Childhood parental loss and schizophrenia: evidence against pathogenic but for some pathoplastic effects

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Abstract

Childhood parental loss has been associated with a number of psychiatric disorders in adulthood. The present article aims to examine, firstly, the etiologic relationship between early parental loss and later development of schizophrenia and, secondly, the pathoplastic effect of the former on the symptomatology of the latter. We have administered semi-structured interviews inquiring into psychopathology and early separation experiences to a representative sample of first-visit patients to the 31 hospitals and clinics all over Japan ($n = 1963$) and also to a community sample in a small city in Japan ($n = 218$). When 225 patients diagnosed with schizophrenia according to DSM-III-R criteria were compared with 122 healthy control subjects without any lifetime psychiatric disorder, controlled for sex and age, there was no statistically significant difference in the rates of childhood parental loss (death or separation). As regards the pathoplastic effects, it was found that schizophrenic men were less likely to present with negative symptoms if they had experienced separation from the father, and were more likely to show panic attacks if they had experienced separation from the mother. Schizophrenic women were more likely to present with hallucinations if they had suffered any loss of the father. Childhood parental loss is not pathogenic of schizophrenia but appears to exert some pathoplastic influences on its presenting symptoms. © 1998 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

Death or prolonged absence of a parent during childhood is obviously a stressful experience for a child and has been associated with a number of psychiatric disorders in adulthood, including most notably depression (Beck et al., 1963; Brown et al., 1977; Kendler et al., 1992) but also anxiety disorders (Hafner and Roder, 1987; Tweed et al., 1989), alcoholism (Tennant and Bernardi, 1988) and personality disorders (Paris et al., 1994).

There have also been a number of studies implicating childhood parental loss as an etiological or pathogenic factor in schizophrenia. In early days such a hypothesis had its underpinnings in psychoanalytic theories which emphasized the role of loss and early experiences in predisposing an individual to later psychopathology. The twin and adoption studies have since proved beyond reasonable doubt that schizophrenia is genetically transmitted; the same studies, however, also establish that environmental influences must also play a major role, because estimates of heritability lie in the range of 0.41–0.87 (Cannon et al., 1998). In other words, something in the past or present environment of the individuals who have developed schizophrenia must explain between 13 and 59% of the variance in liability to schizophrenia. Some of the better studied aspects of these environmental factors include biological ones, such as intrauterine viral infection (O'Reilly, 1994) and perinatal obstetric complications (Verdoux et al., 1997), on the one hand, and psychosocial ones, such as life events (Brown and Birley, 1968; Norman and Malla, 1993) and expressed emotions (Butzlaff and Hooley, 1998), on the other. Childhood parental loss might well be one such factor.

Granville-Grossman (1966) reviewed 13 studies published between 1944 and 1963: five studies found significant and eight found non-significant differences between the rates of parental death in schizophrenic and control populations. Results of more recent studies have also been mixed. Birtchnell (1972) compared 6795 patients referred to the psychiatric services in Scotland and 3425 control subjects recruited from the general population of the same regions. Adjusting for the decade

of birth, he concluded that early bereavement was not a significant factor among the psychotics except for the depressives. The relationship between parental death and psychiatric diagnoses was examined in the Chestnut Lodge Follow-Up Study, but no significant association emerged: patients experiencing childhood parental loss did not cluster preferentially within any diagnostic group including schizophrenia and the mood disorders (Ragan and McGlashan, 1986). On the other hand, Watt and Nicholi (1979) studied the frequencies of childhood parental death in three separate samples of psychiatric patients and found that the schizophrenic patients had significantly greater frequencies of bereavement than the control subjects or than the non-schizophrenic patients.

