PREDICTION OF ADOPTEE PSYCHIATRIC DISORDERS BY INTERACTION OF GENETIC RISK OF SCHIZOPHRENIA AND COMMUNICATION DEVIANCE DIVIDED BY THE WORD COUNT OF ADOPTIVE PARENTS

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TAUSTA: Vaikka geenien ja ympäristön toisistaan riippumaton vaikutus skitsofrenian etiologiaan on osoitettu, ei aiemmissa tutkimuksissa ole kiinnitetty huomiota näiden yhdysvaikutuksiin. Suomalaisessa skitsofrenian adoptiolapsitutkimuksessa geeni-ympäristö yhdysvaikutuksen on havaittu olevan yhteydessä yleisesti adoptiolasten psykiatrisiin häiriöihin.

TUTKIMUSONGELMA: Ennustimme adoptiolasten seurannassa todettuja mielenterveyden häiriöitä perustuen heidän adoptiovanhempiensa yksilö-Rorschach -testissä todettuihin kommunikaatiohäiriöihin standardisoituna puheen pituudella. Vertasimme tätä menetelmään, jossa kommunikaatiohäiriöt oli standardisoitu transaktioiden (vastausten) lukumäärällä löytääksemme mahdollisia eroja tuloksissa näiden kahden metodin välillä.

MENETELMÄ: Adoptiolapset (n=108), joilla ei ollut DSM-III-R diagnoosia alkumittauksissa, jaettiin geneettisen riskin perusteella korkean- ja matalan riskin ryhmiin perustuen heidän biologisen äitinsä skitsofrenian spektriryhmän häiriön diagnoosiin. Ympäristöriskimuuttujana käytimme tässä tutkimuksessa vanhempien kommunikaatiohäiriötä (Communication Deviance, CD). Adoptiolapsen perinnöllisellä riskillä ja adoptiovanhempien kommunikaatiohäiriöillä sekä näiden yhdysvaikutuksella ennustettiin keskimäärin 12.5 vuoden seurannan jälkeen adoptiolasten mielenterveyden häiriöitä.

TULOKSET: Lapsen perinnöllisen riskin sekä vanhemman kommunikaatiohäiriöihin kuuluvan osa-asteikon ”ajattelun häiriöt ja ristiriitaisuudet” yhdysvaikutuksella todettiin olevan yhteys adoptiolasten mielenterveyden häiriöihin. Ainoastaan perinnöllisellä riskillä sairastua skitsofreniaspektrin ryhmän häiriöön todettiin olevan yhteys adoptiolapsen mielenterveyden häiriöihin, kun selitysmallissa olivat mukana perinnöllinen riski, adoptiovanhempien kaikki kommunikaatiohäiriöt ja näiden yhdysvaikutus.

JOHTOPÄÄTÖS: Käyttämämme menetelmä, jossa vanhempien kommunikaatiohäiriöpisteet jaettiin heidän testiosassa puhumiensa sanojen määrällä, ei osoittanut genetiikka-ympäristöyhdysvaikutusta lasten psykiatristen häiriöiden selittäjänä lukuun ottamatta viidettä CD-alaryhmää (ajattelun häiriöt ja ristiriitaisuudet). Vertailukohtana käyttämämme menetelmä, jossa kommunikaatiohäiriöpisteet oli jaettu transaktioiden määrällä, osoitti vahvan ympäristö-genetiikka yhdysvaikutuksen, vaikka geneettiset- ja ympäristöriskitekijät eivät yksinään osoittautuneet merkittäviksi. Näin ollen geneettinen päävaikutus ylikorostuu, mikäli kommunikaatiohäiriöpisteitä standardisoidaan puheen pituudella.

