Natural History of Ashkenazi Intelligence

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The fourth is the existence of the Ashkenazi sphingolipid, DNA repair, and other disease clusters, groups of biochemically related mutations that could not plausibly have reached their present high frequencies by chance, that are not common in adjacent populations, and that have physiological effects that could increase intelligence.

Other selective factors have been suggested. “Winnowing through persecution” suggests that only the smartest Jews survived persecution. Why this should be so is not clear. There was no similar outcome in other groups such as Gypsies who have faced frequent persecution (Crowe and Kolsti, 1991). Another theory suggests that there was selective breeding for Talmudic scholarship. This seems unlikely to have been an important selective factor, since there weren’t very many professional rabbis, certainly less than one percent of the population. A selective force that only affects a tiny fraction of the population can never be strong enough to cause important evolutionary change in tens of generations. A plausible variant of the Talmudic scholarship model suggests that it was like a sexually selected marker and that rich families preferred to marry their daughters to males who excelled (Weyl and Possony, 1963; MacDonald, 1994) so that the payoff to intelligence was indirect rather than direct as we suggest. Without detailed historical demographic information it will be difficult to evaluate this hypothesis.

We proceed by summarizing IQ psychometrics and IQ as a quantitative genetic trait. We then describe relevant aspects of Ashkenazi social and demographic history with a focus on the centuries between 800 and 1600AD, after which we think many of the unique selective pressures were relaxed. We show that plausible mechanisms

significance because IQ (as measured by IQ tests) is the best predictor we have of success in academic subjects and most jobs. Ashkenazi Jews are just as successful as their tested IQ would predict, and they are hugely overrepresented in occupations and fields with the highest cognitive demands. During the 20th century, they made up about 3% of the US population but won 27% of the US Nobel science prizes and 25% of the ACM Turing awards. They account for more than half of world chess champions.

While the mean IQ difference between Ashkenazim and other northern Europeans may not seem large, such a small difference maps to a large difference in the proportion of the population with very high IQs (Crow, 2002). For example if the mean Ashkenazi IQ is 110 and the standard deviation is

matures. The phenomenon of heritability increasing with age is characteristic of many quantitative traits in mammals (Falconer, 1981).

The heritability of IQ is probably lower than 0.80 in most human populations, and it may

between 0.3 and 0.5 in childr

selective differential, the change per generation is $R = h^2S$ with no gene flow. If the local

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Empire, but there was a substantial population of Roman Jews, along with other poorly documented western settlements such as Cologne. After the Moslem conquests, the great majority of Jews live

The Ashkenazi population, established in northern France by the early 900s, prospered and expanded. They settled the Rhineland and England after the Norman Conquest. At first they were international merchants who acted as intermediaries with the Moslem world. As Moslems and Christians, especially Italians, increasingly found it possible to do business directly, Ashkenazi merchants moved more and more into local trade. When persecution began to be a serious problem and the security required for long-distance travel no longer existed, the Ashkenazim specialized more and more in one occupation, finance, left particularly open to them because of the Christian prohibition of usury. The majority of the Ashkenazim seem to have been moneylenders by 1100 AD (Ben-Sasson, 1976; Arkin, 1975), and this continued for several centuries. Such occupations (sales, trade, finance) had high IQ demands, and we know of no other population that had such a large fraction of cognitively demanding jobs for an extended period.

In some cases, we have fairly detailed records of this activity. For example (Arkin, 1975, p.58), concerning the Jews of Roussilon circa 1270: “The evidence is overwhelming that this rather substantial group of Jews supported itself by money lending, to the virtual exclusion of all other economic activities. Of the 228 adult male Jews mentioned in the registers, almost 80 percent appear as lenders to their Christian neighbors. Nor were loans by Jewish women (mostly rj 50 0 0 50 485 0 Tm (l) 0 0 50 10 1658 0 Tm(e) Tj 50 0 0 50 242 0 Tm (w) Tj 50

As they had in Western Europe, the Jews of Poland had a very unusual occupational profile. The very first to immigrate were mainly moneylenders, but that soon changed. They became tax-farmers, toll-farmers, estate managers, and they ran mills and taverns. According to Weinryb (1972) in the middle of the fourteenth century, “about 15 percent of the Jewish population were earners of wages, salaries and fees. The rest were independent owners of business enterprises.” They were the management class of the Polish-Lithuanian Commonwealth. Besides literacy, success in those specialized occupations depended upon skills similar to those of businessmen today, not least the ability to keep track of complex transactions and money flows.