The available evidence has therefore been inconclusive up to the present day, and it is indeed difficult to reconcile these various findings in the literature. Gregory (1958) pointed out methodological difficulties of these studies, such as the representativeness of the patient group and the failure to control for confounding variables. We must also entertain some skepticism as to the diagnostic reliability of the so-called schizophrenics of the earlier studies before the era of operational diagnostic criteria. The study by Ragan and McGlashan (1986) was the only study to apply modern diagnostic criteria, but they did so only retrospectively to the data obtained from clinical chart abstracts. The ascertainment of childhood parental loss was also done through chart reviews in some studies and may have been subject to some unintended omissions. The variation in the definition of parental 'loss' is another factor undoubtedly contributing to the confusion in the findings.

In contrast to these pathogenic investigations, some authors have recently suggested a pathoplastic effect of childhood parental loss in schizophrenia. Regardless of whether childhood parental loss may or may not contribute to the development of the schizophrenia (pathogenesis), it may influence the form of the disease once it has developed (pathoplasy) (Birnbaum, 1923). Roy (1981) studied parental loss before 17 years of age among 100 patients with chronic undifferentiated schizophrenia as defined in DSM-III and found

that it was significantly associated with the development of a depressive syndrome. Stastny et al. (1984) found, in two samples of chronic schizophrenic patients diagnosed according to DSM-III, early parental absence defined as either death or physical separation longer than 6 months before age 16 was significantly more frequent among chronic inpatients than among outpatients. The authors therefore concluded that parental loss in pre-schizophrenic children may be an early indicator for course and outcome of the disorder.

The Group for Longitudinal Affective Disorders Study (GLADS) in Japan has been conducting a multi-center prospective follow-up study of a broad spectrum of affective disorders under the sponsorship of the Ministry of Health and Welfare (Furukawa et al., 1995). In the first stage of the collaborative study, we interviewed representative samples of psychiatric patients visiting the participating centers and collected data on their psychopathology and childhood parental loss. We have also conducted a separate general population psychiatric epidemiological study in a city in Japan and inquired about the inhabitants' psychiatric status as well as experiences of early parental loss through semi-structured interviews (Aoki et al., 1994). We have previously reported on the influence of early parental loss among patients with mood disorders (Furukawa et al., in press) and with alcohol dependence (Furukawa et al., 1998). The present article aims to examine, firstly, the hypothesized pathogenic relationship between early parental loss and later development of schizophrenia and, secondly, the pathoplastic effect of childhood parental loss on the presenting symptomatology of the schizophrenic patients.

2. Methods

2.1. Patients

Out of 1963 subjects (938 men and 1025 women) who were representative samples of patients making their first visit to the 31 hospitals and clinics participating in the GLADS Project, who were aged 16 or over, and for whom relevant information concerning early separation experiences was available, 225 subjects (114 men and 111 women) were diagnosed with schizophrenia according to DSM-III-R by a psychiatrist using a semi-structured interview called the Psychiatric Initial Screening for Affective disorders (PISA) (Kitamura, 1992b).

The 31 hospitals and clinics included psychiatric departments of 15 university hospitals ($n = 79$; 35%), eight general hospitals ($n = 19$; 8%), five mental hospitals ($n = 103$; 46%), a community mental health center ($n = 14$; 6%) and an outpatient clinic ($n = 10$; 4%), and a psychosomatic department of a university hospital ($n = 0$) from all over Japan. Each hospital and clinic examined a representative subset of its first-visit patients according to the predetermined rules; in certain centers, a representative subset meant all the first-visit patients examined by the psychiatrist(s) participating in the GLADS Project; in others, it meant all the first-visit patients on a certain day of the week; still, in some others, it meant only the first such patient to show up on a certain day of the week. The selection of these preset rules was left to the individual center as time and human resources varied in each hospital.

