## COMMUNICATION DEVIANCE OF THE ADOPTIVE PARENTS AS A PREDICTOR OF THOUGHT DISORDER IN THE ADOPTEE

Miia Metsänen, Karl-Erik Wahlberg, Helinä Hakko, Outi Saarento, Taneli Tarvainen, Pekka Koistinen, Pekka Tienari

## Summary

Object: Recognition of the joint effects of genetic and environmental risk factors has significantly improved our understanding of the development of psychiatric disorders. One of the possible vulnerability markers among environmental factors has been Communication Deviance (CD) in families. Correspondingly, thought disorders have attributed to both genetic and environmental components, but also to genotype-environment interaction. The aim of this study was to investigate whether the CD of adoptive parents measured 13 years earlier predicts thought disturbances of high-risk (HR) and low-risk (LR) adoptees.

*Method:* The thought disorders of HR (biologic mother had a schizophrenia spectrum disorder) (n=38) and LR adoptees (n=51) were assessed based on the Thought Disorder Index (TDI).

Results and Conclusions: An association emerged between the thought disorder of the adoptees and the CD of their parents assessed 13 years earlier. However, the CD of the adoptive parents predicted thought disorders at follow-up only in the low-risk adoptees. This may be due to the decreasing contacts between the adoptees and their parents after the adult children have moved away from home. The thought functions of high-risk adoptees are probably also shaped more by the present environment, and they are likely to be more sensitive to and dependent on environmental influence that than those of low-risk adoptees.

Key Words: Communication Deviance - Thought Disorder - Schizophrenia

#### **Declaration of interest:** None

M. Metsänen<sup>1</sup>, K-E. Wahlberg<sup>2</sup>, H. Hakko<sup>3</sup>· O. Saarento<sup>3</sup>, T. Tarvainen<sup>3</sup>, P. Koistinen<sup>3</sup>, P. Tienari<sup>2</sup>

¹Päijät-Häme Central Hospital, Lahti, Finland, ²University of Oulu, Department of Psychiatry, Oulu, Finland and ³University Hospital of Oulu, Clinic of Psychiatry, Oulu, Finland

## Corresponding author

M. Metsänen, Päijät-Häme Central Hospital, Keskussairaalankatu 7, FIN-15850 Lahti, Finland. Phone: 358-40-590 69 75 - Fax: 358-3-819 3011

E-mail: miia.metsanen@oulu.fi

## 1. Introduction

Several studies have shown the importance of early detection of and intervention in schizophrenia (Falloon et al. 1996, McGlashan and Johannessen 1996, McGorry et al. 2000, Vaglum 1996, Wahlberg and Wynne 2001). Therefore, a need to explore the possible vulnerability markers of schizophrenia has become apparent. Previous studies have especially focused on the anatomical, molecular, physiological, chemical, and other biological abnormalities as signs of vulnerability to schizophrenia (Carpenter and Buchanan 1994). It is obvious that genetic factors play an important role in the development of schizophrenia. At the same time, environmental factors, such as complications of delivery (Cannon et al. 1993, Isohanni et al. 2004, Jones

et al. 1998, McNeil 1991) and viral infections of the mother in the second trimester (Sorensen et al. 2004, Tochigi et al. 2004) have been found to be risk factors for schizophrenia. Unwanted pregnancy (Myhrman et al. 1996) and depression of the mother during the antenatal period (Jones et al. 1998) have also been associated with the development of schizophrenia. In contrast to the differentiation between genetic and environmental factors. Kendler and Eaves (1986) pointed out that comprehensive understanding of the development of psychiatric disorders presumes recognition of the joint effect of genetic and environmental risk factors. Today, it is widely accepted that genotype-environment interaction is essential in the development of schizophrenia (Carter et al. 2002, Tienari et al. 2004, Wahlberg et al. 2004).

One possible environmental risk factor is the Communication Deviance (CD) present in families (Wynne et al. 1977). Parental CD is a relative stable (Wahlberg et al. 2001) and enduring "environmental" stressor during the child's development. The effects of unclear, amorphous, or fragmented communication have turned out to be quite destructive for a child with a biological predisposition to schizophrenia (Singer et al. 1978). Wahlberg, Wynne et al. (1997) have reported that the interaction of the genetic risk in adoptees with high Communication Deviance in the adoptive rearing parents was related to subsyndromal thought disorder in the high-risk adoptees. Furthermore, a more specific study by Wahlberg et al. (2000) revealed a certain kind of thought disorder (idiosyncratic verbalization) to be linked with genetic and environmental variables, whereas another form of thinking disturbance (fluid thinking) was more related to the genetic risk. Previous research has also revealed that the joint effect of genetic liability to schizophrenia spectrum disorder and Communication Deviance of the adoptive parents predicted psychiatric disorders in the adoptees at adult age (Wahlberg et al. 2004). Correspondingly, Tienari et al. (2004) found adoptees at high genetic risk for schizophrenia to be more sensitive to problems in the rearing adoptive family.

