Does obesity run in families because of genes?

An adoption study using silhouettes as a measure of obesity

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A number of studies, including the Danish adoption study, have shown that, in adults, the familial resemblance of obesity, as measured by the body mass index (weight in kg/(height in m)^2), is mainly due to genes. The body mass index may reflect both fat and fat-free body mass. In this further analysis of the Danish adoption study, the degree of obesity was assessed by a silhouette score. There was a significant relationship in scores between the adult adoptees and their biological mothers and between the adoptees and their biological full siblings reared by the biological parents. Weaker, nonsignificant associations were found for the biological fathers and for the maternal and paternal half-siblings. There were no relationships in silhouette scoring between adoptees and adoptive parents. The results confirm the results of our previous analysis of body mass index. We conclude that human obesity is under genetic control, whereas the childhood family environment has little, if any, influence on obesity in adults. It is an important task for future research to identify the genes involved.

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The common saying that obesity runs in families means in quantitative terms that the degree of obesity exhibits an intrafamilial correlation at about 0.20 to 0.25 for parent-offspring relations and 0.25 to 0.35 for full sibling relations (1, 2). Twin and adoption studies (3–10), including one based upon the Danish Adoption Register (7–9), have indicated that genes play a major role in the familial resemblance of obesity. In most of these studies the assessment of obesity was based on measurement of height and weight, usually combined in the body mass index (weight in kg/(heigh in m)^2). Since these measurements are correlated with both fat and fat-free body mass, it is not possible to distinguish between effects on these two components.

In the Danish adoption study (7–9), we also asked the subjects to score the degree of obesity using a series of silhouette drawings showing bodies of increasing obesity ranging from very thin to very obese (11). This study addresses the genetic and familial environmental influence on obesity as assessed by the silhouette method.

Material and methods

The study used the information assembled in the Danish Adoption Register on 5455 non-familial adoptions granted in the Copenhagen area between 1924 and 1947 (12). The study population and methods have been described in detail in the previous publications that focused on body mass index (7–9).

Briefly, by mailed questionnaire we obtained information allowing calculation of current and maximum body mass index on 3580 and 3476 adult adoptees, respectively. After stratification by sex and age, we selected for further study 4 groups on the basis of current body mass index – thin, medium weight, overweight and obese – each comprising 137 (4%) of the population in the extremes and around the median. Four groups of 133 (4%) were similarly selected on the basis of maximum body mass index. Of the total of 840 selected adoptees, 240 belonged to both the current and the maximum weight groups.

The adoptive parents, the biological parents and other offspring of the biological parents (full and half-siblings of the adoptees not adopted away) were traced through the population registers. Questionnaires were mailed to the parents asking about their height, weight and silhouette score (Fig. 1) at the time when the adoptees went to school. The selected adoptees and the biological siblings received questionnaires asking about the same infor-

Fig. 1. Silhouettes from which the subjects picked the one that best represented themselves or their parents

mation on the parents and about their own height, current and greatest ever weight, and corresponding silhouette scores. Table 1 shows the number of subjects from whom silhouette scores were obtained.

The silhouette scoring has been validated by correlations with the body mass index, although not with measures of body composition. Within the present sample, the correlation coefficient between the self-reported silhouette scores and the self-reported body mass index of the adoptees was 0.88 and 0.87 for current and maximum values, respectively. Owing to the greater weight put on the extremes of the distribution by the sampling scheme, these estimates are somewhat exaggerated. Thus, for siblings the corresponding, less biased, correlations were 0.79 and 0.81. The offspring's scoring of silhouettes of their parents according to their recall of the parents' degree of overweight 15 years earlier was compared with measurements of these parents carried out 15 years earlier as part of the repeated health examinations of the population in Tecumseh, Michigan (13). The correlations of these silhouette scores with the previously measured body mass index were 0.74 and 0.63 for the mothers and fathers, respectively, and the correlations of the scores with the sum of several skinfold thicknesses were 0.66 and 0.39, respectively.

