

Multisensory Conflict Resolution: Should I Stay or Should I Go?

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Swift action is often required in the face of indeterminate sensory evidence. In this issue of *Neuron*, Song et al. (2017) describe an inhibitory circuit in the posterior parietal cortex that evaluates conflicting auditory and visual cues and supports resolute perceptual decision making.

The American novelist F. Scott Fitzgerald famously remarked, “The test of a first-rate intelligence is the ability to hold two opposed ideas in the mind at the same time, and still retain the ability to function” (*The Crack-Up*). In this issue of *Neuron*, Song et al. (2017) put this idea to the test by describing a neural circuit in the mouse cerebral cortex that weighs conflicting sensory evidence and provides a singular output in support of purposeful behavior. Many regions of the cerebral cortex are modulated—if not explicitly driven—by inputs from more than one sensory modality. In fact, accumulating evidence suggests that purely unimodal regions of sensory cortex may be more the exception than the rule (Ghazanfar and Schroeder, 2006). Contemporary multisensory research has identified a set of principles that describe how moderately effective, spatially and temporally co-registered stimuli from distinct sensory modalities are combined in key regions of the brain to elicit a neural response that is more than the sum of its parts (Stein and Meredith, 1993). Recent findings suggest that distributed cortical networks reassemble congruent signals flowing in from distinct mechanical and chemical senses to construct a perceptual gestalt that supports better informed perceptual decision making than could be derived from any one sense alone (Bizley et al., 2016).

But what if signals from distinct sensory modalities are conflicting rather than congruent? In a classic multisensory illusion known as the McGurk effect, pairing the audio track of a spoken phoneme (e.g., “ba”) with the video of someone producing a mismatched phoneme (e.g., “ga”) often elicits the perception of a third

sound that lies somewhere in between the auditory and visual stimuli (e.g., “da”) (McGurk and MacDonald, 1976). Whereas the *perception* of incongruent stimuli might reflect an intermediate mixture of their unisensory components, *action* must be swift, decisive, and singular. Suppose, for example, that a crosswalk signal visually indicates that it is safe to cross the street but the squeal of tires from an approaching car suggests otherwise. Should you cross the street or stay put? Executing the intermediate motor behavior would not be rewarded. Clearly, taking definitive action in the face of conflicting perceptual evidence is a matter of paramount importance to our survival, but how does the brain reach a timely solution?

Here, Song et al. (2017) perform an ingenious set of experiments to identify a neural circuit in the mouse parietal cortex that performs just such an operation. Head-fixed mice were trained in a Go-Nogo task arranged in two different configurations. In the first configuration, licking a spout after an auditory stimulus triggered a water reward, but licking after a visual stimulus resulted in a puff of air to the face. The second configuration was just the opposite; licking after an auditory stimulus triggered an air puff, while licking after a visual stimulus elicited a water reward. Once mice were well trained and the stimulus intensities from each modality were matched for perceptual salience, unreinforced multisensory trials would occasionally occur, in which both auditory and visual stimuli were presented simultaneously. In the face of conflicting sensory cues, would the mice execute the behavior consistent with the auditory stimulus, visual stimulus,

or something in between? The answer was clear; the behavior followed the auditory cue, regardless of its hedonic association (Figure 1A).

Song et al. (2017) hypothesized that the neural circuit responsible for this auditory primacy would likely be found in the cortex, either in early stages of auditory or visual processing (ACTx and VCtx, respectively), or in a downstream multisensory region (Figure 1B). They addressed this hypothesis through a series of experiments designed to home in on a neural circuit responsible for converting conflicting auditory and visual cues into a singular, auditory-guided behavior. Unsurprisingly, auditory cues continued to dominate in multisensory conflict trials when VCtx was inactivated with muscimol (Experiment 1, Figure 1C). Interestingly, inactivating ACTx switched the behavioral outcome on multisensory trials to visual dominance, such that Go-Nogo responses followed the visual cue instead of the auditory cue (Experiment 2, Figure 1C). Song et al. (2017) then confirmed that direct optogenetic activation of excitatory neurons in either region could be substituted for natural sensory stimulation, with ACTx dominance in trials where both cortical regions were simultaneously activated (Experiment 3, Figure 1C). Having demonstrated that the activity of excitatory neurons in ACTx was both necessary and sufficient for auditory dominance in multisensory conflict trials, the most straightforward interpretation was that ACTx activation directly suppressed unit responses in VCtx. However, unit recordings from VCtx failed to show any evidence of cross-modal suppression when ACTx was activated alone

