Our molecular knowledge of mitophagy has greatly expanded in the last decade, mainly due to investigations of stimulus-induced mitophagy *in vitro*. During multicellular organism development, mitophagy occurs under the control of developmental signaling and in a context-dependent and cell-specific manner [3]. The clearance of mitochondria in the *Drosophila* midgut provides a premium model for exploring fundamental questions about mitophagy, including how the mitochondrion-surrounding isolation membrane forms, where the membrane comes from for the formation and expansion of the isolation membrane, how ubiquitin is involved in this process, and how mitophagy affects cellular remodeling.

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Speech Comprehension: Stimulating Discussions at a Cocktail Party

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When humans listen to speech, ongoing cortical oscillations entrain to the acoustic signal. New research demonstrates that electrically stimulating the brain in time with speech rhythm can improve intelligibility for speech in noise.

In the midst of a noisy conversation, some people are typically more interesting to listen to — or more important to listen to — than others. One of our challenges as listeners is to focus our attention on what a target speaker is saying so we can hear them above the din (or above a less-interesting conversational partner). This situation is frequently referred to as the

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'cocktail party' phenomenon [1], although in fact it commonly occurs in the absence of mixed drinks. A central focus for speech research has been understanding the mechanisms and limitations of perception in the midst of background noise or competing talkers. Converging evidence indicates that ongoing brain activity is sensitive to the rhythm of spoken sentences, providing a possible mechanism for listeners to 'lock on' to a talker of interest. A new study by Riecke *et al.* [2], reported in this issue of *Current Biology*, demonstrates that experimentally altering cortical oscillations using noninvasive brain stimulation improves a listener's ability to understand speech in noise.

The concept of oscillatory entrainment is critical to understanding the approach taken by Riecke *et al.* [2]. When human brain activity is measured noninvasively using electroencephalography (EEG) or magnetoencephalography (MEG), periodic fluctuations (i.e., oscillations) can be observed that reflect shifts in population-level neural activity. Neural oscillations are described in terms of their frequency, amplitude, and phase. Oscillatory activity is ubiquitous in the brain, and has been suggested to underpin computational processes including cross-region communication, sensory prediction, and attentional selection [3,4].

In the context of language processing, recent years have seen a flurry of interest in the role of low-frequency (3–7 Hz) cortical oscillations in speech comprehension [5,6]. These experiments have been motivated in part by findings in animals showing that the phase of ongoing cortical oscillations align (or entrain) to external stimuli, and that this entrainment can aid perception [7]. In humans, numerous studies have shown that oscillations in the 3–7 Hz range lock on to the acoustic speech signal, and can discriminate between different sentences being presented [8], show stronger locking to the speech signal when speech is intelligible [9], and represent the attended-to speaker more strongly than the ignored speaker in divided attention tasks [10]. Low-frequency oscillations also appear to form the foundation for a hierarchy of nested oscillations spanning multiple brain regions [11], consistent with both animal work [12] and theoretical models of packet-based speech perception [13].

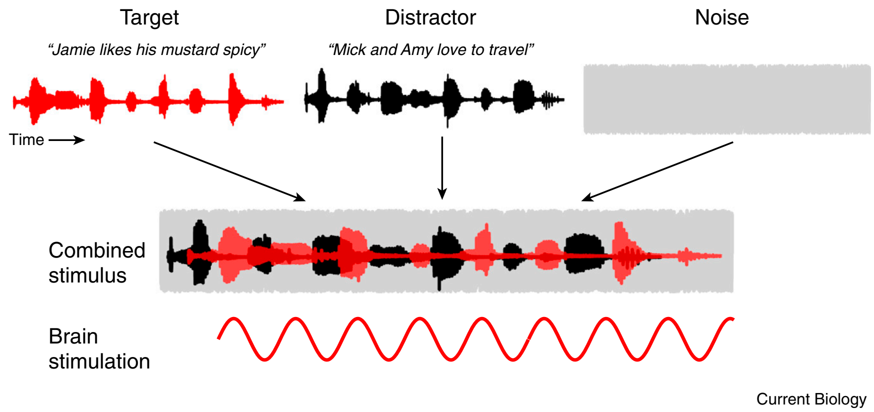

Figure 1. Noninvasive brain stimulation improves speech perception.
In the first experiment reported by Riecke *et al.* [2], listeners heard two simultaneous talkers in background noise. The rhythm of the two talkers was fixed to 4 Hz and the talkers adjusted so that the sentences alternated (more precisely than in this toy example). tACS stimulation was then applied sinusoidally to line up with the target talker (in red: "Jamie likes his mustard spicy") rather than the distractor (in black: "Mick and Amy like to travel"). The authors found this alignment resulted in improved perception for the target talker. The implication is that rhythmic brain stimulation altered the excitability of neural populations involved in speech processing.