Mean silhouette scores were calculated for each type of relative within each adoptee weight class. Separate analyses were carried out for families with data on 1, 2 or 3 or more of each type of sibling, and all siblings within such set were then included in the analysis. Silhouettes corresponding to current and maximum weight of the siblings were analyzed in relation to the current and maximum weight classes of the adoptees, respectively. The differences in mean silhouette scores across adoptee weight class were statistically evaluated by one-way analysis of variance, including test for linear trend. In addition to the statistical significance of each analysis, the consistency of the results among similar analyses of different subsets of the data was considered: analysis of current and maximum weight classes, of fathers and mothers and of families with 1, 2 or 3 or more siblings. It should be noted, however, that these analyses are not fully independent replications, and specific hypothesis about different effects, for example for current and maximum degree of obesity, might also be put forward.

Results

The mean silhouette scores are shown in Fig. 2–4 and the results of the analysis of variance in Table 1. To appraise the magnitude of the effects, the mean silhouette scores of the adoptees are shown in each figure as well. When the scores of the adoptees and their biological relatives are compared, it should be kept in mind that first-degree relatives share half of their genes and second-degree relatives only a quarter of their genes.

The scores of the biological mothers increased by about 1 unit through the thin, median and overweight class of adoptees in both the current and the maximum weight class groups, and the effects were highly significant. The biological fathers showed smaller and nonsignificant trends across the adoptee weight classes.

The scores of the adoptive mothers showed no trends and the scores of the adoptive fathers even a slight, but statistically significant inverse trend across the adoptee weight classes.

The full sibling scores generally showed increasing trends across the adoptee weight classes, which were statistically significant in 4 of 6 analyses. The average scores among the 3 groups of siblings in the 4 current weight classes were 3.7, 4.1, 4.4 and 4.9, and 4.6, 4.9, 5.5 and 5.6 in the 4 maximum weight classes, respectively.

The scores of the 6 groups of half-siblings increased slightly across the 4 weight classes: within each adoptee weight class, the average scores were 3.9, 4.1, 4.2 and 4.2 for current weight, and 4.4, 4.8, 5.0 and 5.0 for maximum weight. Only one analysis, however, was statistically significant: maximum weight class, 2 maternal half siblings per adoptee.

There were no differences in the silhouette scores of biological parents and half-siblings between the overweight and obese classes of adoptees. For the full siblings there was a distinct difference in the current weight classes but not in the maximum weight classes.

Discussion

The significant relationships in silhouette scores between adoptees and biological mothers and between adoptees and full siblings confirm the findings of studies of body mass index (3–10). Assuming that the silhouette method is measuring the fat mass rather than the fat-free body mass, our findings support the interpretation that the degree of obesity is under genetic control.

Our previous analysis of body mass index showed significant relationships between adoptees and biological fathers and between adoptees and maternal half-siblings, but not between adoptees and their paternal half-siblings (7–9). The silhouette method showed weaker, mostly nonsignificant, trends for these relatives across the adoptee weight classes. These negative findings could be due to methodological problems arising from using the silhouette method combined with expected

Table 1. Results of one-way analysis of variance of silhouette scores of relatives of adoptees across the 4 adoptee weight classes, defined either by their current or greatest ever body weight (Fig. 2–4)

		Current weight classes			Maximum weight classes		
			Effects			*Effects*	
	Relative of adoptee	*n*	Main *P*	Linear *P*	*n*	Main *P*	Linear *P*
Parents (Fig. 2)	Biological mother	379	0.0001	0.0001	369	0.0001	0.0001
	Biological father	294	0.35	0.18	285	0.10	0.27
	Adoptive mother	447	0.29	0.24	424	0.31	0.85
	Adoptive father	412	0.09	0.04	394	0.08	0.01*
Full siblings (Fig. 3)	1**	42	0.02	0.003	48	0.001	0.0001
	2	27	0.88	0.55	25	0.20	0.05
	3+	45	0.02	0.002	51	0.49	0.99
Maternal half-siblings (Fig. 4)	1	205	0.17	0.08	174	0.44	0.18
	2	128	0.11	0.09	108	0.03	0.005
	3+	136	0.69	0.24	94	0.62	0.93
Paternal half-siblings (Fig. 4)	1	156	0.07	0.06	145	0.55	0.30
	2	102	0.96	0.81	79	0.35	0.17
	3+	124	0.76	0.55	101	0.15	0.04

* *Inverse trend.* ** Numbers of siblings per adoptee available for analysis.