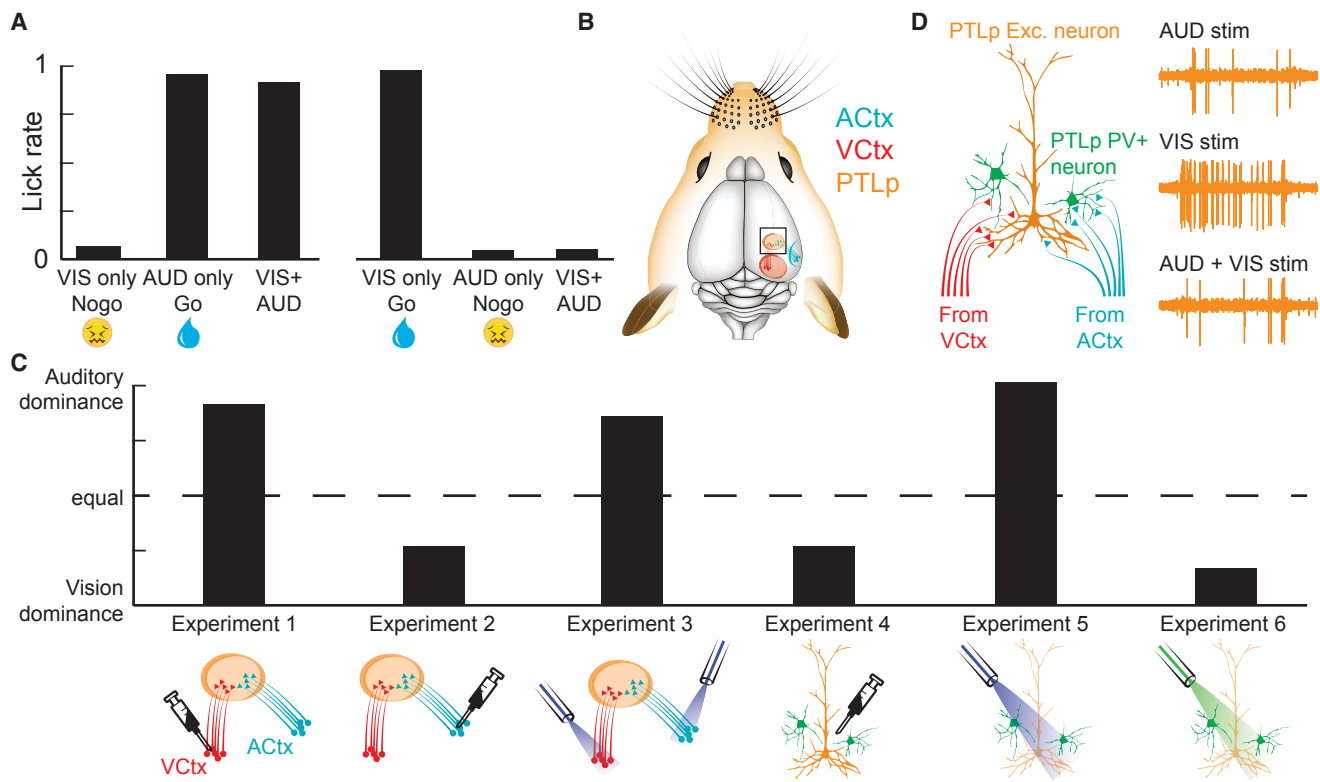


Figure 1. A Neural Circuit for Auditory Primacy in Multisensory Conflict Resolution

(A) Head-fixed mice were trained on a Go-Nogo behavior that rewarded licking after auditory cues (AUD) but not visual cues (VIS, left), or vice versa (right). On trials where both cues are presented simultaneously, licking behavior follows the auditory cue.

(B) In the mouse, auditory and visual cortex (ACtx and VCtx, blue and red, respectively) project to the posterior parietal cortex (PTLp, orange, marked with black square).

(C) Auditory dominance in multisensory conflict behavioral trials was characterized in six experiments. Experiments 1–3, activity levels were manipulated in ACtx and VCtx. Experiment 4, non-selective inactivation of PTLp. Experiments 5 and 6, selective manipulations of parvalbumin-expressing (PV) GABA neurons (green). Syringe denotes muscimol injection. Blue and green light represent activation of neurons expressing ChR2 or silencing of neurons expressing ArchT, respectively. (D) ACtx projections disproportionately target PV interneurons in PTLp. Spiking in PTLp units that respond to VIS but not AUD cues are suppressed when both modalities are presented simultaneously, perhaps on account of stronger feedforward connectivity from ACtx onto PTLp GABA neurons.

or in combination with VCtx. This suggested that the dominance of audition over vision might reflect processing in a downstream area that received and compared inputs from earlier stations of cortical sensory processing.

