feeding rhythm during the Arctic polar day and night [14], and the emperor penguin (*Aptenodytes forsteri*) loses its melatonin rhythm during the Antarctic mid-winter [15]; on the other hand, several Arctic rodents and carnivores have been reported to exhibit 24-h activity rhythms during the polar day and/or in constant conditions [16–19]. Clearly, further comparative studies are needed to determine the species characteristics that lead to differential dependence on circadian control at the poles.

Importantly, circadian arrhythmia in reindeer does not mean complete arrhythmia. Indeed, as Lu *et al.* [1] point out, they display precisely timed annual reproductive cycles, perhaps involving a distinct 'circannual' clock. They also exhibit robust ultradian activity rhythms (with periods <24 h) throughout the year, which may represent the frequency best-suited to the energy and digestive requirements of a large Arctic herbivore [3]. Suppression of circadian and enhancement of ultradian rhythmicity is also a known feature of a non-Arctic rodent, the common vole (*Microtus arvalis*), and laboratory experiments have begun to dissect the underlying mechanisms [20]. Animals everywhere are confronted by environments that demand specialized behavioral and metabolic responses; for those of us intent on understanding the adaptive significance of clocks and rhythms, the premier experimental resource remains the richness and diversity of the natural world.

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Auditory Neuroscience: Recalibration of Space Perception Requires Cortical Feedback

Behavioral implications for the massive feedback connections from auditory cortex to the inferior colliculus have been elusive, but at last one has been identified — cortical feedback is required for recalibration of spatial hearing following changes to the auditory periphery.

Asif A. Ghazanfar

Most of us are probably more familiar with the story of Vincent van Gogh's missing ear than with his paintings (Figure 1A). The urban legend — the one you probably heard in elementary school — is that he cut off his own ear to demonstrate his unrequited love for a woman. The official version of the story, according to the Van Gogh Museum in Amsterdam, is that he cut off his ear after fighting with his friend and roommate, the French artist Paul Gauguin, and then presented the severed ear to Rachel, a favorite prostitute at a local brothel. The revisionist story, based on a re-examination of witness accounts and the artist's letters, is that he did not in fact cut off his own ear, but that Gauguin hacked it off during a sword fight [1]. The two artists agreed to cover up the truth. What is not in dispute by either Gauguin, historians, van Gogh's physician or subsequent physicians reviewing his case, is that van Gogh suffered from mental illness; the physicians diagnosed temporal lobe epilepsy severely exacerbated by his heavy drinking of absinthe [2]. There is also the possibility that the epilepsy and heavy drinking led to lesions in the temporal lobe [3].

Modern neuroscientists might add to this story the following: that immediately after he or Gauguin cut of his outer ear, van Gogh would have problems localizing sounds on the side of his body missing the ear, but that over time, however, these localization deficits would disappear. Even in adulthood, changing the shape of the mammalian outer ear leads to problems with identifying the location of a sound source, but continued experience coupled with neural plasticity allows for a ‘recalibration’ of the auditory system. Over the course of days or weeks, problems identifying the locations of sounds disappear. For example, altering spatial cues by fitting moulds in the outer ears of human subjects disrupts their elevation judgments, but their errors disappear after weeks of wearing the moulds [4]. Similarly, adult ferrets with one of their ears chronically plugged make localization errors that disappear over the course of days if the ferrets continue their training regime [5].

In all likelihood, therefore, a mangled outer ear would have given van Gogh a different set of auditory cues leading to spatial hearing problems soon after the incident — just as a similar affliction might affect an animal injured in a fight. Through the use of on-going auditory experience, the mammalian brain evolved the ability to recalibrate our hearing. But what of the hypothesized lesions to van Gogh’s neocortex? The cortex of a mammal’s brain has an amazing ability to remap after injury, and many neuroscientists would claim that were van Gogh’s epilepsy or absinthe-drinking to have damaged his auditory cortex, his ability to recalibrate might be lost. New data from a remarkable experiment suggest that this is true, but that it involves an unexpected neural pathway.

Bajo and colleagues [6] investigated what role the auditory cortex may play in the recalibration of spatial hearing. They were specifically interested in whether feedback connections from layer V of the auditory cortex to the inferior colliculus play a pivotal role. The inferior colliculus is sensitive to many acoustic features, including the three cues that we use to localize sounds in space: differences in the level or the time-of-arrival of sounds at the two ears, and spectral cues provided by the filtering properties of the outer ear. These cues are combined in the inferior colliculus. This structure also receives a massive feedback projection from layer V of the auditory cortex [7,8] and the response properties of collicular neurons are modulated when the auditory cortex is electrically-stimulated [9]. But while the anatomy and physiology show an influence of auditory cortex on the inferior colliculus, a direct demonstration that this cortical feedback influences *behavior* had not been forthcoming.

