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Fitness among individuals with early childhood deafness: studies in alumni families from Gallaudet University

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Summary

The genetic fitness of an individual is influenced by their phenotype, genotype and family and social structure of the population in which they live. It is likely that the fitness of deaf individuals was quite low in the Western European population during the Middle Ages. The establishment of residential schools for deaf individuals nearly 400 years ago resulted in relaxed genetic selection against deaf individuals which contributed to the improved fitness of deaf individuals in recent times. As part of a study of deaf probands from Gallaudet University, we collected pedigree data, including the mating type and the number and hearing status of the children of 686 deaf adults and 602 of their hearing siblings. Most of these individuals had an onset of severe to profound hearing loss by early childhood. Marital rates of deaf adults were similar to their hearing siblings (0.83 vs. 0.85). Among married individuals, the fertility of deaf individuals is lower than their hearing siblings (2.06 vs. 2.26, $p=.005$). The fitness of deaf individuals was reduced ($p=.002$). Analysis of fertility rates after stratification by mating type reveals that matings between two deaf individuals produced more children (2.11) than matings of a deaf and hearing individual (1.85), suggesting that fertility among deaf individuals is influenced by multiple factors.

Keywords

Deafness; Fertility; Fitness; Assortative Mating

INTRODUCTION

Deafness is a common sensory deficit, affecting the communication of nearly 70 million people worldwide. In the United States, roughly one per 1000 newborn infants has severe to profound sensorineural deafness, and an additional one-two children per 1000 are born with less severe but clinically significant bilateral or unilateral hearing loss (Morton, 1991; White, 2003). Deafness is an etiologically heterogeneous trait with many recognised genetic and environmental causes (Tekin et al., 2001; Morton & Nance, 2006). Genetic causes account for nearly 60% of childhood deafness and can be classified by the presence or absence of distinctive features that permit the recognition of specific syndromes, as well by the pattern of inheritance (Marazita et al., 1993). More than 300 syndromic forms of

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deafness have been recognised but, in 70% of cases of genetic deafness, hearing loss is the only clinical feature (i.e. non-syndromic) (Toriello et al., 2004). Of those with non-syndromic genetic deafness approximately 80% exhibit autosomal recessive inheritance, 15–20% exhibit autosomal dominant inheritance, and 1–2% exhibit either an X-linked or matrilineal (i.e., mitochondrial) pattern of transmission (Chung et al., 1959; Nance, 1977; Marazita et al., 1993). Remarkable progress has been made in the identification of genes for deafness, with over 110 loci being mapped, including a Y linked locus, and 42 genes being identified (Van Camp & Smith, 2009; Wang et al., 2004). Loci for deafness have now been mapped to every chromosome. Surprisingly, mutations at a single locus, DFNB1 on chromosome 13, account for 30–40% of non-syndromic deafness in many populations (Denoyelle et al., 1997; Zelante et al., 1997). The DFNB1 locus includes the *GJB2* and *GJB6* genes which encode the Connexin 26 and Connexin 30 protein subunits, respectively, which form gap junction proteins that are expressed in the inner ear. These proteins form channels between adjacent cells that permit the exchange of small molecules, and may facilitate the recycling of potassium ions from the hair cells, after acoustic stimulation, back into the cochlear endolymph. More than 100 *GJB2* mutations have been identified, but a single truncating mutation, 35delG, accounts for up to 70% of pathologic alleles in many populations. DFNB1 deafness is common in Western Europeans and in the Middle East, while much lower frequencies have been observed in Asia (Downs & Yoshinaga-Itano, 1999; Orzan et al., 1999; Kudo et al., 2000; RamShankar et al., 2003). A 309 kb deletion spanning the *GJB6* locus that causes deafness when present in *trans* with a single pathologic *GJB2* mutation explains hearing loss (HL) in many individuals heterozygous for a pathogenic mutation in *GJB2* (Del Castillo et al., 2003; Pandya et al., 2003). DFNB1 deafness is almost always recessive with an early childhood onset of severe to profound hearing loss.