DSM-III-R diagnoses were given by psychiatrists who administered the PISA. The PISA lists 33 symptoms corresponding to diagnostic criteria of schizophrenia, mood disorders, anxiety disorders, somatoform disorders, dissociative disorders, organic mental disorders and substance use disorders, and the inter-rater reliability of these psychopathological variables has been reported to range between kappas of 0.71 and 1.00 (median = 0.85) (Furukawa et al., 1995). The PISA also contains a section inquiring after each parent's current age if alive, or each parent's age and the patient's age when the parent died, and whether (and when and how long) the patient lived apart from each parent for a period longer than a month before the patient's 16th birthday. The reasons for death and separation were also to be specified. In the event of more than one period of separation from a parent longer than one month, regardless of the cause, only the first separation was considered. Other studies in the

literature have also used the same conventions as ours to adopt the age limit of the 16th birthday (Brill and Liston, 1966; Munro and Griffiths, 1969; Stastny et al., 1984), to use the cut-off of 1 month for the length of separation (Tennant and Bernardi, 1988; Oakley-Browne et al., 1995) and to count only the first separation in the event of multiple separations (Brill and Liston, 1966). We were thus able to collect data on the patients' parental loss through direct and systematic interviewing. Approximately half of the cases were accompanied by their relatives and, where necessary, corroborative information was obtained from them.

2.2. Control subjects

Control subjects were taken from a separate epidemiological study in Kofu, Japan. The city is situated in Eastern Japan, approximately 100 km to the West of Tokyo, and has a population of 195 000. A total of 218 inhabitants (95 men and 123 women) aged 18 or more were successfully contacted by lay interviewers trained in the use of a semi-structured psychiatric interview called the Time-Ordered Stress and Health Interview (TOSHI) (Kitamura, 1992a). Seventy subjects were found to suffer from lifetime diagnoses of one or more DSM-III-R disorders, and for 26 further subjects relevant information concerning early separation experiences were lacking; in the following, data for the 122 healthy control subjects (52 men and 70 women) are therefore used. The interrater reliability (intraclass correlation) of the TOSHI, using case vignettes, was 0.75 for major depressive episode, 0.41 for dysthymia, 0.75 for manic episode, 0.60 for generalized anxiety disorder, 0.85 for panic disorder, 0.48 for phobic disorder and 0.64 for obsessive-compulsive disorder (Kawakami et al., 1996). The section of the TOSHI dealing with early loss experiences is identical to that of the PISA.

2.3. Analysis

Statistical analyses were conducted using SPSS 6.1 for Macintosh (SPSS Inc., 1994). All the significance tests are two-tailed.

3. Results

In order first to test the pathogenic hypothesis about the relationship between childhood parental loss and schizophrenia, we compared the rates of death of a parent, separation from a parent and loss (i.e. either death or separation) of a parent among the patients and the control groups. Because the loss of a parent may have a different meaning for a child of the same sex or the other sex, we calculated the odds ratios separately for men and women. Furthermore, because there were statistically significant differences in the age of the patient and the control groups (mean $\pm$ S.D. = 31.5 $\pm$ 10.1 vs. 57.4 $\pm$ 16.9; t = 12.3, d.f. = 164, $P < 0.001$ for men: 34.6 $\pm$ 12.6 vs. 55.5 $\pm$ 15.0; t = 10.1, d.f. = 179, $P < 0.001$ for women), we conducted multiple logistic regression analyses and calculated the odds ratios adjusted for age (Table 1).

Ninety-five percent confidence intervals of all the odds ratios included the value of 1.0 and therefore could not demonstrate either increase or decrease in the incidence of parental death and/or separation among the schizophrenic patients as compared with the normal control subjects.

The causes of parental loss were as follows. Among the schizophrenic patients, the reasons for paternal death were the father's illness (n = 7, 77.8%) or accident (n = 2, 22.2%), and those for maternal death were the mother's illness (n = 3, 100%). Separation from the father was due to the child's illness (n = 3, 11.5%), the father's illness (n = 2, 7.7%), the father's job (n = 5, 19.2%), the child's attending boarding school (n = 1, 3.8%), being adopted (n = 4, 15.4%), the parents' separation (n = 2, 7.7%), the parents' divorce (n = 4, 15.4%) and others (n = 5, 19.2%); separation from the mother was due to the child's illness (n = 3, 17.6%), the mother's illness (n = 1, 5.9%), the mother's job (n = 2, 11.8%), the child's attending boarding school (n = 1, 5.9%), being adopted (n = 4, 23.5%), the parents' divorce (n = 1, 5.9%) and others (n = 5, 29.4%).