The presence of thought disorder has been considered one of the possible indicators of vulnerability to schizophrenia (Arboleda and Holzman 1985, Hurt et al. 1983, Nuechterlein et al. 1986, Koistinen 1995, Ott et al. 2001, Wahlberg et al. 1997, Wahlberg et al. 2000). Furthermore, thought disorder has turned out to be a prospective sign of other mental disorders as well (Metsänen et al. 2004). The stable, trait-like features of thought disorder have further added to the prognostic value of thought disturbances (Metsänen et al. 2005, Metsänen et al. 2006).

Previous research has shown that deviant thinking is not only characteristic of schizophrenic patients but also of the nonpsychotic relatives of persons with schizophrenia (Hain et al. 1995, Johnston and Holzman 1979, Kinney et al. 1997, Shenton et al. 1989). These results have strongly suggested the presence of a genetic component in thought disorder. According to the vulnerability/stress and stress diathesis models, disturbances in thinking and other cognitive functions are a product of genotype-environment interaction (Wahlberg et al. 1997), but the presence of these difficulties does not automatically lead to the development of schizophrenia (Nuechterlein 1987, Rosenthal 1963, Zubin and Spring 1977). Therefore, the probability of possible psychiatric disorder depends on whether the environment includes either protective or predisposing factors.

## 1.1 Aims of the study

Our purpose here was to investigate whether Communication Deviance in adoptive parents measured 13 years mean interval earlier will predict thought disturbances in high-risk (HR) and low-risk (LR) adoptees in the Finnish adoptive family study of schizophrenia.

#### 2 Methods

## 2.1 Subjects

A subgroup of the total sample of the Finnish adoptive family study of schizophrenia was used in this study (Tienari et al. 1987a, Tienari et al. 1987b, Tienari et al. 2000, Tienari et al. 2003). The total Finnish national adoption high-risk sample includes the adoptive families of all children adopted away by women hospitalised because of schizophrenia (or paranoid psychosis) in Finland during 1960-1979 (Tienari et al. 1987a). Women were excluded if they had an organic brain syndrome, severe mental retardation, primary alcoholism (preceding schizophrenia), or any other major physical illness (Tienari et al. 1987a, b; 2000, 2003). The final sample included 190 offspring at high genetic risk (HR) whose biological mothers had verified DSM-III-R diagnoses in the broad schizophrenia spectrum (Tienari et al. 2000, 2003; Kendler et al. 1996). Correspondingly, the control sample consisted of 192 adoptees at low genetic risk (LR) with biological mothers who had a nonspectrum diagnosis or no psychiatric disorder. The adoptees were excluded if they had been adopted by a relative, adopted abroad, or adopted after the age of 4 years. The study was approved by the Ethics Committee of the Medical Faculty of the University of Oulu (Finland). The participation of all subjects was based on their free will. The design, sampling, and diagnostic procedures of the adoption study as a whole have been described earlier (Tienari et al. 1987a, b, 2000). Thought disorders of the adoptees as well as the communication patterns of their adoptive parents were first examined at the initial assessment. The adoptees were re-examined after a follow up period which mean interval in this subsample was 12 years.

The subsample of this report included the adoptees whose thought disorder had been assessed at both the initial and the follow-up evaluations by using the Though Disorder Index (TDI). The inclusion criterion was that the Rorschach records had been tape-recorded and transcribed. Furthermore, the assessment of communication deviance (CD) of both adoptive parents was relevant. Three single-parent families who had never had an adoptive father were also included. In these cases, the CD of the tested mother was multiplied by two. The final subsample included 89 adoptees. Of these subjects, 38 were high-risk (HR) and 51 low-risk (LR) adoptees. The adoptees' mean age at the initial assessment was 20 years ( $\pm 6.7$ ) and at follow-up 33 years ( $\pm 7.9$ ). Other demographic and clinical data of the subjects are presented in Table 1. A comparison of the adoptees' demographic variables in our subsample and in the whole sample revealed no statistically significant differences, with the exception of the adoptee's age and the adoptive family's social status. The adoptees in this study were younger (mean age=20 years, SD=6.72) than those in the whole sample (mean age=29 years, SD=10.32). The adoptive families in the whole sample were more often in social class I (20.6%) than the adoptive families in this subsample (9.0%). These variables, i.e. the adoptee's age and the adoptive family's social status, were therefore controlled in the multivariate model (logistic regression analysis).