A unique feature of the deaf population in the U.S. is the propensity of deaf individuals to marry one another (assortative mating). In East-Asian countries, such as India where arranged marriages are still prevalent, marriages involving two deaf individuals are uncommon (A. Pandya, personal communication). The 1970 National Census of the Deaf Population (NCDP) in the United States revealed that 80–90% of individuals with profound deafness married a deaf partner (Schein & Delk, 1974). This is higher than the 75% frequency reported by Rose (1975) which was based on data collected by E. A. Fay in the early 19th century. This increase has been partly attributed to increasing enrollment of deaf students in residential schools for the deaf resulting in social opportunities and contact with many other deaf students. Assortative mating within a population can have a profound influence on the distribution of genes in that population. In 2000 we proposed that the high frequency of DFNB1 deafness in the United States might be the consequence of the combined effects of the high degree of assortative mating among deaf individuals and the relaxed selection against deafness (Nance et al., 2000). We subsequently showed by computer simulation and by studies comparing contemporary matings with data on matings that occurred more than a century ago in deaf individuals that this mechanism has doubled the frequency of DFNB1 deafness in the United States during the past 200 years (Nance & Kearsey, 2004; Arnos et al., 2008).

Genetic fitness as measured by fertility is an important index of the impact of a genetic disease on a population. In the case of sickle cell anemia, for example, the reduced genetic fitness of affected homozygotes is balanced by the increased survival of juvenile heterozygotes who contract malaria (Allison, 1954). The average number of children born to a specified group is a convenient measure of their genetic fitness. Genetic fitness is usually expressed as the average number of offspring for the group in question compared to the average number for a “control” sample, either drawn from the general population or from normal siblings of the “cases”. The fitness of deaf individuals was generally quite low in

Europe prior to the introduction of sign language and subsequent establishment of schools for the deaf which occurred about 400 years ago (Bender, 1981). The acquisition and use of sign language, by both deaf and hearing family members, is an important factor in improving the “genetic fitness” of deaf individuals. The effect of such factors is evident in population isolates with a high frequency of deafness where the development of indigenous sign languages has allowed for interfamilial communication between both deaf and hearing individuals, to the great benefit of the fitness of the deaf members of these populations. Examples include Martha’s Vineyard in the United States in the 1800s, contemporary Bedouin tribes in Israel where the incidence of deafness is as high as 2.6%, and some current geographical regions of Turkey and Bali (Groce, 1985; Friedman et al., 1995; Scott et al., 1995; Fox, 2007; Tekin & Arici, 2007).

In the latter half of the 20th century, attempts to estimate the fitness of deaf individuals have included two studies of congenitally deaf individuals in China (Sichuan and Shanghai), where the fertility of all probands of “reproductive age” were based on comparisons to normal siblings, and fitness of deaf individuals was noted to be significantly reduced (0.6 and 0.78, respectively) (Hu et al., 1987; Liu et al., 1994). In a study of pre-lingually deaf individuals from Mongolia, the fitness of deaf adults compared to their hearing siblings was 0.62 (Nance et al., 1999). In a US study based on the 1970 National Census of the Deaf Population (NCDP), the fitness of deaf women was reduced when compared to the general US population, and ranged from 0.31 to 0.77, depending on the age category (Schein & Delk, 1974). Although the ascertainment methods differ among these studies, comparison of the fertility and fitness in a contemporary US population of deaf adults would allow a comparison of the change in fitness over time and identification of factors that influence the changes such as geographic location, culture and ethnic background.

The present study was designed to obtain contemporary estimates of the relative genetic fitness of deaf individuals in comparison to their hearing siblings. Contemporary data on fitness and fertility has also been compared to similar information from the deaf population in the United States 40 years ago as well as to data from contemporary deaf populations in other countries.

MATERIALS AND METHODS

Ascertainment of Participants

Contemporary estimates of the genetic fitness of deaf individuals in the United States were obtained by reviewing pedigree data from alumni of Gallaudet University. Gallaudet University is a liberal arts school for deaf and hard of hearing students in Washington, DC that was established in 1864 and currently has nearly 14,000 living, deaf alumni. As part of a larger study on the epidemiology of deafness, a detailed interview was conducted by the project staff and informed consent was obtained as approved by the Institutional Review Board of Gallaudet University (Arnos et al., 2008). Most probands had an onset of severe to profound hearing loss by early childhood. When possible, at least a three-generation pedigree data was collected on all probands and their siblings including: the hearing status of their siblings and spouse/partners, birth year, and marital status. Information on the number and hearing status of the children of alumni probands and their hearing and deaf siblings was also collected. The resulting dataset included families with varying forms of environmentally-caused deafness and hereditary deafness.