BACKGROUND: Although the main effects of genes and the environment have been independently explored in the etiology of schizophrenia, previous research has not paid much attention to possible interactions between these two. In the Finnish Adoptive Family Study of Schizophrenia, gene-environment interactions have been found to be the defining predictive factor for the outbreak of general adoptee mental health problems.
AIMS: We predicted the outbreak of general mental health disorders in adoptees at the follow-up by their parents' Communication Deviance (CD) scores standardized by the length-of-speech in the individual Rorschach tests. We also did comparisons between these and Communication Deviance scores standardized by the number of transactions to find out whether these two standardization methods would yield different results.
METHOD: Adoptees (n = 108) with no DSM-III diagnoses at initial assessment were divided into genetic high-risk and low-risk groups based on their biological mothers' schizophrenia-spectrum diagnoses. We then calculated the Communication Deviance scores for the rearing family adoptive parents by dividing their individual CD scores by the number of words spoken during the individual Rorschach test. We predicted general mental health disorders of the adoptees after a 12.5 year follow-up using the high genetic risk and the adoptive parents Communication Deviance and their interaction.
RESULTS: We found the interaction between the high genetic risk of the adoptee and high scores on the CD subscale "Parental reasoning problems and contradictions" to be predictors of general psychiatric disorders in the adoptee. The main effect of high genetic risk was found to be the only significant predictor of mental disorders in the adoptees when the total CD scores of the adoptive parents and their interaction with the high genetic risk were included in the model.
CONCLUSION: Communication Deviance scores of the adoptive parents standardized by dividing them with the number of words spoken do not show any gene-environment interactions affecting the outbreak of general mental health disorders in the adoptees (except for CD subgroup 5, Reasoning Problems and Contradictions). However, earlier research has verified that total Communication Deviance scores standardized by the number of individual Rorschach test transactions do show a very strong gene-environment interaction, whereas the main effects of genes and the environment become non-significant. The genetic main effects therefore appear to become over-highlighted whenever the length-of-speech standardization method is used.

INTRODUCTION

Although the evidence for the predominant role of genetics in the etiology of schizophrenia and schizotypal personality disorders is indisputable (see, for example, Gottesman, 1991; Tienari et al., 2000, 2003), there have been only relatively few attempts to explore the *interaction effects* between genetics and the rearing environment (Tienari, Wynne, & Wahlberg, 2006; van Os & Sham, 2003). Traditional research designs, such as twin studies, have often considered the effects of genes and the environment independently of each other, resulting in any gene-environment effects present in the data being incorporated into either the genetic or environmental component alone (Iyegbe, Modinos, & Sanchez, 2012). However, more recent research has hypothesized that the complex etiology of schizophrenia is probably best explained by equally complex interaction effects. Activation of pre-existing genetic or pre-symptomatic environmental liabilities by certain acute or chronic environmental triggers – a model generally known as the diathesis (vulnerability)/stress (or stressor) model – has already been widely accepted in the field of schizophrenia study (Nuechterlein & Dawson, 1984; Rosenthal, 1970; Zubin & Spring, 1977). Research has shown us that genetic vulnerabilities can increase a person's sensitivity to environmental factors such as adverse rearing patterns (Hakko, Wahlberg, Tienari, & Räsänen, 2011; Kendler & Eaves, 1986). This gene-environment interaction is also likely to predispose children to other disturbances beyond schizophrenia; even though only a few of the offspring of schizophrenic parents develop a psychosis, the amount of general mental disturbance found among such offspring is high (Schubert & McNeil, 2003).

Several environmental factors have been found to affect the outbreak of schizophrenia. One such risk factor is the Expressed Emotion within the family (Leff & Vaughn, 1985). High EE environments - which have been associated with the relapse of schizophrenic symptoms - have high levels of critical comments, hostility and emotional over-involvement. However, these levels of EE are not stable over time and probably react to the disturbing behavior shown by the patient, indicating a two-way interaction between the patient and his/her environment (Brown, Birley, & Wing, 1972). Other environmental factors, such as maternal influenza (Brown et al., 2004), genital/reproductive infections (Babulas, Factor-Litvak, Goetz, Schaefer, & Brown, 2006), famine during pregnancy (Hoek, Brown, & Susser, 1998) and obstetric complications during pregnancy and delivery (Cannon, Jones, & Murray,