Table 1. Demographic and clinical characteristic of high-risk (HR) and low-risk (LR) adoptees in the Finnish Adoptive Family Study of Schizophrenia

Variables All cases High-Risk (HR n=89 adoptees adoptees comparis n=38 (42-7%) n=51 (57.3%) p-va	ons	R and LR		
Age, years (mean, ±SD): the initial assessment 20 (±6.7)		20 (±6.8)	20 (16.7)	ns <sup>a</sup>
the follow-up assessment	33 (±7.9)	32 (±8.0)	20 (±6.7) 33 (±7.8)	ns <sup>a</sup>
Age at placement,				
months (mean, $\pm$ SD):	16 (±13.5)	17 (±15.2)	14 (±12.0)	ns <sup>a</sup>
Gender n (% of subjects):				$ns^b$
Female	50 (56.2)	20 (50.6)	30 (58.8)	
Male	39 (43.8)	18 (47.4)	21 (41.2)	
Social groups <sup>c</sup>				
n ( % of the subjects):				ns <sup>b</sup>
I group	8 (9.0)	5 (13.2)	3 (5.9)	
II group	47 (52.8)	19 (50.0)	28 (54.9)	
III group	30 (33.7)	12 (31.6)	18 (35.3)	
IV group	4 (4.5)	2 (5.3)	2 (3.9)	
Diagnostic groups				
n (% of the subjects):				
At the initial assessment				ns <sup>b</sup>
No Psychiatric Disorder	74 (83.1)	30 (78.9)	44 (86.3)	
Any Psychiatric Disorder	15 (16.9)	8 (21.1)	7 (13.7)	
At follow-up				<.01
No Psychiatric Disorder	53 (59.6)	16 (42.1)	37 (72.5)	
Any Psychiatric Disorder	36 (40.4)	22 (57.9)	14 (27.5)	

<sup>&</sup>lt;sup>a</sup> Student's t-test was used to assess the group differences

#### 2.2. Instruments

## 2.2.1. Thought disorders of the adoptees.

The thought disorders of the adoptees were assessed by using the Thought Disorder Index (TDI) (Johnston and Holzman 1979). TDI is a multidimensional scale for tagging, classifying, and measuring thinking problems both qualitatively and quantitatively. Most commonly, responses to the Rorschach cards are used, although any verbal sample is possible. The revised version of Thought Disorder Index includes 24 categories weighted along a continuum of severity (0.25, 0.50, 0.75, and 1.0). In this study, we used the sum of weighted TDI scores divided by the number of Rorschach responses (TD<sub>R</sub>). The following formula was applied to calculate TD<sub>R</sub>,

 $TD_{R} = 0.25 (A) + 0.50 (B) + 0.75 (C) + 1.00 (D)_{X 100}$ 

Total number of Rorschach responses where A= the number of responses scored at the level of 0.25, B= the number of responses scored at the level of 0.50, C= the number of responses scored at the level 0.75, and D= the number of the responses scored at the level of 1.00. At the initial assessment, four psychologists scored pairwise the records without prior knowledge of the subjects' relatedness to their biological and adoptive families or their psychiatric diagnoses. They only knew the subject's age, sex, and occupation. The intraclass correlation coefficient (ICC) between the pairs of psychologists was 0.94 for  $TD_R$ , 0.92 for the 0.25 level, 0.92 for the 0.50 level, 0.86 for the 0.75 level, and 0.66 for the 1.0 level. At follow-up, the scoring was made by one psychologist (Metsänen), again unaware of the subjects' relatedness to their biological and adoptive families and their psychiatric diagnoses. As at the initial assessment, she only knew the subjects' age, sex, and

<sup>&</sup>lt;sup>b</sup> The differences in the groups was assessed by using Chi-square

<sup>&</sup>lt;sup>c</sup> Social group classification is based on the main provider's occupation and education. The basis to this classification was the social respect to different occupation. The first group included occupations which were in managerial positions, the second one enterpreneurs, foremen, upper functionaries, the third one skilled workers and lower functionaries and the fourth class unskilled workmen.

occupation. Reliability was checked (n=31) by the single-measure intraclass correlation coefficient (ICC) between the two psychologists (Metsänen and Wahlberg). The ICCs were 0.85 for the .25 level, 0.92 for the .50 level, and 0.95 for the .75 level. The 1.0 severity level was omitted because only one subject had had scores at this level at the initial assessment.

