FAMILY PREDICTORS OF SEVERE MENTAL DISORDERS AND CRIMINALITY IN THE NORTHERN FINLAND 1966 BIRTH COHORT

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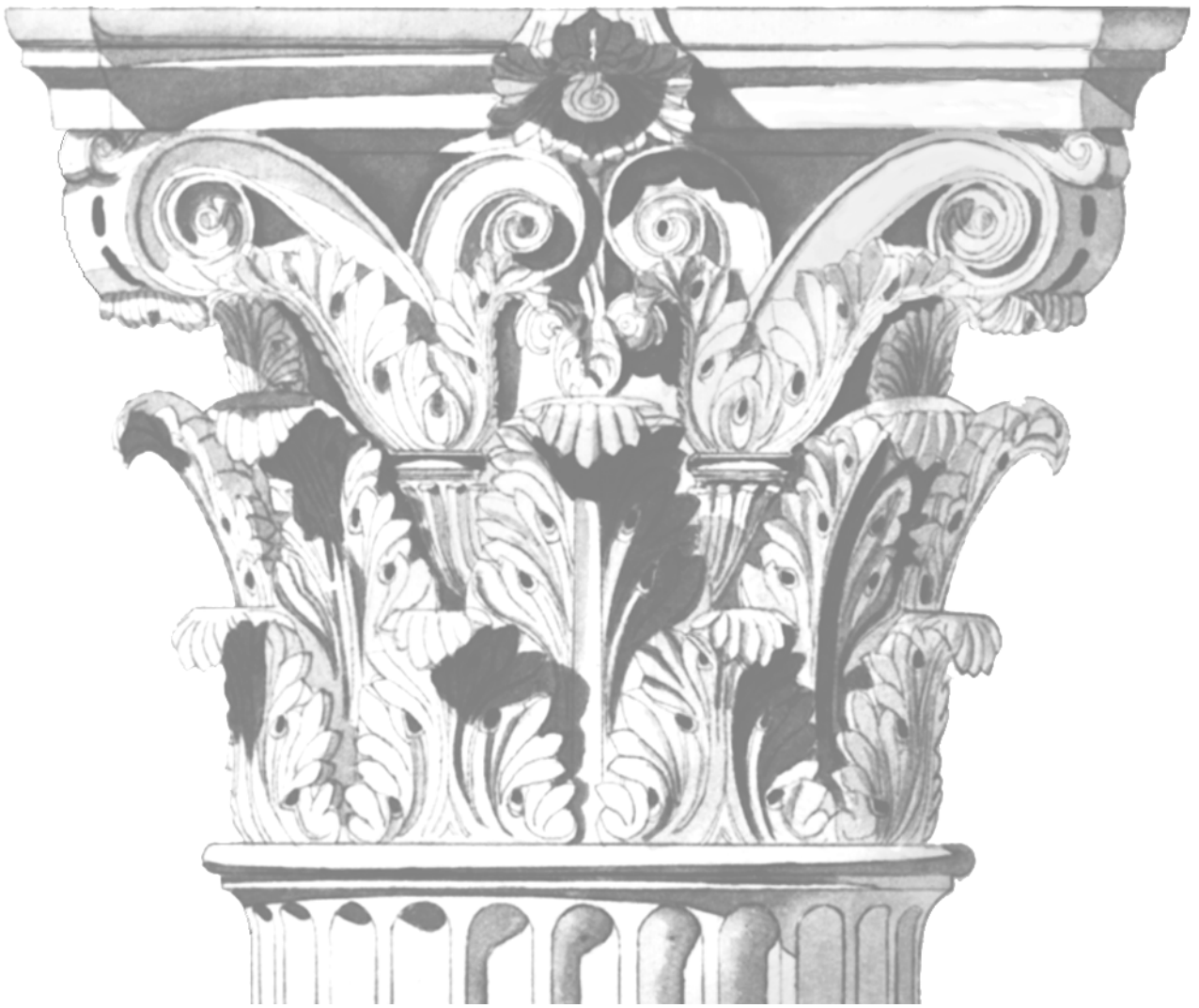

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Academic Dissertation to be presented with the assent of the Faculty of Medicine, University of Oulu, for public discussion in the Väinö Pääkkönen Hall of the Department of Psychiatry, on November 9th, 2001, at 12 noon.

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Abstract

Early family characteristics may influence the later development of severe mental disorders and criminality of a child. The association between an adverse family environment during childhood and its later consequences in adulthood, however, are still widely open. The aim of the present study was to analyse in a longitudinal perspective, family risks of severe hospital-treated mental disorders and criminal behaviour in the Northern Finland 1966 Birth Cohort and to develop a descriptive life span model of schizophrenia.

A large, general population birth cohort (N = 11 017), the Northern Finland 1966 Birth Cohort was used as a study population. This database provides the information of prospectively collected data on both biological and social aspects of pregnancy, the characteristics of family, the mother, the father, and the child. The information of psychiatric outcomes was gathered from the Finnish Hospital Discharge Register (FHDR) and the data on registered criminal behaviour of the cohort members come from computerized files maintained by the Ministry of Justice.

Children born to multiparous mothers (GMP) i.e. those that had undergone at least six deliveries were more commonly treated in mental hospitals later in life (4.5% vs. 3.4%; p = 0.028) than children born to mothers that have fewer children. Of the diagnostic groups, the risk of psychoses other than schizophrenia (OR 2.3; 95% CI 1.2–4.7), and depressive disorders (OR 2.2; 1.0–4.5) was elevated among adult children of those mothers.

Birth order was associated with adult schizophrenia. The risk was elevated among male firstborns (ratio 1.5; 95% CI 1.0–2.2), but it was lower than expected among male lastborns (ratio 0.7; 95% CI 0.5–0.9). The elevated risk was not significantly associated with female schizophrenia patients. On the contrary, the risk was lower than expected among females who were not first, not last or not only children in the family (ratio 0.6; 95% CI 0.3–0.9).

Among males the risk for violent crimes later in life was elevated among the only children (OR 1.8; 95% CI 1.1–3.0). If perinatal risk was additional exposure, the risk increased up to 4-fold (OR 4.4; 95% CI 1.9–10.8). Combining with maternal risks increased the risk up to 6-fold (OR 5.9; 95% CI 3.1–11.3) and with paternal risk up to 8-fold (OR 8.4; 95% CI 3.9–18.1), respectively.

Among females the absence of the father during childhood until the age of 14 was the strongest risk factor in predicting later criminality (OR 2.5; 95% CI 1.4–4.3). Further, in the families, where the father was present, maternal smoking during pregnancy together with being born unwanted increased the prevalence for criminal offending significantly up to 7.2%.

In conclusion, some characteristics of the early childhood family environment were associated with mental disorders and criminality in adulthood and form part of the developmental trajectory of these disorders. Early detection of such children at risk is important in preventing mental disorders and criminality in adulthood.

Keywords: criminality, birth order, early childhood family, descriptive model, mental disorders

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Finally, my loving gratitude belongs to my husband Markku and our children. I dedicate this work to you.

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Abbreviations

CNS	Central nervous system
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised
FHDR	Finnish Hospital Discharge Register
GMP	Grand multiparity
GGMP	Grand grand multiparity
ICD-8	Manual of International Statistical Classifications of Diseases, Injuries and Causes of Death, eight revision
ICD-9	Manual of International Statistical Classifications of Diseases, Injuries and Causes of Death, ninth revision
ICD-10	Manual of International Statistical Classifications of Diseases, Injuries and Causes of Death, tenth revision
MRI	Magnetic Resonance Imagin
IQ	Intelligence Quotient
OR	Odds ratio
RR	Risk ratio
95% CI	95% Confidence interval

List of original papers

The present thesis is based on the following original papers, which are referred to in the text by the Roman numerals I-V.

I. Kemppainen L, Mäkikyrö T, Jokelainen J, Nieminen P, Järvelin M-R & Isohanni M (2000) Is Grand multiparity associated with offsprings´s hospital-treated mental disorders? A-28-year follow-up of the North Finland 1966 birth cohort. Social Psychiatry Psychiatric Epidemiology 35: 104-108.

II. Kemppainen L, Veijola J, Jokelainen J, Hartikainen A-L, Järvelin M-R, Jones P, Croudace T& Isohanni M (2001) Birth order and risk for schizophrenia: A 31-year follow-up of the Northern Finland 1966 Birth Cohort. Acta Psychiatrica Scandinavica 104: 148-152.

III. Kemppainen L, Jokelainen J, Järvelin M-R, Isohanni M & Räsänen P (2001) The one-child-family and violent criminality: A 31-year follow-up study of The Northern Finland 1966 Birth Cohort. The American Journal of Psychiatry 158: 960-962.

IV. Kemppainen L, Jokelainen J, Isohanni M, Järvelin M-R & Räsänen P (2001) Predictors of female criminality: Findings from the Northern Finland 1966 Birth Cohort Study. Submitted manuscript.

V. Isohanni M, Jones P, Kemppainen L, Croudace T, Isohanni I, Veijola J, Räsänen S, Wahlberg K-E, Tienari P& Rantakallio P (2000) Childhood and adolescent precursors of schizophrenia. A review. European Archives of Psychiatry and Clinical Neuroscience 250: 311-319.

1 Introduction

Although the genetic aetiology of schizophrenia is well documented, the mechanisms for its inheritance remain unknown (DeLisi 1997). Furthermore, there is considerable evidence that environmental, epigenetic factors are also involved in the aetiology. However, schizophrenia is still a scientific mystery in many ways. Of the adverse environmental factors, an association between obstetric complications and later development of schizophrenia has been indicated in several studies (Verdoux *et al*. 1997, Geddes & Lawrie 1995, Hultman *et al.* 1999). Further, the infectious exposure as one part of the aetiology of schizophrenia is well demonstrated during both perinatal period and early childhood (Mednick *et al.* 1988, Sham *et al.* 1992, Sham *et al.* 1993, Rantakallio *et al.* 1997, Suvisaari *et al*. 1999, Westergaard *et al*. 1999). Further, the role of the rearing environment during early childhood is also considered to be of great importance (Alanen 1997), although it is partly speculative and only proposed on the basis of some evidence. Many possible adverse psychosocial predicting factors have been suggested, such as disturbances in the parent-child relationship (Jones *et al.* 1994), unwantedness of pregnancy (Myhrman *et al.* 1996), communication deviance in the family (Wahlberg *et al*. 1997) and low social status of parents (Jones *et al.* 1993).

Of the family structural factors, birth order has been investigated for many decades as a factor associated with later adverse mental outcomes, especially schizophrenia, but the results have been controversial (Goodman 1957, Schooler 1964, Granville-Grossman 1966a, 1966b, Solomon & Nuttal 1967, Barry & Barry 1967, Erlenmeyer-Kimling 1969, Hare & Price 1970, Wild *et al.* 1974, Weller & Miller 1978). In two more recent studies, the firstborn status has been noted as a risk position for schizophrenia (Stompe *et al.* 1999, Bender *et al.* 2000). However, being raised in a single-parent family during childhood has not been found to be a predictor of later schizophrenia (Mäkikyrö *et al.* 1998). Surprisingly, such "positive" premorbid features as high social class of father (Mäkikyrö *et al.* 1997) had also been linked with later schizophrenia of a child.

There are diverse forms and manifestations of schizophrenia suggesting several aetiological causes. This aetiological and phenomenological uncertainty is also true regarding different precursors, which not necessarily are specific to schizophrenia but common to other psychotic disorders as well (Jones & Tarrant 1999). It remains the true that no single premorbid sign or risk indicator has yet been identified that is specific for schizophrenia. Empirical studies of all aspects during the course of a lifetime have been

carried out, suggesting that genetic, environmental, individual and social contexts interact in the genesis of schizophrenia (Jones 2001). Since Kraepelin around the turn of the century, different efforts to formulate causal factors and developmental models have been made. However, the aetiology of schizophrenia is still mostly unknown.

As with schizophrenia, the explaining risk factors, which predict later antisocial and criminal behaviour are equally complex. Genetic vulnerability (Cadoret *et al.* 1997, Alsobrook & Pauls 2000), adverse primary psychosocial family characteristics and perinatal biological risks have this far found to be associated with the antisocial behaviour of a child. There is evidence that perinatal complications (Pasamanic *et al*. 1956, Lewis *et al.* 1979), born unwanted (Rantakallio *et al*. 1992a) single-parenthood (Sauvola 2001), and smoking during pregnancy (Rantakallio *et al.* 1992a, Fergusson *et al.* 1998, Brennan *et al*. 1999, Räsänen *et al.* 1999) predict later criminality. However, the precise nature and timing of these hypothesized biological or psychosocial insults are not known.

Previous findings of the association between early risks and later criminality are mainly based on male study samples. Of female studies, the most important associations with later criminality have been found to be linked with unmarried and teenage mothers (Conseur *et al.* 1997). According to Rantakallio *et al*. (1995) an unmarried mother was a significant predictor for later delinquency among girls, but this association did not exist among males. Interestingly, a follow-up study of Lewis *et al.* (1991) revealed that early biopsychosocial variables predictive for males were not associated with female delinquency.

Professor (emerita) Paula Rantakallio has started the prospective Northern Finland 1966 Birth Cohort. The original purpose of this cohort was to describe and analyse the risk factors for perinatal deaths and low birth weight. Recent studies concerning severe mental disorders (Isohanni *et al*. 1997, 2000) and criminality (Rantakallio *et al.* 1992a, 1992b, 1995, Räsänen *et al.* 1998, 1999) have been the most important areas of psychiatric research. This study is part of the psychiatric follow-up project of the ongoing Northern Finland Health and Well-being Study. The purpose of the present study is to extend the previous work of early environmental risk factors predicting severe mental disorders and criminality by analysing factors related to the childhood family environment.

2 Review of the literature

2.1 Early environmental risks of schizophrenia

2.1.1 Infections during pregnancy and early childhood

There is considerable evidence that infections are involved in the aetiology and development of schizophrenia. Many studies have underlined an increased risk in individuals whose second and third trimesters of foetal life coincided with an epidemic of influenza. In a large original epidemiological study of adults who were at risk for exposure to the 1957 influenza A2 epidemic while in utero, those at risk for second trimester had significantly more hospitalisations for schizophrenia (Mednick *et al*. 1988). Further, in a study by Sham *et al.* (1992) influenza epidemics, which occurred between 1939 and 1960 elevated the risk for exposed individuals.

In a study of the Northern Finland 1966 Birth Cohort, neonatal meningitis was associated with an increased risk for schizophrenia in the adulthood. This finding was based on an epidemic in which 16 neonates were infected, and two of the five viral infections were caused by Coxsackie B5 (Rantakallio *et al.* 1997). Further, in a recent population based study of hospitalised schizophrenia cases born between 1951 and 1969 the authors were able to link the information from the Finnish Hospital Discharge Register concerning maternal exposure to polio infection and later schizophrenia of a child. They pointed out that the occurrence of poliomyelitis was associated with a higher rate of births 5 months later of individuals who later developed schizophrenia (Suvisaari *et al*. 1999).

Common infections have also been suggested to be associated with an elevated risk for later schizophrenia. In a population based cohort study from Denmark with 2669 schizophrenia cases Westergaard *et al.* (1999) found a 1.26 times elevated risk for schizophrenia when coming from a sibship size of 4 (95% CI 1.11-1.44) and a 1.46 times elevated risk when coming from sibship of 5 or more (95% CI 1.22-1.75) compared with a sibship of 2, suggesting that common respiratory infections during childhood can be risk factors. Similar results came from a Swedish family study with 270 schizophrenia cases by Sham *et al.* (1993). According to the authors a pregnant mother with young

children at home may be particularly at risk for adverse effects on the foetus due to viral infections transmitted by older siblings. This can increase the risk for later schizophrenia in individuals who have siblings of a young age while in utero.

2.1.2 Perinatal complications

A relation between obstetric complications and later schizophrenia has been suggested by a significant number of studies and confirmed in two recent meta-analyses, but there is still considerable uncertainty about which specific exposures and pathopsychological mechanisms are involved. Geddes & Lawrie (1995) performed a meta-analysis of 20 case-control and two cohort studies and calculated that subjects who later developed schizophrenia were twice as likely to have been exposured to obstetric complications of different kinds when compared with controls. Further, Verdoux *et al.* (1997) found out a significant association between obstetric complications and early age of onset using data based on all available studies. The schizophrenia patients were 10 times more likely to have had a history of complicated Caesarean birth. On the contrary, in a study of two case-control studies on structured obstetric record Kendell *et al.* (2000) surprisingly pointed out that the evidence that schizophrenia was associated with raised incidence of obstetric complications was weaker than assumed. The authors reported that not a single complication of pregnancy or delivery was associated with later schizophrenia of a child.

