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Genetic Analysis of Cognitive Failures (CFQ): A Study of Dutch Adolescent Twins and Their Parents

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Abstract

A substantial part of the inter-individual variation in everyday cognitive failures in memory, perception and motor control can be attributed to genetic factors. Cognitive failures were assessed with the Cognitive Failures Questionnaire (Broadbent, Cooper, FitzGerald and Parkes, 1982) in a large sample of Dutch adolescent twin pairs and their biological parents. The heritability for CFQ scores was around 50 per cent. There was no association between CFQ scores and age or educational level. Both in the parental generation (aged 46 years on average) and in the offspring generation (aged 17.7 years on average) women had somewhat higher mean CFQ scores than men. There were no sex differences in heritabilities. The part of the variance that could not be attributed to genetic factors was best explained by environmental influences unique to the individual. There was no evidence for the influence of shared environment on CFQ scores. CFQ scores of husband and wife were correlated ($r = 0.22$) and this association was modeled as phenotypic assortment. The correlations between parents and offspring were somewhat lower than the correlations between dizygotic twins. Under a model with equal heritabilities in parents and offspring, there was some evidence that the genetic factors that influence cognitive failures in the two generations are partly different.

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INTRODUCTION

The Cognitive Failures Questionnaire (CFQ) developed by Broadbent, Cooper, FitzGerald and Parkes (1982) is an instrument designed to measure everyday failures in memory, perception and motor control. It comprises 25 items that assess the frequency of particular mistakes such as forgetting names, failing to notice road signs, bumping into people and getting unintentionally distracted. Such slips and lapses

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have been called execution failures (Reason, 1988). Proneness to these failures seems to be governed by a global factor that exerts its influence across a variety of memory lapses and action slips (Larson, Alderton, Neideffer and Underhill, 1997; Reason, 1988). People tend to show stable individual differences in their tendency toward cognitive failures across a variety of situations. Broadbent *et al.* (1982) found a 3 month test–retest stability of 0.82 and in a different sample a 16 month stability of 0.54. They also obtained significant correlations between CFQ self-ratings and ratings of the respondents by their spouses.

CFQ scores seem largely independent of standard measures of personality and intelligence, but show a relationship with self-reported psychiatric symptoms, especially symptoms experienced during or following periods of stress (Reason, 1988). Broadbent *et al.* (1982) report a significant association between CFQ scores and minor psychiatric symptoms in nurses who had worked on high-stress wards. In nurses who had worked on low-stress wards no such association was seen.

Broadbent *et al.* (1982) argue that the CFQ measures vulnerability to externally imposed stress. When exposed to life stress, individuals with high CFQ scores develop neurotic symptoms, because they are less successful in adopting active coping strategies. Reason (1988) reviews the various lines of research that suggest that a certain style of cognitive resource management can lead to both absent-mindedness and to inappropriate matching of coping strategies to stressful situations. He poses the question of whether this cognitive management style has a relatively fixed constitutional basis. This question is addressed in this paper by analysing individual differences in CFQ scores in a large sample of monozygotic and dizygotic twin pairs and their parents. With this twin–family sample the extent to which variation in CFQ scores is caused by genetic and by environmental variation between individuals can be examined.

The etiology of individual differences in vulnerability to stress such as that assessed by the CFQ can be studied by comparing the similarity in CFQ scores within pairs of monozygotic twins to CFQ similarity within pairs of dizygotic twins. Monozygotic (MZ) twins share all their genetic material. If a trait is influenced by genetic factors they should be more alike than dizygotic (DZ) twins who share on average 50 per cent of their segregating genetic material (as do ordinary siblings). Parents and offspring also share 50 per cent of their genes. If genetic factors that influence trait variation are stable across the age span, then the correlation between parents and offspring is expected to be of the same magnitude as the correlation in DZ twin pairs.