2002; Mäki et al., 2005) have also been established in the etiology of schizophrenia. The cumulative adversity index (e.g. the accumulation of factors such as childhood illness, disrupted rearing environment, parental mental illness, and cannabis use) in childhood and adolescence has been associated with narrow schizophrenia (Husted, Ahmed, Chow, Brzustowicz, & Bassett, 2012). Urbanization (Mortensen et al., 1999), migration (Cantor-Graae & Selten, 2005; Mäki et al., 2005) and neuroanatomical abnormalities (van Haren et al., 2012) have also been found to be associated with an increased risk of schizophrenia.

However, one particularly interesting environmental risk factor – the one in the focus of this current study – is the level of Communication Deviance (CD) measured in the rearing parents. This parental CD has been previously studied by Singer and Wynne (1965) and Wahlberg et al. (1997, 2001, 2004). A high CD score indicates that a person´s speech is hard to follow, as well as difficulties in the sharing of common attention and meaning in conversation (Wahlberg et al., 2001; Wynne, Singer, Bartko, & Toohey, 1977). Generally it is thought that high scores of CD found in the rearing parents are indicative of the growing child being predisposed to factors that could impair their cognitive development (Roisko, Wahlberg, Hakko, Wynne, & Tienari, 2011). Communication Deviance is stable during adulthood, making it a good measure of environmental risk (Wahlberg et al., 2001).

Adoption studies are currently our best bet in unveiling the complex gene-environment interactions underlying schizophrenia, because they give us the possibility to distinguish between the environmental and genetic factors involved (Petersen & Sørensen, 2011a; Tienari et al., 2004). However, for example, in the much-quoted Danish adoption register data studies, there has been no attempt to explore the gene-environment *interaction*; only the main effects taken separately have been considered. In the data, genetic liabilities were found to be the defining predictive factor in the outbreak of schizophrenia, not environmental influences (Ingraham & Kety, 2000; Kety, 1983; Kety et al., 1994; Petersen & Sørensen, 2011b). Results from the Finnish Adoptive Family Study of Schizophrenia, however, have shown that genetic and environmental factors considered independently of each other are insufficient to predict the triggering of schizophrenia in a person (Tienari et al., 2004; Wahlberg et al., 2004); instead, the results seem to indicate that the only statistically significant model of predicting the outbreak of schizophrenia is the interaction *between* the genetic background and the rearing environment. These findings have also found support within the Palauan adoption study by Ierago et al. (2010), which concluded that

adoptees at a high genetic risk of schizophrenia were more likely to report psychotic and depressive symptoms if they had negative family relations – respectively, significantly fewer symptoms were present if the family relations were good. However, this study was cross-sectional, so it is possible that poor family relations developed only after the outbreak of psychosis.

The aim of the current study was to see whether parental CD scores divided by the number of words (i.e. standardized for the length-of-speech) could be used to predict the outbreak of general mental disturbances in adoptees. The main point of interest here was a methodological one: Wynne et al. (1977) had previously proposed that CD scores should be calculated by dividing them by the number of transactions, but Hirsch and Leff (1975) had shown that CD scores and the number of words spoken are highly correlated. They proposed that all Communication Deviance scores should instead be calculated by dividing them by the word count used by the interviewee during the Rorschach test. Our study set out to clear up this difference in methodology, and we compared our results to those of Wahlberg et al. (2004), showing that mental disorders of adoptees are connected with the Communication Deviance of their adoptive parents (they had followed the Wynne et al. 1977 standardization methodology). We also wanted to predict the mental disturbances of the adoptees simply by looking at the word count used by their rearing parents during testing, to find any similarities to the Hirsch & Leff study.