Hultman *et al*. (1999) performed a study where they linked birth register and nationwide inpatient register in order to examine the association between obstetric complications and later schizophrenia. They pointed out that schizophrenia was statistically significantly associated with multiparity (OR 2.0; 95% CI 1.0-3.8), maternal bleeding during pregnancy (OR 3.5; 95% CI 1.2-10.3) and birth in late winter (OR 1.4 95% CI 1.0-2.0). In the Northern Finland 1966 Birth Cohort study, Jones *et al.* (1998) found that combination of birth weight < 2500g and gestation age < 37 weeks (OR 3.5; 95% CI 1.3-9.6) as well as perinatal brain damage (OR 7.5; 95% CI 3.2-17.6) increased the risk for later schizophrenia significantly. Although many studies have confirmed the association between obstetric complications and later schizophrenia, it remains, however, uncertain, whether or not obstetric complications are the results of preceding foetal abnormalities. According to McNeil and Cantor-Graae (1999), there is no support for suggestions that pre-existing foetal abnormalities precede obstetric complications in the history of individuals who suffer from schizophrenia

2.1.3 Mother's parity

Evidence that history of obstetric complications may contribute to the development of later schizophrenia has made aspects of social and medical characteristics of mothers of schizophrenia patients scientifically interesting. Still, the association between mother's parity and schizophrenia of a child is complex and opposing results exist. Cantor-Graae *et al.* (1996) showed that parity was the only maternal characteristic significantly associated with increased obstetric complications in mothers of preschizophrenic persons. When compared with nulliparous control mothers, nulliparous mothers of preschizophrenics had significantly increased rates of obstetric complications, while primi- and multiparous mothers did not have. On the contrary according to Hultman *et al.* (1999), mother's multiparity was associated with later schizophrenia (OR 2.0; 95% CI 1.0-3.8) as well as with reactive psychoses (OR 2.1; 95% CI 1.3-3.5).

Furthermore, multiparous mothers are regarded as being at risk for complications of pregnancy, labour and puerperium. Such mothers are known to show an increased incidence of somatic complications, Rhesus incompatibility, rupture of uterus, abnormal presentation and operative delivery (Nelson & Sandmeyer 1958, Israel & Blatsar 1965), as well as an increased perinatal morbidity and mortality (Baskett 1977, Tanbo & Bungum 1987). Juntunen (1997) however, concluded in her recent study that even the mothers who had given birth to ten or more children (grand grand multiparity; GGMP) were not at major risk for obstetric complications provided that the health care system was organized well at every level. Although the association between mothers' parity and maternal outcomes are well studied, to the best of my knowledge the association between a mother's grand multiparity (GMP) i.e. giving birth to her sixth or more children and later mental disorders of the child has not previously been studied.

2.1.4 Early childhood family

2.1.4.1 Birth order

Birth order has long been investigated as a variable in trying to understand childhood and adult outcomes. It has been evaluated from the point of psychology, economics and society for its relation to intelligence, education, and occupational achievements, personality, psychopathology and other indicators of mental health (Elliot 1992). Especially the relation of birth order to pathogenesis of schizophrenia has been investigated for many decades. Typically, non-epidemiological samples of schizophrenic patients have been examined for any systematic deviation of birth order from a uniform distribution. However, results of these previous studies, mainly from the 1960s, have been inconsistent and blamed to have serious methodological problems due to changes in birth rate and family size (Hare & Price 1970). Previously, Böök & Rayner (1953), Wahl (1954), Goodman (1957), Gregory (1959) and Tsuang (1966) as well as Westergaard *et al.* (1999) in a more recent study failed to point out any association between birth order and risk of developing schizophrenia.

Of those studies indicating an association between birth order and schizophrenia, Goodman (1957) identified over-representation among lastborn males, which according to the author, may be a feature of the general population. Further, according to a study by Schooler (1964) there existed an overrepresentation among laterborn females but the possible age and social class differences by sex could not be controlled. Weller & Miller (1978) found such an association among middle and lastborn females, Wild *et al.* (1974) among firstborn males, Barry & Barry (1967), Solomon & Nuttal (1967) and Erlenmeyer-Kimling (1969) among earlierborn males, Granville-Grossman (1966a, 1966b) lastborn males and Hare & Price (1970) laterborn males in small sibships.

Previous research on birth order has been carried out with hypotheses of psychodynamics on the relationship between personality and position in the sibship and theories and role of heredity and environment (Ernst & Angst 1983). One new hypothesis for the present association between birth order and schizophrenia has been maternal respiratory infections during pregnancy transmitted by older siblings, as presented by Sham *et al.* (1993). According to the author this association shows up as a decreased risk for schizophrenia in firstborn children and an increased risk in individuals who had siblings of young age while in utero. In another recent birth order study, an increased risk of schizophrenia associated with having many siblings, independent of birth order and short intervals to the nearest older or younger sibling, was suggestive of environmental factors being involved in the aetiology probably due to common infections at home (Westergaard *et al*. 1999). Recently Bender *et al.* (2000) reported an over-representation among eldest children in a birth order study in Pakistan (62.5% eldest vs. 37.5% not eldest, p=0.002). According to the authors the aetiological phenomena might be obstetric complications, season of birth, the viral hypothesis or psychological stress caused by over-expectations concerning firstborns but these factors were not available for statistical testing.

A summary of studies on birth order and schizophrenia is presented in Table 1. In the light of the earlier studies it seems that extreme position (firstborn or lastborn) carries an increased risk to develop schizophrenia.

*Table 1. Summary of studies on the relation between birth order and schizophrenia**

Author	Country	Number of schizophrenia cases	Overrepresented position
Böök & Rayner 1953	Sweden	103	Not noted
Wahl 1954	USA	309	Not noted
Wahl 1956	USA	568	Laterborns, only children
Goodman 1957	England	306	Lastborn males
Hallgren & Sjögren 1959	Sweden	214	Not noted
Gregory 1959	Canada	440	Not noted
Farina *et al*. 1963	USA	167	Laterborns
Smith & McIntyre 1963	USA	283	Not noted
Burton & Bird 1963	USA	241	Not noted
Schooler 1964	USA	724	Laterborn females
Tsuang 1966	England	206	Not noted
Granville-Grossman 1966a,b	England	1252	Lastborn males
Barry & Barry 1967	USA	1009	Earlierborn, laterborn males
Solomon & Nuttal 1967	USA	291	Earlierborn males
Erlenmeyer-Kimling 1969	USA	1347	Earlierborn males
Erlenmeyer-Kimling 1970	USA	264	Not noted
Hare & Price 1970	England	1761	Laterborn in small sibships
Schooler 1972	USA	500	Firstborns, lastborns
Mentzos *et al.* 1972	USA	400	Only children
Birtchnell 1972	Scotland	666	Not noted
Wild *et al.* 1974	USA	409	Firstborn males
Leonhard 1976	Germany	466	Laterborns
Weller & Miller 1978	Israel	264	Middle and lastborn females
Malama *et al.* 1988	Greece	221	Not noted
Sham *et al.* 1993	Sweden	270	Laterborns
Westergaard *et al.* 1999	Denmark	2669	Not noted
Stompe *et al.* 1999	Pakistan	379	Firstborn males
	Austria	144	Not noted
Bender *et al*. 2000	Pakistan	64	Firstborn males

*Modified and updated from Ernst & Angst; Table 45; p. 204 (1983).

2.1.4.2 Maternal psychosocial factors

Contrary to the biological environmental risks the association between psychosocial factors during pregnancy and later schizophrenia are not widely studied. Only a few original studies have been performed concerning factors that suggest adverse early familial environment. In the Northern Finland 1966 Birth Cohort Myhrman *et al.* (1996) have shown that the risk of developing schizophrenia later in children of unwanted pregnancies was elevated when compared with children born from wanted pregnancies (OR 2.4; 95% CI 1.2-4.8). This association was not explained by adverse sociodemographic, pregnancy or perinatal variables used as confounding factors. Further, according to Jones *et al.* (1998) maternal antenatal depression was associated with later schizophrenia compared with children whose mothers didn't feel themselves as depressed during pregnancy (OR 1.8; 95% CI 1.1-3.1). Further, abnormal social interaction in the family has been considered to be associated with later schizophrenia (Jones *et al.* 1994, Tienari *et al*. 1994). Extreme maternal stress during pregnancy due to loss of husband (Huttunen & Niskanen 1978) has been shown to be related with the risk for later schizophrenia of a child. In a recent study by van Os & Selten (1998) prenatal exposure to maternal stress during the five-day invasion and defeat of the Netherlands by the German army was associated with later schizophrenia (RR 1.28; 95% CI 1.07-1.53).

On the contrary, there exist some studies linking family features in common thinking considered as positive to later schizophrenia. Mäkikyrö *et al*. (1997) have pointed out an association between high social class of childhood family and adult schizophrenia. According to the author the cumulative incidence of early onset schizophrenia until 23 years was higher (1.14%; 9/726) among children coming from the highest social class I compared with children from lower social classes (0.47%; 48/10225), being statistically significant ($p< 0.05$). Further, single parenthood was not found to be a risk factor for later schizophrenia (Mäkikyrö *et al.* 1998). Most studies indicate that schizophrenia is linked with poor social status of the parents (Jones *et al.* 1993).

2.1.4.3 Other epigenetic family factors

The role of non-genetic family factors is complicated. Much discussion, particularly from the earlier literature, (see e.g. Alanen 1997 for review) has been carried out. Empirical testing of supposed interactions has been one major cause of dispute in the scientific community. Weinberger (1995) has stated that psychological and social theories on the development of schizophrenia are scientifically unfounded and only blaming families and society. However, many studies have suggested possible psychosocial predisposing factors, such as disturbances in parent (or mother)-child relationship (Jones *et al*. 1994), communication deviance in the family (Wahlberg *et al.* 1997) and several social factors. The direction of causality is, however, not clear; the relationship may be circular or confounded by e.g. genetic factors. The offspring, known to be deviant developmentally, may have elicited abnormal responses from or toward adults.

2.2 Early predictors of male criminality

2.2.1 Factors during pregnancy and perinatal period

2.2.1.1 Biological factors

There is some evidence that perinatal complications (Pasamanic *et al.* 1956, Lewis *et al.* 1979) and central nervous system trauma (Rantakallio *et al.* 1992b) are associated with delinquency. The incidence of delinquency was increased by 10.3% among males who had a central nervous system trauma by the age of 14, and this remained significant when social and demographic factors were taking into the statistical model with an odds ratio of 1.9 fold for all crime and 3.15 fold for those who had been arrested by the police for a violent crime (Rantakallio *et al*. 1992b).

Many studies have confirmed the association between smoking during pregnancy and adult violent criminality. According to Rantakallio *et al.* (1992a) the incidence of delinquency by the age of 22 was 4.6% among the sons of mothers who did not smoke during the pregnancy and 10.3% among those of smokers ($p<0.001$). Furthermore, Fergusson *et al.* (1998) have examined possible sex differences with regards to the effect of maternal smoking during pregnancy on conduct disorder symptoms. According to the authors the rate of increasing conduct disorder symptoms was more marked for males than for females. Further in a recent study by Räsänen *et al.* (1999) the prevalence of smoking among the mothers of those with a criminal record was found to be 1.8 times that of mothers of subjects with no criminal record. In a birth cohort study of 4169 males in Denmark, Brennan *et al*. (1999) pointed out that maternal smoking predicted significantly both non-violent (OR 1.13; 95% CI 1.06-1.21) and violent crimes (OR 1.19; 95% CI 1.09-1.30). However, the explanation for the relation between maternal smoking and criminality of a child is open. Maternal smoking during pregnancy may be symptomatic of an antisocial lifestyle of the mother rather than being an agent with a direct causal role. This lifestyle can exert an effect on the offspring and increase later criminal behaviour of the child (Rantakallio *et al.* 1992a). The meaning of it could be biological like for example causing reduced serotonin uptake (King *et al*. 1991) and alternations in dopaminergic neurons in the foetal brain due to nicotine exposure (Richardson & Tizabi 1994, Fung & Lau 1989).

2.2.1.2 Psychosocial factors

It is known that biological and psychosocial birth circumstances are related to later criminal offending. In a study of juvenile delinquency in the USA, Conseur *et al.* (1997) found that for both males and females such characteristics as mother being unmarried, young age at childbirth, and young age at first birth were related to risk of juvenile delinquency, being highest when the mother was under 18 at the time of delivery. Males born to unmarried, teenage mother have an 11-fold risk of chronic offending compared with males born to married non-teen mothers. Further, according to Rantakallio *et al*. (1995) low social class of the father (OR 1.2; 95% CI 1.0-1.6), social mobility downward (OR 1.3; 95% CI 1.0-1.7), urban residence at birth (OR 1.3; 95% CI 1.1-1.6), and a mother's low education (OR 1.3; 95% CI 1.0-1.8) were related to delinquency among males in the Northern Finland 1966 Birth Cohort.

Furthermore, Raine *et al.* (1994) have noted a significant association between violent offending at the age 18 and a combination of early maternal rejection and obstetric complications. Virkkunen *et al*. (1996) have linked the absence of the father and later criminality of a son in a prospective follow-up study of alcoholic violent offenders and fire setters. In her thesis, Sauvola (2001) has found that being raised in single-parent family could be considered as adverse family environment in many ways. According to her the risk for committing suicide was significantly up to 2.5-fold elevated among young adult males from single-parent families (OR 2.5; 95% CI 1.1-5.8). Further, the general mortality risk was increased (OR 1.8; 95% CI 1.1-2.9) among males with single-parent background. Furthermore, the risk of repeated violent offending was nearly 8-fold higher among males being raised in a single-parent family (OR 7.76; 95% CI 3.11-9.36).

2.2.1.3 Birth order and criminality

There are only a few studies that occupy themselves with an association between birth order and adult antisocial behaviour and criminality; moreover the findings are conflicting. Two studies of 70 years ago by Ward (1930) and Levy (1931) suggested that being an only child disposes one to delinquency. In a German study of sexual offenders, 38% were firstborns and one third of them were without siblings (Fehlow 1973). In a study of Indian criminals, Mukherjee *et al*. (1961) found an overrepresentation among middle borns. Further, according to Horton & Whitesell (1979) being a firstborn was associated with a lower risk of recidivism. Ernst & Angst (1983) concluded that all of these previous studies were methodologically inadequate and that there was no evidence that birth order had an influence on the development of criminal behaviour. In a recent, methodologically sound study by Conseur *et al*. (1997), juvenile offenders were slightly more likely to be born as third or more in family when compared with non-offenders, but this result was not further discussed. The percentage of offenders being third in the birth order was 15.5% compared with 13.5% of third born non-offenders and 12.9% of fourth borns compared with 10.6% of non-offenders being fourth borns.

Thomson (1974) had previously speculated that children of one-child-families were maladjusted, self-centred, self-willed and lacking social skills when compared with those

with siblings. Further, they have been criticized to develop narcissistic personalities due to parental overindulgence and lack of restriction and social responsibility (Millon & Everly 1985). It has also been suggested that, because of missing older siblings, only children in the family acquire more autocratic, less interactive interpersonal styles and that this may have negative consequences for peer popularity (Miller & Maryana 1976). In a recent study, peer rejection during childhood was found to be the strongest independent predictor of adolescent antisocial behaviour among males (Lewin *et al.* 1999). However, previous studies covering these psychosocial developmental risks among the only children are incompatible, and frequently involve sporadic observations, qualitative notions or small/ biased data samples (Falbo 1984).

Eronen *et al.* (1996) have studied the risk of homicidal behaviour among forensic psychiatric patients and found that the risk committing a homicide among schizophrenics was up to 9,7-fold elevated. Further, according to Tiihonen *et al*. (1996) schizophrenia increases the risk for homicidal violence up to 8-fold among males. Furthermore, Funahashi *et al.* (2000) have studied birth order from the viewpoint of self-violent behaviour. The authors conducted a clinical investigation of suicides among 80 schizophrenia patients in Japan and found that a total of 39.5% of those who committed a suicide were in the middle position in the sibling order compared with 18.8% being in the control group (not middle). Therefore birth order may be on important factor when analysing violent behaviour.

