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Report

Familial Aggregation of Absolute Pitch

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Absolute pitch (AP) is a behavioral trait that is defined as the ability to identify the pitch of tones in the absence of a reference pitch. AP is an ideal phenotype for investigation of gene and environment interactions in the development of complex human behaviors. Individuals who score exceptionally well on formalized auditory tests of pitch perception are designated as "AP-1." As described in this report, auditory testing of siblings of AP-1 probands and of a control sample indicates that AP-1 aggregates in families. The implications of this finding for the mapping of loci for AP-1 predisposition are discussed.

Absolute pitch (AP [MIM 159300]) is distinct from most complex human behaviors in that virtually all AP possessors have been exposed to a single, measurable environmental factor—namely, early music training. Although studies have pointed to the possibility of a genetic predisposition for development of AP (Profita and Bidder 1988; Baharloo et al. 1998), there has been a paucity of systematic evidence for such a genetic contribution to AP. We have now attempted to quantify the familial aggregation of AP by estimating the sibling recurrence risk (lambda sib [λ_s]) for a particularly distinct form of AP, termed "AP-1." λ_s is defined as the risk to siblings of probands, over the population prevalence, for a specific disease or trait (Risch 1990). AP-1 individuals are those who exhibit the most clear-cut AP ability on an auditory test developed in our laboratory. This test consists of identifying the pitch of 40 pure tones and 40 piano tones, presented to the subject at 3-s intervals. On the basis of this test, AP possessors were grouped into distinct phenotypic classes; AP-1 individuals are those who score at least three standard errors above the mean score of a randomized group of musicians (self-reported AP possessors and nonpossessors) who received comparable music training (Baharloo et al. 1998). We therefore consider individuals with AP-1 as those able to identify pitches accurately and instantaneously and without relying on reference tones.

The λ_s has been estimated for a wide range of behavioral traits, for which prevalence data are available for siblings of probands as well as for the general population; for example, for schizophrenia, the sibling recurrence rate is ~9%, versus 1% in control populations—that is, $\lambda_s = 9$. The degree of risk (we use this standard epidemiological term for simplicity, although AP is obviously not a disorder) of the siblings of AP probands can be estimated by careful interviewing of AP probands (to determine which sibs are possible AP possessors), followed by direct auditory testing of the sibs. To obtain an estimate of the population prevalence, similar assessment procedures can be applied to a suitable population control group. In the case of AP-1, however, it is also necessary to pay careful attention to its major environmental covariate, early music training (Sergeant 1969; Miyazaki 1988; Profita and Bidder 1988), which itself may be familial. Therefore, in any family-aggregation study of AP, it is important to stratify subjects by the age at which they initiated music training. Studies (ours and others) suggest dichotomizing age at onset of music training at 6 years; virtually all AP-1 individuals have had music training by that age, although the rate of AP-1 does not increase substantially with onset of music training earlier than that age.

AP-1 probands had been recruited for participation in possible genetic mapping studies of AP, without our

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having knowledge of their family history for either music training or AP. All the AP-1 individuals ($n = 74$) recruited into the genetic studies at the time that we initiated the current investigation were asked whether they had siblings who had started music training at <6 years of age (table 1). All probands had music training at <6 years of age. These probands reported that they had 113 siblings, of whom 53 had started music training at <6 years of age. The probands reported that 25 of these 53 individuals possessed AP ability either identical or very similar to their own AP abilities. Of 60 siblings who did not receive music training at <6 years of age, only 1 was reported by a proband to have AP. To obtain an estimate on accuracy of the AP reports about siblings by the probands, we tested all 13 sibs to whom we had ready access and who were reported, by the probands, to possess AP; 12 (92%) of these 13 individuals were confirmed as AP-1. These 13 sibs were tested with the same auditory test and procedures as were used to test the probands.