Eventually, as the Ashkenazi population of the Polish-Lithuanian Commonwealth increased, more and more Jews became craftsmen—there are after only so many managerial and financial slots. Still, for 800 to 900 years, from roughly 800 AD to 1650 or 1700 AD, the great majority of the Ashkenazi Jews had managerial and financial jobs, jobs of high complexity, and were neither farmers nor craftsmen. In t

significant change over historical time. It is likely that the selective pressures affecting the medieval Ashkenazi were far stronger and somewhat different, because such a high percentage had cognitively demanding jobs, and because the Ashkenazi niche was so specifically demanding of accounting and management skills, while upper classes elsewhere experienced a more diverse set of paths to wealth.

Genetic Evidence about Ashkenazi History and the Bottleneck Hypothesis

Evidence from Polymorphic Gene Frequencies

The prevalence of several inherited diseases among Ashkenazim is often attributed to one or more population size bottlenecks in the past. Since the only evidence for such a bottleneck is the mutations themselves, it is important to look at other genetic markers for signs of any bottleneck. Episodes of small effective size could have allowed deleterious mutants to increase in frequency by chance. While the concentration of Ashkenazi mutations in a few pathways is a very strong argument against the bottleneck hypothesis, it is nevertheless important to evaluate the bottleneck hypothesis with available genetic data. The conclusion of this section is that Ashkenazi gene frequencies are so similar to those of Europeans that any bottleneck of fewer than five or ten thousand effective size is excluded by the data and that drift cannot account for the Ashkenazi diseases.

Patterns on the Y-chromosome and mitochondrial DNA suggest that the Ashkenazi founding population originated in the Middle East, in accord with tradition and the historical record. Gene

of the bottleneck. In either case drift could not have been strong enough to allow deleterious mutants to increase to high frequencies.

The small genetic distance between Ashkenazim and other Europeans

Mediterranean fever (Aksentijevic

by defective sphingolipid catabolism, while MLIV involves abnormal lysosomal sorting and trafficking. In each case the main storage substances are sphingolipids.

Each of these diseases is surprisingly common among the Ashkenazi Jews, particularly surprising because Tay-Sachs, Niemann-Pick, and MLIV homozygotes do not reproduce, while Gaucher homozygotes often have health problems. Table 2 shows the relevant gene frequencies and allele variants.

Each of these gene fre

Biology of the Sphingolipid Mutations

The sphingolipid storage mutations were probably favored and became common because of natural selection, yet we don't see them in adjacent populations. We suggest that this is because the social niche favoring intelligence was key, rather than geographic location. It is unlikely that these mutations led to disease resistance in heterozygotes for two reasons. First, there is no real evidence for any disease resistance in heterozygotes (claims of TB resistance are unsupported) and most of the candidate serious diseases (smallpox, TB, bubonic plague, diarrheal diseases) affected the neighboring populations, that is people living literally across the street, as well as the Ashkenazim. Second and most important, the sphingolipid mutations look like IQ boosters. The key datum is the effect of increased levels of the storage compounds. Glucosylceramide, the Gaucher storage compound, promotes axonal growth and branching (Schwartz et al., 1995). In vitro, decreased glucosylceramide results in stunted neurons with short axons while an increase over normal levels (caused by chemically inhibiting glucocerebrosidase) increases axon length and branching. There is a similar effect in Tay-Sachs (Walkley et al., 2000; Walkley, 2003): decreased levels of GM2 ganglioside inhibit dendrite growth, while an increase over normal levels causes a marked increase in dendritogenesis. This increased dendritogenesis also occurs in Niemann-Pick type A cells, and in animal models of Tay-Sachs and Niemann-Pick.

Figure 1, from Schwartz et al. (1995) shows the effect of glucosylceramide, the sphingolipid that accumulates in Gaucher disease. These camera lucida drawings of cultured rat hippocampal neurons show the effect of fumonisin, which inhibits glucosylceramide synthesis, and of conduritol B-epoxide (CBE) which inhibits lysosomal glycocerebrosidase and leads to the accumulation of glucosylceramide, thus mimicking Gaucher disease. Decreased levels of glucosylceramide stunt neural growth, while increased levels caused increased

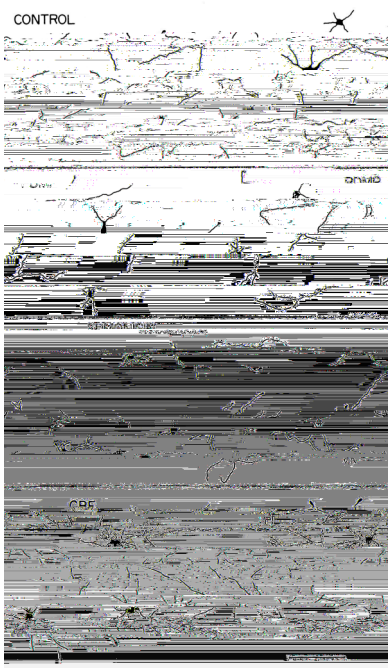

Figure 1: Glucosylceramide Increases Axon Growth, from Schwartz et al. (1995), reproduced by permission of the Journal of Biological Chemistry.

