and events are in space. The ventriloquism effect illustrates an illusory sound localization induced by the apparent visual stimuli in space [11]. This effect can be explained by better resolution in vision compared to audition for the space perception. In other words, when an object is detected by the perceptual search, the visual information in space dominates other senses and makes the observer believe other sensory modalities are co-localized at the visual location. However, the spatial information also exists in other modalities including audition [19], and this can help the space perception in vision. For example, the pre-cued auditory stimuli can facilitate the visual search for the stimulus [20,21]. Thus, perceptual localization of the sensory stimuli in space can be facilitated by the cross-modal integration.

The timing of the sensory stimuli

Temporal coherence between the modalities helps binding between different modalities and enhances perception [22]. If temporal mismatch occurs between the modalities, it can induce an illusory perception. One example is the sound-induced flash illusion (SiFi), which shows auditory inputs from the beeping sounds generate illusory visual perception of the flashing light [10]. In this case, audition dominates vision. This effect can be explained by the higher temporal resolution in audition than vision, and thus audition leads vision in the audiovisual integration of the temporally mismatching stimuli [23].

Circuits for the multisensory integration

Sensory inputs first enter the primary sensory cortex in a modality selective manner. Visual, auditory and somatosensory cortices not only receive modality-specific inputs but they innervate each other and receive information from other modalities [14••,24–31] (Figure 1). Direct projection from the auditory cortex to the visual cortex can modulate visual processing and perception [32,33], and neurons in the visual cortex even show direct response to the auditory stimuli [26]. This circuit can be responsible for sound-induced illusory visual perception as shown in SiFi [34]. The auditory cortex also receives a direct projection from the visual cortex, which modulates auditory responses in it [35,36]. The cross-modal projections between unisensory cortices can mediate faster integration process and might play a crucial role during the temporal integration of multisensory inputs. Supporting this idea, a recent study in ferrets shows visual inputs to the auditory cortex can promote perceptual binding of temporally modulated sounds [37].

Output projections from the sensory cortices reach to higher association cortices, where multisensory integration occurs as well [8••,38–40] (Figure 1). Indeed, many frontal areas receive converging inputs from the sensory cortices (Figure 1a). One important region is the posterior parietal cortex (PTLp), which has been identified as playing an important role in the cross-modal integration [8••,41–44]. Another interesting area is the retrosplenial cortex (RSP), which receives stronger inputs from the visual cortex than other sensory cortices. It forms an important network with other brain areas processing spatial information [14••] (Figure 1, purple lines). The biased convergence of multisensory inputs to the RSP might be responsible for dominance of visual stimuli in space perception. When animals experience multisensory perception, association cortices are activated simultaneously. Interaction among cortical areas needs to be measured to understand how the association cortices act in concert to generate a coherent multisensory percept in behaving animals. Future studies are required to understand the relationship between the connectivity between higher association areas and multisensory perception in behaving animals.

Top-down modulation of the multisensory integration

The bottom-up information in the sensory cortex can be modulated by the top-down signals that represent the