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Childhood Hyperactivity Scores Are Highly Heritable and Show Sibling Competition Effects: Twin Study Evidence

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Hyperactivity has consistently been shown to be familial. Until recently however, due to a lack of systematic twin evidence, it has remained uncertain to what extent familial transmission can be explained by genetic factors. We used a systematically ascertained population-based sample of twin pairs aged between 8 and 16 years old to explore the role of genetic influences on maternally rated hyperactivity scores. Hyperactivity scores were found to be substantially heritable. The data were best explained by a model which incorporated sibling competitive effects as well as additive genetic factors. These findings suggest not only that hyperactivity scores are influenced by genetic factors but that sibling interaction effects are also of importance.

KEY WORDS: Twin studies; hyperactivity; attention deficit hyperactivity disorder; sibling interaction.

INTRODUCTION

The question of how hyperactivity should best be defined is one which has provoked much debate. It is still uncertain whether hyperactivity is best viewed as a dimension or as a category, and even when considered as a diagnostic category, concepts of hyperactivity vary. Transatlantic differences in the concept of hyperactivity are highlighted by the findings of epidemiological surveys. These have shown that estimated prevalence rates of hyperactivity vary from 6 to 19% (Schachar *et al.*, 1981, 1991; Shekim *et al.*, 1985; Anderson *et al.*, 1987; Szatmari *et al.*, 1989; Taylor *et al.*, 1991) for the relatively broad DSM III (American Psychiatric Association, 1980) attention deficit disorder, with hyperactivity to a rate of 1.7% (among school boys) for the more narrowly defined ICD 10 (World Health Organization, 1992) hyperkinetic disorder (Taylor *et al.*, 1991).

Despite these difficulties, it has been acknowledged for some years that hyperactivity aggregates in families. In some of the earliest studies, relatives of hyperactive children showed higher rates of hyperactivity than controls (Morrison and Stewart, 1971; Cantwell, 1972; Nichols and Chen, 1981). Although these studies may be criticized on methodological grounds, similar results have been obtained in a more recent series of studies in which standardized assessment measures and diagnostic criteria were used (Biederman *et al.*, 1986, 1992; Faraone *et al.*, 1991).

Familial transmission of a condition or a behavioural dimension can of course be accounted for by shared environmental factors as well as by genetic factors (McGuffin *et al.*, 1994). Given the observed association between environmental factors such as social disadvantage and family discord and hyperactivity (Schachar, 1991; Taylor, 1994), twin and adoption studies which enable us to tease apart the effects of genes and environment are of partic-

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ular importance. Unfortunately there have been very few twin and adoption studies of hyperactivity or psychopathology in childhood (Rutter *et al.*, 1990; LaBuda *et al.*, 1993).

Although the findings of several early adoption studies suggested that hyperactivity may well be genetically influenced (Morrison and Stewart, 1973; Cantwell, 1975; Alberts-Corush *et al.*, 1986), these studies are open to methodological criticism. To date there has been only one published systematic twin study of hyperactivity in which hyperactivity was considered both as a dimension and as a category using questionnaire scores (Goodman and Stevenson, 1989b; Stevenson, 1992). In this study of 13 year olds, genetic influences appeared to be of considerable importance for behavioral and attentional components of hyperactivity in different settings.

The aim of this study was to explore the role of genetic influences on hyperactivity scores in a systematically ascertained sample of twins aged between 8 and 16 years.

METHOD

Subjects

The Cardiff Births Survey (CBS) is a database which was set up in 1965 (Andrews *et al.*, 1986) and consists of detailed obstetric information and demographic details on all births in the county of South Glamorgan, Wales, UK (approximate population 400,000). A population-based sample of twins was obtained by identifying and tracing twin pairs born between 1976 and 1984 from the CBS (Thapar and McGuffin, 1994). In this phase of the study, the sample consisted of 376 pairs of twins.

Measures

The parents of all twins were sent questionnaires by post with two reminders if there was no response. For twins born between 1976 and 1980, additional self-ratings were obtained separately and three reminders sent. Twin zygosity was determined by a twin similarity questionnaire which consists of questions regarding physical similarity and the extent to which the twins are confused by others. This method of distinguishing between identical (monozygotic; MZ) and nonidentical (dizygotic; DZ) twins has been shown to be over 90% accurate (Nichols and Bilbro, 1966; Cohen *et al.*, 1975). A questionnaire measure of environmental sharing (Loehlin and Nichols, 1976) was also obtained.