In this paper the familial resemblance in CFQ scores is analysed in a large sample of adolescent Dutch twins and their parents. CFQ data are available for over 3000 twins, for 1418 fathers and 1603 mothers. Structural equation models are used to test whether familial resemblance in CFQ scores is due to shared genes, a common environment shared by family members or to cultural transmission from parents to their offspring (Neale and Cardon, 1992).

METHOD

Subjects

Twin families were recruited by asking all 699 city councils in The Netherlands for addresses of twins aged 13–22 years. A positive response was received from 252 city

councils that supplied 3859 addresses; 177 addresses were available from other sources. After contacting these twin families by letter, 2375 families indicated that they were willing to complete a questionnaire on health and lifestyle and 1700 families returned these questionnaires (Boomsma, Koopmans, Van Doornen and Orlebeke, 1994; Koopmans and Boomsma, 1996). The sample consisted of monozygotic (MZ) and dizygotic (DZ) male and female twin pairs and of dizygotic twin pairs of opposite sex (DOS). Twin zygosity was determined by questionnaire, using items on physical similarity and frequency of confusion of the twins by family members and by others. For a group of 405 same-sex twin pairs zygosity information based on blood group and DNA polymorphisms was also available. The agreement between zygosity based on the questionnaire data and zygosity based on DNA marker data was 95 per cent (six DZ same-sex pairs were misclassified as MZ and 15 MZ pairs were misclassified as DZ based on the questionnaire data). In the total sample there were 275 MZM, 258 DZM, 360 MZF, 322 DZF and 485 DOS pairs. Average age of the twins, fathers and mothers was 17.7 (SD = 2.3), 47.8 (SD = 5.6) and 45.7 (SD = 5.2) years, respectively. Data on educational attainment were collected by questionnaire. The sample is representative of the general Dutch population with respect to educational level (Koopmans, Boomsma, Heath and Van Doornen, 1995).

Measures

The Dutch translation of the Cognitive Failure Questionnaire (CFQ) developed by Broadbent *et al.* (1982) was administered (Das-Smaal, De Jong and Koopmans, 1993; Muris and Merckelbach, 1995). The CFQ consists of 25 items that measure the frequency of everyday cognitive lapses on a five-point scale (0, never; 4, very often). Items refer to particular types of mistake such as forgetting appointments, bumping into people, dropping things and forgetting names. The total CFQ score was the sum of the all individual responses to the 25 items. Higher scores thus indicate a higher frequency of cognitive failures. Subjects with more than two missing items were discarded from the analyses. There were 1651 twin pairs, 1418 fathers and 1603 mothers with complete CFQ data. There were 1360 families in which both parents and both twins completed the CFQ.

Statistical analysis

Sex and generation differences in CFQ scores were tested with Spss-Anova. Within each sex and generation the correlation between CFQ score, educational level and age was computed with Spss.

Resemblances among family members for CFQ scores were first summarized by correlations. Correlations were estimated separately for monozygotic (MZ) and dizygotic (DZ) male and female, and DZ opposite-sex twin pairs, for fathers and mothers with their male and female offspring, and for spouses (husband–wife pairs).

Different models of familial resemblance were fitted to covariance matrices, that were computed with PRELIS2 (Jöreskog and Sörbom, 1993). First, a series of models was fitted to the five 2×2 covariance matrices of twins (i.e., MZM, MZF, DZM, DZF, and DOS twin pairs). These genetic models specified the variation in phenotype as a function of genotype and environment. Sources of variation considered were A, additive genetic influences (i.e., the sum of the effects of the individual alleles across

all loci), C, common environmental influences shared by twins living in the same household, and E, a random environmental deviation that is not shared by family members. Their influence on the phenotype is given by parameters h , c , and e that are equivalent to the standardized regression coefficients of the phenotype on the latent variables A, C, and E, respectively. The proportion of variance due to each source is the square of these parameters. Under a model in which twin resemblance is explained by additive genetic factors, MZ twins, who are 100 per cent genetically identical, are expected to be twice as similar as DZ twins, who share 50 per cent of their segregating genes. Under a shared environmental model MZ and DZ correlations are predicted to be the same. If MZ correlations are larger than DZ correlations, but less than twice the DZ correlation, both additive genetic and shared environmental influences are implicated.