# 2.2.2. Communication disturbances of the adoptive parents.

Communication deviance (CD) was used to assess the communication patterns in the adoptive families. CD is a scale to measure the degree to which the members of the family are unable to share and maintain a focus of attention during communication (Singer and Wynne 1966). In this study, we used 42 categories adapted from the Singer-Wynne Rorschach scoring manual (Singer et al. 1978, Singer and Wynne 1966, Singer and Wynne unpublished 1986 version). Dr Singer provided training to Dr Wahlberg in the scoring of Communication Deviance (CD), and the minor modifications of scoring in Finnish compared to English were discussed (Wahlberg 1994). CD was calculated separately for each parent as the frequency of the scored CD categories divided by the number of responses in the individual Rorschach test. The quotients were used as the Communication Deviance (CD) for each parental pair. Two psychologists scored CD from the tape-recorded and transcribed individual Rorschach records of the adoptive parents. The intra-class correlation coefficient for CD between the psychologists was 0.95 (51 records scored).

## 2.2.3. Adoptees' DSM-III-R diagnoses

The psychiatric status of the adoptees was assessed by using the best-estimate, hierarchically most

severe lifetime diagnoses. 90 % of the adoptees' interviews were carried out at the initial assessment as semi-structured, and at follow-up as structured (the Present State Examination, PSE (Wing et al. 1974); the Structured Clinical Interview for Axis II Personality Disorders, SCID-II (Spitzer et al. 1989); the Structured Interview for Schizotypy, SIS (Kendler et al. 1989) personal interviews. The diagnostic evaluation was made according to the DSM-III-R criteria for Axis I or Axis II psychiatric disorders based on all available data for all adoptees. Psychiatrists who evaluated the adoptees' mental disorders were blind to their high-risk/low-risk status. The kappa coefficient for inter-rater reliability was found to be good (kappa 0.71-0.80) (Tienari et al. 2000). In this study, the adoptees were divided into two diagnostic groups. The first group included adoptees without any psychiatric disorder (NPD). The second group consisted of adoptees with any psychiatric disorder (APD).

#### 2.3. Statistical methods

Distributions of the Thought Disorder Index (TDI) of the adoptees and the Communication Deviance (CD) of the adoptive parents were skewed to the right and therefore non-parametric methods were used. The group differences in the categorical variables were investigated with Pearson's Chi-square test or Fisher's Exact test, while the differences in the continuous variables were subjected to Student's t-test (Bland 1995). The association of parental CD with the likelihood for high  $\mathrm{TD}_{\mathrm{R}}$  scores at follow-up was examined with a logistic regression model after controlling for gender, age, and psychiatric status at follow-up of the high- and low-risk adoptees separately (McCullagh and Nelder 1989). The statistical software used was the SPSS, version 12.0.

Table 2. Though Disorder Index of adoptees at the initial and follow-up assessments in relation to Communication Deviance (CD) scores of adoptive parents measured 13 years earlier in the Finnish Adoptive Family Study of Schizophrenia

	CD of the adoptive parents Low CD n (%)	High CD n (%)	p-value*
$TD_R$ of the adoptees			
At the initial assessment			
Low TD <sub>R</sub>	54 (80.6%)	13 (59.1%)	0.04
High TD <sub>R</sub>	13 (19.4%)	9 (40.9%)	
At follow-up assessment			
Low TD <sub>R</sub>	53 (79.1%)	15 (68.2%)	ns
High TD <sub>R</sub>	14 (20.8%)	7 (31.8%)	

Note: High TD<sub>p</sub> and high CD indicate the scores belonging to upper quartile of the distribution of a variable.

<sup>\*</sup> Chi-square test, df=2, two-tailed significance.

## 3. Results

The upper quartiles in the distribution of both the adoptees'  $TD_R$  and the parents' Communication Deviance (CD) were classified as the most deviant groups (high  $TD_R$ , high CD) compared to the other subjects (low  $TD_R$ , low CD). At the initial assessment, the proportion of adoptees with high  $TD_R$  scores was twofold if the adoptive rearing parents had high CD scores compared to those with parents with low CD scores (40.9% vs. 19.4%, p-value = 0.04) (Table 2). However, this difference was no longer significant at follow-up, even though it was similar in direction (1.5 fold) as at the initial assessment.