Hyperactivity scores were derived from maternal ratings on the Rutter A questionnaire (Rutter *et al.*, 1970). Previous work (Schachar *et al.*, 1981; Goodman and Stevenson, 1989a) has shown that a dimensional measure of hyperactivity can be obtained by summing scores for the three hyperactivity items (''very restless, has difficulty staying seated for long,'' ''squirmy, fidgety child,'' and ''cannot settle to anything for more than a few moments'') in this questionnaire. As each item is scored as 0, 1, or 2, the total hyperactivity score ranges between 0 and 6.

Obstetric data were obtained from the CBS and pregnancy and birth complications (PBC) were scored using the Parnas scale (Parnas *et al.*, 1982). This scale was designed to rate pregnancy and birth complications using data based on birth records. The scale can be used to calculate frequency scores (the number of recorded PBCs) and total scores (the sum of weighted PBCs).

Genetic Analysis

The basis of the twin study design is that MZ twins are genetically identical, whereas DZ twins share only 50% of their segregating genes on average. Thus, assuming that MZ and DZ twins share environment to the same extent, MZ twins will be more alike than DZ twins for traits that are under genetic influence.

The total observed variation of a trait (phenotypic variance) can be subdivided into a proportion due to additive genetic factors (h^2; heritability), a proportion accounted for by shared environment (c^2), and a remaining proportion attributed to nonshared environmental factors and error (e^2). Observed twin correlations ($r$mz and $r$dz) can then be expressed in terms of heritability and the variance due to shared environmental factors as follows:

$$r\text{mz} = h^2 + c^2$$

$$r\text{dz} = \frac{1}{2}h^2 + c^2$$

Model fitting allows us to test whether observed patterns of twin correlations can be explained by simpler models, that is, by additive

Table I. Frequency of Hyperactivity Scores by Zygosity and Sex

Hyperactivity score	MZ Females (n = 138)	MZ Males (n = 88)	DZ Females (n = 80)	DZ Males (n = 90)	Opposite sex (n = 164)	Total
0	94	57	51	46	98	346
1	18	12	13	16	19	78
2	14	12	5	7	15	53
3	8	5	7	10	12	42
4	4	1	2	5	6	18
5	—	1	2	2	6	11
6	—	—	—	4	8	12

genes only (AE) or by shared environment only (CE) or by neither genes nor shared environment (E).

Hyperactivity scores on the Rutter questionnaire range between 0 and 6 and the data were treated as categorical. Models were fitted directly to contingency tables rather than to correlation matrices using the program Mx (Neale, 1991), so that a model allowing phenotypic interaction could also be tested (see later). This approach is similar to that used in LISREL (Joreskog and Sorbom, 1989) but allows for greater flexibility. The goodness of fit of the tested model is given by the chi-square value, with a smaller chi-square indicating a better fit. The degrees of freedom (df) are equal to the number of estimated parameters (including 6 threshold values for the hyperactivity categories) subtracted from the number of observed statistics (2 groups with 7 × 7 contingency tables = 96 observed statistics). The fit of the full ACE model is compared against the fit of the reduced models by subtracting the chi-square values. This distribution follows a chi-square distribution with degrees of freedom equal to the df of the reduced model minus the df of the full model. Further details of model fitting are described by Neale and Cardon (1992).

RESULTS

Sample

The response rate for the parent rated questionnaires in this phase of the study was 76% (287/376). Responders were similar to nonresponders in terms of age, sex, and social class. However, mothers of nonresponders were significantly younger (χ^2 = 16.03, df = 2, $p < .001$) and more often single, widowed, divorced, separated, or remarried at the time of birth (χ^2 = 13.1, df = 3, p = .005) than responders.

Zygosity

Zygosity was determined by using parent and twin (where available) ratings for the twin similarity questionnaires which had been sent in two phases of the study. The total sample consisted of 113 MZ, 85 same-sex DZ, and 83 opposite-sex DZ twin pairs. Zygosity was not assigned to six twin pairs where ratings were inconsistent, missing, or ambiguous. MZ twin pairs were comparable to DZ twin pairs in terms of age, sex, and social class. However, MZ twin pairs scored significantly higher than DZ twin pairs on the measured index of environmental sharing (t = 4.86, df = 180, $p < .001$). This finding has been reported elsewhere (Loehlin and Nichols, 1976) and suggests that MZ twins share environment to a greater extent than DZ twins, which would violate a basic assumption of the twin method. However, further analyses showed that the environmental sharing score was not associated with MZ twin similarity for hyperactivity scores (Spearman rank correlation r = −.12, p = .23).