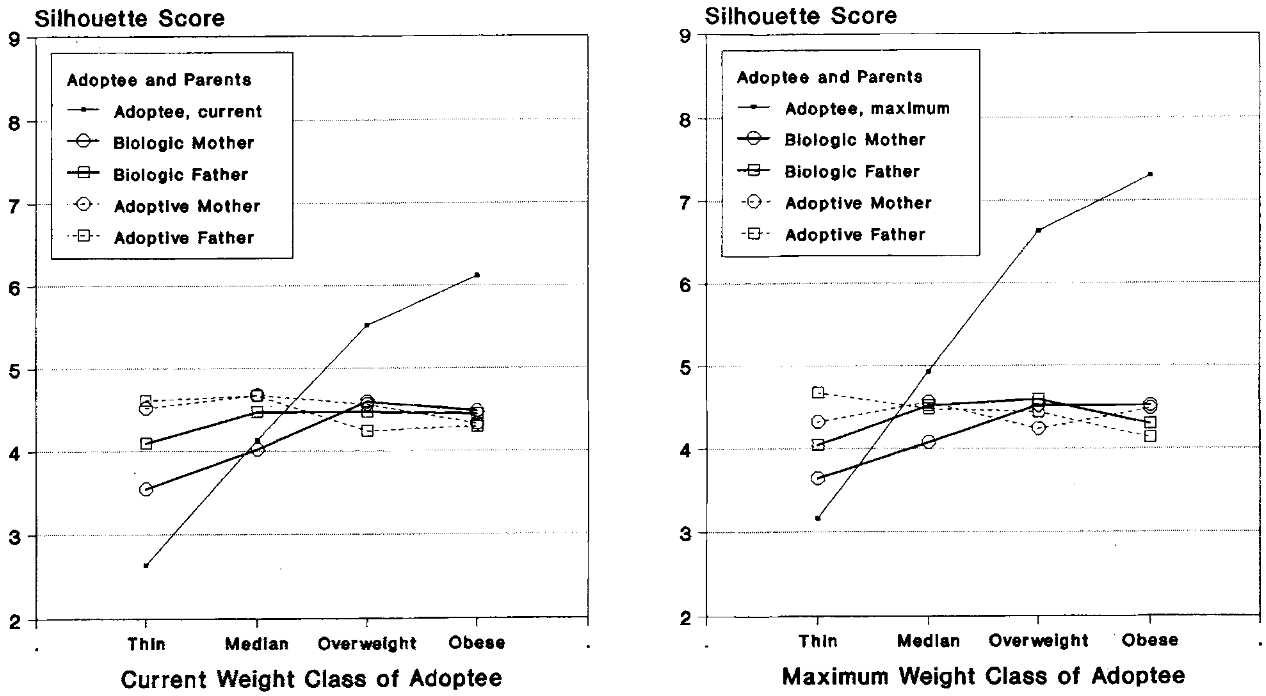

Fig. 2. Average silhouette scores of adoptees and their biological and adoptive parents in the four weight classes of adoptees as defined the body mass index (weight in kg/(height in m)^2) derived from either their current weight (left panel) or their greatest ever weight (right panel). The silhouette scores of the adoptees corresponds to the current and maximum weight, respectively. The scores for the parents referred to the time when the adoptees went to school and were reported by themselves or their adult offspring. The results of the statistical analysis are given in Table 1.