The predictive power of the Communication Deviance (CD) of the adoptive parents measured 13 years before the manifestation of thought disorder in the adoptees was also analyzed with logistic regression analyses separately for the high-risk (HR) and low-risk (LR) adoptees (Table 3). The covariates in the model were the adoptee's gender, psychiatric status, and age at follow-up as well as the social status of the adoptive family. The low-risk (LR) adoptees reared by adoptive parents with high Communication Deviance (CD) scores were shown to have a statistically significantly increased likelihood for high TD<sub>R</sub> scores at follow-up, while the corresponding association in high-risk (HR) adoptees was not significant (p= 0.18). In separate analyses of male and female adoptees no significant association between the parents' CD and the adoptees' TD<sub>p</sub> at follow-up was observed in this study sample.

#### 4. Discussion

The aim of the study was to investigate whether Communication Deviance (CD) in adoptive parents measured a mean of 13 years earlier predicted thought disturbances in high-risk (HR) and low-risk (LR) adoptees in the Finnish adoptive family study of schizophrenia.

We observed that high Communication Deviance (CD) of the adoptive parents was related to high TD<sub>p</sub> scores of the adoptees at the initial assessment, supporting the earlier finding of Wahlberg et al. (Wahlberg et al. 1997). However, the association between the adoptee's TD<sub>R</sub> and the adoptive parents' CD measured 13 years earlier no longer existed at follow-up. As we have previously shown, Thought Disorder Index (TDI) scores decreased over time despite the stable characteristic of thought disturbances (Metsänen et al. 2005, 2006). One possible explanation for our present results could be the same phenomena as before, the maturation of thought processes. In our previous study concerning the stability of thought disorder only the genetic risk for schizophrenia was taken into account, while the environmental factors were not. We found that the genetic risk did not affect the stability of thought disorder. In the present study the environmental factor, Communication Deviance (CD) of adoptive parent was assessed. The result indicates that stability of thought disorder among highrisk adoptees was not so apparent, while there was more variation than among low-risk adoptees. The CD of adoptive parent did not predict the thought disorder of the high-risk (HR) adoptees at follow-up probably because of their sensitivity to the changes in the environment. It is very probable that nearly all adult adoptees had moved away from home during the follow-up period. Thus, they were no longer exposed to the Communication Deviance (CD) of their adoptive parents, but possibly had a less confusing and thus more "protective" environment.

Wahlberg et al. (1997) used partly the same study population as in this study, and they found in their crosssectional study that high-risk (HR) adoptees to be more sensitive to and dependent on the environment than lowrisk (LR) adoptees. This was shown by the finding that HR adoptees had more thought disorder than LR adoptees if their adoptive parents had high levels of Communication Deviance (CD). However, high-risk (HR) adoptees had a lower incidence of thought disorders than low-risk (LR) adoptees if they were living with low-CD adoptive parents. Correspondingly, Tienari et al. (2004) showed adoptees at high genetic risk to be significantly more sensitive to adverse vs. 'healthy' rearing patterns in their adoptive families than were adoptees at low genetic risk. The joint interaction (genetic liability and environment) was also pointed out by Wahlberg et al. (2004). They found that adoptees' genetic liability to schizophrenia spectrum disorder and high Communication Deviance (CD) of adoptive parents measured 14 years earlier predicted significantly broadly defined psychiatric disorder in high-risk (HR) adoptees but in low-risk (LR) adoptees. Additionally, they found that low Communication Deviance of adoptive parents and genetic liability to schizophrenia spectrum disorder did not predict psychiatric disorders in either HR or LR adoptees. In the present study, an association between the adoptee's follow-up TD<sub>R</sub> and the adoptive parents' Communication Deviance (CD) measured 13 years earlier was only present among the low-risk adoptees. Thus, it could be speculated that the high-risk adoptees were more sensitive to the possible positive changes in their environment and therefore no longer displayed the association of TD<sub>R</sub> with CD at follow-up. It could be possible that the joint interaction of a 'healthy' environment and genetic liability protects high-risk adoptees from vulnerability to schizophrenia. The corresponding relationship between the thought disorders of low-risk (LR) adoptees and Communication Deviance (CD) of their adoptive parents was not similar. When LR adoptees were younger and lived with their parents their thought processes were not connected with the communication atmosphere in the family (Wahlberg et al. 1997) as we can assume when a young person is separating from his parents and developing to an autonomous one. However, later in their lives they are identifying more with the characteristics of the adoptive parents and therefore the connection between their thought disorders and communication of the adoptive parents is more probable than earlier.