METHOD

Subjects

The total sample in the Finnish Adoptive Family Study of Schizophrenia consists of 382 adopted-away children. This sample includes 190 genetic high risk (HR) adoptees, whose biological mothers had DSM-III-R diagnoses (APA, 1987) of the broad schizophrenia spectrum (Kendler et al., 1996; Tienari et al., 2003). The control group of the sample consisted of 192 genetically low risk (LR) adoptees of biological mothers without schizophrenia-spectrum diagnoses. The design, sampling, and diagnostic procedures of the whole adoption study have been described in more detail earlier by Tienari et al. (2000, 2003).

Our current study focuses on a subsample of 108 adoptees and their parents. Of these adoptees, 66 belonged to the LR group and 42 to the HR group. This subsample includes only cases where the adoptee did not have any psychiatric disorders at initial assessment. The only exception to these exclusion criteria was Adjustment Disorder (DSM III-R), which was included in the sample if it was identified as a reaction to some known stressor that had appeared 6 months or less before the assessment. We excluded cases of adoptees where either adoptive parent was dead and/or the Communication Deviance (CD) measures of both parents had not been completed. The only exception to this was three single-parent families in which the adoptive fathers had never existed. The adoptees were re-diagnosed at the follow-up, approximately 12.5 years after the initial assessment.

In the LR group there were 37 girls and 29 boys, and in the HR group 16 girls and 26 boys. In the LR group the mean age of placement was 14.58 months, and in the HR group 17.26 months. The initial evaluations of this study were started at the beginning of the year 1977, when the mean age of the adoptees was 19.42 ± 6.42 years (19.61 ± 6.22 years in the LR group, and 19.12 ± 6.79 years in the HR group). The mean ages of the adoptive mothers were 53.33 ± 7.38 years in the LR group, and 52.83 ± 7.65 years in the HR group; as for the adoptive fathers, 55.55 ± 7.97 years in the LR group, and 54.73 ± 7.90 in the HR group. Follow-up evaluations were made 12.5 ± 4.2 years after the initial evaluations. The mean age of the adoptees at the end of the follow-up was 31.75 ± 7.44 years. The social class of the adoptive families was classified into four groups based on the Finnish 4-level classification of the main provider´s occupation and education (The Center of Statistics, 1983). The first group included parents in managerial positions; the second group entrepreneurs, foremen, and higher officials; the third group skilled workers and lower officials; and the fourth group unskilled workers. In the LR group, 5 adoptees (7.58 %) belonged to social class I, 38 (57.58 %) to class II and 23 (34.85 %) to social class III. Social classes of the adoptees belonging to the HR group were divided as 7 adoptees (16.67 %) in class I, 17 (40.48 %) in class II, 17 (40.48 %) in class III, and 1 (2.38 %) in class IV. Demographic variables did not differ statistically significantly between the LR and HR groups.

INSTRUMENTS

Diagnostic procedure

In our subsample, 42 biological mothers had the DSM-III-R diagnosis of schizophrenia spectrum disorders. Of these mothers, 30 were defined as having ´typical´ schizophrenia and 12 as having a diagnosis of the broad schizophrenia spectrum (4 schizophreniform, 1 schizoaffective, 3 schizotypal personality disorders (PD), 1 schizoid PD, 1 avoidant PD, 1 bipolar psychosis, 1 depressive psychosis).

Our adoptees were divided into two groups based on their DSM-III-R diagnoses at the follow-up assessment. None of the adoptees had typical schizophrenia during the follow-up, but 24 (7 LR and 17 HR) were diagnosed as having some other psychiatric disorder.

All high risk (HR) and low risk (LR) adoptees, as well as their biological mothers and adoptive parents, were interviewed by psychiatrists who were experienced in psychiatric diagnostics and who were kept blind about the index/control status of the subjects. In the follow-up evaluation, adoptees were individually re-interviewed by a new research psychiatrist who was blind to the prior information. The kappa coefficient for inter-rater reliability in diagnostics varied between raters from 0.71 to 0.80. Diagnoses and diagnostically relevant information about the adoptees has been gathered and followed up from national health and hospital registers until the end of the year 2000.

