Letters to the Editor

Am. J. Hum. Genet. 65:911–913, 1999

Absolute Pitch: Prevalence, Ethnic Variation, and Estimation of the Genetic Component

To the Editor:

Absolute pitch (AP), also known as "perfect pitch," is a distinct cognitive ability possessed by a minority of musicians. The essential feature of this trait is the capacity to recognize and name the pitch of a musical note or ambient sound without the use of a reference pitch and with a minimum of deliberation. Elegant studies by Miyazaki (1988) have provided a method of measuring this ability, and Baharloo et al. (1998) recently reported on the characterization of a population of AP possessors, using a modification of this approach. These studies have emphasized that, although there is some variation in levels of accuracy in AP possessors, musicians with this ability are nevertheless distinct from those who do not possess AP. As such, AP ability is one of the few cognitive phenotypes that exhibit a clear qualitative difference between those who possess it and those who do not.

Although informal prevalence estimates for AP ($\leqslant$1:1,500 among amateur music students) have been suggested (Profita and Bidder 1988), the study by Baharloo et al. (1998) represents the only published data concerning the prevalence of the AP phenotype. In a survey of 612 highly accomplished musicians, Baharloo et al. (1998) observed a prevalence rate of 15%. We have now completed a survey of 2,707 music students at music conservatories as well as at university and college music programs in the United States. We surveyed student populations ranging in size from 20 to 390 students (mean [$\pm$ SD] 104 $\pm$ 78), using a two-page questionnaire asking about the presence of AP in the students and in their family members. We assumed AP ability to be present if students reported both the ability to perceive tones in an absolute manner and the ability to sing a note when given the letter name, but without a reference pitch. In our experience (see below), this correlates reasonably well with AP ability on objective testing, as has been observed by others (Takeuchi and Hulse 1991; Baharloo et al. 1998).

We observed large variations in AP prevalence among different student populations (range 0%–35%). There was a significant association ($P < .001$) between the type of institution or music program and the prevalence of AP in the students: conservatory (24.6% with AP), university-based school of music (7.3% with AP), or liberal arts/state university music program (4.7% with AP). We also noted a strong correlation between the prevalence of AP and the percentage of students in these schools who reported their ethnic background as "Asian or Pacific Islander" ($r = .81$, $P < .0001$, Spearman rank correlation coefficient). This raised the possibility that AP is more prevalent in Asian students in general.

Table 1

Prevalence of AP in Asian Music Students, Stratified by Type of Music Program

Type of Music Program (No. of Students Surveyed)	No. (%) of Students with AP
Conservatory (73)	36 (49.3)
University music program (152)	39 (25.7)
Liberal arts college (12)	1 (8.3)
All programs combined (237)	76 (32.1)

The prevalence data in table 1 (Asian students) and table 2 (non-Asian students) indicate that AP is significantly more prevalent in Asian students compared with all other ethnic groups (non-Asian) combined (32.1% vs. 7.0%, $P < .001$). Furthermore, the higher rate of AP in Asian students is observed in all types of educational institutions. Even among non-Asians, however, the rate of AP was significantly higher in students at major music conservatories (table 2). A multivariate logistic regression indicated that Asian ethnicity and attendance at a conservatory were independently associated with AP in the student populations. Asian ethnic background had a relative risk (RR) of 5.0 (95% CI 3.6–7.0), whereas attendance at a music conservatory (vs. other music programs) had RR = 3.5 (95% CI 2.6–4.8). There were insufficient numbers of Hispanic or African American students to perform a meaningful subgroup analysis within the non-Asian group. Most of the individuals in the non-Asian group were white, and there were no obvious trends among the other broad ethnic groupings.