Possible sex differences in genetic architecture were assessed by comparing a model in which estimates for h , c , and e were allowed to differ in magnitude between males and females, to a model in which they were constrained to be equal in both sexes.

Parameters h , c , and e were estimated by maximum likelihood, using the computer program Mx (Neale, 1997). Goodness-of-fit for different models of familial resemblance (e.g., ACE and AE) was assessed by likelihood-ratio χ^2 tests. The overall χ^2 test indicates the agreement between the observed and the predicted variances and covariances in the five twin groupings. A large χ^2 (and a low probability) indicates a poor fit, while a small χ^2 (accompanied by a high probability) indicates that the data are consistent with the model. Submodels were compared by hierarchical χ^2 tests, in which the χ^2 for the full model is subtracted from that for a reduced model. The degrees of freedom (df) for this test are equal to the difference between the degrees of freedom for the full and the submodel.

Next, data from twins and parents were summarized into 4×4 covariance matrices and analysed simultaneously. A series of models for the parent-twin data was evaluated. In the first model the correlation between CFQ scores of spouses was represented as phenotypic assortment and modeled with a copath (Cloninger, 1980). This path induces correlations among spouses' latent variables without affecting their within-person covariance structure before assortment. Assortative mating may increase the correlations in first-degree relatives and thereby affect heritability estimates. If assortative mating induces a correlation γ between latent genetic factors of parents, then the genetic correlation between first-degree relatives increases from 0.5 to $0.5(1 + \gamma)$.

In addition to genetic transmission from parents to offspring, cultural transmission from parents to children was considered and modeled as transmission from the father's and mother's phenotype to the environment of the children. In this model the parents create part of the environment of the child according to their phenotypic resources. Additionally, there may be environmental effects that are shared by offspring only. The effects of genetic and cultural transmission induce a correlation, s , between genes and environment (Boomsma and Molenaar, 1987; Fulker, 1982; 1988; Neale, Walters, Eaves, Maes and Kendler, 1994), that can be expressed as a function of the other parameters in the model. A test for differential expression of genes at different ages was carried out by estimating the correlation between genetic factors in parents and genetic factors in offspring, instead of constraining it at 0.5 (or $0.5(1 + \gamma)$ in the case of assortative mating).

RESULTS

Figure 1 gives the frequency distributions of the Cognitive Failures Questionnaire for both sexes in the parental and offspring generations. In all four groups, the data show a normal distribution. The mean scores and standard deviations for CFQ scores are listed in Table 1 for first- and second-born male and female twins and for their parents. There were no significant differences between the two generations in the average number of Cognitive Failures that were reported by parents (32.2) and their offspring (32.0). As can be seen in Table 1, however, there is a difference in CFQ scores of males and females. In each generation, women reported significantly more cognitive failures than men (mean values are 33.5 and 30.4, for all females and for all males, respectively). Within each generation and sex, there was no association of CFQ scores with age or with educational level.

The degree of familial resemblance for the CFQ is summarized in Table 2. For monozygotic twins the average correlation for CFQ scores was around 0.50 and for dizygotic twins it was 0.25. Correlations for male and female twin pairs were about the same and the correlation for opposite-sex twin pairs was of the same magnitude as the correlations for same-sex pairs. This pattern of twin correlations for CFQ scores implies that around 50 per cent of the variance can be attributed to genetic factors, without contributions of shared environmental factors and without significant sex differences in heritability.

The resemblance between parents and offspring was somewhat, but not very much, lower than the DZ correlation with an average correlation around 0.20. Correlations between fathers and offspring were of the same magnitude as between mothers and offspring, again suggesting the absence of sex differences in heritabilities. There was a significant association between CFQ scores of spouses (0.22).