The present study adds to the previous research concerning the association between thought disorders and Communication Deviance. Our results raise several clinically important questions. Could it be possible to prevent schizophrenia in high-risk individuals by means an environmental intervention? Does a clearly communicating and consistent environment minimize

Table 3. Association of high Communication Deviance (CD) scores of adoptive parents measured 13 year earlier with the likelihood for high scores in Thought Disorder Index at follow-up of low- and high-risk adoptees in the Finnish Adoptive Family Study of Schizophrenia

	Likelihood for high scores in TDR at follow-up*				
	LR adoptees (n=51) OR (95% CI)	p-value	HR adoptees (n=38) OR (95%CI)	p-value	
High CD of adoptive parents Psychiatric status (APD)	6.93 (1.30 - 36.89) 2.72 (0.54 - 13.79)	0.02 0.23	0.21 (0.02-2.04) 1.38 (0.22-8.54)	0.18 0.73	
Gender, male	1.07 (0.23 - 4.90)	0.94	0.99 (0.19-5.08)	0.99	
Age at follow-up	1.11 (0.98 - 1.23)	0.11	1.03 (0.93-1.14)	0.63	
Social status of the adoptive family	1.08 (0.23-5.04)	0.92	0.85 (0.17-4.34)	0.84	

Note: High TD<sub>p</sub> and high CD indicate the scores belonging to upper quartile of the distribution of a variable.

possible thought disturbances to such an extent that the risk for schizophrenia and other mental disorders could decrease? Due to the limitations of this study, more studies are needed. It was not possible here to study reliably enough the changes in the adoptees' place of residence during the follow-up period. It would be especially important to clarify high-risk adoptees' sensitivity to the environment. In addition, further studies could investigate whether different Thought Disorder Index (TDI) subscales are associated with Communication Deviance (CD) more often among high-risk adoptees than low-risk adoptees. Another limitation of our study was the small number of cases. On the other hand, however, the follow-up time was long, and the reliability of the methods was good.

## Acknowledgements

This research was supported in part by grant MH39663 from the Public HealthService, by a grant from the Scottish Rite Schizophrenia Research Program, N.M.J., U.S.A., by The Academy of Finland, The Alma and K.A. Snellman Foundation, Oulu, Finland, The Emil Aaltonen Foundation, The Jalmari and Rauha Ahokas Foundation, The Finnish Konkordia-Union, The Paulo Foundation, Päijät-Häme Central Hospital, and Oulu University Hospital, Department of Psychiatry. We thank Heljä Anias, M.A., Ilpo Lahti, M.D., Juha Moring, M.D., Mikko Naarala, M.D., Anneli Sorri, M.D., Pekka Koistinen, Ph.D., and Taneli Tarvainen, Lic.Psych. for contributing to the psychological testing and psychiatric diagnosing of subjects in this study.

## References

Arboleda C, Holzman PS (1985). Thought disorder in children at risk for psychosis. *Archives of General Psychiatry 42*, 1004-1013.

Bland M (1995). *An Introduction to Medical Statistics*. Oxford University Press, Oxford.

Cannon TD, Mednick SA, Parnas J, Schulsinger J, Praestholm J, Vestergaard A (1993). Developmental brain abnormalities in the offspring of schizophrenic mothers. I Contributions of genetic and perinatal factors. *Archives of General Psychiatry* 50, 551-564.

Carpenter WT Jr, Buchanan RW (1994). Schizophrenia. New England Journal of Medicine 330, 681-690.

Carter JW, Schulsinger J, Parnas J, Cannon T, Mednick SA (2002). Multivariate prediction model of schizophrenia. *Schizophrenia Bulletin* 28, 649-682.

Falloon IRH, Kydd RR, Coverdale JH, Laidlaw TM (1996). Early detection and intervention for initial episodes of schizophrenia. *Schizophrenia Bulletin* 22, 271-282.

Hain C, Maier W, Hoechst-Janneck S, Franke P (1995). Subclinical thought disorder in first-degree relatives of schizophrenia patients. Acta Psychiatrica Scandinavica 92, 305-309.

Hurt SW, Holzman PS, Davis JM (1983). Thought disorder: the measurement of its changes. *Archives of General Psychiatry* 40, 1281-1285.

Isohanni M, Isohanni I, Koponen H, Koskinen J, Laine P, Lauronen E, Miettunen J, Maki P, Riala K, Rasanen P, Saari K, Tienari P, Veijola J, Murray G (2004). Developmental precursors of psychosis. *Current Psychiatry Reports* 6, 168-175.

Johnston MH, Holzman PS (1979). Assessing Schizophrenic Thinking. Jossey-Bass Publishers, San Francisco.

Jones P, Rantakallio P, Hartikainen A-L, Isohanni M, Sipilä P (1998). Schizophrenia as a long-term outcome of pregnancy, delivery and perinatal complications: a 28 year of follow-up of the 1966 Northern Finland general population birth cohort. *American Journal of Psychiatry* 155, 355-364.