As has been reported by others, we also observed a significant association between AP and the age at which an individual first began playing music. For the AP group as a whole, the mean age of starting musical activities

Table 2

Prevalence of AP in Non-Asian Music Students, Stratified by Type of Music Program

Type of Music Program (No. of Students Surveyed)	No. (%) of Students with AP
Conservatory (276)	50 (18.1)
University music program (1,844)	107 (5.8)
Liberal arts college (350)	16 (4.5)
All programs combined (2,470)	173 (7.0)

was 5.4 ± 2.8 years, whereas, for the non-AP group, the mean age was 7.9 ± 3.2 years ($P < .0001$). This same trend was observed for Asian students as well as non-Asian students.

The issue of familial aggregation of AP is important for assessing the genetic contribution to this phenotype. In a small study (Gregersen and Kumar 1996), we estimated λ_s (recurrence risk to sibs divided by population prevalence) at ~20, whereas the data of Baharloo et al. (1998) suggested a λ_s of ~7 (Gregersen 1998). Because our current survey populations have such highly variable rates of AP, we estimated λ_s using the recurrence risk in *sibs of unaffecteds* as the denominator in the RR calculation. For this survey population, the recurrence rate for AP in siblings was reported as 14.1% for probands with AP and 1.7% in the siblings of subjects who did not have AP, leading to an estimate of $\lambda_s = 8.3$. By this method, the λ_s estimate for Asians was 11.1. Of course, this approach to estimating λ_s will tend to underestimate its value, since the background prevalence of AP in the general population is undoubtedly much lower than it is in the sibs of unaffected musicians. Notably, the prevalence of AP in the parents of AP probands is also higher than in the parents of music students without AP (6.5% vs. 1.6%), similar to our previous report (Gregersen and Kumar 1996).

These data indicate that estimates of the prevalence of AP are highly dependent on the selection of the population under study. Although AP may occur in non-musicians, the method of ascertainment of the AP phenotype restricts prevalence surveys to musically educated populations. This fact makes it especially difficult to separate the environmental from the genetic factors that predispose to AP, since exposure to music is both required for ascertainment as well as implicated in the development of the phenotype. In addition, the presence of AP almost certainly increases the probability that musical education will be pursued, and it may well provoke educational activities at an earlier age, thus confounding the interpretation of the association between early-childhood musical activities and AP. Our data also suggest that more-professionally oriented music schools are especially likely to attract or admit individuals with AP, independent of the ethnic background of students in these schools.

There are several possible reasons for the markedly increased prevalence of AP in students of Asian background. The presence of AP in a child may provoke more-serious parental efforts at music education in certain cultural groups and may lead to preferential selection of this population into higher levels of music education. Alternatively, certain childhood educational systems (for example, the Yamaha method in Japan) may foster the development of AP. We do not currently have information on our study population concerning childhood exposure of the Asian students to these methods. Finally, the possibility that certain Asian populations may have a higher prevalence of AP susceptibility genes should be considered.

Because these data are derived from a survey, the results must be treated as preliminary. In our experience, self report for AP is a very good indicator of AP ability; >80% of 173 subjects who reported AP have passed a rigorous test of their pitch-naming ability (E. Kowalsky and P. K. Gregersen, unpublished data). However, the reliability of reporting on AP ability in sibs or parents is uncertain and needs to be validated. It would also be valuable to obtain data on early-childhood music exposure and education from sibs of AP probands, to better control for the influence of environment on the development of AP. Familial aggregation of AP appears to be common, yet the measurement of background prevalence is not possible in the general population. Thus, more-extensive contact with the family members of a large number of AP subjects will be required, to provide further epidemiological evidence for genetic predisposition to AP, independent of environment. On the other hand, many subjects report the spontaneous appearance of AP in very early childhood. It is likely that inheritance plays a significant role in AP, perhaps in the setting of environmental exposure to music during a "critical" period (Goodman and Schatz 1993).