CD of adoptive parents

In this study, the Communication Deviance (CD) of the rearing parents was used as the primary environmental (E) variable. The CD of the adoptive parents was assessed from transcribed tape-recordings of their individual Rorschach test protocols by two psychologists. The intra-class correlation coefficient between the psychologists was 0.95. The amount of CD was calculated separately for each adoptive parent by dividing their CD scores by the number of words spoken (i.e. standardized for the length-of-speech). The final CD score used was the sum of quotients of both adoptive parents. We divided the adoptees into two groups by the median (0.14) of their adoptive parents' CD.

Our CD assessment and categorization was based on the Singer-Wynne Rorschach scoring manual. CD was divided into six subgroups: 1) disruptions of task and relationship with tester, 2) problems with commitment and sustaining task set, 3) unstable and unclear references, 4) language anomalies, 5) reasoning problems and contradictions, and 6) indefinite and cryptic comments (Singer & Wynne, 1966; 1986).

Statistical analyses

Our data was not normally distributed, so we used logistic regression to model the genetic, environmental, and interactive associations found between the parental CD scores and the adoptee psychiatric diagnoses. Our dependent variable was the presence of any DSM-III-R-based mental disorders of the adoptees at the time of the follow-up. Separate logistic regression models, in which the association of genetic risk and environmental factors (i.e. parental CD), separately, and in combination to the mental disorder of the adoptees, were calculated by adjusting for the essential covariates. These were the age of the adoptees at initial assessment and at the time of their placement into families, as well as their gender and social class, which were introduced into all the models as covariates. Our methodology was in line with that of Wahlberg et al. (2004) to keep our results comparable. All tests were two-tailed and a limit for statistical significance was set at $p < 0.05$. The analyses were performed by using PASW Statistics, version 19.

RESULTS

Genetic factor

As seen in Table 1, 40.5 % of high genetic risk (HR) adoptees and 10.6 % of low genetic risk (LR) adoptees had DSM-III-R-based mental disorders at the follow up. The results of a logistic regression analysis showed that the HR adoptees had an increased likelihood for mental disorder compared to the LR adoptees (adj. odds ratio, OR, for genetic risk, 5.84, p=0.001, 95 % confidence interval (CI) 95 % 2.02-16.93).

Environmental factor

For the environmental variable, as assessed with the Communication Deviance of the parents, 29.6 % of adoptees with high CD rearing parents and 14.8 % of adoptees with low CD parents had a mental disorder at the follow up (Table 1). However, the results of the logistic regression analysis showed that the environmental factor alone was not a significant predictor for mental disorder in adoptees (adj. OR 2.50, p=0.08, CI 95 % 0.90-6.91).

Table 1. The prevalence of DSM-III-R-based psychiatric disorders of the adoptees according to their genetic and environmental risk status

Genetic liability of the adoptees	Communication Deviance of the adoptive parents					
	Low CD		High CD		Total sample	
	n	%	n	%	n	%
Low risk	3/37	8.1	4/29	13.8	7/66	10.6
High risk	5/17	29.4	12/25	48.0	17/42	40.5
Total	8/54	14.8	16/54	29.6	24/108	22.2

Genetic * Environmental factors

When both the genetic risk of the adoptee and the levels of CD in the rearing parents were high, 48.0 % of the adoptees had mental disorders at the follow up, compared to adoptees with low genetic risk and low parental CD, who had an incidence rate of 8.1 % (Table 1). After entering into a logistic regression model both the genetic and environmental risk factors and their interaction (Table 2), the only statistically significant result was found in the model including the adoptive parents' CD. In that model, the genetic risk was associated with the adoptee's mental disorder (OR 5.32, CI 95 % 1.02-27.68), but not the CD of the adoptive parents or G * E interaction.