2.2.1.4 Special early environmental features of female offenders

It is well known that females have fewer antisocial behavioural problems than males, but antisocial tendencies among females are increasing (Durant *et al.* 1995, Loper & Cornell 1996). It had also been assumed that most antisocial girls eventually "outgrew" their deviances and that the course of events was relatively benign (Kunzel 1993). Rosenbaum (1989), in a 20-year follow-up study of 240 nonviolent females, reported that 96% of them had been arrested mostly for offences more serious than prostitution or drug possession. Further, in a follow-up study of 21 delinquent girls, 71% of them had adult arrest records seven years later and 13 of them had relationships with violent men. 15 girls had become mothers of at least one child and 8 of them had given up their children (Lewis *et al.* 1991). Although the unfortunate consequences of female criminality are known, the lack of original studies leaves the developmental pathway of offending wide open.

Causes for female criminality can be sought from equal biological, psychological and social factors like those implicated in male criminal studies. According to Rantakallio *et al.* (1995), the demographic, social, educational and health factors predictive of delinquency are very similar to males and females. On the contrary, a follow-up study by Lewis *et al.* (1991) revealed that early biopsychosocial variables predictive for males were not associated with female delinquents. In a follow-up study of female delinquents Conseur *et al*. (1997) have found that young maternal age was an important risk factor for later criminality also among females. According to the authors females born to mothers

younger than 18 years of age were more likely be offenders (OR 2.2; 95% CI 1.8-2.6) and more likely to become chronic offenders (OR 2.8; 95% CI 1.1-6.9), compared with children born to mothers of ages between 20-24 years. Further, several studies have indicated that unmarried and teenage mothers have difficulties in getting attached to and nurturing their infants (Crnic *et al.* 1983, Culp *et al.* 1988). This leads to poor parenting practices and inadequate supervision (Hechtman 1989). Further, a study of juvenile offenders by Rantakallio *et al.* (1995) revealed that the unmarried status of a mother was a significant predictor for later delinquency among girls, but not among boys. Females born to an unmarried mother were more likely to become delinquents when compared with females born to married mothers (OR 2.9; 95% CI 1.3-6.3).

2.3 Summary of the literature

Although there is consensus that genetic factors (DeLisi 1997) are associated with the aetiology of schizophrenia, it is obvious that the childhood family has a decisive influence on the psychic development of a child. Since Sigmund Freud's time family structures are taken into considerations on the pathogenesis of psychic illness. In the Northern Finland 1966 Birth Cohort some important studies concerning childhood family and later outcomes have been carried out. Myhrman *et al.* (1996) have found an elevated risk regarding schizophrenia in a child born from an unwanted pregnancy. Further, the association between childhood low social class and later outcomes has been studied (Rantakallio *et al.* 1995). On the contrary, there exist some studies linking family features not considered as adverse to later disorders. For example Mäkikyrö *et al.* (1997) have found an association between high social class in childhood family and adult schizophrenia, but single parenthood was not found to be a risk factor for later schizophrenia (Mäkikyrö *et al.* 1998). In her recent thesis, Sauvola (2001) relates effects of a single-parent family to later physical morbidity, mortality and criminal behaviour in a child. Although the majority of children born from single-parent families did well during the follow-up period, being raised in single-parent family could be considered a risk for elevated mortality and morbidity and criminal behaviour of a child (Sauvola 2001).

Of the childhood family risks, birth order has long been investigated and is understood to influence adult adverse outcomes. A large body of original studies on the putative association between birth order and schizophrenia has been performed and all variants of over-and under-presentations have been reported (Ernst & Angst 1983). Although identified from the earlier literature that extreme birth position (first or last born) carries an increased risk of future schizophrenia, most of the studies are blamed to have serious methodological problems (Price & Hare 1969). Some recent methodologically sound studies have revealed that the firstborn position is a risk for schizophrenia (Stompe *et al.* 1999, Bender *et al.* 2000). The possibility to study these associations by taking into account a variety of biological and social characteristics of the family, the mother, the father and the child, which were recorded prospectively since mid-pregnancy, gives an unique opportunity.

There are diverse forms and manifestations of schizophrenia, suggesting a variety of aetiological causes. No single premorbid sign or risk indicator has yet been identified that

is specific for schizophrenia. Empirical studies of all aspects of a life course have been carried out suggesting that genetic, environmental, individual and social contexts interact in the genesis of schizophrenia. To consider any one without the others is going to generate neither a realistic nor a valid aetiological model of schizophrenia (Jones 2001).

In contrast to schizophrenia studies, the association between birth order and criminality has not received a great deal of scientific attention. The lack of birth order studies of criminal offenders is especially evident among data samples of female criminals. In conclusion, controversial findings of schizophrenia and birth order studies on the one hand and the lack of birth order and criminality studies on the other hand formed the bases to perform this study, highlighting methodologically sound study design.

3 The aims of the study

The general purpose of the present study was to investigate specific predisposing and predicting childhood family factors associated with the development of later schizophrenia, other hospital treated psychiatric disorders and criminality. The numbers I-V hereafter refer to the original publications. The detailed aims of the present study were:

1. To investigate if parity is associated with any mental disorders (I).

2. To investigate if birth order is associated with schizophrenia (II).

3. To investigate if birth order is associated with criminal behaviour (III).

4. To investigate the early family risks of criminal behaviour of girls (IV).

5. To review childhood and adolescent predictors of major mental disorders, especially schizophrenia and to build a developmental life-span model (V).

4 Material and methods

4.1 Study population and data collection

The study population in the present thesis was the Northern Finland 1966 Birth Cohort originally assembled by Professor (emerita) Paula Rantakallio. It is based on 12068 pregnant women and their 12058 live-born children in the provinces of Oulu and Lapland with an expected delivery date during 1966 representing 96% of all births in the region. The majority of the cohort members are Finns (white Caucasians) and less than 1% being Gypsies and Lapps. The original purpose of the Cohort was to describe and analyse the risk factors for perinatal deaths and low birth weight. Data for biological, socio-economic and health conditions, living habits and family characteristics of cohort members have been collected prospectively since pregnancy during follow-ups in various ages. Of the cohort members 284 had died and 757 emigrated, leaving 11017 individuals alive and living in Finland at the age of 16 for the present study.

Data on the cohort members and their families have been gathered at the antenatal clinics at various ages since the pregnancy of the mother and at the time of birth in 1966, and then during follow-ups at various ages. Such sociodemographic characteristics of mother and family as housing conditions, education, occupational level and social status and maternal smoking during pregnancy have been collected. Further, details of a mother's obstetric history and information on the postnatal course of events have been gathered during routine post-natal clinic visits (Rantakallio 1969, 1988).

4.1.1 Follow-ups

The data gathering has been continued to date from several registers, such as hospital discharge registers and the National Crime Register of the Ministry of Justice. Three main follow-ups have been performed. The first follow-up was performed at the routine post-natal clinic visit at age 1 when information on growth, development and health status of the children at that time was gathered (Rantakallio 1988).

The second follow-up was performed when the cohort members were 14 years of age. Information on health, schooling, living habits, social situation of the family and family background variables were gathered using postal questionnaires (Rantakallio 1988, Järvelin *et al.* 1997). The number of cohort members alive at the time was 11780. Response rates on the children's and parents' inquiry was up to 97% (Rantakallio 1988).

The latest follow-up, the Northern Finland Health and Well-being Study, was conducted between the years 1997 and 1998, when cohort members were 31 years old (Sorri & Järvelin 1998). The response rate for the postal questionnaire was 77%.

One of the most important follow-ups for the present study has been the 14-year follow-up when data on the family were gathered. Further, the psychiatric follow-up with the data on FHDR and validation of diagnoses has also been very important for the present thesis (Isohanni *et al*. 1997) In Figure 1 study population and variables of the Northern Finland 1966 Birth Cohort database up to the end of 1998, are presented.

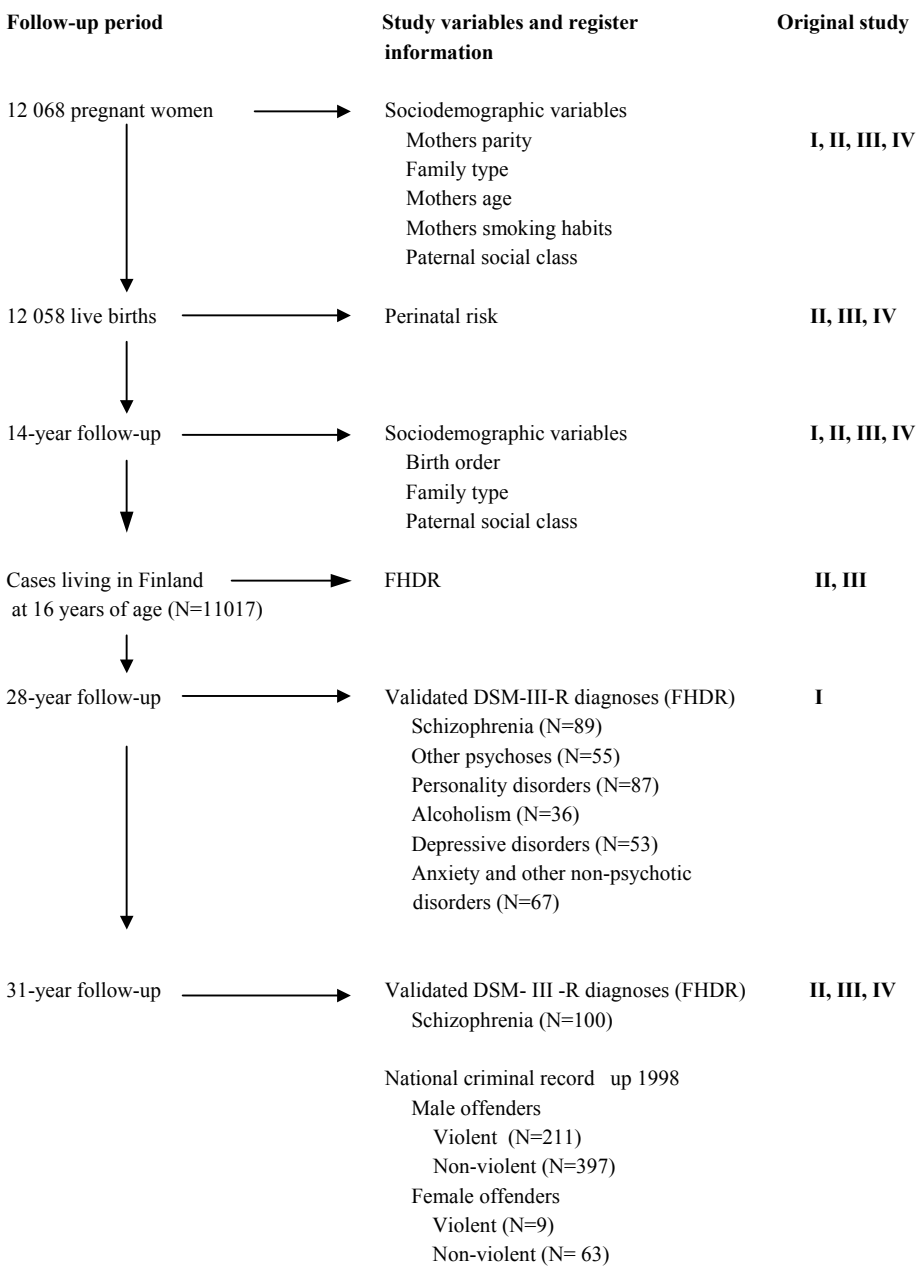

Fig. 1. Study population and variables of the Northern Finland 1966 Birth Cohort database used in this study.

4.2 Exposure variables

4.2.1 Parity (I) and birth order (II, III, IV)

Mother's parity was used as an exposure variable for future severe hospital treated mental disorder of a child in the first original study. Parity number was assessed in 1966 as 6 children or more (grand multiparity; GMP) vs. 5 children or less (non-GMP) (Juntunen 1997). 12% (1230) of them were GMPs and 88% (9680) were non-GMPs.

In the original study (II), the birth order status, another exposure variable, was calculated for each cohort member using data on a mother's parity at 1966 and the information gathered from the family size during the 14 year follow-up. The family size was enquired using a questionnaire as follows: *"How many children are there or have been in your family?"* Case assessment was the following: Firstly, if the cohort member was the mother's first parity at 1966 and sibsize remained the same until 1980, the child was determined as the only child. Secondly, if the parity number was one in 1966 and the number of children in the family was more than one in 1980, the child was assessed as firstborn. Thirdly, if the parity number and the number of the children in 1980 was more than one, then the child was identified as lastborn. Fourthly, if the parity number was more than one and smaller than the number of children in the family in 1980, the birth order status was middle (not only child, not first, not last). 5.0% of the cohort members were only children in the family, 27.3% firstborns, 37.1% lastborns, and 30.6 % of them were in the middle of the sibship (i.e. not only child, not first not last).

4.3 Outcome variables

4.3.1 Psychiatric morbidity (I, II)

The nation-wide Finnish Hospital Discharge Register (FHDR) covers all mental and general hospitals, as well as bed wards of local health centres, military wards, prison hospitals and private hospitals. The FHDR contains the personal and hospital identification code, and data on length of stay and primary diagnoses at discharge, together with three possible subsidiary diagnoses. Diagnoses are coded routinely between 1969 and 1986 using ICD-8, between 1987 and 1995 according to ICD-9 with DSM-III-R criteria, and since 1996 ICD-10. All case records were scrutinized and diagnoses were validated for the DSM-III-R criteria (Isohanni *et al.* 1997).

In the original study I the follow-up of psychiatric diagnoses and diagnostic validation was performed to the end of 1994 resulting in 387 psychiatric cases. The six diagnostic categories used in this study were DSM-III-R schizophrenia (N=89), other psychoses (N=55), personality disorders (N=87), alcoholism (N=36), depressive disorder (N=53), and anxiety and other non-psychotic disorders (N=67). Inter-rater reliability was ensured in many phases, with good kappa values from 0.6-0.9 (Isohanni *et al.* 1997).

In the original study II the follow-up period continued up to the end of 1997 and the second diagnostic validation resulted in 444 psychiatric cases. The diagnostic validation procedure is discussed in detail by Moilanen *et al*. (submitted). A total of 100 cases (65 or 65% men) of DSM-III-R schizophrenia arose by the end of the 31st year (cumulative incidence (0.91%: 95% CI 0.7-1.08). Two of them were treated as outpatients.

The case ascertainment and diagnostic validation process used in the Northern Finland 1966 Birth Cohort Study up to 1997 is presented in Figure 2 (Moilanen *et al.* submitted).

The diagnostic categories and number of cases in different diagnostic groups are presented in Table 2.

