Action–perception mismatch in tone-deafness

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The source of conscious experience has fueled scientific and philosophical debates for centuries. In the auditory and motor domains, it is not yet known how consciously and unconsciously obtained information combine to enable the production and perception of speaking and singing. Both forms of vocalization rely upon the interaction of brain networks responsible for perception and action. While perceptual experience and executed actions are usually well coupled, dissociations between perception and action can be informative. Here we report such a dissociation: tone-deaf individuals, who cannot consciously perceive pitch differences, can paradoxically reproduce pitch intervals in correct directions. Our results suggest that multiple neural pathways have evolved for sound perception and production, so that pitch information sufficient for intact speech can be obtained separately from pathways necessary for conscious perception.

Pitch perception is a central function of the human and animal auditory system [1,2]. Humans are generally able not only to consciously perceive pitch differences, but also to produce pitch intervals accurately via the interaction of perceptual and motor neural systems [3], thus enabling the communication of musical and linguistic information. However, this ability is selectively impaired in one special population: people affected by tone-deafness, also known as congenital amusia, report musical difficulties or have been told that they sing out of tune, but have normal audiometry and no obvious language problems [4,5]. Psychophysically, one hallmark of tone-deaf individuals is their inability to consciously discriminate pitches less than one semitone apart [5,6]. This dichotomy offers a unique model to test the relationship between conscious perception and unconscious actions, and between brain mechanisms responsible for action and perception. We tested the hypothesis that tone-deaf individuals might have dissociated abilities in pitch perception and production. Using psychophysics combined with sound analysis of singing in tone-deaf and control samples, we provide evidence for intact but imprecise abilities in pitch production despite impaired perception.

Tone-deaf listeners were identified based on their performance on the Montreal Battery of Evaluation of Amusia (MBEA) (see Supplemental Data). In a first experiment assessing perception and production, pairs of pure tones, forming different small intervals, were presented to tone-deaf and normal control individuals. Listeners reproduced the tone intervals by humming (*production task*), and then indicated verbally whether the second tone was higher or lower than the first (*perception task*).

Tone-deaf listeners performed at chance for the perception task, and were significantly worse than controls. In the production task, however, tone-deaf individuals were above chance at producing the correct pitch direction, with performance being indistinguishable from controls (Figure 1). This dichotomy between perception and production points to a dissociation between action and perception pathways in the auditory system [7], possibly analogous to action-blindsight in the visual system [8].

Pitch extraction of sung intervals showed that, while directions of interval production were intact, variability in produced pitches compared to target pitches was significantly higher in tone-deaf listeners than in controls (Figure 2A,B). Thus, although tone-deaf listeners could produce pitch intervals in target directions, the pitches they produce are imprecise and highly variable. This leads to the common observation that tone-deaf individuals are unable to sing in tune.

To further characterize the dichotomy between production and perception, we conducted adaptive staircase procedures on a subset of subjects (tone-deaf group: N = 3; control group: N = 3) to assess the psychophysical thresholds of production and perception (see Supplemental Data for details). For tone-deaf individuals, production thresholds (mean = 12.3 Hz, SD = 2.5 Hz) were much smaller than perception thresholds (mean = 36.2 Hz, SD = 2.0 Hz). In contrast, control subjects showed nearly identical thresholds for production and perception, with a slightly larger production threshold (mean = 2.5 Hz, SD = 1.0 Hz) than perception threshold (mean = 2.0 Hz, SD = 0.8 Hz). Paired t-tests comparing thresholds for perception and production were conducted for each individual subject using confidence intervals obtained from reversal points in the adaptive staircase procedure (in Hz). The results show significantly different perception and production thresholds for every tone-deaf subject (subject 1: $t(5) = 5.9$, $p = 0.002$; subject 2: $t(5) = 2.6$, $p = 0.047$; s3: $t(5) = 3.6$, $p = 0.02$) but no such dissociation between perception and production thresholds for every control subject (subject 1: $t(5) = 1.3$, $p = 0.3$; subject 2: $t(5) = 2.0$, $p = 0.1$; s3: $t(5) = 1.0$, $p = 0.4$; see Figure S1 in the Supplemental Data). These individual statistics confirm that perception and production are mismatched in tone-deaf individuals but not in controls.

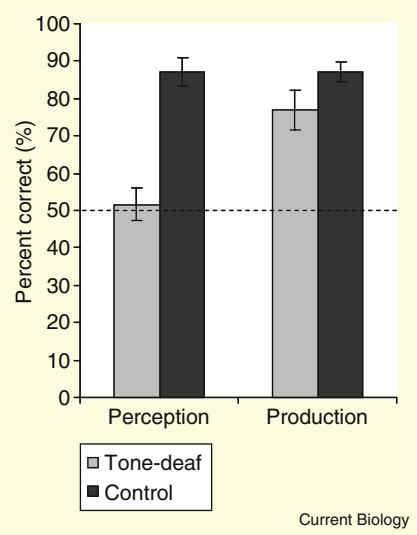

Figure 1. Perception and production accuracy in tone-deaf and control listeners.