Table 2. Genetic risk, parental Communication Deviance (CD) and their interaction as predictors for DSM-III-R-based mental disorder of adoptees

	Adoptive parents CD (n=108)		Adoptive mothers CD (n=145)		Adoptive fathers CD (n=111)	
Risk factor	Adj.OR* (95 % CI)	*p*	Adj.OR* (95 % CI)	*p*	Adj.OR* (95 % CI)	*p*
CD	2.18 (0.43-11.09)	0.35	0.37 (0.10-1.40)	0.14	1.14 (0.20-6.52)	0.88
Genetic risk	5.32 (1.02-27.68)	0.001	1.59 (0.45-5.63)	0.47	2.69 (0.56-13.00)	0.22
G X E Interaction	1.09 (0.13-8.97)	0.94	4.03 (0.67-24.04)	0.13	5.77 (0.67-50.01)	0.11

* Adjusted by the adoptees' age, gender, social class, and time of placement into families

Subscales of Communication Deviance

Because the Communication Deviance scale consists of 6 subgroups, we predicted the outbreak of mental health disorders in the adoptees in each of these subscales separately. The results of the model, including both the genetic and environmental factors and their interaction, indicated that only subgroup 5 (Reasoning problems and contradictions) was associated with an increased likelihood of mental disorder in adoptees (OR 9.24, p=0.04, CI 95 % 1.09-78.51).

Word count of adoptive parents

An additional analysis examining the effect of the adoptive parents' word count (WC) alone as a predictor of mental disorder in the adoptees was also performed. The WC of the adoptive parents was dichotomized at the median. The results of the logistic regression model indicated that high WC as an environmental risk factor alone was related to an increased risk of the adoptees' mental disorder (OR 2.93, p=0.04, CI 95 % 1.06-8.11); however, when the genetic variable and the interaction between the genetic factor and WC were added into the same model, the influence of a high number of words disappeared (OR 1.25, p=0.84, CI 95 % 0.14-11.30). A Spearman correlation test indicates that the amount of CD and the number of words spoken are highly correlated (r=0.80, p<0.001).

DISCUSSION

Our main goal in this study was to predict the development of mental disturbances in adoptees from the combined variables of their parents' Communication Deviance (CD) and genetics. Our analyses had the CD scores standardized by dividing them by the number of words spoken during the Rorschach test – effectively a method for controlling the length-of-speech. We also wanted to compare these word-count standardized CD scores (i.e. those standardized using the Hirsch & Leff 1975 method) to CD scores that were divided by the number of transactions in the Rorschach tests (i.e. according to the original Wynne et al. 1977 method). These two ways of computing the CD variable appear to yield highly differentiated results.

As far as the word-count standardized CD scores go, they were not a risk factor for mental disturbances when considered on their own (in our environmental model) nor when considered as a part of the gene-environment interaction (in our gene-environment model). Instead, genetic effects were the only factor affecting the development of mental disturbances in our study: in the family genetic model, the chance for a high-risk adoptee (compared to a low-risk adoptee) to suffer from some sort of mental disorder was almost six-fold. When both the effect of genetics and the rearing environment and their interaction were entered into the same logistic regression model (the gene-environment model), the impact of genetics was the only significant variable (five-fold risk) but the total CD of the adoptive parents or the gene-environment interaction term were not significant variables in the model. Overall, genetics was highlighted and environmental effects dismissed in our spectrum of analyses.

Gene-environment interactions were only found in one subgroup within the family gene-environment model: the CD subgroup 5 (indicating a nine-fold risk). Generally defined as "Reasoning problems and contradictions", these cognitive disturbances are apparently a powerful risk factor for high-risk children suffering from a genetic liability to schizophrenia. This finding is well in line with previous evidence: subgroup 5 was already identified to be a risk factor in the Wahlberg et al. (2004) study, where it showed a gene-environment interaction predicting a 28-fold risk for mental disturbances in high-risk vs. low-risk adoptees. Subgroup 5 might therefore be a particular point of interest for further studies that insist on following the Hirsch & Leff methodology of standardizing for the length-of-speech, as all

the other CD sub-groups in our study seemed to consistently pick up only the genetic influences within the data.