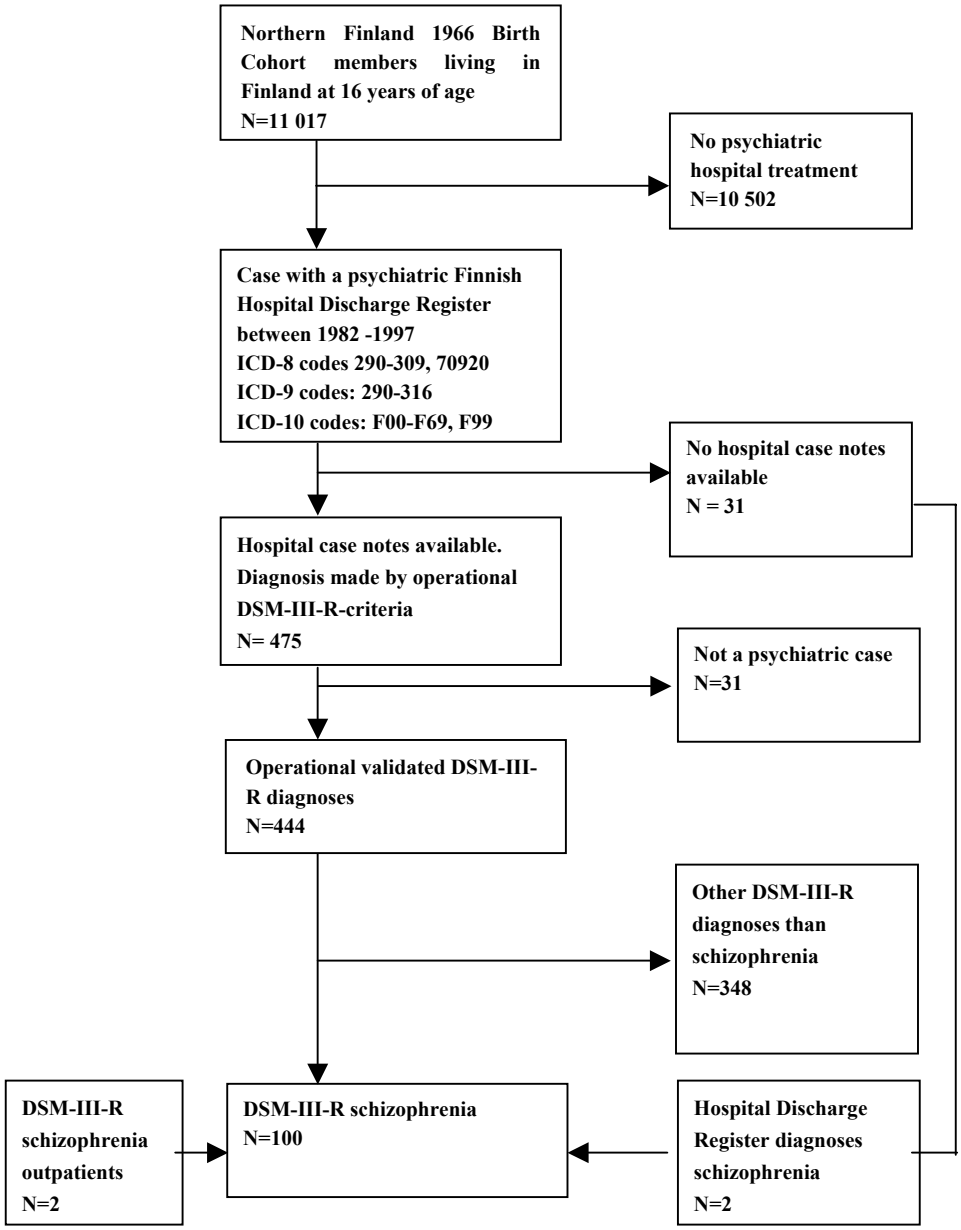

Fig. 2. The case ascertainment and diagnostic validation process used in the Northern Finland 1966 Birth Cohort Study until 1997 (Moilanen *et al.* submitted manuscript).

Table 2. The diagnostic categories with DSM-III-R codes of hospital treated mental disorders in the Northern Finland 1966 Birth Cohort up to 1997. The number of cases in different categories is presented in parenthesis.

DSM-III-R diagnostic categories			
Schizophrenia	Other psychoses	Non-psychotic disorders*	N
29510(3), 29511(1), 29512(8), 29514(1), 29520(1), 29522(1), 29530(9), 29532(15), 29534(2), 29539(1), 29590(22), 29591(5), 29592(25), 29594(6)		30390(1), 30490(1), 3050 0(7), 30750(1)	100
	29540(16), 29570(4), 29624(5), 29634(1), 29644(6), 29654(1), 29664(1), 29710(10), 29880(2), 29890(9)	30000(1), 30021(1), 30023(1), 30390(1), 30410(1), 30500(6), 31100(1), 30122(1), 30183(1)	55
		29620(1), 29622(7), 29623(17), 29631(2), 29632(2), 29633(9), 29653(2), 29670(4), 30000(18), 30001(8), 30002(3), 30015(1), 30023(12), 30029(4), 30030(1), 30040(1), 30090(27), 30300(1), 30290(1), 30390(66), 30410(3), 30440(1), 30490(10), 30500(55), 30520(1), 30540(3), 30550(1), 30570(1), 30590(2), 30710(2), 30740(1), 30742(2), 30750(1), 30900(18), 30921(1), 30922(1), 30924(16), 30928(20), 30940(3), 30982(1), 30989(1), 31100(18), 31220(1), 31231(1), 30100(1), 30122(2), 30150(1), 30160(1), 30170(20), 30181(1), 30182(2), 30183(24), 30190(14), 31010(2)	315

* multiple diagnoses are possible in this category, and the number of diagnoses exceeds the number of cases

4.3.2 Data on crimes (III, IV)

Data on registered crimes of the cohort members were collected from computerized files maintained by the Ministry of Justice available to the end of 1998 for the present thesis. This national register includes records of all crimes known to the police committed anywhere in Finland after the 15th birthday.

Crimes were categorised as non-violent and violent. The category of violent crimes included homicide, assault, robbery, arson, sexual crime, and violation of domestic peace. The category of non-violent crimes included severe traffic violations, crimes against property, i.e. theft, fraud or treachery, disorderly conduct or illegal sale or possession of alcohol or narcotics (Tiihonen *et al.* 1997).

A total of 608 (10.9%) males and 72 (1.3%) females had committed at least one crime during the follow-up time. The percentage of criminal offending among males at the age of 32 was 3.8% (N=211) for violent crimes and 7.1% (N=397) for non-violent crimes. Of the female criminals 9 (0.2%) had committed at least one violent crime and 63 (1.2%) had committed at least one non-violent crime.

4.4 Confounding variables

The potential confounding variables used in this thesis are presented in Table 3.

Table 3. Confounding variables used in the original papers (I-V)

Confounding variables	Original paper
Perinatal risk: no versus yes: low birth weight (<2500g), preterm birth (<37 weeks) or perinatal brain damage	II, III, IV
Maternal smoking during pregnancy: smoked daily during the entire duration of pregnancy versus stopped before pregnancy/no smoking	III, IV
Mother's attitude to the pregnancy: did not want the pregnancy/mistimed pregnancy versus wanted the pregnancy.	I, II, III, IV
Mother's age at delivery: low maternal age (≤20 years) Mother's age at delivery (18-35 years versus ≤ 17 year or ≥ 36 year)	III, IV II
Paternal risk: absent from the family during childhood until the age 14.	III, IV
Paternal socio-economic status (social classes I-V)	I
Mother's self-reported antenatal depression yes versus no	I
Family type Full versus single	II

4.4.1 Biological variables

4.4.1.1 Perinatal risk (II, III, IV)

The data on the obstetric histories of the mothers and perinatal complications of the children were obtained at the delivery and puerperal period from hospital records. The perinatal risk included low birth weight (<2500g), preterm birth (<37 weeks gestation) or perinatal brain damage. Perinatal brain damage was defined as the occurrence of one or more of the following: low Apgar score (0 at 1 min, or <5 min at 15 min), neonatal convulsions, neonatal asphyxia (based on blood gas analyses or clinical signs as need of extra oxygen or assisted ventilation), brain injury or intraventicular hemorrhage (Rantakallio *et al.* 1987, Järvelin *et al.* 1997, Jones *et al.* 1998). Children with CNS malformation, cromosomal aberration or hereditary CNS degeneration were excluded (Rantakallio *et al.* 1987).

4.4.1.2 Maternal smoking habits during pregnancy (III, IV)

The first information of mother's smoking habits was collected during the routine visit at antenatal clinics in the sixth and seventh month of pregnancy. The mother was asked whether she had smoked during the last 12 months before pregnancy and whether she had changed her smoking habits during the pregnancy. After the delivery, mothers were again asked if they had smoked during the last three months of the pregnancy and if the smoking habits had changed (Rantakallio *et al.* 1992a). Maternal smoking was classified as "yes" if the mother smoked during the pregnancy (after second month of the pregnancy) and "no" if the mother did not smoke or stopped before the pregnancy (Järvelin *et al.* 1997, Räsänen *et al*. 1999).

4.4.2 Psychosocial variables

4.4.2.1 Paternal absence (III, IV)

Variable paternal absence during a cohort member's childhood was assessed using data on family background collected during the14 year follow-up (Moilanen & Rantakallio 1988, Mäkikyrö *et al.* 1998, Sauvola 2001). The cohort members were asked if the father was alive, alive but not living at home, dead or unknown. The father was considered as absent, when he was dead, unknown or not living at home.

4.4.2.2 Family type (II)

The family type was assessed in both 1966 and 1980. The type of single family was determined as follows: 1) "All time" when the mother was unmarried at the child's birth up to the child's age of 14 (N=163). 2) "At birth", when the child was born to an unmarried mother who got married later by the time the child was 14 years of age (N=228). 3) The mother (N=108), father (N=580) or both parents (N=19) had died before the child reached 14 years of age (N=707). 4) The parents got divorced or were permanently separated before the child's age of 14 (N=989) (Moilanen & Rantakallio 1988, Mäkikyrö *et al.* 1998).

4.4.2.3 Mothers' self-reported antenatal depressions (I)

During the routine visit to antenatal clinics in the sixth and seventh month of pregnancy mothers were asked if they felt depressed during the pregnancy. The variable was dichotomised as yes vs. no (Rantakallio 1969, Jones *et al.* 1998, Veijola *et al.* 1998).

4.4.2.4 Wantedness of pregnancy (I, II, III, IV)

During the routine visit to antenatal clinics in the sixth and seventh month of pregnancy it was inquired if the mother did not want the pregnancy, preferred it later or if she wanted the pregnancy (Rantakallio 1974, Myhrman *et al*. 1996)

4.4.2.5 Social class (II)

Social class was determined by the father's occupation and prestige, and it was assessed in 1966 for the present study (Rantakallio 1969). In class I, the father's occupation was highest and usually required academic education. Social class II fathers were professionals with lower valuation and shorter education than in the first class. Class III consisted of skilled workers and class IV unskilled workers and persons on a disability pension. Class V was formed by farmers. When the father's occupational status was not known the mother's information was used (Rantakallio 1979, Mäkikyrö *et al.* 1998).

4.5 Statistical methods

The data were analysed using basic methods to conduct cohort studies (Rothman & Greenland 1998). Associations between exposure and outcome variables were analysed in using cross-tabulations and regression models adjusted for confounding.

In the original study I cross-tabulation was first used to present the distribution of the offspring's mental disorders in adulthood as well as maternal sociodemographic and health factors by parity. The statistical significance of differences in the frequency tables was tested using the chi-square test. The continuation ratio model was then used to estimate the adjusted odds ratios of psychiatric disorders for parity. It partitions the analysis of the original response variable (e.g. psychiatric disorder) into six different logistic models (logistic regression models for dichotomous response) (Agresti 1990).

In the original study II the cumulative incidences of schizophrenia until the age of 31 and the risk ratio with 95% CI for comparing the firstborn status with other statuses was calculated. The observed number of schizophrenia cases was compared with expected number of schizophrenia cases, which were calculated using internal standardisation (Breslow & Day 1987).

In the original study III, in order to explore the effect of the only child status on offences in combination with other risk factors, odds ratios with 95% CI were calculated for violent and non-violent offences for subjects characterized by various combinations of risk factors. Cross-tabulation with chi-square tests or Fisher's exact tests, as appropriate, were used in assessing relationships among nominal variables.

In the original study IV the number and percentage of criminal and non-criminal females in each risk group were presented and the difference between criminals and non-criminals was tested using the chi-square test. A Chi-Squared Automatic Interaction Detector (CHAID) analysis (Magidson 1993) in the Statistical Package for the Social Sciences (SPSS, 1994) was utilized in order to study the associations between psychological and biological risk factors during childhood and later criminality of cohort females.

The statistical programs used were the SPSS for Windows version 6.1 (Norusis 1994), and in original study II additionally the SAS 6.12 for Windows (SAS institute, 1997, 1999a, 1999b).

4.6 Ethical considerations

Permission for gathering data for the entire Cohort was obtained from the Ministry of Social Welfare and Health Affairs in 1993. The research plan for the 31-year follow-up study design of the Cohort named the Northern Finland Health and Well-being Study (Sorri & Järvelin 1998) was under review by the Ethics Committee of the Faculty of Medicine, University of Oulu on 17th of June 1996. During the 31-year follow-up, after having been given a complete description of the study, the cohort members have had an opportunity to refuse the use of their data at any point of the data collection.

This study has been approved by the Postgraduate Research Committee of the Faculty of Medicine on 7th of December 1999. The permission by the Ethics Committee of Faculty of Medicine on 17th of June 1996 covers also the present study.

5 Results

5.1 Parity and mental disorder (I)

During the follow-up period up to age 28, children of grand multiparity mothers (GMP, i.e. those having undergone six or more deliveries) were more commonly treated in psychiatric hospitals (4.5% vs. 3.4%, p=0.028) than children of mothers with fewer children. Of all the diagnostic groups used, psychoses other than schizophrenia (OR 2.3; 95% CI 1.2-4.7) and depressive disorders (OR 2.2; 95% CI 1.0-4.5) were significantly associated with maternal GMP after adjustment with social class, maternal antenatal self-reported depression and wantedness of pregnancy. Table 4 shows the associations between a mother's parity and hospital treated mental disorders.

Figure 3 (I: Figure 1) presents the "tree structure" of the six logistic regression models, analysing the seven diagnostic categories. In the GMP variable, the non-GMP category was used as a reference group to calculate the odds ratios for GMPs. The associations are between GMP and different psychiatric disorders are expressed as both crude and adjusted odds ratios.

Table 4. Cumulative incidences and adjusted odds ratios with 95% confidence intervals of an offspring's mental disorder until 28 years of age by a mother's parity in 1966 in the Northern Finland Birth Cohort 1966. Percentages are calculated by columns.

Mental disorder	Mother's parity				OR[c]	95%CI
	No GMP[b]		GMP			
	N=9680	%	N=1320	%		
Hospital diagnosis[a]						
Schizophrenia	74	0.8	14	1.1	1.1	0.6-2.1
Other psychoses	44	0.5	11	0.8	2.3	1.2-4.7
Personality disorder	79	0.8	8	0.6	0.5	0.2-1.1
Alcoholism	28	0.3	8	0.6	2.0	0.8-4.7
Depressive disorder	40	0.4	13	1.0	2.2	1.0.4.5
Anxiety disorders and other non-psychotic disorders	60	0.6	6	0.5	0.8	0.3-1.6
All cases treated in hospital	325	3.4	60	4.5	1.3	0.9-1.8
No hospital treatment	9355	96.6	1260	95.5	1.0	[reference]

[a] p=0.008

[b] grand multiparity

[c] odds ratio, adjusted for social class, self-reported antenatal depression, wantedness of pregnancy

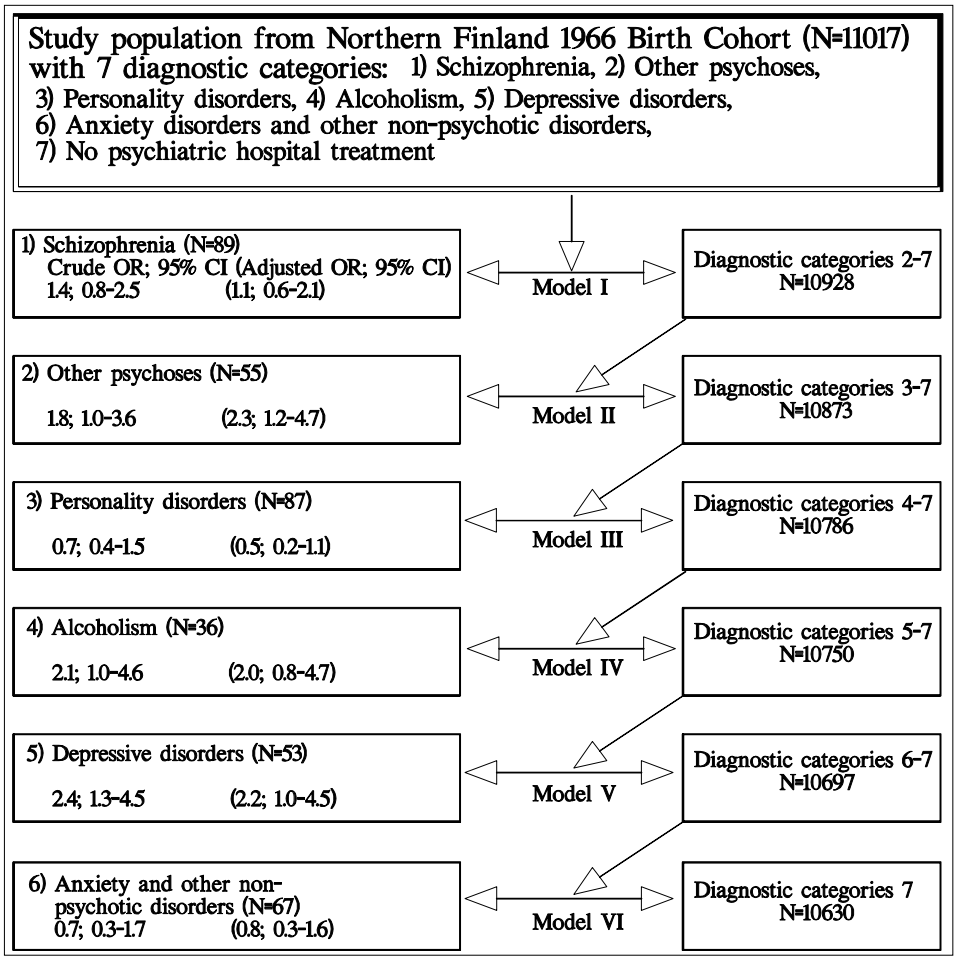

Fig. 3. The "tree structure" of the six logistic regression models presenting the odds ratios (OR) and confidence intervals (95%) of grand multiparity for seven diagnostic categories.