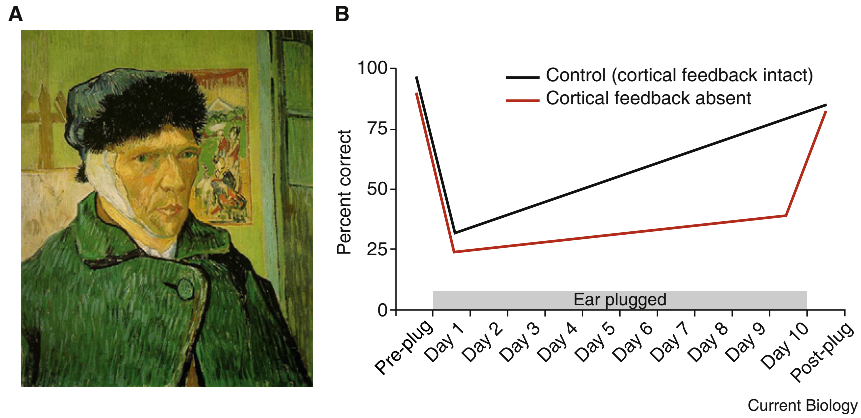

Figure 1. Recalibrating spatial hearing after a peripheral perturbation — with and without cortical feedback to the inferior colliculus.

(A) ‘Self-portrait with cut ear’ by Vincent van Gogh. (B) Recalibration is hampered in the absence of cortical feedback to the inferior colliculus. Percentage correct scores (averaged across all speaker locations) for sound localization accuracy in the session before one ear was plugged (Pre-plug), on each of the 10 days over which the plug was worn (day 1–10) and in the session following its removal (Post-plug).

Bajo *et al.* [6] trained ferrets to localize sound in a circular arena with speakers distributed evenly along the wall. When a burst of broadband noise was played through one of the speakers, the ferrets simply had to identify the correct speaker by moving towards it to receive a reward. Following this training, two critical manipulations were applied. The first was to lesion only those cortical neurons that sent projections to the colliculus. This goal precluded the use of standard cortical inactivation techniques, such as cooling or infusing GABA-agonists, because these methods would disrupt all layers of the neocortex as well as neurons in layer V that do not project to the colliculus. This would obscure the role of cortical feedback as any subsequent behavioral deficits could not be attributed to a specific pathway. To make the lesion specific, the authors used a technique called ‘chromophore-targeted photolysis’. Briefly, microbeads conjugated with chlorine e_6 are injected into the inferior colliculus. There, they are taken up by axon terminals and retrogradely transported to cell bodies. When near-infrared light is shown on those cell bodies, it activates the chlorine e_6 that then produces singlet oxygen, a toxic free-radical that kills the cells. In the present case, while many neurons projecting to the colliculus probably took up the chromophore, only those neurons that were targeted by the light (that is, the cortical neurons) were killed. In this way, Bajo and colleagues lesioned only those layer V cortical neurons that sent feedback projections to the inferior colliculus.

The second critical manipulation was blocking one of the ferrets’ ears (the ear contralateral to the side of the lesion). As alluded to above, blocking a single ear results in immediate problems with localizing sounds, particularly those on the same side as the blocked ear. After 10 days of training, ferrets adjust their auditory system to deal with the attenuated signals coming from the blocked ear and could localize sounds just fine. The key question is this: could they do this without that feedback pathway from the auditory cortex to the inferior colliculus? The answer is no: relearning sound localization using the new cues induced by blocking one ear was severely disrupted by the lesion of that feedback pathway (Figure 1B) [6].

Importantly, the cortical lesions did not affect sound localization per se: before plugging the ear, ferrets with lesions performed the sound localization task just as well as control ferrets. Furthermore, putative damage to the colliculus caused by the injections of microbeads did not lead to any discernable deficits either, showing that the effect could not be the result of nonspecific collicular damage.

Beyond hypothetical scenarios about the consequences of van Gogh's mangled ear, Bajo *et al.*'s [6] discovery of a role for auditory cortical feedback to the inferior colliculus in recalibrating sound localization behavior has important clinical ramifications for current sufferers of hearing loss. In particular, the escalation of military deployments has created an unprecedented amount of auditory impairment. Historically, nearly one-third of Union soldiers from the United States suffered hearing loss in one ear (which ear depended upon which side they held their rifles) [10]. Modern soldiers often experience blast exposure leading to peripheral hearing loss accompanied by traumatic brain injury [11]. Soldiers exposed to blasts have a high chance of being hit by flying objects or of being picked up by the blast wave and colliding with a stationary object, such as a vehicle or a wall. In both cases, there is a significant chance that the brain suffered impact, and the auditory areas of the temporal lobe are among the most commonly affected regions [12].

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