Although prior studies have consistently shown a relationship between the acoustic speech signal and brain oscillations, they have failed to answer a critical question regarding causality: is cortical oscillatory entrainment to speech a result of perception, or might it cause perception? Or, put another way, is it possible to adjust a listener's brain activity, and by doing so improve their perception? In order to experimentally manipulate the timing of a listener's brain oscillations independently of what they heard, Riecke *et al.* [2] used transcranial alternating current stimulation (tACS). In tACS, electrodes are placed on a participant's head and a low voltage current is passed between them [14]. The current travels through the skull into the brain, altering the electrical activity in the regions it passes through. The current is assumed to thus alter the excitability of neural populations. tACS therefore provides a method for inducing brain oscillations that align with a speech signal that can be used to test whether doing so alters a listener's performance.

For a well-controlled experiment, it would be ideal to have clear phase differences between the speech of two talkers, so that brain stimulation could be unambiguously aligned to a target or a distractor. This approach is challenging, however, because conversational speech is seldom temporally regular. Riecke *et al.* [2] therefore cleverly constructed stimuli that sounded relatively normal, but which had a regular pattern. This allowed them to create two-talker stimuli in which the target talker and distractor alternated, and to deliver brain stimulation at a regular frequency that could be selectively aligned with the speech of a target talker (Figure 1). Alternatively, brain stimulation could be delivered at the same frequency, but shifted in time relative to the target talker. The authors found that tACS pulses delivered in synchrony with a target talker improved the accuracy of listeners' perception for the target talker, an effect that disappeared as the temporal alignment between the tACS and the talker changed.

As a further test of the effect of rhythmic tACS on speech perception, Riecke *et al.* [2] performed a second experiment with a single talker, but with digitally-manipulated speech that removed the amplitude changes most associated with speech rhythm [15]. In other words, now the acoustic signal was not suited to drive cortical oscillations. Using tACS, the authors applied stimulation that matched the rhythm of the original speech, and found once again that aligned tACS improved perception. Thus, the findings of these two experiments are in agreement, and suggest that when cortical oscillations are aligned with the speech signal listeners have an easier time understanding it. Consistent with this conclusion, recent work combining tACS with fMRI shows that speech-timed brain stimulation leads to increased responses for intelligible speech in regions associated with language processing [16].

There are a number of questions that might be addressed in further investigations using tACS to alter brain oscillations during listening. For example, is it possible to disentangle effects of tACS on attention from effects of tACS on perceptual sensitivity? In addition, some prior studies with nonspeech auditory stimuli have found striking individual differences in the relationship of cortical oscillations to the acoustic signal [17] — that is, all listeners displayed cortical oscillations that entrained to what they were hearing, but at different temporal lags. Do these individual differences in temporal lag also influence the efficacy of tACS timing? Another area ripe for study is how to apply findings from temporally regular speech (as used by Riecke *et al.* [2]) to speech that has a rhythm closer to everyday conversation, which is predictable but seldom periodic [18].

Perhaps the most tantalizing aspect of this new work is it helps pave the way for real-time modulation of brain oscillations to aid speech perception. Noise-cancelling headphones reduce the influence of background sound by performing real-time calculations and generating shaped acoustic signals to counteract unwanted noise. Is there a future in which we use real-time neuromodulation to help us understand each other at a cocktail party? Thankfully, it will no doubt still be important that we have something worthwhile to say.

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Brain Rhythms: Higher-Frequency Theta Oscillations Make Sense in Moving Humans

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The hippocampal theta rhythm is critical for learning and memory. New research demonstrates that theta oscillations in freely moving humans are similar in frequency and function to those observed in rodents and are modulated by movement speed and exploratory behavior.

Going for an early morning run in El Moro Canyon is an unforgettable experience. Despite its familiarity, it somehow feels a tad different every time. The sensory barrage around each turn is a welcome change from the office setting that will occupy the rest of my day. Each point in the breathtaking landscape leaves a lasting memory, one that I myself help create as I move through the landscape. Much of our lives is spent moving and exploring in the same way, crafting experiences that are the result of our unique interactions with the world. In the evolutionary sense, we are

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