



Research report

Genetic and familial environmental effects on suicide attempts: A study of Danish adoptees and their biological and adoptive siblings



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ABSTRACT

Objectives: Genetic factors have been found to influence the risk of suicide. It is less clear if this also applies to attempted suicide. We have investigated genetic and familial environmental factors by studying the occurrence of suicide attempts in biological and adoptive siblings of adoptees who attempted suicide compared to siblings of adoptees with no suicide attempts.

Method: We used a random sample of 1933 adoptees from the Danish Adoption Register, a register of non-familial adoptions of Danish children, i.e. the adoptive parents are biologically unrelated to the adoptee. Analyses were conducted on incidence rates of attempted suicide in biological and adoptive siblings given occurrence of attempted suicide in the adoptees while also taking into account psychiatric disorders. Information about suicidal attempt and history of psychiatric disorder was based on hospital admissions.

Results: The rate of attempted suicide in full siblings of adoptees who attempted suicide before age 60 years was higher than in full siblings of adoptees who had not attempted suicide (incidence rate ratios (IRR)=3.45; 95% confidence interval [CI]=0.94–12.7). After adjustment for history of psychiatric admission of siblings the increased rate was statistically significant (IRR=3.88; 95% CI=1.42–10.6).

Limitations: Information on attempted suicide and psychiatric history was limited to that which involved hospitalisation.

Conclusions: Genetic factors influence risk of suicide attempts.

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1. Introduction

Genetic factors have been found to influence the risk of suicide (Brent and Melhem, 2008; Voracek and Loibl, 2007; Petersen et al., 2013). It is less clear if this also applies to attempted suicide. In a Swedish study of familial clustering of suicide attempts in the general population, there appeared to be a familial influence beyond transmission of mental illness (Mittendorfer-Rutz et al., 2008). Such a genetic effect may be separated from familial environmental effects by twin or adoption studies (Voracek and Loibl, 2007; Petersen et al., 2013; Neale and Cardon, 1992). Suicidal behavior (i.e. suicide and attempted suicide investigated jointly), is significantly more frequent in monozygotic than in dizygotic twins (Voracek and Loibl, 2007; Tidemalm et al., 2011), suggesting

genetic contributions to suicidal behavior. In 3372 male twin pairs from the Vietnamese Era Twin Register, suicide attempts were seen significantly more frequently in monozygotic than in dizygotic twins (Fu et al., 2002). However, drawing the conclusion about genetic contribution to suicidal behaviour from twin studies assumes that the common environmental influences in utero and due to living in the same families, as well as at total genetic variance is identical in mono- and dizygotic pairs (Neale and Cardon, 1992). Moreover, genetic influences may be additive (i.e. due to different genetic variants) typically being expressed in parents and their offspring or they may be non-additive (i.e. dominance effects by genetic variants or by interactions among genes), expressed among full siblings (Neale and Cardon, 1992). An example of a non-additive effect was found in an earlier adoptions study; when analyzing incidence and case-fatality of infectious disease in adoptees and their siblings there appeared to be a strong non-additive genetic influence on risk of fatal outcome (Petersen et al., 2010a). In twin studies common environmental

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influences cannot be distinguished from non-additive genetic influences (Neale and Cardon, 1992). Unfortunately, there are extremely limited data on risk of suicide attempts in twins reared apart compared to those reared together; such data might provide information on the contribution of both common environmental effects and genetic effects (Voracek and Loibl, 2007).

A Swedish adoption study of familial as well as non-familial adoptees, born between 1973 and 2003, suggested increased suicidal behavior (defined as death by suicide or suicide attempt) in adoptees whose biological parent had exhibited suicidal behavior (von Borczyskowski et al., 2011). The study included no separate analyses of suicide attempts alone. When adopted by relatives in the biologically-related family, the adoptee is brought up in a family environment that is not clearly separated from their genetic background. Investigations of non-familial adoptions, as in the Danish Adoption Register (Petersen and Sørensen, 2011) enable better separation of genetic and familial environmental effect. Restricting analyses to siblings would also enable better assessment of non-additive genetic effects and reduce the potentially confounding influences from generational changes.