Kendler KS, Eaves LJ (1986). Models for the Joint Effect of Genotype and Environment on liability to Psychiatric Illness. *American Journal of Psychiatry* 143, 279-289.

Kendler KS, Lieberman JA, Walsh D (1989). The Structured Interview for Schizotypy (SIS). A preliminary report. *Schizophrenia Bulletin* 15, 559-571.

Kendler KS, O'Neill FA, Burke J, Murphy B, Duke F, Straub RE, Shinkwin R, Ni Nuallain M, MacLean CJ, Walsh D (1996). Irish study of high-density schizophrenia families: Field methods and power to detect linkage. *American Journal of Medicine Genetics* 67, 179-190.

Kinney DK, Holzman PS, Jacobsen B, Jansson L, Faber B,

<sup>\*</sup> Each odds ratio is adjusted for by all the other variables in table.

- Hildebrand W, Kasell E, Zimbalist ME (1997). Thought disorder in schizophrenic and control adoptees and their relatives. *Archives of General Psychiatry* 54, 475-479.
- Koistinen P (1995). Thought disorder and the Rorschach. A study on psychopathology and vulnerability of subjects. *Acta Universitatis Ouluensis, Series D, Medica* 346.
- McCullagh P, Nelder JA (1989). *Generialized linear models*. 2 nd ed., Chapman and Hall, New York.
- McGlashan TH, Johannessen JO (1996). Early detection and intervention with schizophrenia: rationale. *Schizophrenia Bulletin* 22, 201-222.
- McGorry PD, Krstev H, Harrigan S (2000). Early detection and treatment delay: implications for outcome in early psychosis. *Current Opinions in Psychiatry* 13, 37-43.
- McNeil TB (1991). Obstetric complications in schizophrenic patients. *Schizophrenia Research* 5, 89-101.
- Metsänen M, Wahlberg K-E, Saarento O, Tarvainen T, Miettunen J, Koistinen P, Läksy K, Tienari P (2004). Early presence of thought disorder as a prospective sign of mental disorder. *Psychiatry Research* 125, 193-203.
- Metsänen M, Wahlberg K-E, Saarento O, Hakko H, Tarvainen T, Koistinen P, Tienari P (2005). Stability of Thought Disorder Index among High-Risk and Low-Risk adoptees in the Finnish Adoptive Family Study of Schizophrenia. *European Psychiatry* 20, 35-40.
- Metsänen M, Wahlberg K-E, Hakko H, Saarento O, Tienari P (2006). The Thought Disorder Index: A longitudinal study of severity levels and schizophrenia factors. *Journal of Psychiatric Research* 40, 258-266.
- Myhrman A, Rantakallio P, Isohanni M, Jones P, Partanen U (1996). Unwantedness of a pregnancy and schizophrenia in the child. *British Journal of Psychiatry* 169, 637-640.
- Nuechterlein KH, Edell WS, Norris M, Dawson ME (1986). Attentional vulnerability indicators, thought disorder, and negative symptoms. *Schizophrenia Bulletin* 12, 408-426.
- Nuechterlein KH (1987). Vulnerability models for schizophrenia. State of the art. In SR Steinhauer, JH Gruzelier, J Zubin (eds) *Search for the Causes of Schizophrenia*, pp. 297-316. Springer-Verlag, Giessen.
- Ott SL, Allen J, Erlenmayer-Kimling L (2001). The New York high-risk project: observations on the rating of early manifestations of schizophrenia. *American Journal of Medical Genetics* 105, 25-27.
- Rosenthal D (1963). A suggested conceptual framework. The gain quadrpulets: A case study and theoretical analysis of heredity and environment in schizophrenia. Basic Books, New York.
- Shenton ME, Solovay MR, Holzman PS, Coleman M, Gale HJ (1989). Thought disorder in the relatives of psychotic patients. *Archives of General Psychiatry* 46, 897-901.
- Singer MT, Wynne LC (1966). Principles for scoring communication defects and deviances in parents of schizophrenics: Rorschach and TAT scoring manual. *Psychiatry* 29, 260-288.
- Singer MT, Wynne LC, Toohey ML (1978). Communication disorders and the families of schizophrenics. In, LC Wynne, RL Cromwell, S Matthysse (eds) *The nature of schizophrenia*. Wiley & Sons, New York.
- Sorensen HJ, Mortensen EL, Reinisch JM, Mednick SA (2004).
  Association between prenatal exposure to analgesics and risk of schizophrenia. *British Journal of Psychiatry* 185, 366-371
- Spitzer RL, Williams JBW, Gibbon M (1989). Structured Clinical Interview for DSM-III-R Personality Disorders. SCID-2 (9/1/89 Version). New York: Biometric Research Department, New York State Psychiatric Institute.
- Tienari P, Lahti I, Sorri A, Naarala M, Wahlberg K-E, Rönkkö T, Moring J, Wynne LC (1987a). The Finnish adoptive