5.2 Birth order and risk of schizophrenia (II)

Of all cohort members, 5.0% were only children i.e. children without siblings in the family, 27.3% were firstborns, 37.1% lastborns, and 30.6 % of them were in the middle of the sibship in the childhood family. Among male schizophrenia cases 38.5% (N=25) were firstborns, 27.7% (N=18) lastborns, 3.1% (N=2) only children in the family, and 30.8% (N=20) were born in the middle. 31.4% (N=11) of female schizophrenia patients were firstborns, 51.4% (N=18) lastborns, 2.9% (N=1) only children in the family and 14.3% (N=5) held the middle status.

Table 5 presents the distributions of observed and expected cases of schizophrenia by birth order. During the follow-up period (between ages 16-31) being the firstborn in the family increased the risk for schizophrenia later in life significantly among male subjects with complete data, up to 1.5-fold (RR 1.5; 95% CI 1.0-2.2). Being the lastborn female increased the risk statistically marginally up to 1.3-fold (RR 1.3%; 95% CI 0.9-1.9). The observed number of schizophrenia cases was 0.7-fold lower than expected (RR 0.7; 95% CI 0.5-0.9) among the lastborn sons. Further, among the females being in the middle, the risk was 0.6- fold lower than expected (RR 0.6; 95% CI 0.3-0.9).

Table 2 (II: Table 2) presents observed number of male schizophrenia cases and Table 3 (II: Table 3) observed number of female cases, all until the age of 31 in the Northern Finland 1966 Birth Cohort subdivided according to different birth order status with corresponding adjusted number in brackets.

Among male schizophrenia cases an over-representation was associated with the firstborn status and an under-representation with lastborn status. In all different subgroups the observed number of cases was higher than expected among firstborns and lower than expected among lastborns. Among female schizophrenia cases, being firstborn in a big family (three siblings or more) or lastborn in a small family (two siblings or less) increased the risk statistically significantly. The effect in other strata of confounding factors was impossible to estimate due to the small number of cases.

Table 5. The observed and expected number of schizophrenia cases and adjusted odds ratios with 95% confidence intervals until the age of 31 in the Northern Finland 1966 Birth Cohort classified by birth order. Ratio estimates (observed/expected number of cases with 95% confidence intervals) are also reported.

	Male			Female		
Birth order	Observed	Expected*	Ratio (95% CI)	Observed	Expected*	Ratio (95% CI)
Only child	2	3.2	0.6 (0.2-1.8)	1	2.3	0.4 (0.1-1.4)
First born	25	16.9	1.5 (1.0-2.2) [a]	11	10.1	1.1 (0.7-1.8)
Last Born	18	25.6	0.7 (0.5-0.9) [a]	18	13.7	1.3 (0.9-1.9)
Other status	20	19.3	1.0 (0.7-1.4)	5	8.9	0.9 (0.3-0.9) [a]

* Adjusted for wantedness of pregnancy, maternal age at delivery, perinatal complications, family type and number of siblings.

[a] p-value < 0.05.

5.3 Birth order and criminality (III)

During the follow-up period (between ages 16-31) a total of 32 only children in the family had committed a crime and 225 had not. Of the crimes 6.2% (N=16) were violent and 6.2% (N=16) were not. The corresponding percentages and numbers of cases for not only children were 3.6% (N=177) and 6.9% (N=342), respectively. During the follow-up period (between ages 16-31) being an only child increased the crude odds ratio for committing a violent crime later in life relative to not being an only child up to 1.8-fold (OR 1.8; 95% CI 1.1-3.0). No association with non-violent offending was noted (III: Table 1).

Table 1 (III: Table 1) presents the results of the analyses with multiple risk factors. Being an only child combined with a perinatal risk increased the odds ratios for violent crimes up to 4.4-fold (OR 4.4; 95% CI 1.9-10.0). If maternal or paternal risks were present, the odds ratios for violent offences were higher, reaching six-fold (OR 5.9; 95% CI 3.1-11.3) and eightfold levels (OR 8.4; 95% CI 3.9-18.1), respectively. However, only children in the family were not at risk for non-violent offending, except in cases were the father was absent (OR 2.5; 95% CI 1.0-5.9).

Table 6 presents the distributions of criminal behaviour by birth order among male cohort members.

Table 6. Distributions of violent and non-violent crimes by birth order among males in the Northern Finland 1966 Birth Cohort

	Only child N=257		Not only child N=4984	
Crime type	N	%	N	%
Violent	16	6.2	177	3.6
Non- violent	16	6.2	342	6.9
No crime	225	87.6	4465	89.5

5.4 Predictors of female criminality (IV)

Figure 4 (IV: Figure 1) presents a Chi-squared Automatic Interaction Detection Analysis (CHAID) flowchart of the best segmentation for prediction of criminality rates (%) and number of cohort females in each sub-sample. The strongest risk factor in predicting female criminality was the paternal factor, i.e. absence of the father (p=0.0008) The percentage of criminal girls in families in which the father was absent and in families in which the father was present were 2.8% and 1.0%, respectively. None of the other risk factors used in this model were significant predictors of outcome of female criminality in the category of absent father families. However, a trend that maternal young age at the time of delivery predicted criminality was noted, the cumulative incidence of criminal girls being 6.6% among daughters of mothers under the age of 20 (p= 0.10).

In families in which no paternal risk existed, maternal smoking during pregnancy segmented the data sample into two subsets (p= 0.005). Further, among smoking mother families, the daughters' criminality rates were up to 7.2% elevated when the pregnancy was unwanted or mistimed (p= 0.01).

A logistic regression analysis of risk for criminal offending among females was performed. The potential exposure variables used were birth order, wantedness of pregnancy, maternal smoking during pregnancy, father's absence, perinatal risk and maternal age at birth. The major finding was that the paternal absence during childhood increased the daughters' risk for criminal offending up to 2.5-fold (OR 2.5; 95% CI 1.4-4.3). Of the maternal risks, only maternal smoking during pregnancy was statistically significantly associated with later criminality of the daughter (OR 1.8; 95% CI 1.0-3.3). Further, if the female offspring was the firstborn or in her primary family, the criminality risk was 2-fold (OR 2.2; 95% CI 1.1-4.4).

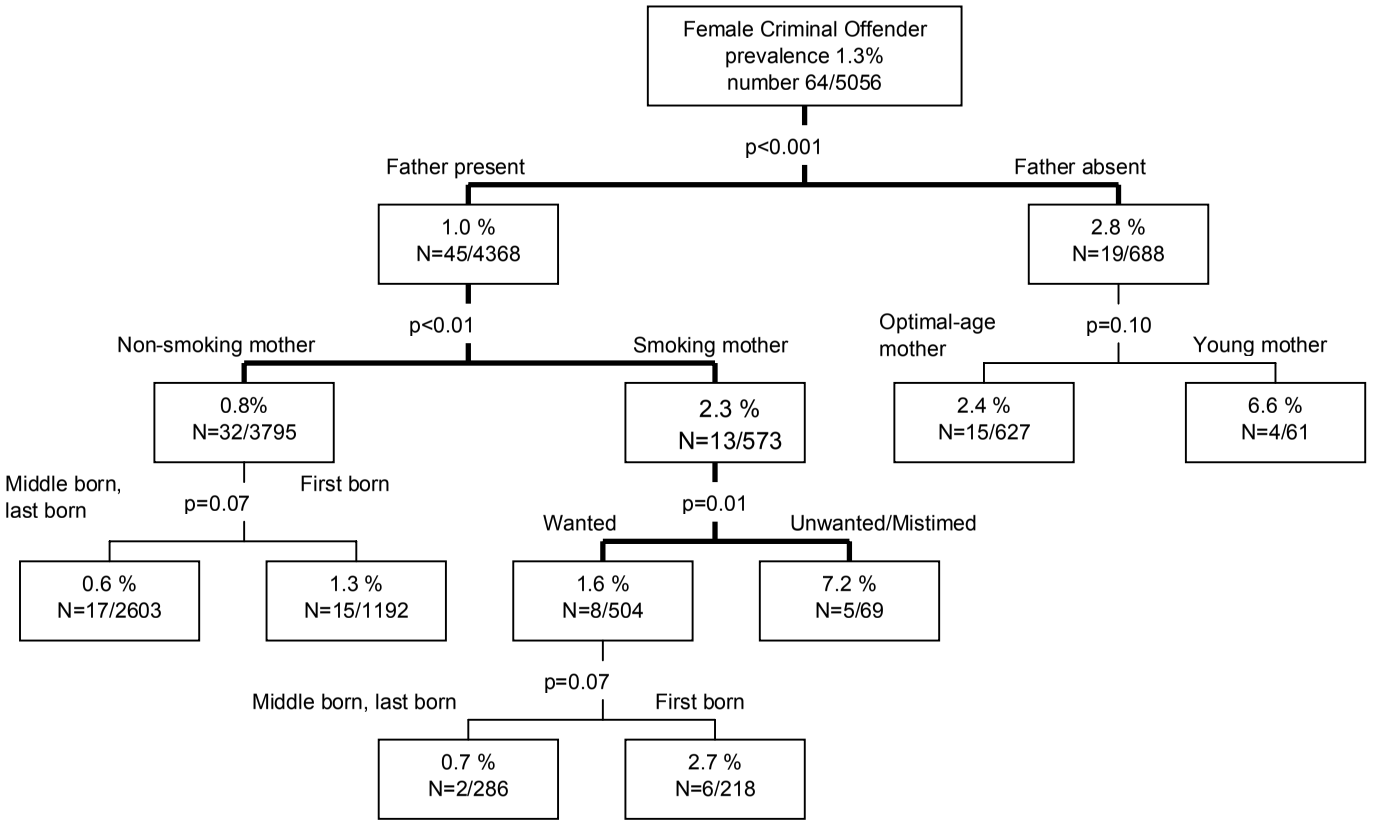

Fig. 4 A chi-squared automatic interaction detection analysis (CHAID) flowchart of the best segmentation for the prediction of female criminality in the Northern Finland 1966 Birth Cohort.

6 Discussion

6.1 Discussion of the results

6.1.1 Parity and mental disorders (I)

The main finding of this study was that grand multiparity (GMP) was not associated with later schizophrenia but was related to other psychoses and hospital-treated non-psychotic depressions in adulthood. Alcoholism was also more common among the offsprings of GMP mothers but this result did not reach statistical significance.

If our results can be replicated, there may be some theoretical explanations for linking grand multiparity and mental disorders. Psychological or biological factors can be associated with the elevated risk for later psychoses and depressive disorders. Firstly, some adverse factors not identified here may be linked with GMP families. Mothers of large families may be stressed and therefore incapable to provide psychological support equally for all of their children. Those families may also have more financial problems than non-GMP families even in the Nordic welfare states where large families receive economic support. In a recent study, Kahn *et al*. (2000) pointed out that women of low of social class with young children were at substantially high risks of depression and poor health. According to Brown & Harris (1978), one vulnerability factor of depression in women was if there were several children under the age of 14 living at home. Further, maternal depressive syndromes are known to be associated with later depressive syndromes of a child (Shiner & Marmorstein 1998). In the present study 26.7% of the GMP mothers and 12.3% of the non-GMP mothers were depressed during pregnancy. It can be speculated that the depression of the mother contributed to the depression of the child.

Paternal factors may also be associated with our results. In a recent study by Malaspina *et al.* (2001), advancing paternal age had been pointed out to be a risk factor of up to 2.8-fold for later psychotic disorders of a child. According to the authors, the elevated risk was not explained by the age of the mother, suggesting mutations arising in paternal germ cells to being related to later psychoses and schizophrenia of a child.

Furthermore, an association between common infections in early childhood and adulthood psychoses can only be speculated. According to Torrey & Yolken (1998), exposure to infectious agents, which are more common in big families, may be a risk factor for psychotic disorders.

In conclusion, some association between a mother's GMP-status and later hospital treated mental disorders of a child was noted. Yet, the vast majority of such children managed without treatment in psychiatric hospitals. Generalization of the results to persons suffering from non-psychotic disorders but receiving treatment outside the hospital remains uncertain. Further, the explanations remained highly speculative suggesting maternal parity or other factors unidentified here to be associated with the aetiology and developmental pathways of psychoses and depression.

6.1.2 Birth order and risk for schizophrenia (II)

In this study, the association between birth order and later schizophrenia was confirmed. The main finding was that the risk for schizophrenia in adulthood was elevated up to 1.5-fold among firstborn sons. On the contrary, the risk was lower than expected among lastborn sons.

Previously, some studies have also supported the over-representation of firstborns and lastborns (Goodman 1957, Schooler 1964, Solomon & Nuttal 1967, Barry & Barry 1967, Erlenmayer-Kimling 1969), but due to methodological limitations of those studies discussed in detail by Prize & Hare (1969), the results have not been replicated in further studies leaving the association between birth order and schizophrenia open. Most of these studies were large samples of hospital treated schizophrenia patients with different ages. Further, they failed to take into account changes of birth rates and family sizes and other background variables associated with birth order.

Recently, a methodologically sound study by Bender *et al.* (2000) also supported the over-representation of firstborn sons among schizophrenia patients. The observed number of schizophrenia cases among firstborns was 2.7 times higher than the expected number, being statistically significant. The authors speculated whether season of birth, obstetric risk, viral infection or psychological stress might be explanations of the association. Yet, they were unable to test these hypotheses.

In the present study the possibility to explore the confounding by perinatal complications, maternal age at delivery, wantedness of pregnancy, number of siblings and family type was the main advantage of the study.

The under-representation of schizophrenia cases in a specific birth order has not been supported in previous literature. Interestingly, the elevated risk for schizophrenia was not associated with birth order among female patients. On the contrary, the risk for later schizophrenia was lower than expected among daughters belonging to the middle status (i.e. not first, not last, not only child).

How can the results be explained? It is obvious that if a birth order status has a causal role in schizophrenia it is by no means a necessary condition for the disorder. More probably it indicates only one aspect of a multi-factorial aetiology. Identifying the true causal factors remains problematic. It is possible that the results are a statistical artefact

and a chance phenomenon, although statistical testing suggests the rejection of the null hypothesis. Although the number of females was low, boosted by a large study sample, the study does give, however, reasonable statistical power to the primary analyses although some confidence limits come close to unity.

It is also possible that residual confounding by unknown and unobserved variables may account for the findings. It is worth considering that the variables of perinatal events used in the present study controlled only major mishaps, not minor ones, probably more prevalent among firstborns than laterborns.

If the association does indicate causation, explanations may be either biological or psychological. However, an elevated risk among firstborns is not in accordance with the common infection theory introduced by Sham *et al.* (1993) and Westergaard *et al.* (1999). This association should show an increased risk for schizophrenia among subjects with siblings a few years older (Sham *et al.* 1993). Further, it is tempting to speculate that the association between birth order and elevated risk for schizophrenia could be linked to psychological stress.

Furthermore, there is also potential for other biological or psychological interactions between birth order and family size. Both firstborn and lastborn children are usually considered to have a special position in the family, while children born in the middle have less status (Lester 1989). Maybe lastborn children in the family are pampered and the expectation of the parents are not so high. It is possible that especially firstborn sons, have a special and conflicting position in some families (Sethi & Gupta 1971). It is also possible, that boys are treated with much indulgence during childhood and on the contrary girls are soon encouraged to shoulder responsibility. This may change during adolescence, when the eldest sons are expected to take over responsibilities (Stompe *et al* 1999). Further, it is possible that in some cultures parents prefer their firstborn child to be a boy (Williamson 1976). They can be targets for ambitious parental attitudes, which can be too hard to follow for fragile individuals. It means a lot to lose that special position of care and privilege by the birth of a younger sib. However, being the firstborn or lastborn may bring its own stresses that may independently associate with schizophrenia. It is also possible to speculate that sons and daughter are treated differently, irrespective of whether firstborn or lastborns.