Neuroanatomical tracer studies identified the posterior parietal cortex (PTLp) as a prime candidate because it received inputs from both ACtx and VCtx. Indeed, inactivating PTLp with muscimol had no effect on unisensory detection but caused a switch from auditory dominance to visual dominance during multisensory conflict trials (Experiment 4, Figure 1C). This result confirmed that PTLp was involved in the expression of auditory dominance, but how was the circuit organized? One possibility was that excitatory projections from ACtx disproportionately contacted GABAergic interneurons within PTLp.

Song et al. (2017) tested this hypothesis by tracing the monosynaptic inputs onto excitatory and inhibitory PTLp neurons with a pseudotyped rabies virus. This experiment confirmed that parvalbumin-expressing (PV+) and somatostatin-expressing interneurons in PTLp were biased toward inputs from ACtx, as compared to VCtx (Figure 1D). Furthermore, PTLp units driven by visual stimulation, but not auditory stimulation, were nonetheless strongly suppressed when auditory and visual stimuli were presented simultaneously, suggesting that ACtx inputs suppress visual responses in PTLp by disproportionately activating select populations of inhibitory interneurons (Figure 1D, right). If this were the case, then activating PV+ neurons in PTLp would exacerbate the normal auditory dominance, whereas silencing PV+ neu-

rons in PTLp would switch the dominance in multisensory conflict trials from auditory to vision. A final series of optogenetics experiments supported both of these predictions by showing that increasing or decreasing the activity of PV+ neurons in PTLp was sufficient to shift the bias in behavioral choice from extreme auditory dominance to extreme visual dominance, respectively (Experiments 5 and 6, Figure 1C).

The work of Song et al. (2017) uses a powerful combination of techniques to dissect a neural circuit subserving auditory primacy during perceptual decision making based on conflicting audiovisual cues. Most impressively, they demonstrate that auditory dominance may be the default state, but it was not the obligatory state. Song et al. (2017) were able to smoothly shift their subjects' behavior

between auditory and visual bias by adjusting (1) the physical intensity of the auditory and visual sensory cues, (2) the activity of excitatory neurons in ACtx or VCtx, and (3) the activity levels of PV+ GABA neurons in PTLp. Thus, it seems that PV+ neurons in PTLp are in a key position to adjudicate between competing sensory signals and rule in favor of one modality over another. Although this study used pharmacologic and optogenetic methods to artificially override the normal activity in PTLp, one is tempted to speculate that PTLp PV+ neurons might be naturally engaged to dynamically shift the weighting of evidence-based cues in support of flexible multisensory perceptual decision making (Morcos and Harvey, 2016). As an example, self-initiated locomotion suppresses sound-evoked activity in the auditory pathway but simultaneously enhances visually evoked responses in the visual pathway (Williamson et al., 2015). Based on the evidence presented here, reducing the gain on ACtx output while increasing VCtx gain might flip the mode of conflict resolution from auditory to visual dominance as mice transition from still to running. Clearly, the findings reported in this paper will inspire many future studies to monitor the natural forms of engagement and modulation in this multisensory circuit.

The data presented here also raise several interesting questions about the organization of GABA circuits in PTLp. Silencing activity in PTLp with muscimol, a GABA_A agonist, switched sensory dominance in multisensory conflict trials from auditory to visual (Experiment 4 in Figure 1C), yet selectively activating PV+ GABA neurons in PTLp made the auditory bias more extreme (Experiment 5, Figure 1C). This comes as a surprise, as optogenetic activation of PV+ interneurons is often used to suppress all local network activity and thus would be expected to have the same outcome as muscimol, not the opposite. The results of Experiments 4–6 (Figure 1C) and others described in their study hint that the organization of GABA circuits in PTLp might differ from the typical organization described in earlier stages of cortical sensory processing. On a final note, one cannot help but wonder to what extent the findings reported by Song et al. (2017) reflect a broader principle of multisensory processing as opposed to a peculiarity of their behavioral paradigm or neural circuit organization in the rodent brain. After all, it is not clear why, all things being equal, the behavioral report of the mouse would side with the auditory input and not the visual input. The same bias may not be shared with other species.

What is clear is that the brains of many species have evolved strategies to resolve internal conflict between the senses. For example, when the pitching and rolling of a boat in rough seas sends our sensory systems into turmoil, staring at the horizon can help resolve the mismatched multisensory signals generated by the motion of the ship versus the motion of the body (Mayo et al., 2011). When confronted with incongruous sensory inputs, the mouse brain may be predisposed to follow its ears over its eyes.

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