In the Wahlberg et al. 2004 study, which had the CD scores divided by the number of parental responses, both the main effects of genetics and the environment were found to be non-significant – however, there was a gene-environment interaction that predicted the outbreak of general mental health disorders among the adoptees. This gene-environment interaction was not found in our own study although we used the same data set (except for one case, in which – when the data was controlled – the adoptee was found to have a diagnosis at initial assessment and was therefore excluded). Apparently the Hirsch & Leff method of standardizing the CD scores by dividing them by the number of words "lost" the previously found gene-environment interactions within our data and replaced them with genetic influences only. These results lead one to think that long and complex transactions during the Rorschach test are probably, in themselves, a form of CD, and should not be "standardized away". This assumption was supported by the high correlation between our CD and Word Count (WC) variables. It may be problematic to divide a variable (the amount of Communication Deviance) by another highly correlating variable (Word Count), as this may lead to a non-existent variation between the two observations. This may mean that CD divided by WC cannot predict the mental disorders of the adoptees. This conclusion, however, needs more statistical consideration and confirmation in other study samples in the future.

Taken from a conceptual viewpoint, one could argue that standardizing the CD scores by the number of transactions (responses) instead of WC would give a more accurate representation of Communication Deviance, as it does not hide the effect of long speeches. Payne, Caird, & Laverty (1964) considered high verbosity as a part of over-inclusive thinking; this, then again, could be thought to have something in common with both Communication Deviance and Word Count. CD at its core is a failure in the sharing of focus of attention and meaning, as defined by Wynne et al. (1977). Each response in the Rorschach test can therefore be viewed as an attempt to share one meaning unit, and CD found within any such meaning unit is indicative of varying degrees of difficulty in sharing this particular piece of information. In this sense, CD scores obtained by standardizing them with the number of transactions would depict the essence of Communication Deviance more accurately. If this is true, then it would be methodologically unwise to try and remove the effect of the length-of-speech of participants from the

data, as this would basically result in the CD scores being divided by the CD scores themselves, undermining their effect.

More broadly, our results hint that the role of genetics has a tendency to become over-highlighted whenever the role of the interaction between genes and the environment is not taken into account. This could be thought to at least partly explain the differences found between the Danish and Finnish adoption studies regarding the etiology of schizophrenia. It is likely that the gene-environment interaction would also have been found to have a major predictive value within the Danish data set, had it only been searched for. It is of utmost importance that future studies take this viewpoint into account when planning their methodology. Our findings imply that the gene-environment interaction should always be taken into account in research, not just the main effects of genes and the environment alone.

Moreover, Hirsch and Leff had also previously found a strong correlation between the CD scores and word count – this hypothesis gained some indirect support within our study as well, as we tried to predict the development of mental disorders by the word count alone. When only the word count was entered into the model, it appeared to have predictive value, indicating a three-fold risk of developing a disorder. However, this effect was no longer present in the gene-environment model, most likely due to the genetic influences "eating away" any significance that the length-of-speech alone might have had. Nevertheless, our findings seem to indicate that lengthy speech is likely to correlate with high CD scores to at least some extent.

All in all, in the light of our results, we wish to emphasize the importance of properly accounting for the gene-environment interactions within data sets studying schizophrenia and mental disturbances in general. Whenever these interactions are ignored, we are likely to see varying over-emphasis on either the genetic or environmental components. Complex phenomena are likely to have complex etiologies as well; future research should reflect this by exploring the possible interaction effects further, giving them equal thought alongside the main effects. Neither environmental nor genetic influences alone suffice to make up a person – the whole is always the sum of its parts.

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