To obtain an estimate of the population prevalence of AP-1 (the denominator of the λ_s equation), we surveyed and pitch tested all 625 students attending a summer music camp at Florida State University (FSU). The music camp at FSU was randomly selected from a list of the first 10 summer camps identified in an Internet search using "summer music camp" as the key word. Students attending the FSU camp consisted of two groups: (1) students, with ⩾1 year of music training, in grades 7 and 8 and (2) students, with ⩾2 years of music training, in grades 9–12. Surveys were distributed to and completed by all students attending the camp during their regular class hours. The aim of the survey was to identify those students who had begun music training at <6 years of age. Immediately after they completed the surveys, all students in the camp took the auditory test that we have used to assess AP status. The only difference from the testing procedure used previously was that the students in each class (~20 students per class) listened to the tones played over speakers rather than on headphones. To assess whether this difference could influence the results, we, using speakers, retested seven individuals who had previously scored in the AP-1 range when tested via headphones; all seven of these subjects continued to score as AP-1 in this retest. Thus, it does not appear that use of speakers, rather than headphones, leads to a more difficult test, which could artificially deflate the rates of AP-1 in this control group versus those in the family group that we studied.

Of the 625 camp students tested, 139 reported music training at <6 years of age (table 1). Nineteen of 139 students with early music training reported AP; after auditory testing, 4 (21.1%) of these 19 students were determined to be AP-1. Thirty-nine students with a history of music training beginning at >6 years of age reported AP, yet none of these students tested as AP-1. All individuals with AP-1 found by our test reported early music training.

Because we were unable to test all the sibs of the AP-1 probands, we can provide only a range of estimates for the recurrence rate of AP-1 in this group. At the lower end, we identified 12 siblings who tested as AP-1, giving a lower-bound estimate of 22.6% (12/53) for this group. However, an additional 12 siblings were reported, by history from the probands, to have AP. If we assume the same rate of AP-1 among this group as among the 13 sibs whom we tested (i.e., 92.3%), we obtain an estimate of 43.5% ([12+11.8]/53), which we use as the upper end of the range.

These results strongly support familial aggregation of AP-1, even after control for early music training. When a rate of 2.9% (4/139) is used as the population frequency of AP-1 among those with early music training, the rate of AP-1 among the early-trained sibs of AP-1 probands is significantly increased, even when the lower end of our range (22.6% [12/53] vs. 2.9% [4/139]; $\chi^2 = 17.2$, $P < .001$) is used. Using the same sib recurrence-rate figure (22.6%) gives a value of $\lambda_s = .226/.029 = 7.8$. If we use the more realistic upper-

Table 1

Absolute Pitch (AP) in Siblings of AP-1 Probands and in a Control Sample

	Sibs of AP-1 Probands ($n = 113$)				Controls ($n = 625$)			
	Music Training at <6 Years of Age		Music Training at >6 Years of Age		Music Training at <6 Years of Age		Music Training at >6 Years of Age	
	AP	Not AP	AP	Not AP	AP	Not AP	AP	Not AP
By proband or self-report	25 (47.2%)	28 (52.8%)	1 (1.7%)	59 (98.3%)	19 (13.7%)	120 (86.3%)	39 (8.0%)	447 (92.0%)
Tested for AP	13	0	0	0	19	120	39	447
AP-1	12 (92.3%)	…	…	…	4 (21.1%)	0	0	0

Note.—The rates for the sibs are based on reports made by the probands about their sibs. The rates for the controls are based on self-report. All available sibs ($n = 13$) and all controls were evaluated using a test for AP ability (Baharloo et al. 1998). From the results of these tests, we computed the rates of AP-1 in the sibs of probands (lower and upper bounds were 12/53 [22.6%] and 25/53 [43.5%], respectively) and in controls (4/139 [2.9%]), considering only those individuals with music training beginning at <6 years of age.

bound estimate of recurrence rate, we obtain a value of $\lambda_s = .435/.029 = 15.1$. Thus, a plausible range for λ_s is 7.8–15.1, although the higher end of this range is more likely to be appropriate.

There are several additional interesting observations from the data in table 1. First, the data suggest that early music training is itself familial. All the AP-1 probands had music training at <6 years of age. Among their 113 sibs, 53 (46.9%) had early music training. By contrast, among the 625 controls, 139 (22.2%) had music training at <6 years of age. This approximately twofold excess in frequency is highly significant ($\chi^2 = 29.0$, $P < .001$). A second observation relates to the false-positive rate of self-report and family-history report of AP ability. We found a very-low false-positive rate among the tested siblings reported by their AP-1 sibs to possess AP (7.7% [1/13]) but a very-high false-positive rate among the controls self-reported to have AP (78.9% [15/19] for those with music training at <6 years of age; 100% [39/39] for those without music training at <6 years of age). These observations are the opposite of what is typically found in family studies—namely, greater accuracy of self-report than of the family-history report. The explanation in this case is not clear. It may be that individuals with true AP ability are excellent judges of similar ability in their sibs. Alternatively, since most of the AP-1 probands were considerably older than the students at the music camps, it may be that younger people uniformly overestimate their AP ability. In any event, these results demonstrate the importance of direct AP testing and indicate that investigators of AP should not rely exclusively on self-report or family history. If we had simply used the self-report data for the controls, we would have obtained a population prevalence of 13.7% (19/139) for those with music training at <6 years of age, greatly attenuating the estimate of λ_s.