Among the control subjects, the reasons for paternal death were illness (n = 11, 84.6%), accident (n = 1, 7.7%) or unknown (n = 1, 7.7%), and

Table 1
Association between childhood parental loss and schizophrenia: raw counts (%) and odds ratios adjusted for age (95% CI)

	Death of		Separation from		Any loss of	
	Father	Mother	Father	Mother	Father	Mother
Men						
Schizophrenics ($n = 114$)	3 (6.1%)	2 (1.8%)	8 (7.0%)	6 (5.3%)	11 (9.6%)	8(7.0%)
Control subjects ($n = 52$)	4 (7.7%)	5 (9.6%)	12 (23.1%)	10 (19.2%)	15 (28.8%)	13(25.0%)
Odds ratio adjusted for age (95% CI)	1.55 (0.24−10.07)	0.41 (0.05−3.13)	0.58 (0.14−2.33)	0.32 (0.07−1.42)	0.84 (0.25−2.86)	0.44 (0.12−1.62)
Women						
Schizophrenics ($n = 111$)	6 (5.4%)	1 (0.9%)	18 (16.2%)	11 (9.9%)	24 (21.6%)	12 (10.8%)
Control subjects ($n = 70$)	9 (12.9%)	7 (10.0%)	10 (14.3%)	6 (8.6%)	18 (25.7%)	12 (17.1%)
Odds ratio adjusted for age (95% CI)	0.65 (0.18−2.35)	0.52 (0.06−4.68)	1.45 (0.50−4.20)	2.15 (0.59−7.84)	1.23 (0.50−3.01)	1.61 (0.52−4.96)

those for maternal death were the mother's illness ($n = 9$, 75.0%) or unknown ($n = 3$, 25.0%). Separation from the father was due to the father's illness ($n = 3$, 13.6%), the father's job ($n = 4$, 18.2%), the child's attending boarding school ($n = 1$, 4.5%), being adopted ($n = 2$, 9.1%) and others ($n = 12$, 54.5%); that from the mother was due to the child's illness ($n = 1$, 6.3%), the mother's illness ($n = 3$, 18.8%), the child's attending boarding school ($n = 1$, 6.3%), being adopted ($n = 2$, 12.5%), the parents' divorce ($n = 1$, 6.3%) and others ($n = 8$, 50%).

Next, in order to examine the pathoplastic effects of childhood parental loss, we confined our analyses to the 225 patients with schizophrenia. Table 2 lists the odds ratios of presenting with symptoms of depression, hallucination, delusion and so on among the schizophrenic patients with childhood parental loss as compared to the schizophrenic patients without. In some instances the odds ratios could not be calculated because there was no one who had experienced the childhood loss and who did not present with that particular symptom in our sample.

Among male schizophrenic patients, those who had experienced separation from the father were 0.19 (95% CI: 0.04–0.95) times less likely to present with negative symptoms (defined as affective flattening or blunting, alogia, avolition-apathy, or anhedonia-asociality), and those who had experienced separation from the mother or had experienced any loss of the mother were 6.93 (95% CI: 1.08–44.63) and 9.60 (95% CI: 1.84–50.09) times, respectively, more likely to experience panic attacks during the current episode. Among women, those who had experienced loss of the father were 3.52 (95% CI: 1.20–10.34) times more likely to suffer from hallucinations. To compensate for the many statistical inferences made in Table 2 and to avoid possible spurious findings due to Type I error, we also calculated 99% confidence intervals for these odds ratios. They were 0.02–1.56, 0.60–80.14, 1.09–84.18 and 0.85–14.50 in the order listed above; the men with schizophrenia were still more likely to experience panic attacks when they had experienced death of or separation from the mother than when they had not.