Hyperactivity Scores

The distribution of hyperactivity scores by zygosity and sex are shown in Table I. The mean hyperactivity score for the total sample was 0.90 (SD = 1.46). In previous studies a score of 3 or more has been taken as a measure of categorical hyperactivity (Schachar *et al.*, 1981; Goodman and Stevenson, 1989a, b). Defined in this way, the rate

Table II. Contingency Tables of Hyperactivity Scores by Sex and Zygosity (r = Polychoric Correlation)

MZ-TWIN1 score	MZ-TWIN2 score 0	1	2	3	4	5	6
	Male MZ twins (r = .71)						
0	22	0	2	1	0	0	0
1	8	2	0	0	0	0	0
2	1	0	3	2	0	0	0
3	1	0	1	0	0	0	0
4	0	0	0	0	0	0	0
5	0	0	0	0	1	0	0
6	0	0	0	0	0	0	0
	Female MZ twins (r = .58)						
0	38	6	3	1	2	0	0
1	3	2	2	0	0	0	0
2	2	2	2	0	0	0	0
3	1	1	1	1	1	0	0
4	0	0	0	1	0	0	0
5	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0
DZ-TWIN1 score	DZ-TWIN2 score 0	1	2	3	4	5	6
	Same-sex male DZ twins (r = −.22)						
0	11	5	2	2	1	1	1
1	2	2	0	0	1	0	1
2	1	1	1	0	0	0	1
3	5	1	0	1	0	0	0
4	3	0	0	0	0	0	0
5	0	1	0	0	0	0	0
6	1	0	0	0	0	0	0
	Same-sex female DZ twins (r = .05)						
0	16	4	0	1	1	0	0
1	5	1	0	0	0	0	0
2	2	1	1	0	0	0	0
3	4	1	0	0	0	0	0
4	1	0	0	0	0	0	0
5	1	0	0	1	0	0	0
6	0	0	0	0	0	0	0
	Opposite-sex twins (r = .23)						
0	34	6	3	2	2	2	2
1	3	1	1	2	0	0	0
2	4	1	0	1	0	1	1
3	4	0	0	1	0	0	0
4	0	1	1	0	1	0	0
5	0	2	0	1	0	0	0
6	2	1	2	0	0	0	0

Table III. Basic Model Fitting for Hyperactivity Scores (n = 198 Pairs)[a]

	h^2	c^2	χ^2	df	p
ACE	0.59	0.00	88.14	87	.45
AE	0.59	[0]	88.14	88	.48
CE	[0]	0.25	98.70	88	.20
E	[0]	[0]	108.3	89	.08

[a] [0] parameter fixed at zero.

of categorical hyperactivity was found to be 14.8%. Hyperactivity was not associated with age or birth order but was significantly commoner among boys (Mann–Whitney $Z = -2.66$, $p = .008$).

However, MZ and DZ twins did not appear to be comparable in terms of hyperactivity scores. DZ twins scored significantly higher than MZ twins ($DZ\bar{X} = 1.13$, $MZ\bar{X} = 0.65$; Mann–Whitney $Z = -2.6$, $p = .01$) and the variances of hyperactivity scores were significantly different ($DZ6^2 = 3.10$, $MZ6^2 = 1.16$; Kruskall–Wallis one-way ANOVA $\chi^2 = 6.55$, $p = .01$).

Pregnancy and Birth Complications

There were no significant differences between MZ twins and DZ twins in terms of PBC frequency scores ($MZ\bar{X} = 1.15$, $DZ\bar{X} = 1.06$) and PBC total scores ($MZ\bar{X} = 2.37$, $DZ\bar{X} = 2.07$). Frequency and total PBC scores were not found to be significantly associated with either hyperactivity scores or categorical hyperactivity.

Genetic Analyses

Contingency tables of hyperactivity scores and polychoric correlations for MZ and DZ twins are shown in Table II.