Statistical Methods

Only the data on the families of deaf alumni and their deaf and hearing siblings who were at least 35 years old were included in the analysis. This age was chosen to minimise the

potential effects of incomplete childbearing. For the purposes of this study, individuals with long term partners were considered married, regardless of marital status; all individuals with children fell into the “married” category. Fertility was calculated as the average number of children born to specific subsets of the alumni families. Relative fertility is the fertility of one group divided by the fertility of a specified control group. In our study, the fertility of deaf males and females was compared to hearing male and female siblings of the deaf probands. Genetic fitness was defined as the ratio of the overall fertility of affected subjects to their unaffected siblings, including those who do not reproduce. Summary statistics were calculated using SAS v9.0. P-values were obtained using the SISA online statistical calculator (Uitenbroek, 1997).

RESULTS

Data for 686 deaf probands and their deaf siblings and 602 of their hearing siblings who were at least 35 years old was analysed. Data was further subdivided into four groups based on partnering status (married or “in a relationship” vs. single, never married) and gender. Hearing siblings were slightly more likely ($p=0.035$) to have a partner (85%) than were deaf individuals (83%). The average age of the four groups of adults ranged from a low of 50 (single deaf males) to 58 (married hearing males) (data not shown).

Assortative Mating and Marital Rates among Deaf Probands

Data was evaluated for evidence of assortative mating by determining the frequency of deaf by deaf (DxD) matings vs. deaf by hearing (DxH) matings among all deaf individuals. Overall the majority of deaf individuals choose a deaf partner (0.79), as shown in Table 1, which appears to be somewhat influenced by the hearing status of their parents. Deaf individuals who have 2 deaf parents are more likely to choose a deaf partner than individuals who have 2 hearing parents ($p=0.01$). Although the numbers are small, deaf individuals with only one deaf parent are more likely to choose a hearing partner than those with either two hearing or two deaf parents. In addition, deaf males are significantly more likely to choose a deaf partner than are deaf females, irrespective of their parental mating type ($p=0.02$).

We next investigated the effect of the hearing status of an individual’s parents (parental mating type) and the individual’s gender and hearing status on the “marital rate” (i.e., choosing a partner). As mentioned above and shown in Table 2, the proportion of deaf adults who choose a partner is slightly less than their hearing siblings (0.83 vs. 0.85, $p=0.035$). Among deaf individuals, males with two deaf parents have the highest marital rate (0.9) while males with only one deaf parent have the lowest rate of choosing a mate (0.68). Deaf females are only slightly more likely to choose a partner than are deaf males (0.83 vs. 0.82); however, this does vary with parental mating type. In contrast, among hearing siblings, males with one deaf parent have the lowest marital rate, while females with two deaf parents have the highest. Hearing females are more likely to have a partner than are hearing males, irrespective of the parental mating type.

Fertility and Fitness Among the Deaf

Fertility was calculated as the average number of children born to individuals with a partner, irrespective of their marital status. As seen in Table 3, the overall fertility of deaf individuals was lower than their hearing siblings ($p=0.005$), with a greater difference between females ($p=0.006$). We further stratified the deaf individuals and their hearing siblings by gender, by their parental mating type and by the hearing status of their partner to assess for effects of these factors on fertility rate. Overall, while hearing siblings who choose a hearing partner (HxH) have the highest average number of children (2.24), deaf individuals who choose a deaf partner produce more children (2.11) than those who choose a hearing partner (1.85)

(data not shown). As seen in Table 4, the average number of children born to deaf females who have a deaf partner (2.11) is slightly more than if they have a hearing partner (1.94), although this is not statistically significant. However, deaf males with a deaf partner have more children (2.11) than those who have a hearing partner (1.83; $p=0.02$). When the parental mating type is factored in, deaf females have significantly more children ($p=0.02$) if both parents were hearing (2.12), than if they were both deaf (1.97). Although the sample size is small (15), deaf males who have a single deaf parent have fewer children (1.67) than if both parents are hearing (2.05) or are both deaf (2.08). Overall the average genetic fitness for deaf individuals is 0.88, while deaf males appear to have a greater genetic fitness compared to deaf females (0.94 vs. 0.83).