Dendritogenesis appears to be a necessary step in learning. Associative learning in mice significantly increases hippocampal dendritic spi

sample, given a base rate of 2.25%, is approximate

group of functionally related proteins involved in DNA repair. This is mainly an Ashkenazi cluster, but the common Ashkenazi BRCA1 mutation 187delAG is also common in Sephardic populations, while the Tyr978X BRCA1 mutation exists in 1-2% of Iraqi and Iranian Jews. There are two Ashkenazi BRCA1 mutations: 187delAG has an Ashkenazi carrier frequency of 0.96-1.14% and 5382insC has a carrier frequency of 0.15-0.28%. Table 3 lists the relevant gene frequencies and allele variants, from Dong et al. (2002).

All of these DNA repair mutations participate in homologous recombination repair (HRR), a process that is im

embryonic death in homozygotes, while milder mutations with residual function cause Fanconi anemia. Thus there are really two kinds of Fanconi anemia among

that the observed positive select

averaging over the allele age and the distribution of the number of ancestral lineages at the time of the hypothesized bottleneck. Notice that he is not concerned with the probability that a new mutant actually could have reached observed proportions, he is only concerned with the evidence of linkage disequilibrium about the need to invoke selection. Perhaps not surprisingly he is able to reject very few hypotheses about these genes and their history, but he does conclude from consideration of allele age that an earlier bottleneck, around 70AD, rather than a late medieval bottlene

reproductive compensation. With no gene flow and no selection, i.e. the neutral model, the corresponding probability is 15%: the answer given by the neutral model is wrong by a factor of 15.

		$N_0 = 150$	$N_0 = 600$	$N_0 = 3000$
	$N_1=600$	0.01	0.002	0.0001

Functio

Canavan	P45381	ACY2_HUMAN	ASPA
familial dysautonomia	Q8N516	-	IKBKAP
congenital adrenal hyperplasia	Q16874	-	CYP21A2
torsion dystonia	O14656	TO1A_HUMAN	DYT1
Cystic fibrosis	P13569	CFTR_HUMAN	CFTR
familial Mediterranean fever	O15553	MEFV_HUMAN	MEFV
connexin-26	P29033	CXB2_HUMAN	CXB2
Factor XI	P03951	FA11_HUMAN	F11
familial hyperinsulinism	Q09428	ACC8_HUMAN	ABCC8
familial hypercholesterolemia	P01130	LDLR_HUMAN	LDLR
glycogen storage disease type VII	P08237	K6PF_HUMAN	PFKM
Cystinuria	Q07837	SC31_HUMAN	SLC3A1

In practice these raw P-values must be corrected. The inference algorithm is more complicated both because of multiple testing issues and because of the dependency structure of the network. First, testing several hypotheses at a time (such as whether a cluster is involved in lipid metabolism, vacuole assembly, or DNA repair) can result in false positives if the hypothesis test threshold is not calibrated to account for multiple tests. Second, many of the hypotheses tested in a GO analysis are dependent. For example, an assessment of whether a given cluster is involved in lipid metabolism is not statis

Table 6: Clustering of mutations into pathways. The last two columns are the number out of 21 Ashkenazi genes in the cluster and the number out of 24,021 human genes in the cluster.

The results are summarized in Table 6. We note that the software picked up most of the clusters we had independently discovered, and several of them (lytic vacuole assembly, sphingolipid metabolism, glycosyl hydrolase activity) have statistical significance far beyond the 0.01 heuristic for corrected P-values. Furthermore, the DNA-repair cluster we identified is right on the edge of this heuristic with a P-value of .015. In sum, it is highly unlikely that several such tightly functionally linked groups would be present in a random collection of 21 genes. This is extremely strong evidence against the hypothesis that these mutations became frequent through drift rather than natural selection.

Conclusion

Our general hypothesis is that high IQ test scores of Ashkenazim, along with their unusual pattern of abilities, are a product of natural selection, stemming from their occupation of an unusual social niche. All the required preconditions–low inward gene flow and unusually high reproductive reward for certain cognitive skills, over a long-enough period–did exist. These preconditions are both necessary and sufficient, so such a selective process would almost inevitably have this kind of result. The pattern of high achievement among Ashkenazi Jews and the observed psychometric results are certainly consistent with this hypothesis.

Our more specific prediction is that some or most of the characteristic Ashkenazi genetic diseases are by-byproducts of this strong selection for IQ. In particular we find

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