In conclusion, the main finding was that the risk for later schizophrenia was significantly elevated among firstborn sons. On the contrary, the risk was lower among lastborn males and females belonging to the middle group status. The associations were specific only for schizophrenia, not any other psychoses. These results are in support of environmental stress-hypotheses suggesting a multi-factorial aetiology and developmental pathway for schizophrenia as discussed in detail in the original paper V. However, assessing the true causal relations remains an open question.

6.1.3 Birth order and criminality (III)

The main finding was that the risk of violent crimes later in life was elevated among males, who were only children in the childhood family. When perinatal risk, identified as low birth weight, preterm birth or perinatal brain damage, was combined with the only child position, the risk increased up to 4-fold. Furthermore, maternal risk, identified as an age at birth of under 20 and a negative attitude towards the pregnancy, increased the risk up to 6-fold and combined with paternal absence as even as high as 8-fold. Interestingly, paternal absence during childhood was the strongest combined risk factor being double that of the perinatal risk.

Previously, Virkkunen *et al*. (1996) have also reported that paternal absence through divorce during childhood was associated with later criminality among males. They pointed out that the percentage of absent fathers among recidivist was about 3-fold higher than non-recidivists. A novel finding in the present study was, however, that paternal absence among only children resulted in an eightfold greater risk for violent offending, but increased the risk for non-violent offending much less. Further studies are required to confirm whether the association between paternal absence and later violent criminality of a male child is correlated with paternal genetic factors or environmental risks. It can be supposed that fathers suffering from antisocial personality disorders might perhaps more often be absent from home and that therefore genetic associations could, in part, explain our findings. However, Lahey *et al*. (1999) proposed that genetic influences would exert only indirect effects on the antisocial behaviour of a child.

In the present study (III), also maternal risks together with being the only child predicted significantly violent but not non-violent offending. It is possible, that this effect may be linked to the fact that a solo mother's capacity to contribute to the development of her child's sense of justice is impaired. A novel finding in the present study was, however, that the mother's negative attitude towards the pregnancy and/or young age among the only children in the family increases also the risk for violent offences in adulthood.

Earlier, some perinatal biological risks have been found to be related with adult violent behaviour (Farrington 1978, Sheline *et al.* 1994). This study not only confirms the previous result, but also highlights the effect of psychological risks (unwantedness, solo mother and lack of siblings) during the perinatal period in predicting violent but not non-violent offending later in life. A secure, loving and supportive family environment is known to be highly effective in teaching social learning of a child (Fernald *et al.* 1997). In addition, the solo mothers of the only children need special support of both somatic and psychosocial nature in maternity clinics, so that violent behaviour in childhood as well as adulthood can be prevented or at least minimized.

6.1.4 Early family predictors of female criminality (IV)

The main finding of this study was that the strongest risk factor in predicting female criminality, either violent or non-violent, proved to be the absence of the father in the original, childhood family. A similar finding was earlier reported in this thesis (III) in relation to males. In addition, in the families where the father was present, maternal smoking during pregnancy and being a firstborn doubled the risk of criminal offending of the daughter. In families, in which the father was present, maternal smoking during pregnancy together with being born unwanted increased the prevalence for criminal offending significantly up to 7.2%.

Interestingly, maternal smoking during pregnancy was the only biological risk factor associated with later criminal offending and none of the other perinatal biological risk factors used in this study were significant predictors of female criminality. Furthermore, in this study perinatal complications were not significantly associated with later criminality. Previously, perinatal complications were shown to be associated with violent criminality among males, but only if linked with the only child status (III). Thus, long-term effects of perinatal complications among females might be different. This could be due to different genetic and perinatal vulnerabilities of girls and boys, boys being more vulnerable. However, due to the low number of violent females in the Cohort the sub-classification of female criminals into non-violent and violent was not possible. If the relation between perinatal complications and criminality is specific for violent behaviour, it is natural that the association was not found in this study among females.

Recently, Conseur *et al.* (1997) have shown that young maternal age was an important risk factor for criminality among females. Girls born to mothers younger than 18 years of age were 2.2 times more likely to be offenders and 2.8 times more likely to become chronic offenders, than daughters born to mothers aged between 20-24 years. Several other studies have also indicated that unmarried and teenage mothers have difficulties in attaching to and nurturing their infants (Crnic *et al.* 1983, Culp *et al.* 1988), which leads to poor parenting and inadequate supervision (Hechtman 1989). However, in this study (IV), maternal age was selected into the statistical model (CHAID) only if the father was absent from the family. An increase of criminal daughters to over 6% was noted in those families in which a father was present and the mother was young, but due to the small number of female criminals only a trend towards criminality and not actual significance existed. Since young maternal age increased the proportion of criminal daughters only together with a father's absence, this finding might be associated with worse cognitive and affective skills of young mothers, as is discussed by Trad (1995), to alone contribute to the development of a young mother´s child's sense of justice. According to Jones *et al.* (2000) the highest level of delinquency is usually associated with lower levels of both paternal acceptance and firm maternal control. Thus, mothers' and fathers' parenting styles together may matter the most and not simply the existence of both parents in the childhood family.

Some studies have noted an association between unwanted pregnancy and later criminality (Rantakallio *et al.* 1992a, Raine *et al.* 1994) and in many studies maternal smoking during pregnancy has also been linked with later criminality, especially among males (Rantakallio *et al.* 1995, Ferguson *et al*. 1998, Brennan *et al*. 1999, Räsänen *et al.* 1999). However, in this study such an association was demonstrated also among females.

Earlier Ferguson *et al.* (1998) found an association between maternal smoking during pregnancy and conduct disorder symptoms among females, but it was markedly milder than among males. Maternal smoking during pregnancy may be symptomatic of an antisocial lifestyle of the mother that might exert an effect on the daughter and increase later criminal behaviour of hers (Rantakallio *et al.* 1992a). It might also be a symptom of severe psychological disturbance in the mother-child relationship. As noted previously in a study of the Northern Finland 1966 Birth Cohort, women who smoked during pregnancy may be to some extent badly off socially (Isohanni *et al.* 1995). Further, the effect of smoking during pregnancy could be biological, like, for example, causing reduced serotonin uptake (King *et al.* 1991) and cause alterations in dopaminergic neurons in the foetal brain due to nicotine exposure (Fung & Lau 1989, Richardson & Tizabi 1994).

Previously, observations by Virkkunen *et al*. (1996) pointed to an association between paternal absence and criminality among males but the present finding that paternal absence was the strongest risk factor predicting later criminality of a girl is novel. The percentage of absent fathers among recidivist was about 3-fold higher when compared with non-recidivists. It can only be speculated whether the effect of a missing father is correlated with paternal genetic factors or environmental risks. The role of the father in causing delinquency is likely to be greater than that of the mother's. Distance from the father may be more predictive of antisocial behaviour than distance from the mother (Johnson 1987).

In summary, the prospectively collected Northern Finland 1966 Birth Cohort enabled me to investigate preceding perinatal biological and psychosocial risk factors in predicting female criminal offending in adulthood. Because female criminality is rather rare and no extensive exposures exist, further studies with larger databases are needed to define the complex associations between predicting factors during pregnancy, perinatal period and later impulsive behavioural problems of female offspring.

6.2 Theoretical discussion

6.2.1 Descriptive life span model (I-V)

The present study focuses on early childhood family factors and later mental disorders (I, II, V) and criminality (III, IV) based on both biological and psychosocial aspect of the family. Both schizophrenia and criminality can be regarded as the endpoints of adverse outcomes started partly already during the early perinatal period. When compared with schizophrenia, research traditions of seeing criminal behaviour as a part of a person's life span development are shorter and moreover criminal outcomes are more difficult to define.

Empirical studies of the developmental pathway embracing schizophrenia of all aspects of a person's life course have been carried out suggesting that genetic, environmental, individual and social contexts interact in the genesis and developmental trajectory of schizophrenia. To consider any one without the others is going to generate neither a realistic nor a valid aetiological model of schizophrenia (Jones 2001). In original publication V, the main risk factors of schizophrenia are reviewed and a descriptive life-span model constructed.

Psychosocial risk factors in the childhood family have been the main focus for the present thesis. The firstborn status was found to be associated with an elevated risk of schizophrenia (II), but maternal GMP was not (I). The risk of developing schizophrenia later was higher than expected among firstborn sons, but lower than expected among lastborn sons. On the contrary, the risk of later schizophrenia was decreased among daughters being in the middle of the family. In my opinion the firstborn status might be regarded as a stressful position in the family with multiple psychosocial expectations towards a male child, which can be hard for a child who is vulnerable to major mental disorders. The causality is, however, complex and needs further investigation. The level of stress, which may become unbearable to a vulnerable person, may appear normal to others.

Some biological and other psychological adverse factors during pregnancy and early childhood are known to be associated with later schizophrenia. Of the biological factors in this Cohort, perinatal risk (Jones *et al.*1998) and childhood central nervous system infections (Rantakallio *et al.* 1997) were found to be associated with the elevated risk for schizophrenia. Further, in this Cohort being born from an unwanted pregnancy (Myhrman *et al.* 1996) and maternal antenatal depression (Jones *et al* 1998) as maternal psychological risk factors were also found to be associated with later schizophrenia. For example stress for a mother due to the unexpected death of a spouse, has been found to be associated with an elevated the risk for schizophrenia of the child (Huttunen & Niskanen 1978). Of the psychosocial risk factors, communication problems in the family (Wahlberg *et al.* 1997) and disturbance in the parent-child relationship (Jones *et al*. 1994) have also been shown to be associated with schizophrenia later in life.

A descriptive aetiological model of schizophrenia is presented in Figure 5. This comprehensive life-course model is based on the reviewed literature and previous studies of risk factors of schizophrenia in this Northern Finland 1966 Birth Cohort and the present thesis. This figure is modified from Figure 1 in the original paper V by adding to

the model the findings of this thesis (II) in bold letters. The model is divided into pregnancy, premorbid period, prodromal period ending in the clinical course of schizophrenia. Biological and psychosocial predicting factors during the pregnancy and early childhood are stressed. The findings from this cohort and from previous other notable studies show that some young adults destined to develop schizophrenia show deficits in motor, cognitive, and social performance long before they have psychotic symptoms; some abnormalities are present in very early life. In addition, some hypothetical and speculative ideas on protective factors, which are not evidence-based are also proposed, for example normal pregnancy and delivery and good parent-child relationship.

One can easily criticize the value of this kind of model. The descriptive model proposed gives minimal aid to clinical decision-making. The model may not be very heuristic for an experienced scientist - who may, and who already has built a model of his/her own - but it may help young investigators to orient with the topic and literature, localise their research interest, place their hypotheses and results within a framework, and communicate with other scientists.

Both biological and psychosocial family risk factors are also known to predict criminality and/or violent behaviour of a child and formulate the developmental pathway at the beginning of a person's life span to those adverse outcomes. Genetic aetiology of violent criminality is supported by many studies (Cadoret *et al.* 1997, Alsobrook & Pauls 2000). Further, perinatal complications have been found to be associated with criminality (Pasamanic *et al.* 1956, Lewis *et al* 1979) as well as maternal smoking during pregnancy (Rantakallio *et al*. 1992a, Räsänen *et al.* 1999) and so has being born unwanted (Rantakallio *et al.* 1992a). Maternal young age at delivery and being unmarried (Conseur *et al.* 1997) are also known to be associated with an elevated risk for later criminality.

How could childhood factors create an increased risk for later criminality? It is possible that the effects may be indirect, in which case factors in the family are markers for others, maybe more important factors, or direct, in which case these factors form a causal pathway of criminality or both. However, further studies of criminal behaviour, using large and unbiased study samples of both males and females need to be carried out in order to formulate an evidence based descriptive life span model of criminal behaviour.

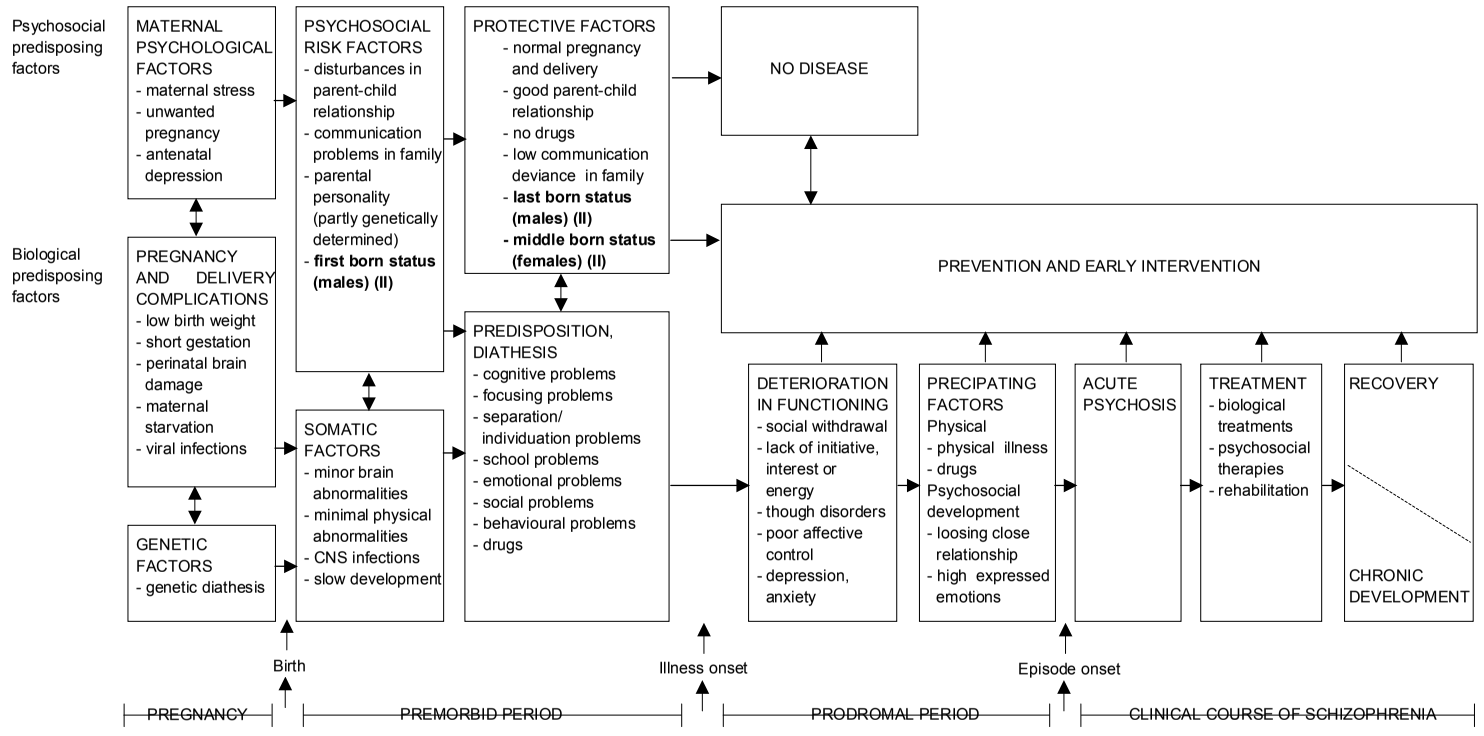

Fig. 5. Life span development model of schizophrenia (modified from original study V). Factors identified in this thesis (II) are presented in bold letters.

6.3 General discussion

6.3.1 Strengths of the study

The major strength of the present study comes from its data sources. The study was based on the unselected general population birth cohort including 96% of all births (N=12 068) in 1966 that occurred in the provinces of Lapland and Oulu. Data on biological, socioeconomic and health conditions, living habits and family characteristics of cohort members were collected prospectively since pregnancy (Rantakallio 1988). This makes analysis of intervening and confounding factors possible. Boosted by a large study sample, the study gives reasonable statistical power for primary analyses although main outcomes (hospital-treated mental disorders and criminality) were rather rare.