DISCUSSION

Genetic fitness may be determined by a variety of methods. One definition often used is the ratio of the overall fertility of affected subjects to their unaffected siblings. Genetic fitness may also incorporate information on the number of grandchildren. We have chosen the former method as this is employed in other contemporary studies of deaf individuals. In addition, there are too few probands or family members with grandchildren to obtain reliable estimates. While the fitness of deaf subjects in our study compared to their hearing siblings is reduced ($p=0.002$), it would appear to have improved substantially in the past 200 years. However, an improved fitness of 0.88 still will have a significant impact over time. Although data on fertility from that time period are lacking, Mygind (1894) reported that in Denmark only 29.4% of male deaf-mutes over the age of 20 years were married in comparison to 71.6% in the hearing population. If we assume that the fertility of those who married in both groups was the same, we can obtain an admittedly imperfect estimate that the relative fitness of deaf individuals at that time may well have been less than $0.716/0.294 = 0.33$. The comparable fitness estimate for deaf individuals from our contemporary data would be $0.83/0.85 = 0.98$. The acquisition of sign language undoubtedly had a major impact on the genetic fitness of deaf individuals. It seems logical that the acquisition and use of sign language along with the establishment of largely residential schools for deaf individuals during the past several hundred years also promoted assortative mating among deaf individuals which in turn accelerated the increase in the frequency of the commonest form of deafness to approach a new equilibrium value. Our fitness estimates are substantially higher than contemporary values reported from China where oralism is favoured over sign language at educational institutions for deaf children (Hu et al., 1987; Liu et al., 1994). In fact sign language is discouraged or forbidden in most schools, and marriage rates among deaf individuals in China are much lower than for hearing individuals. As noted previously, this reflects the situation that existed in Europe and the US several hundred years ago.

The fitness of deaf individuals in the US has continued to approach that of hearing subjects as shown by a comparison of the NCDP data with that from the present study (Schein & Delk, 1974). It also appears that the overall fitness of deaf individuals in the US has increased primarily in the last 40 years (Supplemental Table 1). The comparison of these two data sets may be valid, despite the fact that the fitness in the NCDP study was based on a comparison of deaf individuals with the general population, rather than with their siblings.

The majority of deaf individuals from the Gallaudet alumni choose a deaf partner, with males choosing a deaf partner slightly more often than females. However, this is a reduction compared to the results from the NCDP, where 80–90% chose a deaf spouse (Schein & Delk, 1974). Furthermore, in that study, females were slightly more likely to have a deaf spouse than were males. Our study also found that deaf individuals have more children if they have a deaf partner than if they have a hearing partner. Interestingly, deaf females

choose a deaf partner less frequently than they did 40 years ago. In addition to general fertility and partner selection, a detailed comparison of fitness within age groups can be made between the NCDP data and the Gallaudet sample as shown in Supplemental Table 1. While the fitness of deaf females in the 35–39 age group is greater in the NCDP study, the fitness of the Gallaudet sample is greater in the remaining two age groups. It is possible that the behaviours of the highly educated Gallaudet alumni families do not reflect the practices of the deaf community at large, and that the differences between the total deaf population of the US and the NCDP would be much less. Further efforts to explore possible differences between the Gallaudet alumni/families and deaf individuals/families who did not attend college will be required to resolve this question. In addition, the majority of the Gallaudet families include a high proportion of individuals with an early onset severe to profound hearing loss. Individuals with a later onset of deafness, e.g. by the end of their second decade of life, are likely to have their fitness impacted less than those with an early onset of deafness.

As we were most interested in the effect of the phenotype of deafness on fitness, we did not attempt to categorise families by the underlying etiology, i.e. genetic vs. environmental. For the individuals in our study, most were unlikely to know the specific cause of their deafness prior to reproduction. In general, those families with two or more affected individuals or the result of a consanguineous mating are generally accepted to have a genetic etiology, while those simplex probands from unrelated parents are a mixture of genetic and environmental causes. Within some of the multiplex families, there may be several forms of deafness segregating, so that even siblings may have two different genetic etiologies. A number of the probands with an affected parent do not have a dominant form of deafness, but rather a pseudo-dominant form, with mutations in *GJB2* and/or *GJB6* the most likely explanation for their deafness.

Nearly a decade ago, we speculated that a combination of relaxed selection and assortative mating might account for the high frequency of DFNB1 deafness, which is generally transmitted as recessive with a congenital to early childhood onset of profound hearing loss, in many populations (Nance et al., 2000). This hypothesis postulated that the genetic fitness of the deaf had improved, that marriages involving deaf individuals did not occur at random but exhibited a high degree of assortative mating, and that these two features of the mating structure had a synergistic effect. We subsequently showed by computer simulation that plausible estimates of these two parameters could in fact lead to a doubling of the frequency of the commonest form of recessive deafness in less than 200 years. We next documented the high level of assortative mating among the alumni of Gallaudet University and used two approaches to show that the frequency of DFNB1 deafness has in fact increased in this population during the past century (Arnos et al., 2008). In the present article, we have completed the presentation of the evidence supporting our original hypothesis by documenting the changes in the genetic fitness of deaf individuals that have occurred during the recent past.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Pattern of Assortative Mating by Sex and Parental Mating Type