4. Discussion

The present report represents the first attempt to apply systematically and prospectively operational diagnostic criteria in the study of the pathogenic relationship between childhood parental loss and schizophrenia, and provides another piece of evidence against the hypothesized association.

Several criticisms can be raised, however, concerning the present study design. Firstly, our failure to find a statistically significant difference might be attributable to the low statistical power of our data, especially because the number of subjects reporting parental loss was relatively small. However, our sample size is fairly large, with n values between 52 and 114, and visual inspection of the obtained results reveals that the rates of parental loss are in fact not elevated among our patient sample and the non-significant findings in our study are in all likelihood not due to a type II error. Moreover, we believe that negative evidence also merits to be reported in the literature in order to avoid publication bias or the so-called 'file drawer' phenomenon, particularly in view of the recent emphasis on systematic reviews or meta-analyses. Secondly, some may argue that the strict comparability between our patient sample and the control group is not assured because they were not drawn from the same population. This problem can only be addressed by an epidemiological study in which a cohort from the same regions is examined as to the diagnosis of schizophrenia and to the early experiences of parental loss. One would then need a prohibitively large cohort in order to obtain a sample of schizophrenic patients who had experienced childhood parental loss that is large enough to allow meaningful statistical analyses. It must also be added that the city of Kofu, where the epidemiological study was conducted, is not known to be particularly different from the rest of Japan in terms of ethnicity, religion or industry. Japan is as a matter of fact a rather homogeneous society, where more than 99% of the population have the Japanese nationality, are Japanese in

Table 2
Association between childhood parental loss and symptomatology among schizophrenic patients: odds ratios (95% CI)

	Death of		Separation from		Any loss of	
	Father	Mother	Father	Mother	Father	Mother
Men						
Depressed mood	−	3.32 (0.20−55.01)	0.92 (0.18−4.71)	0.63 (0.07−5.67)	0.62 (0.13−3.01)	1.08 (0.21−5.72)
Hallucinations	−	−	1.29 (0.31−5.46)	1.28 (0.22−7.31)	2.03 (0.52−7.98)	1.98 (0.38−10.31)
Delusions	−	0.38 (0.02−6.35)	0.76 (0.18−3.28)	2.03 (0.23−18.09)	1.20 (0.30−4.76)	1.19 (0.23−6.25)
Negative symptoms	1.51 (0.13−17.14)	0.74 (0.05−12.18)	0.19 (0.04−0.95)[a]	0.35 (0.06−2.01)	0.33 (0.09−1.17)	0.42 (0.10−1.85)
Panic attack	−	12.50 (0.71−219.11)	1.45 (0.16−13.12)	6.93 (1.08−44.63)[a]	1.02 (0.12−8.97)	9.60 (1.84−50.09)[a]
Women						
Depressed mood	0.74 (0.13−4.25)	−	0.58 (0.19−1.79)	0.41 (0.11−1.60)	0.60 (0.22−1.60)	0.37 (0.10−1.41)
Hallucinations	4.11 (0.46−36.41)	−	2.91 (0.88−9.61)	2.88 (0.74−11.11)	3.52 (1.20−10.34)[a]	3.23 (0.85−12.31)
Delusions	0.50 (0.10−2.61)	−	1.30 (0.42−4.02)	1.86 (0.48−7.21)	0.97 (0.37−2.56)	2.08 (0.54−7.97)
Negative symptoms	0.67 (0.12−3.85)	−	0.71 (0.24−2.10)	1.21 (0.38−3.88)	0.68 (0.26−1.77)	1.04 (0.33−3.23)
Panic attacks	5.88 (0.93−37.16)	−	1.38 (0.27−7.16)	1.98 (0.37−10.52)	2.77 (0.71−10.81)	3.39 (0.76−15.05)

[a] 95% CI of odds ratios not including 1.0.