The data on hospital-treated mental disorders of the cohort members have been collected from the Finnish Hospital Discharge register (FHDR). The FHDR covers all mental and general hospitals as well as bed wards of local health centres, military wards, prison hospitals and private hospitals. The accuracy of transfer between hospital case records and the FHDR has been shown to be good (Poikolainen 1983, Keskimäki & Aro 1991).

In the Cohort all case records have been scrutinized and diagnoses have been carefully validated for the DSM-III-R criteria. Interrater reliability had been good with kappa values from 0.6-0.9 (Isohanni *et al.* 1997).

Previous birth order studies have been blamed to have serious methodological limitations concerning birth rates and family size as highlighted by Price & Hare (1969). In this cohort study design with available data on confounding factors, these limitations were partly avoided.

Data on registered criminal behaviour of the cohort members to the end of 1998 were collected from computerized files maintained by the Ministry of Justice. This national register includes records of all crimes known to the police committed anywhere in Finland and it is therefore representative.

6.3.2 Limitations of the study

The association between childhood family variables and later severe hospital-treated mental disorders and criminality have been investigated in a large population sample. The data have been collected prospectively. However, due to the large study sample only part of the potential confounders can be assessed as is the case with most large population-based samples.

In the study of grand multiparity and later mental disorder of the child (I), the follow-up period up to the age 28 may be biased towards the inclusion of more severe forms of disorders. Therefore, the results are relevant with regard to disorders that occurred at a fairly young age at onset. Further, there are many large families in Northern Finland due to religious reasons and, therefore, maybe religious background can be reflected in the results. However, any exact data about the religious background were not available.

Furthermore, only hospital-treated mental disorders were taken into account. In Finland the vast majority of schizophrenia and other psychoses are treated in some phase of a person's life in a mental hospital, and are thereby included in the FHDR. Thus, schizophrenia cases in this study sample were representative, but non-psychotic cases highly selected. We were missing the data on possible treatment as outpatients of other diagnostic entities, who are more likely to be treated outside the hospital (Isohanni *et al.* 1997). Therefore, generalizations of the results to include the non-psychotic majority treated outside hospital have to be made with caution.

Tienari *et al.* (2000) have recently demonstrated interactions between genetic and environmental factors in the development of schizophrenia. In the study of birth order and schizophrenia (II), data on genetic factors and family aspects were not available. Although the number of schizophrenia cases was large (100), stratification led to a limited statistical power for some comparisons. Furthermore the database did not allow the use of such sibship characteristics as age intervals or gender. Further, birth order alone was too robust a measurement in explaining the later mental disorder of a child without the information on other factors of social characteristics of the family.

In the original study III the only child status was robust alone to explain the elevated risk of later criminality in a male child. Similarly the data on social relations of the only child would have been needed. Further, more information was needed on socio-demographic factors and mental health status of the parents. Furthermore, to be raised alone without other siblings and a biological father present does not mean that the only child is without positive experiences of other persons in learning social skills.

In a study of female criminals (IV) neither biological nor psychosocial information was available from absent fathers. Furthermore, it was not known weather the fathers who were present represented "more decent types" than the absent fathers. All explanations of the associations are therefore highly speculative and the findings need replications. Any future studies, however, should aim at a detailed analysis of the paternal factors.

7 Conclusions

7.1 Main results

This study showed that when the cohort member was born to a mother, who had undergone at least six deliveries (GMP), the risk of being treated in a psychiatric hospital in adulthood was elevated. The risks for psychoses other than schizophrenia (OR 2.3; 95% CI 1.2-4.7) and for depressive disorder (OR 2.2; 95% CI 1.0-4.5) were statistically significantly higher than in adult offspring whose mother had fewer children. However, the vast majority of such children managed without treatment in a psychiatric hospital during the follow-up period up to age 28 (I).

During the follow-up period (between ages 16-31) birth order was associated with adult schizophrenia. The risk of schizophrenia was elevated among firstborn sons (ratio 1.5; 95% CI 1.0-2.2), but lower than expected among lastborns (ratio 0.7; 95% CI 0.5-0.9). Among females, birth order was not associated with an elevated risk for the schizophrenia. On the contrary, the risk for schizophrenia was lower than expected (ratio 0.6; 95% CI 0.3-0.9) when the daughter grew up in the middle of the family (not only child, not first and not last) (II).

Up to the age of 31 the risk of violent offending was significantly elevated among males who were the only children in the primary family (OR 1.8; 95% CI 1.1-3.0). Combining the only child status with perinatal risks, the odds ratios for violent crimes increased up to 4-fold (OR 4.4; 95% CI 1.9-10.8), with maternal risks up to 6-fold (OR 5.9; 95% CI 3.1-11.3) and with paternal risk even over up to 8-fold (OR 8.4; 95% CI 3.9-18.1). Interestingly, the only child position in the family was not at risk for non-violent offending, except in cases were the father was absent during the cohort members childhood (OR 2.5; 95% CI 1.0-5.9) (III).

Among female cohort members before the age of 31 the strongest risk factor in predicting criminality was the absence of the father during childhood. The percentage of criminal daughters in the families in which the father was absent and in the families were the father was present were 2.8% and 1.0%, respectively. In the families were the father was present, maternal smoking during pregnancy predicted later criminality of a daughter. The percentage of criminal daughters in the families where the father was present and the mother was smoking was 2.3% compared to 0.8% of criminal daughters

in the reference population. Further, in those families where the father was present and the mother was smoking, the percentage of later criminality among girls who were born unwanted was 7.2% compared with 1.6% born from wanted pregnancies (IV).

7.2 Clinical and practical implications

The majority of the children born to big families seemed to be mentally healthy; at least not treated in a mental hospital. However, in this study some adverse risk factors due to the position in a big family were found. In explaining these findings, parents may be stressed and therefore unable to provide psychological support to their children. It is also possible that large families may have more financial problems. Mothers may be tired and stressed and therefore children, especially if there are many of them to take care of may lack maternal support. Probably, social and economic support might prevent or at least decrease some problems connected with large families.

Being the firstborn son of the family may be more stressful and might predict schizophrenia when compared with other positions in the sibship. Yet, the true causality of the phenomenon remains open. The first delivery is a unique happening, with possibly unexpected consequences. There may exist some other, herein, unidentified biological and psychological risks associated with the first delivery, which can also have different consequences for boys and girls. Adequate medical treatment during the delivery as well as the perinatal period is obviously always of great importance.

The association between the only child status and the increased risk of later violent criminality among boys partly breaks up the ”ideal picture” of a family with a mother, a father and one child. To be the only child in the family may to be related to being raised alone with a young mother, who may herself have many social problems. The early detection of those mothers at the maternity clinics and special support of both a somatic and psychosocial nature may prevent violent offending of the child or at least minimize it.

It seems in the light of these results, that maternal smoking during pregnancy should be taken into account very seriously. In addition to the adverse somatic outcomes for the mother, smoking during pregnancy can nowadays be considered to have negative psychological consequences i.e. violent and other aggressive behaviour in the child to be born.

7.3 Implications for future studies

This study was conduced in order to analyse early childhood family predictors and mental disorders and criminality in adulthood. It revealed some associations between early family environment and adult mental disorders and criminality only among a minority of Cohort members, and the odds were not so high. Although the database is unique and prospectively collected, making analysing the confounding factors possible, the variables describing family factors were limited. Further, identifying the true causal factors remained problematic. It is also possible that residual confounding by unknown and unobserved variables may have accounted for the findings.

In this study, only risk factors associated with the outcomes were investigated. Future research should also aim at the meaning of such positive effects as maternal attachment to the child, interaction between siblings and a successful father-child relationship. Further studies should also aim at genetic factors, for which data were not available. The multiplicity of family-environmental factors should be studied in more detailed. The meaning of siblings in the social learning process and the bringing up of only children should also be investigated. Furthermore, it was possible to study only the Cohort members, although it would have been of great interest to study the siblings as well. For example, what would the role of the second eldest child in the family when the firstborn child suffered from schizophrenia in later life?

For the present it was possible only to represent a model, which is surely not considered heuristic. In the future, it might even be possible to present a more sophisticated quantitative model, which can link the diverse factors associated with schizophrenia. Then, single statistical indices from the study of individual risk factors identified in the Cohort shall be used as building blocks for a large structure, which is more explanatory in orientation than purely descriptive. Furthermore, a descriptive life-span model of criminality should be developed.

Further, as a part of the 33-year follow-up of the Northern Finland 1966 Birth Cohort it will be investigated to what extent, in an unselected population sample, schizophrenia and other psychoses are associated with structural brain abnormalities, and in which regions in the brain these patho-morphologies exist. This will be done using structural MRI scans with which an extensive cognitive test battery is combined. The predictive (gender, genetic risk, pregnancy and obstetric complications, delayed development, childhood CNS infections, low IQ) and associative (clinical features, cognitive disability) factors for these brain abnormalities will be identified. In addition to schizophrenia, these associations will be investigated also amongst other psychoses.

8 References

Agresti A (1990) Categorial data. John Wiley & Sons, New York.

Alanen YO (1997) Schizophrenia - its origins and need-adaptive treatment. Karnac Books, London.

Alsobrook JP & Pauls DL (2000) Genetics and violence. Child Adolesc Psychiatr Clin N Am 9: 765-776.

Barry H III & Barry H Jr. (1967) Birth order, family size and schizophrenia. Arch Gen Psychiatry 17: 435-440.

Baskett TF (1977) Grand multiparity - a continuing threat: a 6-year review. Can Med Assoc J 116: 1001-1004.

Bender KG, Azeem N & Morrice J (2000) Schizophrenia and birth order in Pakistan. Schizophr Res 44: 113-120.

Birtchnell J (1972) Birth order and mental illness – A control study. Soc Psychiat 7: 167-179.

Brennan PA, Grekin ER & Mednick SA (1999) Maternal smoking during pregnancy and male criminal outcomes. Arch Gen Psychiatry 56: 215-219.

Breslow NE & Day NE (1987) Statistical methods in cancer research, Volume 2. The Design and Analysis of Cohort Studies. International Agency for Research on Cancer, Lyon, p 103-106.

Brown GW & Harris T (1978) Social origins of depression. A study of psychiatric disorder in women. University Printing House, Cambridge UK.

Burton A & Bird IW (1963) Family constellation and schizophrenia. J Psychol 55: 329-336.

Böök JA & Rayner S (1953) A genetic and neuropsychiatric investigation of a North-Swedish population. Acta Genet, Basel 4: 1-100.

Cadoret RJ, Leve LD & Devor E (1997) Genetics and aggressive and violent behaviour. Psychiatr Clin North Am 20: 301-322.

Cantor-Graae E, McNeil TF, Sjöström K, Nordström LG & Rosenlund T (1997) Maternal demographic correlates of increased history of obstetric complications in schizophrenia. J Psychiatr Res 31: 347-357.

Conseur A, Rivara FP, Barnoski R & Emanuel I (1997) Maternal and Perinatal risk factors for later delinquency. Pediatrics 99: 785-790.

Crnic KA, Greenberg MT, Ragozin AS, Robinson NM & Basham RB (1983) Effects of stress and social support on mothers and premature and full-term infants. Child Dev 54: 209-217.

Culp RE, Appelbaum MI, Osofsky JD & Levy JA (1988) Adolescent and older mothers: comparison between prenatal maternal variables and newborn interaction measures. Infant Behav Dev 11: 353-362.

DeLisi LE (1997) The genetics of schizophrenia: past, present, and future concept. Schizophr Res 28: 163-175.

Durant HR, Gettes AG, Cadenhead C & Woods ER (1995) The association between weapon carrying and the use of violent among adolescents living in and around public housing. J Adolesc Health 17: 376-380.

Elliott BA (1992) Birth order and health: major issues. Soc Sci Med 35(4): 443-452.

Erlenmeyer-Kimling L (1969) The problem of birth order and schizophrenia: a negative conclusion. Br J Psychiatry 115: 659-677.

Erlenmeyer-Kimling L (1970) Birth order of schizophrenics. Br J Psychiatry 116:124-125.

Ernst C & Agnst J (1983) Birth order, its influence on personality. Springer-Verlag, Berlin Heidelberg.

Eronen M, Hakola P & Tiihonen J (1996) Mental disorders and homicidal behavior in Finland. Arch Gen Psychiatry 53: 497-501.

Falbo T (1984) The single-child family. Guilford Press, New York.

Farina A, Barry H & Garmezy N (1963) Birth order of recovered and non recovered schizophrenics. Arch Gen Psychiatry 9: 224-228.

Farrington DP (1978) The family background of aggressive youths. Book Suppl J Child Psychol Psychiat 1: 73-93.

Fehlow P (1973) Über die Ursachen und forensische Begutachtung von Sexualdelikten. Psychiatr Neurol Med Psychol 25: 535-544.

Fergusson DM, Woodward LJ & Horwood J (1998) Maternal smoking during pregnancy and psychiatric adjustment in late adolescence. Arch Gen Psychiatry 55: 721-727.

Fernald LC, Ani C & Gardner JM (1997) Aggressive behaviour in children and adolescents. Part I: A review of effects of child and family characteristics. West Indian Med J 46: 100-103.

Funahashi T, Ibuki Y, Domon Y, Nishimura T, Akehashi &, Sugiura H (2000) A clinical study on suicide among schizophrenics. Psychiatry Clin Neurosci 54: 173-179.

Fung Y & Lau Y (1989) Effects of prenatal nicotine exposure on rat striatal dopaminergic and nicotinic systems. Pharmacol Biochem Behav 33: 1-6.

Geddes JR & Lawrie SM (1995) Obstetric complications and schizophrenia: a meta-analysis. Br J Psychiatry 167: 786-793.

Goodman N (1957) Relation between maternal age at the parturition and incidence of mental disorder in the offspring. Br J Prev Soc Med 11: 203-213.

Granville-Grossman KL (1966a) Parental age and schizophrenia. Br J Psychiatry 112: 899-905.

Granville-Grossman KL (1966b) Birth order and schizophrenia. Br J Psychiatry 112: 1119-1126.

Gregory I (1959) An analysis of family data on 1,000 patients admitted to a Canadian mental hospital. Acta Genet, Basel, 9: 54-96.

Hallgren B & Sjögren T (1959) A clinical and genetico-statistical study of schizophrenia and lower grade mental deficiency in a large Swedish rural population. Acta Psych Neurol Scand suppl 35: 140.

Hare EH & Price JS (1970) Birth rank in schizophrenia: With a consideration of the bias due to the changes in birth rate. Br J Psychiatry 116: 409-420.

Hechtman L (1989) Teenage mothers and their children: risks and problems: A review. Can J Psychiatry 34: 569-575.

Horton AM Jr & Whitesell L (1979) Prediction of recidivism by sex and number of siblings. Psychol Rep 45: 98.

Hultman CM, Sparen P, Takei N, Murray RM & Cnattingius S (1999) Prenatal and perinatal risk factors for schizophrenia, affective psychosis, and reactive psychosis of early onset: case-control study. BMJ 318(7181): 421-426.

Huttunen M & Niskanen P (1978) Prenatal loss of father and psychiatric disorders. Arch Gen Psychiatry 35: 429-431.

Isohanni M, Oja H, Moilanen I, Koiranen M & Rantakallio P (1995) Smoking or quitting during pregnancy: associations with backgroud and future social factors. Scand J Soc Med 23: 32-38.

Isohanni M, Mäkikyrö T, Moring J, Räsänen P, Hakko H, Koiranen M, Partanen U & Jones P (1997) A comparison of clinical and research DSM-III-R diagnoses of schizophrenia in a Finnish national birth cohort. Soc Psychiatry Psychiatr Epidemiol 32: 303-308.

Isohanni M, Jones P, Kemppainen L, Croudace T, Isohanni I, Veijola J, Räsänen S, Wahlberg KE, Tienari P & Rantakallio P (2000) Childhood and adolescent predictors of schizophrenia in the Northern Finland 1966 birth cohort--a descriptive life-span model. Eur Arch Psychiatry Clin Neurosci 250: 311-319.

Israel SL & Blatsar AS (1965) Obstetric behavior of grand multipara. Am J Obstet Gynecol 91: 326-332.

Johnson RE (1987) Mother´s versus father´s role in causing delinquency. Adolescence 22: 305-315.

Jones DJ, Forehand R & Beach SR (2000) Maternal and paternal parenting during adolescence forecasting early adult psychosocial adjustment. Adolescence 35: 513-530.