	Parental Mating Type			
Sex of Individual	DxD	DxH	HxH	Overall
Female	91/108 (0.84)	15/32 (0.47)	131/168 (0.78)	237/308* (0.77)
Male	78/88 (0.89)	9/15 (0.6)	121/149 (0.81)	208/252* (0.83)
Overall	169/196 ⁺ (0.86)	24/47 (0.51)	252/317 ⁺ (0.79)	445/560 (0.79)

* Females vs. Males $p=0.02$ ⁺ DxD vs HxH parental mating type $p=0.01$

Table 2

Marital Rates for All Individuals by Hearing Status, Sex and Parental Mating Type

		Parental Mating Type			Overall
		DxD	DxH	HxH	
Deaf Probands and Siblings	Female	108/125 (0.86)	33/43 (0.77)	168/206 (0.81)	309/374 (0.83)
	Male	88/98 (0.9)	15/22 (0.68)	150/187 (0.80)	253/307 (0.82)
	Total	196/223 (0.88)	48/65 (0.74)	318/393 (0.81)	562/681 * (0.83)
Hearing Siblings	Female	22/24 (0.92)	20/25 (0.80)	214/246 (0.87)	256/295 (0.87)
	Male	10/12 (0.83)	22/32 (0.69)	221/262 (0.84)	253/306 (0.83)
	Total	32/36 (0.89)	42/57 (0.74)	435/508 (0.86)	509/601 * (0.85)

Note: There were 5 deaf individuals and 1 hearing individual for whom we did not have parental mating type.

* Deaf vs. Hearing: $p=0.035$

Table 3
Relative Fertility of Deaf and Hearing Individuals by Gender

	Deaf Adults			Hearing Siblings		
	Male	Female	Total	Male	Female	Total
# of Individuals Ever Married	254	310	564	254	256	510
Average # of children among married	2.04	2.07 ⁺	2.06 [*]	2.17	2.35 ⁺	2.26 [*]
Relative Fertility	0.94	0.88	0.91			

^{*} Deaf vs. Hearing Siblings: p=0.005

⁺ Deaf Females vs. Hearing Female Siblings: p=0.006

Table 4

Average Number of Children born to Deaf and Hearing Siblings by Hearing Status, Parental Mating Type and Their Own Mating Type

Hearing Status	Mating Type	Sex	Parental Mating Type			
			DxD	DxH	HxH	Overall
Deaf	DxD	Female	2.02 (N=91)	2.53 (N=15)	2.11 (N=131)	2.11 (N=238)
		Male	2.12 (N=78)	1.56 (N=9)	2.14 (N=121)	2.11 (N=209)
	DxH	Female	1.71 (N=17)	1.76 (N=17)	2.14 (N=37)	1.94 (N=71)
		Male	1.80 (N=10)	1.83 (N=6)	1.57 (N=28)	1.83 (N=44)
	All	Female	1.97 (N=107)	2.12 (N=33)	2.12 (N=168)	2.07 (N=310)
		Male	2.08 (N=88)	1.67 (N=15)	2.05 (N=150)	2.04 (254)
Hearing	HxD	Female	2.00 (N=1)	.	4.00 (N=1)	3.00 (N=2)
		Male	.	.	.	.
	HxH	Female	2.53 (N=19)	2.53 (N=17)	2.32 (N=198)	2.35 (N=235)
		Male	1.80 (N=10)	2.36 (N=22)	2.12 (N=208)	2.13 (N=240)
	All	Female	2.41 (N=22)	2.35 (N=20)	2.34 (N=213)	2.35 (N=256)
		Male	1.80 (N=10)	2.36 (N=22)	2.16 (N=221)	2.17 (N=254)

Note: There were several individuals for whom we did not have complete parental mating type information and/or the hearing status of their partner. Their information has been included in the marginal totals, when appropriate.

Table 5
Average Number of Children Born to Deaf and Hearing Adults and Fitness of All Deaf Adults*

	Deaf Adults			Hearing Siblings		
	Males (308)	Females (378)	Total (686)	Males (307)	Females (295)	Total (602)
Ave # of children	1.68	1.70	1.69	1.79	2.04	1.91
Fitness	0.94	0.83	0.88			

* Includes individuals who have not had any children, regardless of marital status

Table 6

Comparison of Average Fitness of the Deaf in Three Populations

Population	Average Fitness	Reference Population
Sichuan, China ¹	0.60	Hearing Siblings
Shanghai, China ²	0.78	Hearing Siblings
Current Gallaudet Alumni Survey	0.88	Hearing Siblings

¹Liu et al., 1994 and²Hu et al., 1987