ethnicity and approximately 90% practice an amalgam of Buddhism and Shintoism (a traditional religion native to Japan). The industrial composition of the city is similar to the average in Japan, the primary industry representing 1% of its domestic product, the secondary industry 30% and the tertiary industry 69% (the respective percentages for all Japan are 2%, 37% and 61%). Thirdly, because the present study is a retrospective case-control one, we would not be able to be certain about the causal relationship even if our study could find a statistically significant association. For example, it is possible that it is not the parental loss (and its associated adverse life circumstances) per se that later leads to schizophrenia but the inherited genetic susceptibility to schizophrenia and suicide that leads to a spurious association between parental death, on one hand, and development of schizophrenia in the child, on the other. It must be noted, however, that no parental death was due to suicide among our patients and control subjects. Lastly, our threshold for separation (1 month) might be too low for it to be developmentally influential. In the literature on childhood parental loss and adult psychopathology, however, the definitions of parental separation have been highly variable, ranging from any (Fergusson et al., 1994) through 1 week (Tennant et al., 1981), 1 month (Tennant and Bernardi, 1988; Oakley-Browne et al., 1995), 3 months (Munro, 1966), 6 months (Faravelli et al., 1986), 1 year (Brown et al., 1986; Kendler et al., 1992), and 5 years (Wahl, 1954) to permanent (Makanjuola, 1989; Paris et al., 1994). Although we did collect data on the length of separation if it was longer than 1 month, adoption of a higher cut-off was infeasible in the present analysis as it resulted in too small a number of subjects for statistical comparisons.

It must also be pointed out that all the previous studies on the relationship between childhood parental loss and schizophrenia were conducted in Western countries and that the present study was the first such study among East Asian subjects. Although one would expect that the very long life expectancy and the low divorce rate in Japan would render the proportions of subjects experiencing parental death or separation in our study to be lower than those reported in recent studies in Western countries, they were found to be roughly comparable. The overall rates of death of father or of mother and separation from father or mother in our whole sample were 6, 4, 14 and 10%, respectively. On the other hand, they were reported to be 3, 2, 26 and 16% among primary care visitors in an Australian study which counted death before age 15 and separation longer than 1 month (Tennant and Bernardi, 1988); in an Italian study counting death before age 10 and separation longer than 6 months, they were 6, 4, 18 and 10% (Faravelli et al., 1986); in a US sample counting death before age 17 and separation longer than 12 months, they were 5, 1, 11 and 3% (Kendler et al., 1992). Some of the discrepancies between previous studies and the present one might, however, be due to the cultural differences in family attitudes and parenting practices including responses of the relatives after parental loss. We need further reports from Asian and other non-European cultures to examine such possibilities.

With regard to the pathoplastic effects of childhood parental loss, the present report has provided some suggestive findings. Schizophrenic men had an approximately fivefold decrease in negative symptoms if they had experienced separation from the father, and had a seven to 10-fold increase in rates of panic attacks if they had experienced separation from the mother. Schizophrenic women were three times more likely to present with hallucinations if they had suffered any loss (death or separation) from the father. On the other hand, early loss experiences had no effect on the probability of the patients' presenting with depressed mood as suggested by Roy (1981).

The pathoplastic hypothesis of early parental loss is a relatively unexplored theme in the literature and needs to be further studied. Firstly, the exact mechanisms of how early parental loss may predispose to certain symptoms among adults with schizophrenia are not clear. Our finding of the increased occurrence of panic attacks among bereaved men is in accordance with some studies reporting association between loss in childhood and anxiety in adulthood (Hafner and Roder, 1987; Tweed et al., 1989; Zahner and Murphy,

1989). Heightened anxiety triggered by parental loss in childhood may sensitize the child to anxiety through adulthood. In addition, influences of childhood parental loss on the longer-term symptomatology of schizophrenia could not be examined by the present study, because our symptom assessment focused on those presented by the patients on their first visit to the hospitals and clinics. Future studies are therefore called for which examine the pathoplastic effects of childhood parental loss on the presenting symptomatology and the course and outcome of schizophrenic patients.

Acknowledgements

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