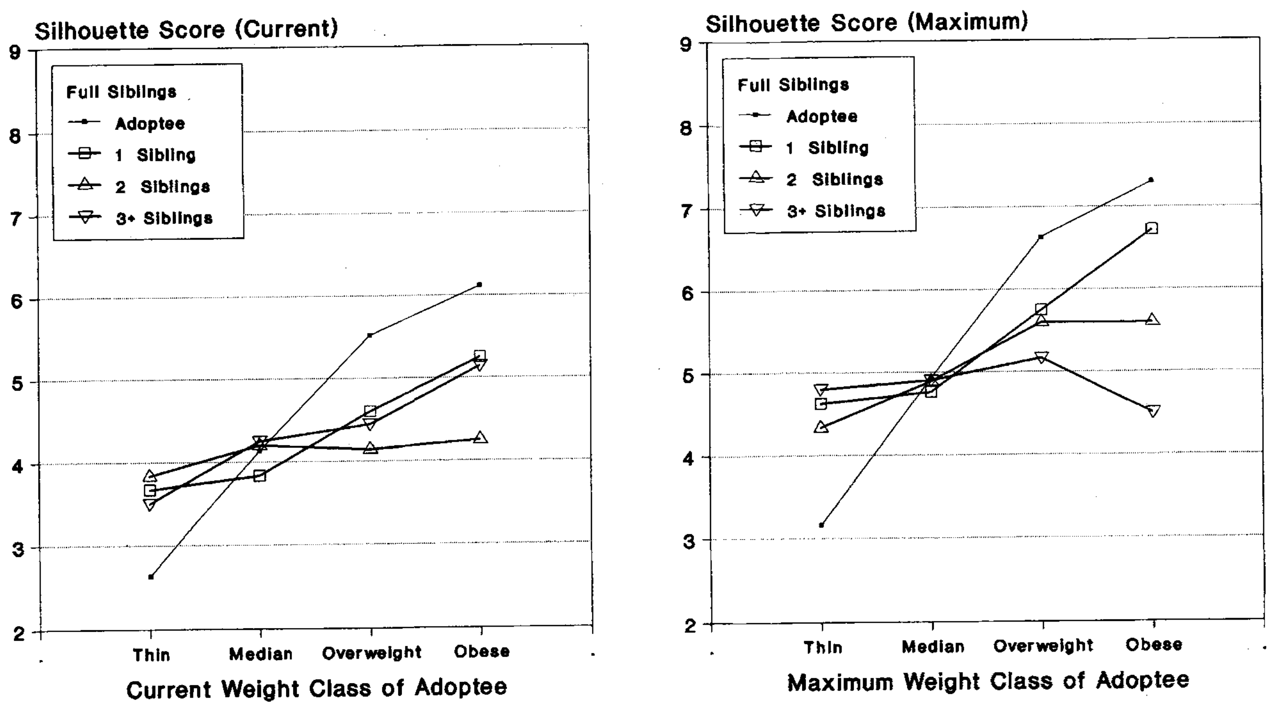

Fig. 3. Average silhouette scores of adoptees and their biological full siblings who also reported their current and maximum score. The families were subdivided according to the number of siblings available for analysis (1, 2 or 3 or more). See legend of Fig. 2 for further explanation.