Table 1. Mean CFQ scores and standard deviations for twins and their parents

| | N | | Mean | SD | | Mean | SD |
|--------|------|------|-------|-------|--------|------|-------|
| MZM | 264 | t1 | 29.0 | 10.31 | t2 | 28.8 | 10.77 |
| DZM | 244 | t1 | 29.8 | 10.92 | t2 | 29.6 | 10.67 |
| MZF | 357 | t1 | 32.7 | 10.47 | t2 | 33.8 | 10.16 |
| DZF | 315 | t1 | 33.8 | 10.27 | t2 | 34.8 | 10.89 |
| DOS | 471 | male | 31.1 | 10.15 | female | 33.6 | 10.31 |
| Father | 1418 | | 30.92 | 10.02 | | | |
| Mother | 1603 | | 33.37 | 9.79 | | | |

Note: MZM, monozygotic males; DZM, dizygotic males; MZF, monozygotic females; DZF, dizygotic females; DOS, dizygotic twins of opposite sex; t1, first-born twins; t2, second born twins.

Table 2. Familial correlations for CFQ scores

| | Twin correlations | | Parent-offspring and spouse correlations | |
|-----|-------------------|------|--|-------------|
| MZM | (264) | 0.50 | Father-son | (1285) 0.18 |
| DZM | (244) | 0.20 | Mother-son | (1431) 0.22 |
| MZF | (357) | 0.53 | Father-daughter | (1519) 0.20 |
| DZF | (315) | 0.33 | Mother-daughter | (1729) 0.21 |
| DOS | (471) | 0.26 | Spouses | (1388) 0.22 |

Note: Number of pairs between brackets.