Basic Model Fitting

As there was no evidence of significant heterogeneity across the sexes (results of model fitting not shown), male and female twins were combined into one group for further analyses. Models were fitted to contingency tables and the results of model fitting are shown in Table III. It can be seen that for the full ACE model (additive genes and shared environment), the lower bound of zero is reached in estimating shared environment (c^2). The AE model does not result in a significantly worse fit

(χ^2 = 88.14–88.14 = 0, df = 1) compared with the full model. It can be seen, however, that for the CE model, the fit is significantly poorer (χ^2 = 10.56, df = 1, p = .001) and that a no transmission model (E) provides a very poor fit for the data (χ^2 = 20.12, df = 2, $p < .0001$). Thus on the grounds of parsimony (accepting the simplest model), the additive genes only model provides the most acceptable explanation of the data.

Model Fitting Incorporating Sibling Interaction Effects

At this point it is important to consider several unexpected findings. First, when hyperactivity scores were treated as continuous, MZ and DZ variances for hyperactivity scores differed significantly (although a higher variance is often associated with a higher mean). Second, a negative tetrachoric correlation was obtained for same-sex male DZ twins and a near-zero value for same-sex female DZ twins. These findings suggest that a different genetic model should be tested. Reciprocal sibling competition (Eaves, 1976) where the behavior or phenotypic trait of one twin has a negative feedback effect on the phenotypic trait of the other twin, and vice versa, could explain these findings (see Discussion for further explanation).

On these grounds, a sibling interaction model which incorporates additive genetic and sibling interaction effects (AE-s) was also tested (see Fig. 1). An AE model is nested within the AE-s model and thus the fit of these models can be compared. As a sibling interaction model predicts different MZ and DZ variances, it was necessary to constrain the total variance, previous to interaction, to unity. This constraint acts as another observed statistic and thus there are now 96 + 1 observed statistics (i.e., df = 97 − 9 = 88). It can be seen from Table IV that there is a significant deterioration in fit when the AE submodel is compared to the full AE-s model (χ^2 = 14.6, df = 1, $p < .0001$).

Thus overall, it appears that the data are best explained by an additive genes and sibling interaction model with heritability estimated as 0.88 and a sibling interaction effect of −0.24.

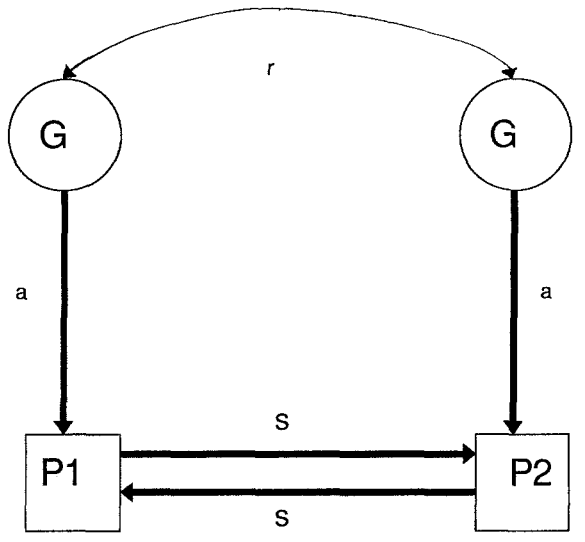

Fig. 1. Additive genetic model with sibling effects. $r$mz = 1, $r$dz = 0.5. G, genotype; P1 and P2, phenotype of twins 1 and 2; a, additive genetic effect; s, sibling effect.

Table IV. Model Fitting Incorporating Sibling Interaction (n = 198 Pairs)[a]

	s	h^2	c^2	χ^2	df	p
AE-s	−0.24	0.88	[0]	73.54	88	.87
AE	[0]	0.59	[0]	88.14	89	.51

[a] [0] parameter fixed at zero.

DISCUSSION

It has long been suspected that hyperactivity may be genetically influenced. There is consistent evidence of familial transmission (Biederman *et al.*, 1992; Faraone *et al.*, 1992), and in an early study of twins, MZ twins were found to be more alike than DZ twins on measures of activity levels and hyperactivity (Willerman, 1973). This study was, however, small, the twin sample was not systematically ascertained, and standardized measurements were not used. Our results suggest that there is a substantial genetic contribution to maternally rated hyperactivity scores. These results replicate the findings of Goodman and Stevenson (1989b), where for 13 year olds, there was evidence of genetic factors influencing hyperactivity scores (h^2 = 42–72%, father- and teacher-rated scores), measures of attention (h^2 = 32–42%), categorical hyperactivity (h^2 = 64%), and extreme hyperactivity (h^2 = 81%) (Stevenson, 1992).