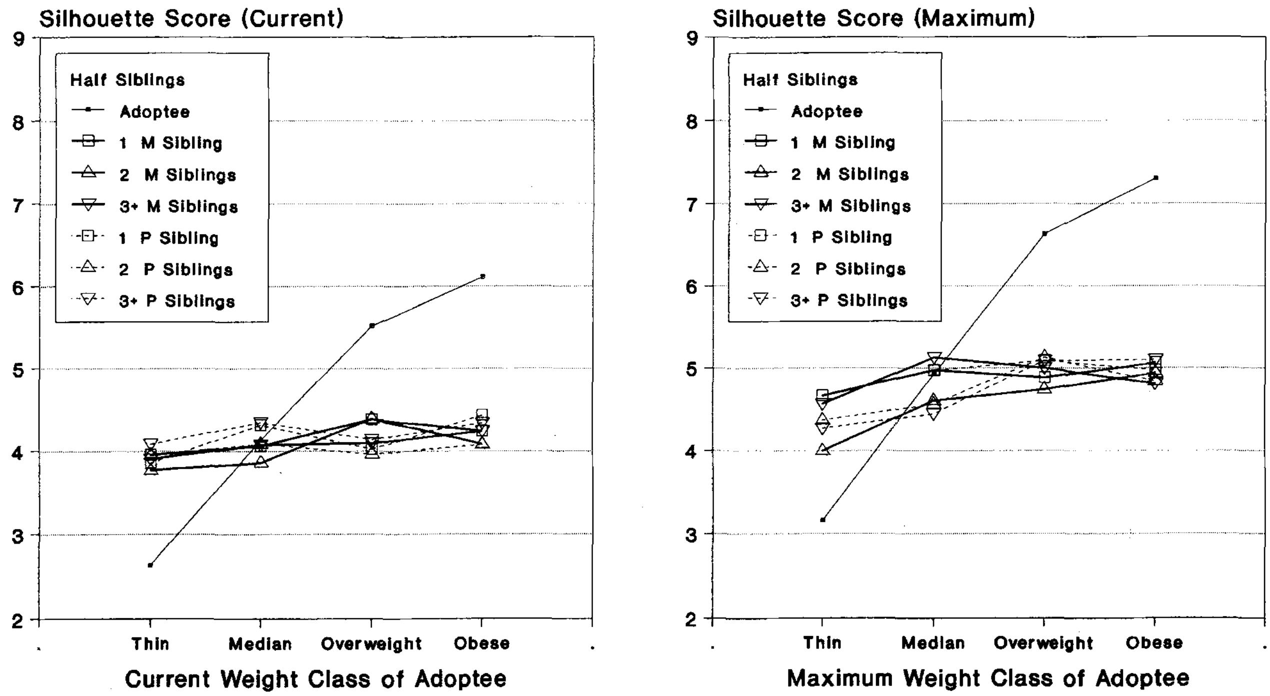

Fig. 4. Average silhouette scores of adoptees and their biological half-siblings on either the biological mother's (M Siblings) or biological father's (P Siblings) side. See legend of Fig. 2 and 3 for further explanation.

weaker relationships for these types of relatives (lower correlations are expected for fathers and paternal half-siblings than for mothers and maternal half-siblings because of the uncertainty about paternity; the sharing of only one quarter of the genes between adoptees and half-siblings results in a correspondingly lower expected correlation than among the adoptees and their first-degree relatives).

The absence of any relationship between degree of obesity in the adoptee and their adoptive parents is in accordance with the analysis of body mass index (7, 9). This suggests that the family environment shared during childhood has no influence on degree of obesity in adulthood. However, several studies (1, 2, 14–16), including an extension of the present study to childhood of the adoptees and their siblings (15) demonstrate that the familial environment does have an effect while the subjects are living together.

Bouchard et al. (17, 18) measured the body composition in a study of twin pairs and families including foster children. They found twin pair and familial correlations of body mass index at the same level as in many previous studies and similar correlations for both fat and fat-free body mass. The analysis of the twin pairs suggested quite strong genetic effects on both body components, strongest for the fat-free mass, but twin studies are often assumed to overestimate genetic effects. Some of the analyses of the family data supported a major influence of the genes; others supported that the family environment was of greater importance. Using analysis based on a comprehensive statistical model, the genetic contribution to the correlations was rather high for fat-free mass, but, in contrast to our results, small for body mass index and for the fat mass, suggesting that family environment is more important than genes for these traits.

However, these findings may be due to the indirect method they used for estimation of genetic effects. It is critically dependent on the assumption that the familial environmental effects among the first-degree relatives are validly expressed in the correlations between spouses, between foster children and the members of the families in which they were reared and between fraternal twins relative to between other biological full siblings. In our study, the genetic effects are directly assessed without confounding the family environment by comparing the adoptees with their biological relatives.

The old observation that obesity runs in families may also mean that there is a familial aggregation of a qualitatively different severe form of obesity, which may be caused by a more specific major gene, as in some obesity syndromes occurring in rodents (19). The previous analysis of body mass index showed a far stronger difference between full siblings than between biological parents and half-siblings of adoptees in the overweight and obese weight classes. As we have noted elsewhere, this finding could be explained by the effect of a major recessive gene (8, 20). The pattern of results using the silhouette method confirms that found with the use of body mass index. Analysis of the distribution of body mass index in populations of families (21–23) and of twin pairs (24) supports the contention about a major gene, and it will be a task for future research to identify the gene.

The twin and family study carried out by Bouchard et al. (17, 18) suggested that the distribution of body fat is also under genetic control. The silhouette method used in the present study may have favored a particular type of fat distribution (the gynoid lower body obesity). Advances in the understanding of genetic influences on human obesity would be aided by differentiating among subtypes of obesity (16). Further development of the silhouette method may enable it to discriminate among sybtypes based on different body fat distribution, for example gynoid versus android obesity.

Although there now seems to be little doubt about the role of genes in human obesity, the environmental causes are as important, as evidenced by the great variation in its occurrence over time both in individuals (25) and populations (26, 27).

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