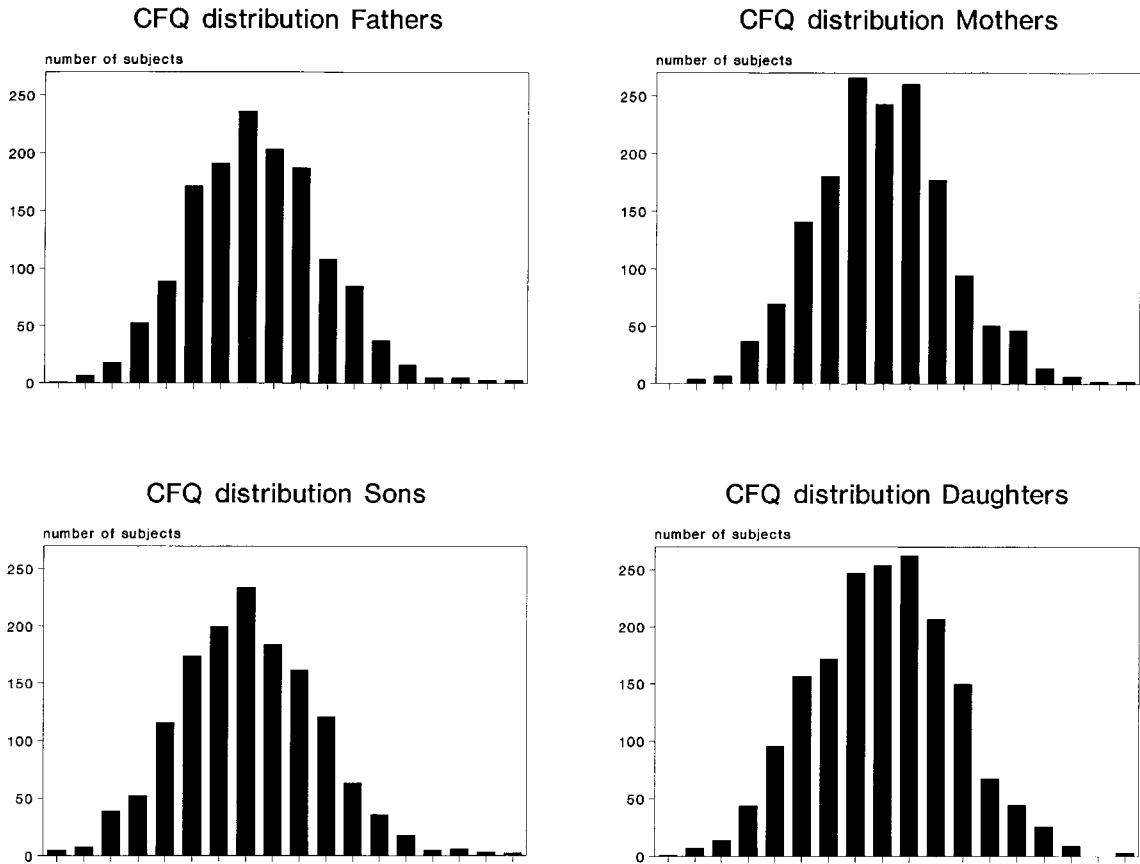


Figure 1. Frequency distributions of the Cognitive Failures Questionnaire for fathers ($N = 1418$), mothers ($N = 1603$), sons ($N = 1465$), and daughters ($N = 1762$)

Table 3. Goodness-of-fit indices for fitting biometrical models to CFQ data from twins

| | χ^2 | df | <i>p</i> |
|-----------------------|----------|----|----------|
| ACE sex differences | 6.45 | 9 | 0.70 |
| CE sex differences | 27.52 | 11 | 0.00 |
| AE sex differences | 6.55 | 11 | 0.84 |
| AE no sex differences | 8.58 | 13 | 0.80 |

Note: A, additive genetic influences; C, common family environment; E, unique environment.

Table 4. Maximum likelihood parameter estimates and χ^2 goodness-of-fit indices for simultaneous analysis of CFQ data from twins and their parents

| | I | II | III | IV |
|--|--------|--------|-------|-------|
| Genetic variance | 56.9 | 64.9 | 40.6 | 50.8 |
| Environmental variance | 55.9 | 52.9 | 61.9 | 51.6 |
| Spouse correlation | 0.23 | 0.23 | 0.23 | 0.23 |
| Twin environment correlation | 0.069 | 0* | 0* | 0* |
| GxE correlation | -0.093 | -0.133 | 0* | 0* |
| Cultural transmission | -0.011 | -0.015 | 0* | 0* |
| Genetic correlation across generations | 0.5* | 0.5* | 0.5* | 0.34 |
| χ^2 | 59.92 | 60.83 | 84.66 | 60.44 |
| Degrees of freedom | 45 | 46 | 47 | 46 |
| Probability | 0.067 | 0.070 | 0.001 | 0.075 |

Note: * parameter fixed at this value.

I, full model: genetic and cultural transmission and phenotypic assortment between spouses

II, as I, no correlated environment in twins

III, as II, no cultural transmission

IV, as III, free genetic correlation across generations.

Different models of familial resemblance were first fitted to the data of the twins. Table 3 gives the chi-squared goodness-of-fit statistics for an ACE model with sex differences in genetic and environmental influences, for a CE model without genetic influences and for an AE model, that leaves out shared environmental influences. As can be seen from the increase in χ^2 , it was not possible to account for the pattern of twin correlations by the influences of a shared family environment. In contrast, the AE model, that leaves out shared environment and accounts for phenotypic resemblance by genetic relatedness, described the data very well. The last model in Table 3 is an AE model without sex differences. This model gave a very good fit to the data and did not describe the data any worse than a model with sex differences in parameter estimates. The heritability for CFQ scores under this model was 52 per cent.