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0002-9297/1999/6503-0035$02.00

Am. J. Hum. Genet. 65:913–917, 1999

Extremely Skewed X-Chromosome Inactivation Is Increased in Women with Recurrent Spontaneous Abortion

To the Editor:

Recurrent spontaneous abortion (RSA), defined as three or more consecutive losses at ⩽20 wk gestation (Stirrat 1990), affects 1%–2% of couples trying to have a family (Stray-Pedersen and Lorentzen-Styr 1979; Roman 1984). Although spontaneous abortion occurs quite frequently in humans, affecting ~15% of all clinically recognized pregnancies (Warburton and Fraser 1964; Edmonds et al. 1982; Wilcox et al. 1988), the observed rate of RSA is much higher than the expected rate of 0.3% due to chance alone. This suggests the presence of factors that may predispose particular couples to multiple pregnancy losses. Nearly 60% of RSA cases can be potentially explained by identifiable autoimmune, endocrine, anatomical, or infectious factors or by structural chromosome rearrangements in one partner (Stephenson 1996). However, >40% of RSA is still unexplained. We suggest that a significant proportion of the unexplained cases of RSA may be caused by a genetic mutation or chromosomal abnormality that would not be discovered by routine investigation.

X-chromosome inactivation (XCI) is the process whereby one of the two X chromosomes present in each cell of female mammals is inactivated during early embryogenesis, to achieve dosage compensation with males (Lyon 1961). Generally, in a given cell type in humans, the maternal X chromosome is inactivated approximately equally as often as the paternal X chromosome (Belmont 1996). However, extremely skewed XCI, defined in this letter as >90% inactivation of one allele, is observed in ~2% of newborns and ~4.5% of 28–32-year-old women (Busque et al. 1996). This extremely skewed XCI pattern may be due to a number of possible causes: (1) chance; (2) a mutation in the XIST gene that is found on the X chromosome and is thought to be critical in the inactivation process (Plenge et al. 1997); (3) selection against cells with a growth disadvantage because of a deletion or mutation on one of the X chromosomes (Pegoraro et al. 1997) or to an X-autosome translocation (Gaal and Laszlo 1977); and (4) a reduction in the fetal precursor-cell pool size, as has been suggested to occur in twinning (Bamforth et al. 1996; Goodship et al. 1996). Trisomy mosaicism has also recently been shown to be associated with extremely skewed XCI (Lau et al. 1997). Extremely skewed XCI (>90% inactivation of one allele) was found in the majority (11 of 18) of prenatally detected mosaic cases when the trisomic cell line was of meiotic origin and absent from most fetal tissues (Lau et al. 1997; W.P. Robinson and M.S. Peñahererra, unpublished data). Skewing is hypothesized to result from a reduction in the number of embryonic precursor cells, because of selection against the trisomic cells shortly after XCI.

At least three causes of skewed XCI are expected to be associated with an increased risk of spontaneous abortion: (1) some deletions or mutations on the X chromosome may be lethal to male fetuses carrying the abnormal X chromosome (Pegoraro et al. 1997); (2) X-autosome translocations can lead to RSA, because some gametes may be deleted and/or duplicated for portions of each chromosome that are involved in the rearrangement (Byrne and Ward 1994); and (3) trisomy mosaicism may also be associated with RSA if the germline is affected, since recurrent aneuploidy may result (Kohn and Shohat 1987; Gersdorf et al. 1990; Satge et al. 1996). Although it is impossible to determine how often the germline is mosaic in individuals with a normal phenotype and blood karyotype, one case was reported in which trisomy 16 was found in placenta and oocytes but in no other fetal tissue (Stavropoulos et al. 1998). To evaluate the degree to which mosaicism or other genetic factors associated with extremely skewed XCI may contribute to RSA, we screened women with RSA in order to determine their XCI status and compared them with controls of similar age.

Patients were ascertained through the Recurrent Pregnancy Loss Clinic at British Columbia's Women's Hospital and Health Centre. Between September of 1997 and December of 1998, all new patients with a history of RSA who were seen by the one of the authors (M.D.S.) were offered participation in this study. RSA was defined as three or more consecutive pregnancy losses prior to 20 wk gestation, with each pregnancy documented by a positive result on serum or urinary hCG, ultrasound, or pathology. Ethics approval was obtained from the