Jones PB (2001) Schizophrenia: social and environmental factors: implications for aetiology. Curr Opin Psychiatry 14: 39-43.

Jones P & Tarrant CJ (1999) Specificity of developmental precursors to schizophrenia and affective disorders. Schizophr Res 39: 121-125.

Jones PB, Bebbington P, Foerster A, Lewis SW, Murray RM, Russell A, Sham PC, Toone BK & Wilkins S (1993) Premorbid social underachievement in schizophrenia. Results from the Camberwell Collaborative Psychosis Study. Br J Psychiatry 162: 65-71.

Jones P, Rodgers B, Murray R & Marmot M (1994) Child developmental risk factors for adult schizophrenia in the British 1946 birth cohort. Lancet 344: 1398-1402.

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 follow-up of the 1966 Northern Finland general population birth cohort. Am J Psychiatry 155: 355-364.

Juntunen K (1997) Grand grand multiparity. A thesis. Acta Universitatis Ouluensis D 432, University of Oulu.

Järvelin M-R, Mäki-Torkko E, Sorri MJ & Rantakallio PT (1997) Effect of hearing impairment on educational out-comes and employment up to the age 25 years in northern Finland. Br J Audiol 31: 165-175.

Kahn RS, Wise PH, Kennedy BP & Kawachi I (2000) State income inequality, household income, and maternal mental and physical health: cross sectional national survey BMJ 321: 1311-1315.

Kendell RE, McInneny K, Juszczak E & Bain M (2000) Obstetric complications and schizophrenia. Two case-control studies based on structured obstetric records. Br J Psychiatry 176: 516-522.

Keskimäki I & Aro S (1991) The accuracy if data on diagnoses, procedures and accidents in the Finnish Hospital Discharge Register. Int J Health Services 2: 15-21.

King J, Davila-Garsia M, Azimia E & Strand F (1991) Differential effects of prenatal and postnatal ACTH or nicotine exposure on 5-HT high affinity uptake in the neonatal rat brain. Int J Dev Neurosci 9: 281-286.

Kunzel RG (1993) Fallen vomen problem girls: unmarried mothers and professionalization of Social Work, 1980-1945. Yale University Press, New Haven (Conn).

Lahey BB, Waldman ID & McBurnett K (1999) Annotion: the development of antisocial behaviour: an integrative causal model. J Child Psychol Psychiatry 40: 669-682.

Leonhard K (1976) Bedeutung von Geschwisterkonstellationen für die Entstehung systematischer Schizophrenien. Arch Psychiatr Nervenkr 222: 27-45.

Lester D (1989) Suicide in a middle-born child Adolescence 24: 909-914.

Levy J (1931) Quantitative study of behavioural problems in relation to family constellation. Am J Psychiatry 10: 237.

Lewin LM, Davis B & Hops H (1999) Childhood social predictors of adolescent antisocial behaviour: gender differences in predictive accuracy and efficacy. J Abnorm Child Psychol 27: 277-292.

Lewis DO, Shanok SS & Balla DA (1979) Perinatal difficulties, head and face trauma, and child abuse in the medical histories of seriously delinquent children. Am J Psychiatry 136: 419-423.

Lewis DO, Yager CA, Cobham-Portorreal CS, Klein N, Showalker C & Anthony A (1991) A follow-up from the female delinquents: maternal contributions to the perpetuation of deviance. J Am Acad Child Adolesc Psychiatry 30: 197-201.

Loper AB & Cornell DG (1996) Homicide by juvenile girls. J Child and Family Studies 5: 323-336.

Magidson J (1993) SPSS for Windows CHAID, Release 6.0, Chicago, IL: Statistical Innovations.

Malama IM, Papaioannou DJ, Kaklamani EP, Katsouyanni KM, Koumantaki IG & Trichopoulos DV (1988) Birth order sibship size and socio-economic factors in risk of schizophrenia in Greece. Br J Psychiatry 152: 482-486.

Malaspina D, Harlap S, Fennig S, Heiman D, Nahon D, Feldman D & Susser ES (2001) Advancing paternal age and the risk of schizophrenia. Arch Gen Psychiatry 58: 361-367.

McNeil TF & Cantor-Graae E (1999) Does preexisting abnormality cause labor-delivery complications in fetuses who will develop schizophrenia? Schizophr Bull 25: 425-435.

Mednick SA, Machon RA, Huttunen MO & Bonett D (1988) Adult schizophrenia following prenatal exposure to an influenza epidemic Arch Gen Psychiatry 45: 189-192.

Mentzos, Knödler, Pittrich (1972) Die Stellung in der Geschwisterreihe als Umweltfaktor in der Pathogenese endogener Psychosen. Zbl Ges Neurol Psychiatric 204: 119-120.

Miller N & Maruyana (1976) G Ordinal position and peer popularity. J Person Soc Psychol 33: 123-131.

Millon T & Everly GS (1985) Personality and disorders. Wiley, New York.

Moilanen I & Rantakallio P (1988) The single parent family and the child´s mental health. Soc Sci Med 27: 181-186.

Moilanen K, Veijola J, Läksy K, Mäkikyrö T, Miettunen J, Kantojärvi L, Kokkonen P, Karvonen JT, Herva A, Joukamaa M, Järvelin M-R, Moring J, Jones PB & Isohanni M The difference berween true positive and false negative schizophrenia cases in the Northern Finland 1966 Birth Cohort. Submitted manuscript.

Mukherjee K & Kundu S (1961) A study of birth order and family positions of criminals. Indian J Psychol 36: 127-132.

Myhrman A, Rantakallio P, Isohanni M, Jones P & Partanen U (1996) Unwantedness of a pregnancy and schizophrenia in the child. Br J Psychiatry 169: 637-640.

Mäkikyrö T, Isohanni M, Moring J, Oja H, Hakko H, Jones P & Rantakallio P (1997) Is child's risk of early onset schizophrenia increased in the highest social class? Schizophr Res 23: 245-252.

Mäkikyrö T, Sauvola A, Moring J, Veijola J, Nieminen P, Järvelin M-R & Isohanni M (1998) Hospital-treated psychiatric disorders in adults with a single-parent and two-parent family background: a 28-year follow-up of the 1966 Northern Finland Birth Cohort. Fam Process 37: 335-344.

Nelson JH & Sandmeyer MV (1958) A study of 812 grand multiparas. Am J. Obstet Gynecol 75: 1262-1266.

Norusis J (1994) SPSS for Windows. Advanced statistics, Release 6. SPSS Inc. Corp. Chicago.

Pasamanic KB, Rodgers ME & Lilienfeld AM (1956) Pregnancy experience and the development of behaviour disorders in children. Am J Psychiatry 112: 613-618.

Poikolainen K (1983) Accuracy of hospital discharge data: five alcohol-related diseases. Drug and Alcohol Depend 12: 315-322.

Price JS & Hare EH (1969) Birth order studies: some sources of bias. Br J Psychiatry 115: 663.

Raine A, Brennan P & Mednick SA (1994) Birth complications combined with early maternal rejection at age 1 year predispose to violent crime at age 18 years. Arch Gen Psychiatry 51: 984-988.

Rantakallio P (1969) Groups at risk in low birth weight infants and perinatal mortality. Acta Paediatr Scand 193 (suppl): 1-71.

Rantakallio P (1974) The unwanted child. Acta Universitatis Ouluensis D 8, Oulu University Press.

Rantakallio P (1979) Social background of mothers who smoke during pregnancy and influence of these factors on the offspring. Soc Sci Med 13: 423-429.

Rantakallio P (1988) The longitudinal study of the Northern Finland birth cohort of 1966. Paediatr Perinat Epidemiol 2: 59-88.

Rantakallio P, von Wendt L & Koivu M (1987) Prognosis of perinatal brain damage: a prospective study of a one year birth cohort of 12 000 children. Early Hum Dev 15: 75-84.

Rantakallio P, Läärä E, Isohanni M & Moilanen I (1992a). Maternal smoking during pregnancy and deliquency of the offspring: An association without causation? Int J Epidemiol 21: 1106-1113.

Rantakallio P, Koiranen R & Möttönen J (1992b) Association of perinatal events, epilepsy, and central nervous system trauma with juvenile deliquency. Arch Dis Child 67: 1459-1461.

Rantakallio P, Myhrman A & Koiranen M (1995) Juvenile offender, with special reference to sex differences. Soc Psychiatry Psychiatric Epidemiol 30: 113-120.

Rantakallio P, Jones P, Moring J & von Wendt L (1997) Association between central nervous system infections during childhood and adult onset schizophrenia and other psychoses: A 28-year follow-up. Int J Epidemiol 26: 837-843.

Richardson S & Tizabi Y (1994) Hyperreactivity in the offspring of nicotine-treated rats: role of the mesolimbic and nigostriatal dopaminergic pathways. Pharmacol Biochen Behav 47: 331-337.

Rosenbaum JL (1989) Family dysfunction and femaledelinquency. Crime & Delinquency 35: 31-44.

Rothman KJ & Greenland S (1998) Modern epidemiology, 2. ed.. Lippincott, Philadelphia.

Räsänen P, Tiihonen J, Isohanni M, Moring J & Koiranen M (1998) Juvenile mortality, mental disturbances and criminality: a prospective study of the Northern Finland 1966 birth cohort. Acta Psychiatr Scand 97: 5-9.

Räsänen P, Hakko H, Isohanni M, Hodgins S, Järvelin M-R & Tiihonen J (1999) Maternal smoking during pregnancy and risk of criminal behaviour among adult male offsprings in the Northern Finland 1966 birth cohort. Am J Psychiatry 156: 857-862.

SAS Institute (1997) SAS/STAT software: Changes and enhancements though Release 6.12, 6.12 edn. SAS Institute Inc., Cary, NC.

SAS Institute Inc. (1999a) SAS Procedures Guide, Version 8. Institute Inc., Cary, NC, p 1729.

SAS Institute Inc. (1999b) SAS/STAT User Guide, Version 8. SAS Institute Inc., Cary, NC.

Sauvola A (2001) The association between single-parent family background and physical morbidity, mortality, and criminal behaviour in adulthood. Acta Universitatis Ouluensis D 629, Oulu Univerity Press.

Schooler C (1964) Birth order and hospitalization for schizophrenia. J Abnorm Soc Psyhol 69: 574-579.

Schooler C (1972) Birth order effects: Not here, not now. Psychol Bull 78: 161-175.

Sethi BB & Gupta SC (1971) Sibling position in India. Psychiatric and nonpsychiatric patients. Am J Psychother 25: 61-69.

Sham PC, O´Callaghan E, Takei N, Murray GK, Hare EH & Murray RM (1992) Schizophrenia following pre-natal exposure to influenza epidemics between 1939 and 1960. Br J Psychiatry 160: 461-466.

Sham PC, Maclean CJ & Kendler KS (1993) Risk of schizophrenia and age difference with older Siblings. Evidence for a maternal viral infection hypothesis. Br J Psychiatry 163: 627-633.

Sheline JL, Skipper BJ & Broadhead WE (1994) Risk factors for violent behaviour in elementary school boys: have you hugged your child today? Am J Public Health 84: 661-663.

Shiner R & Marmorstein NR (1998) Family environments of adolescents with lifetime depression: associations with maternal depression history Am Acad Child Adoles Psychiatry 37: 1152-1160.

Smith CM & McIntyre (1963) Family size, birth rank and ordinal position in psychiatric illness. Can Psychiatr Ass J 8: 244-248.

Solomon L & Nuttal R (1967) Sibling order, premorbid adjustment and remission in schizophrenia. J Nerv Ment 144: 37-46.

Sorri M & Järvelin MR (1998) Well-being and health. Background to the Northern Finland 1966 birth cohort research. Int J Circumpolar Health 57: 82-83.

Stompe T, Orttwein-Swoboda G, Friedmann A & Chaudhry HR (1999) Sibling orders of schizophrenia patients in Austria and Pakistan. Psychopathology 3222: 281-291.

Suvisaari J, Haukka J, Tanskanen A, Hovi T & Lönnqvist J (1999) Association between prenatal exposure to poliovirus infection and adult schizophrenia Am J Psychiatry 156: 1100-1102.

Tanbo TG & Bungum L (1987) The grand multipara- maternal and neonatal complications. Acta Obstet Gynecol Scand 66: 53-56.

Thomson VD (1974) Family size: Implicit policies and assumed psychological outcomes. J Soc Issues 30: 93-124.

Tienari P, Wynne LC, Moring J, Lahti I, Naarala M, Sorri A, Wahlberg K-E, Saarento O, Seitamaa M, Kaleva M & Läksy K (1994) The Finnish adoptive family study of schizophrenia. Implications for family research. Br J Psychiatry (suppl) 23: 15-19.

Tienari P, Wynne LC, Moring J, Läksy K, Nieminen P, Sorri A, Lahti I, Wahlberg KE, Naarala M, Kurki-Suonio K, Saarento O, Koistinen P, Tarvainen T, Hakko H & Miettunen J (2000) Finnish adoptive family study: sample section and adoptee DSM-III-R diagnoses. Acta Psychiat Scand 101: 433-443.

Tiihonen J, Hakola P, Eronen M, Vartiainen H & Ryynänen OP (1996) Risk of homicidal behavior among discharged forensic psychiatric patients. Forensic Sci Int 79:123-129.

Tiihonen J, Isohanni M, Räsänen P, Koiranen M & Moring J (1997) Spesific major mental disorders and criminality: a 26-year prospective study of the 1966 Northern Finland birth cohort. Am J Psychiatry 154: 840-845.

Torrey EF & Yolken RH (1998) Is household crowding a risk factor for schizophrenia and bipolar disorder? Schizophr Bull 24(3): 321-324.

Trad PV (1995) Mental health of Adolescent Mothers. J Am Acad Child Adolesc Psychiatry 34:2 130-141.

Tsuang MT (1966) Birth order and maternal age of psychiatric in-patients. Br J Psychiatry 112: 1131-1141.

van Os J & Selten JP (1998) Prenatal exposure to maternal stress and subsequent schizophrenia. The May 1940 invasion of The Netherlands. Br J Psychiatry 172: 324-326.

Veijola J, Mäki P, Joukamaa M, Järvelin M-R, Rantakallio P & Isohanni M (1998) Offspring of depressed mother. Arch Gen Psychiatry (letter to the editor) 55: 949.

Verdoux H, Geddes JR, Takei N, Lawrie SM, Bovet P, Eagles JM, Heun R, McCreadie RG, McNeil TF, O'Callaghan E, Stober G, Willinger MU, Wright P & Murray RM (1997) Obstetric complications and age at onset in schizophrenia: an international collaborative meta-analysis of individual patient data. Am J Psychiatry 154: 1220-1227.

Virkkunen M, Eggert A, Rugg AJ & Linnoila M (1996) A prospective follow-up study of alcoholic violent offenders and fire setters. Arch Gen Psychiatry 53: 523-529.

Wahl CW (1954) Some antecedent factors in the family histories of 392 schizophrenics. Am J Psychiatry 110: 668-676.

Wahl CW (1956) Some antecedent factors in the family histories of 562 male schizophrenics of the US navy. Am J Psychiatry 113: 201-210.

Wahlberg K-E, Wynne LC, Oja H, Keskitalo P, Pykäläinen L, Lahti I, Moring J, Naarala M, Sorri A, Seitamaa M, Läksy K, Kolassa J & Tienari P (1997) Gene-environment interaction in vulnerability to schizophrenia: Findings from the Finnish Adoptive Family Study of Schizophrenia. Am J Psychiatry 154: 355-362.

Ward A (1930) The only child- a study of one hundred only children living at home with both parents. Smith College Studies in Social Work 1: 41.

Weinberger DR (1995) Schizophrenia: from neuropathology to neurodevelopment. Lancet 346: 552-557.

Weller L & Miller S (1978) Birth order, country of origin and schizophrenia in Israel. Int J Soc Psychiatry 24: 195-198.

Westergaard T, Mortensen PB, Pedersen CB Wohlfarth J & Melbye M (1999) Exposure to prenatal and childhood infections and the risk of schizophrenia: suggestions from a study of shipship characteristics and influenza prevalence. Arch Gen Psychiatry 56: 993-998.

Wild CM, Shapiro LN & Abeling T (1974) Sampling issues in family studies of schizophrenia. Arch Gen Psychiatry 30: 211-215.

Williamson NE (1976) Sons or daughters: a cross-cultural survey of parental preferences. Sage, Beverly Hills, CA.