By contrast, it would appear that the false-negative rate of AP-1 by self-report or family-history report is low. We have yet to encounter any subjects who tested as AP-1 and who had not previously reported such ability or who had had such ability reported for them by relatives.

In any case, the sib recurrence rate for AP-1 appears to be significantly elevated compared with the population prevalence, after control for early music training. With figure A 2.1 in the textbook by Vogel and Motulsky (1997, p. 755), the sibling recurrence rate in combination with the population prevalence was used to estimate heritability of AP under various models of inheritance. For example, the data are not compatible with a polygenic-threshold model. Even when the lower estimate of sib recurrence (22.6%) is used, the heritability estimate is >100%. Such observations often indicate major-locus effects.

If the AP-1 phenotype is the result of interaction between multiple loci, then λ_s per locus could be substantially smaller than our estimates for total λ_s. Estimation of risk to second- and third-degree relatives or identical twins can be used to estimate the probable number of loci involved and their contribution to the trait. For example, λ_s for schizophrenia has been estimated as ~9, yet the λ data from different classes of relatives points to interaction of multiple loci, each with $\lambda_s < 2$. For logistical reasons we were not able to assess the risk to second-degree relatives of AP-1 probands.

A study that examined AP heritability (Gregersen et al. 1999) estimated λ_s of 8.3 for AP, by dividing the risk to the sibs of AP individuals participating in a survey of 2,707 music students by the risk to the sibs of non-AP students participating in the same study. However, that analysis did not involve direct testing of AP ability in all participants and did not differentiate between individuals who had had early music training and those who had not. Elsewhere we have shown that early music training is a major environmental factor contributing to the development of AP-1 (Baharloo et al. 1998). Yet, estimation of λ_s may be confounded by the possibility that exposure to early music training is, in itself, familial. Siblings in the same household are more likely to be exposed to early music training (and, hence, to have a higher likelihood of developing AP) if such training is provided for any one of them. Indeed, we have provided evidence (table 1) that early music training is familial. In considering our estimates of relative risk to the siblings of AP-1 probands and to members of the control population, one must keep in mind that concordance of the AP-1 phenotype in siblings may be partially due to their experiencing of similar environments (aside from music training) that we have not considered or anticipated, and, thus, that our estimated λ_s of 7.8–15.1 may not entirely reflect genetic factors. Furthermore, estimates used in the λ_s calculation were obtained in two different studies. Although we considered only the prevalence of AP-1 in individuals with music training at <6 years of age, the value for the numerator was obtained from the study of sibs with a more rigorous music background (13 sibs tested had $\geq$5 years of music training), and the denominator was obtained from a sample of students with perhaps less music proficiency. This sampling scheme may have led to an inflated value for the numerator of the λ_s equation and, thus, to an inflated estimate of λ_s. On the other hand, it may also be true that children with AP ability are more music oriented and seek out music training at an earlier age than do children without such ability.

In summary, we have obtained a λ_s value of ~8–15 for AP-1, which suggests a strong role for genetic influences on the development of this trait. Furthermore, the calculated sibling recurrence rates and the population rates suggest the possibility that the genetic predisposi-

tion to AP-1 may include a major-gene effect. Since early music training is a requirement for the development of AP-1, we have considered, as the relevant population for λ_s estimation, only the fraction of the population with early music training. This is the first study in which the frequency of AP-1 in the control population was obtained through a randomized process and in which the AP status of all individuals from the control population was confirmed by an auditory test. The high estimates of λ_s, both from our study and from that by Gregersen et al. (1999), suggest that it may be possible to assemble a number of pedigrees or sib pairs that is sufficient to map loci for AP-1.

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Electronic-Database Information

The accession number and URL for data in this article are as follows:

Online Mendelian Inheritance in Man (OMIM), http://www.ncbi.nlm.nih.gov/Omim (for AP [MIM 159300])

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