Each trial was scored as correct if the direction of verbal report (in the *perception task*) or the direction of produced fundamental frequencies (in the *production task*) was the same as target stimuli. Perception was significantly worse in tone-deaf individuals than controls, $t(1,10) = 5.6$, $p = 0.0002$. However, direction of pitch production was above chance in tone-deaf subjects, with performance being statistically indistinguishable from controls, $t(1,10) = 1.05$, $p = 0.3$. A two-way ANOVA with factors of group (tone-deaf vs. control) and task (perception vs. production) showed a significant interaction ($F(1,20) = 13.2$, $p < 0.01$), confirming differential performance in perception but not production in tone-deaf versus control listeners.

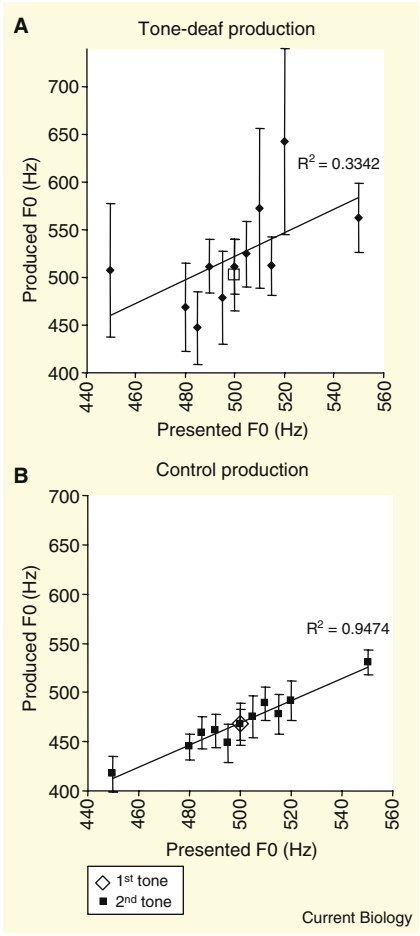

Figure 2. Variable pitch production by tone-deaf individuals.

(A) Mean fundamental frequencies of the two produced tones in tone-deaf listeners. The first tone had a target frequency at a constant 500 Hz, whereas the second tone ranged from 450-550 Hz. (B) Same as A in normal controls. While both groups show a significant positive correlation between target and produced fundamental frequency, the correlation is significantly lower in the tone-deaf group ($t(1,10) = 2.3$, $p = 0.046$) and variability in pitch production is higher for the tone-deaf group, as indicated by a t-test comparing standard error across different subjects producing the same pitch: $t(1,20) = 3.6$, $p = 0.0015$. Error bars indicate between-subject standard error.

Models of vocal communication generally involve interactions between the perception and production systems that allow the tuning of motor commands to achieve sound targets [3]. Our results shed further light on these models by indicating that the auditory pathways necessary for vocal performance are, to some degree at least, distinct from those necessary for conscious perception. The fact that tone-deaf individuals show no clear impairment in perceiving and producing speech provides further support for this conclusion. The distinction between auditory streams for production and perception demonstrated here may be analogous to separate visual streams for action and perception [9]. Further studies may aim to identify the precise neural correlates of this perception–action mismatch, and relate behavioral manifestations of tone-deafness to observed neurobiological anomalies in this unique population [10].

Supplemental data

Supplemental data are available at http://www.current-biology.com/cgi/content/full/18/8/R331/DC1

Acknowledgments

This work was supported by grants from the NINDS (R01 NS045049), NIDCD (RO1 DC008796) and NSF (BCS0518837) to G.S. and NIDCD (R01 DC002852) to F.H.G. We thank three anonymous reviewers for helpful comments.

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FGF induces oscillations of Hes1 expression and Ras/ERK activation

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Many biological processes, such as circadian rhythms and somite segmentation [1], are regulated by molecular clocks. During somitogenesis, mRNAs for Notch signaling molecules, such as the Notch effector Hes1, oscillate periodically [1]. Here, we show that FGF stimulation induces the oscillatory expression of Hes1 in an ERK-dependent manner and also induces oscillatory activation of Ras and ERK activities. Our analysis demonstrates that oscillations in Ras/ERK activity require negative-feedback phosphorylation of Sos by ERK, suggesting that Ras/ERK oscillations could act as a novel molecular clock.

The oscillatory expression of Hes1 is triggered by serum stimulation in several cultured cell lines [2]. As FGF has been implicated in the regulation of somite segmentation [3], we examined whether FGF stimulation induces oscillation of Hes1 expression. Treatment of C3H 10T1/2 cells with bFGF induced the oscillation of *hes1* mRNA and Hes1 protein with a 2 hour cycle (Figure 1A and Figure S1 in Supplemental Data, published with this article online). To examine the potential involvement of the MEK–ERK pathway in triggering the oscillatory expression of Hes1, we examined the effects of U0126, a specific MEK inhibitor. Pretreatment with U0126 almost completely inhibited bFGF-induced oscillatory expression of Hes1 (Figure 1A). Moreover, pretreatment with another MEK inhibitor (PD98059) or expression of the MAPK phosphatase CL100/MKP1 suppressed the ERK activation and Hes1 oscillation (data not shown). DAPT, an inhibitor of γ-secretase, which cleaves Notch, did not prevent the Hes1 oscillation (data not shown). When U0126 was added to cells 110 min after FGF stimulation, the later rise in *hes1* expression was suppressed (Figure 1C). Unexpectedly, we then found that ERK phosphorylation, and therefore activity, oscillated in response