Parameter estimates and goodness-of-fit tests, based on the simultaneous analyses of the parent–offspring data, are shown in Table 4. Column I gives the results under the full model which specifies mixed genetic and cultural transmission, phenotypic assortative mating, and an additional correlation between environmental influences in twins. As was already suggested by the analyses of the twin data, the correlation between environmental influences in twins was not different from zero (column II). It was not possible to remove cultural transmission from the model (column III), as judged by the large increase in χ^2 . Cultural transmission parameters were negative, suggesting that parents who score relatively low on the CFQ create an environment for their children that promotes higher scores. However, a model in which partly

different genes influence CFQ scores in parents and children (column IV) fitted the data as well as the model with negative cultural transmission. The correlation between genetic factors that influence CFQ scores in parents and genetic factors that influence CFQ scores in children was estimated at 0.34, implying that there still is substantial overlap between the genetic influences on cognitive failures in adolescents and in adults. Under all parent–offspring models the heritability for CFQ scores is estimated around 50 per cent.

DISCUSSION

This is the first study of everyday cognitive failures in which the heritability of individual differences in CFQ scores was estimated. The results show that around 50 per cent of the variance in CFQ scores may be attributed to genetic differences between individuals. No sex differences in heritability estimates were found. There is no evidence that shared environmental factors have any influence on CFQ scores. In this respect, the CFQ resembles many other personality variables. The estimate of 50 per cent heritability for CFQ is of the same magnitude as heritability estimates for a large number of personality traits (e.g., Eaves, Eysenck and Martin, 1989; Loehlin, 1992; Plomin, DeFries, McClearn and Rutter, 1997).

The CFQ data showed a moderate correlation between the scores of husband and wife. The model for assortment that was employed is essentially an atheoretical statistical treatment, which seems appropriate at this point, since we know very little about the mechanisms of assortment for human behavioural traits (Fulker, 1988). It is unlikely that the spousal correlation for cognitive failures arises because of the known assortment for intelligence or educational attainment, since the CFQ is largely independent of IQ and this study also found no relationship between CFQ scores and educational attainment.

Correlations between male and female twins for CFQ scores were very similar, as were correlations within opposite-sex pairs. Similar to the results seen in the twins, the resemblance between parents and offspring in CFQ scores did not depend on the sex of the parent or the child, confirming that heritabilities are of the same magnitude in men and women. The correlations between parents and offspring were somewhat smaller than between DZ twins. It is difficult to decide on statistical grounds between a model for these data in which there is negative cultural transmission from parents to the environment of their offspring and a model in which there is a reduced genetic correlation between the generations. It seems difficult, however, to conceive of a mechanism by which low CFQ scores in parents would create an environment for high CFQ scores in their children or vice versa. The model which specifies a reduced genetic correlation between the generations may be the more appropriate one. In this model, the path from parent's genotypes to those of their offspring was estimated at 0.34, which suggests that over half of the genetic factors that cause individual differences at an earlier age are still active at a later age.

In several studies CFQ data seem to correlate with indices of anxiety, depression, and neuroticism. Power (1988) obtained CFQ, anxiety, and depression scores in a sample of students on two occasions. CFQ scores predicted levels of anxiety and depression four months later. For anxiety, CFQ even predicted the time-2 anxiety levels, when time-1 levels were partialled out. Merckelbach, Muris, Nijman and

De Jong (1996) found positive associations between neuroticism, state and trait anxiety, and depression in student and in patient samples. Reason (1988) hypothesized that certain styles of cognitive resource management, as assessed by the CFQ, may lead to both absent-mindedness and to inappropriate matching of coping strategies to stressful situations. It is interesting that the measures found to be associated with the CFQ show positive relations among themselves. Moreover, several large-scale twin studies have established that anxiety and depression (Kendler, Heath, Martin and Eaves, 1986; 1987) and neuroticism and depression (Kendler, Neale, Kessler, Heath and Eaves, 1993) share a common genetic basis. Whether the association between cognitive failures and measures of anxiety, depression, and neuroticism is due to pleiotropic genetic effects, or whether environmental stressors or other environmental influences explain this association, remains to be investigated. In the same families that completed the CFQ, we have collected longitudinal questionnaire data on anxiety and neuroticism and are currently collecting psychiatric interview data. We intend to use these data to look at their associations with CFQ scores and to address the question of the etiology of this association in future multivariate genetic analyses.

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