However, in our study, we have additionally shown that a model in which sibling effects are incorporated appears to be superior to a simple additive genetic model. This is the first report ex-

amining the role of sibling interaction effects in hyperactivity. Genetic models with sibling interaction effects were first described by Eaves (1976) and more recently developed further by Carey (1986). Competition or contrast effects are characterized by the behavior or phenotype of one twin having an inhibitory effect on the behavior of the other twin, with the parameter "s" (see Fig. 1) taking on a negative value. Our findings suggest that, at least for maternally rated hyperactivity scores among twins, competitive effects are of some importance (that is increased hyperactive scores in one twin result in a decrease in the hyperactivity score of the other twin). It has been shown previously that competitive sibling effects predict an increased variance among DZ twins compared to MZ twins (Eaves, 1976, 1978; Carey, 1986). Sibling competitive effects could also account for a negative DZ correlation (Eaves, 1976, 1978), for which there is otherwise no plausible biological explanation. Thus there were several indicators in our data that suggested that it would be appropriate to test a model with sibling competitive effects.

Our findings are of particular interest as there are very few examples of sibling interaction models (competition and cooperation) which have been fitted successfully. This may be in part because sibling interaction can be confounded with other effects (competition mimicking genetic dominance and cooperation mimicking shared environment) (Eaves, 1978). Previous work has suggested that sibling competition may be influential for type A behavior (Sims *et al.*, 1991) and extraversion in adults (Eaves, 1989), and more recently there is preliminary evidence of cooperation effects influencing antisocial behavior in childhood (Neale and Cardon, 1992).

Although our sample of twins is systematically ascertained, the possibility of a biased sample of responders has to be considered. For example, MZ/DZ differences in hyperactivity scores could also arise if there were underrepresentation of high-scoring MZ twins or overrepresentation of low-scoring DZ twins. However, the ratio of MZ twins to same-sex DZ twins (1.3:1) suggests that there is no overrepresentation of DZ twins in the total sample. The sample also appears to be representative in that our rates of maternally rated hyperactivity (14.8%) are intermediate to those obtained in studies in the Isle of Wight [9.9% (Schachar *et al.*, 1981)] and London [17.3% (Goodman and Stevenson, 1989a)]. The observed pattern of results (increased hyperactivity scores among males, no association between hyperactivity scores and pregnancy and birth complications) is also broadly similar to those observed in the London twin study (Goodman and Stevenson, 1989a). Moreover, our overall MZ and DZ correlations of 0.61 and −0.10 (same-sex twins) are strikingly similar to those of Goodman and Stevenson [(1989b) $r$mz = 0.68, $r$dz = −0.08 (same-sex twins) for maternally rated hyperactivity scores]. The lack of association between hyperactivity and birth complications contrasts with a previous study using the CBS (Chandola *et al.*, 1992) where small but significant effects were detected. However, the subjects in this study consisted of singletons who had been referred, and thus sample differences may in part explain the disparate findings.

Another potential source of bias in our twin study is that of expectancy effects, where mothers tend to rate MZ twins as more similar and exaggerate differences between DZ twins. However, even where parents were mistaken about the zygosity status of their twins, the pattern of correlations remained similar ($r$mz-recognized = 0.652, n = 70; $r$mz-unrecognized = 0.667; n = 35). Moreover, this pattern of MZ and DZ correlations was not observed for either depressive (Thapar and McGuffin, 1994) or anxiety (Thapar and McGuffin, 1995) symptoms in the same sample of twins.

Finally, it is important to note, as mentioned earlier, that it can be difficult to disentangle genetic dominance effects (i.e., nonadditive genetic interactions within a locus) from sibling competition effects. Unfortunately, our data do not allow us to test simultaneously for dominance and sibling effects. Although dominance effects would explain MZ correlations of greater than twice the DZ correlations, they would not explain MZ/DZ differences in variance or a negative DZ correlation.

In conclusion, hyperactivity scores appear to be substantially heritable and influenced by sibling competitive effects. One limitation of our study is that we have relied on maternal reports only, and it is possible that the results are demonstrating maternal contrasting effects. As we have analyzed hyperactivity scores across the range, these findings may not necessarily apply to extreme and/or pervasive hyperactivity. However, there is some evidence to suggest that extreme, maternally rated

hyperactivity is also heritable (Stevenson, 1992). It is, of course, possible that sibling effects may vary according to the level of hyperactivity and across different situations. These factors need to be taken account of in future studies, with the consideration that sibling effects could be further explored by studying singletons as well as twins, using direct observational measures of hyperactivity and by including families of different size.

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