- family study of schizophrenia: possible joint effects of genetic vulnerability and family interaction. In K Halweg, MJ Goldstein (eds) *Understanding Major Mental Disorder: The Contribution of Family Interaction Research*, pp. 33-54. Family Process Press, New York.
- Tienari P, Sorri A, Lahti I, Naarala M, Wahlberg K-E, Moring J, Pohjola J, Wynne LC (1987b). Genetic and Psychosocial Factors in Schizophrenia: The Finnish Adoptive Family Study. *Schizophrenia Bulletin* 13, 477-484.
- Tienari P, Wynne LC, Moring J, Läksy K, Nieminen P, Sorri A, Lahti I, Wahlberg K-E, Naarala M, Kurki-Suonio K, Saarento O, Koistinen P, Tarvainen T, Hakko H, Miettunen J (2000). Finnish adoptive family study: sample selection and adoptee DSM-III-R diagnoses. *Acta Psychiatrica Scandinavica* 101, 433-443.
- Tienari P, Wynne LC, Läksy K (2003). Genetic Boundaries of the Schizophrenia Spectrum: Evidence from the Finnish Adoptive Family Study. *American Journal of Psychiatry* 160, 1-8.
- Tienari P, Wynne LC, Sorri A, Lahti I, Läksy K, Moring J, Naarala M, Nieminen P, Wahlberg K-E (2004). Genotype-environment interaction in schizophrenia-spectrum disorder. Long-term follow-up study of Finnish adoptees. *British Journal of Psychiatry* 184, 216-222.
- Tochigi M, Okazaki Y, Kato N, Sasaki T (2004). What causes seasonality of birth in schizophrenia? *Neuroscience Research* 48, 1-11.
- Vaglum P (1996). Earlier detection and intervention in schizophrenia: unsolved questions. *Schizophrenia Bulletin* 22, 347-351.
- Wahlberg K-E (1994). Parental communication and thought disorders of the offspring: an adoptive study. Acta Universitatis Ouluensis D 305.
- Wahlberg K-E, Wynne LC, Oja H, Keskitalo P, Pykäläinen L, Lahti I, Moring J, Naarala M, Sorri A, Seitamaa M, Laksy K, Kolassa J, Tienari P (1997). Gene-environment interaction in vulnerability to schizophrenia: Findings from the finnish adoptive family study of schizophrenia. American Journal of Psychiatry 154, 355-362.
- Wahlberg K-E, Wynne LC, Oja H, Keskitalo P, Anias-Tanner H, Koistinen P, Tarvainen T, Hakko H, Lahti I, Moring J, Naarala M, Sorri A, Tienari P (2000). Thought disorder index of Finnish adoptees and communication deviance of their adoptive parents. *Psychological Medicine* 20, 127-136
- Wahlberg K-E, Wynne LC (2001). Possibilities for prevention of schizophrenia: Suggestions from research on genotype-environment interaction. *International Journal of Mental Health* 30, 91-103.
- Wahlberg K-E, Wynne LC, Keskitalo P, Nieminen P, Moring J, Läksy K, Sorri A, Koistinen P, Tarvainen T, Miettunen J, Tienari P (2001). Long-term stability of Communication Deviance. *Journal of Abnormal Psychology* 110, 443-448.
- Wahlberg K-E, Wynne LC, Hakko H, Läksy K, Moring J, Miettunen J, Tienari P (2004). Interaction of genetic risk and adoptive parent communication deviance: longitudinal prediction of adoptee psychiatric disorders. *Psychological Medicine* 34, 1531-1541.
- Wing JK, Cooper JE, Sartorius N (1974). Measurement and Classification of Psychiatric Symptoms: An Instruction Manual for the PSE and Catego Program. Cambridge University Press, London.
- Wynne L, Singer M, Bartko J, Toohey M (1977). Schizophrenics and their families: Recent research on parental communication. In JM Tanner (ed) *Developments in psychiatric research*. Hodder & Stoughton, London.
- Zubin J, Spring B (1977). Vulnerability a new view of schizophrenia. *Journal of Abnormal Psychology* 103-126.