Absolute pitch: A special group of ears

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Auditory pitch perception is an ability that is pervasive in the animal kingdom, but many features of this ability are not understood. In humans, it is clear that pitch perception is the result of sound processing by the listener, and although the perceived pitch of a sound is strongly related to its frequency, careful psychophysical studies have revealed many surprising features of this auditory function (1). One of the most remarkable aspects of human pitch perception is the phenomenon of absolute pitch (AP), which is the subject of an article by Athos *et al.* (2) in this issue of PNAS.

The Nature of Absolute Pitch

AP is the ability to instantly and effortlessly identify the pitch of a tone without the use of a reference tone. Most of us who do not possess AP require some sort of reference, such as a tone from a pitch pipe, to start a melody on the correct note. However, most non-AP individuals can easily determine the relative distance between two pitches. This ability is called "relative pitch" and is the basis for our ability to recognize a melody, in which successive pitches (notes) occur at specific distances from each other (intervals) on the musical scale. So, although [most of us can recognize a wrong note in a melody], we cannot easily recognize the difference when a melody is played correctly but begins at a higher or lower pitch. In other words, a melody sounds quite similar to most of us in many different musical keys.

Individuals with AP are unique in that they can recognize the absolute value of a musical tone. They can tell whether a single isolated tone is an A or a $C^{\#}$, for example, and can easily distinguish a melody in one key as opposed to another. This remarkable ability exists in a small fraction of the population and appears to be the result of an innate predisposition, combined with musical exposure and training, probably within a critical period during childhood (3). An understanding of the neural basis of AP would provide significant insights into many aspects of neuroscience, including audition, memory, development, and cognition.

An important advance in this understanding came with the recognition that the innate predisposition to AP has a strong genetic component (3–6). This opened the possibility of using human genetic approaches that could ultimately lead to the identification of molecular and cellular mechanisms involved in AP. However, despite familial clustering of this ability, there has been no good evidence for a simple Mendelian pattern of inheritance of AP. This, combined with the demonstrated need for musical exposure and training in the expression of AP, supported the view that AP is a complex trait. In contrast to Mendelian traits, complex traits have proven very difficult to assign to individual genetic variants in humans. Recent successful approaches to this problem have used very large populations and have identified genetic variants that individually make modest contributions to the trait (7).

A Distinct Group

Athos *et al.* (2) report results from an unusually large group of AP subjects, recruited and evaluated through an interactive web site that provided information on >2,000 individuals. Their results are both surprising and significant. Their first observation was that, among the population who took the web-based AP test, scores were not distributed continuously. Assuming that this is not the result of an unknown ascertainment bias, it means that AP individuals comprise a distinct outlier group that resides beyond a clear discontinuity in the distribution. This is surprising because virtually all human complex traits show a continuous distribution, with the affected individuals typically occupying the tail of a bell-shaped curve. In contrast, the distribution of AP test scores resembles that of a Mendelian trait, where affected individuals are easily distinguishable from unaffected individuals and definition of affection status does not depend on assignment of an arbitrary cutoff value at some point in the distribution. This finding suggests that AP may not be the result of the cumulative effects of many different genetic variants in the population, each contributing a small fraction to the phenotype. Instead, it suggests that single major gene effects may be causative in AP and provides the prospect that identification of these genes may be more straightforward.

Most of us can recognize a wrong note in a melody.

The other surprise revealed in the study is a curious anomaly regarding the note A—classically defined as a frequency of 440 Hz on the piano and famous as the note to which orchestras tune. The authors found that AP individuals designated a much broader range of frequencies as "A" than was the case for other notes. Athos *et al.* (2) suggest that this odd phenomenon may be explained by the fact that not all modern orchestras tune to 440 Hz. Some, particularly in Europe, tune to slightly higher frequencies, such as 442 or even 446 Hz. AP individuals, with their exceptional pitch discrimination abilities and unique auditory memory, may have internalized this variability and adjusted for it in their identification of A. Further studies that proved this hypothesis would provide an important adjunct to our understanding of AP and could help to quantify the role of neural plasticity in pitch perception.

Individuals who possess AP frequently comment on changes in pitch perception with aging. To date, this phenomenon has not been well characterized, but the large sample size enrolled in this study allowed the authors to investigate this question on a population level. Indeed, the authors confirmed that pitch perception does shift in later life, with the errors typically in the higher (sharp) direction. This finding may have implications in audiology, where hearing function is typically measured by using pure tones at specific frequencies. The vast majority of the population may well experience alterations in pitch or frequency perception in later life, but they are likely unaware of this because they do not possess AP.

Absolute pitch is an especially tantalizing trait for genetic analysis. It has an onset early in life, it occurs equally in males and females, it is highly heritable, it is rare in the population, and it ap-

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pears to be nonsyndromic, that is, unassociated with other conditions. All of these features bode well for the prospects of gene finding. However, unlike most inherited neurological conditions for which affected individuals present themselves to a medical specialist, AP individuals and families have not been easily ascertained. The demonstration by Athos *et al.* (2) that a web site can be an effective tool for identifying, testing, and recruiting AP subjects is an important development. The identification of the genetic variation that leads to AP is likely to tell us much about a part of the auditory system that is currently obscure, and the results of Athos *et al.* are indeed encouraging in this quest.

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