An earlier adoption study of suicide, based on the Danish Adoption Register, demonstrated that suicide risk was significantly increased in the biological parents and siblings of adoptees who died by suicide compared to the biological parents and siblings of adoptees who did not die by suicide (Schulsinger et al., 1979). In a recent study based also on the Danish Adoption Register, a strong genetic influence on suicide, independent of known psychiatric disorder, was found among siblings of adoptees (Petersen et al., 2013). The effect was strongest in full siblings, suggesting a non-additive effect.

Severe psychiatric disorders necessitating psychiatric hospital admission are strongly associated with risk of suicide (Goldacre et al., 1993; Geddes and Juszcak, 1995; Nordentoft et al., 2011). Schulsinger et al. (1979) found evidence of genetic influence, both among people dying by suicide without any history of psychiatric hospitalization and among people who did have such a history. They discussed whether this suggests a pathogenic factor contributing to suicide independently of psychiatric disease, or whether suicide reflects an acute and severe psychiatric illness which manifests as suicide. A large Danish study strongly suggested that familial history of psychiatric illness increases suicide risk only through increasing the risk of developing a mental disorder. It also showed that family suicide history significantly increases suicide risk independently of familial history of psychiatric illness (Qin et al., 2002).

Given the paucity of information on attempted suicide from studies of adoptees, using the national Danish Adoption Register and Danish health registers we have estimated rate of suicide attempts in biological full siblings and half-siblings of adoptees and in their adoptive siblings. We compared the rate of suicide attempts in siblings of adoptees who had attempted suicide with the rate in siblings of adoptees who had no recorded suicide attempts. The analyses include examination of rate according to history of psychiatric treatment. Our hypothesis was that we would find evidence of both genetically-transmitted risk (i.e. observed in biologically-related siblings) and familial environmentally-determined risk (i.e. observed in adoptive siblings) of attempted suicide, and that these risks would exist irrespective of whether or not siblings had a history of psychiatric treatment.

2. Study population and methods

2.1. Adoption cohort

The study was based on the Danish Adoption Register, which contains records on all 14,425 non-familial adoptions formally

granted in Denmark during the period 1924 through 1947 (Petersen and Sørensen, 2011). We included adoptees born in 1917 or later who were traceable, who were transferred to the adoptive family before the age of 7 years (25% were transferred directly after birth and mean age at transfer were 8 months), who were singletons (or one from each twin pair), and who did not emigrate or die before the age of 12 years. There were 13,061 such adoptees, of whom we for a randomly selected cohort of 1933 adoptees (Petersen et al., 2005) traced their siblings, which is an extremely labour intensive task, because of the regionally organized civil registers from the early 20th century. The study sample consisted of the 1263 adoptees who were alive in 1977 and for whom it was possible to trace adoptive and biological siblings, using information about their parents. Adoptive siblings are children growing up in the same family but not biologically related to the adoptee. Biological full siblings have the same mother and father as the adoptee, and half siblings have the same mother or father as the adoptee, but these biological siblings grew up either with their parents or in another adoptive family. Twins would be adopted together, so they were omitted from the sampled siblings, whereas full siblings and half siblings adopted away were placed in separate adoptive families in 99.8% of the cases. This means that the biological siblings in our study did not grow up together with the adoptee.

2.2. Siblings of adoptees

The Danish regional population registers cover the period between 1924 until 1968 in paper files and as a computerized national register from April 1968. The parents and the children are linked (Pedersen, 2011). Siblings who were alive in 1977 were followed up through national registers with respect to occurrence of suicide attempts between 1977 and 2010, and psychiatric admissions from 1970 onward. There are some restrictions by design, as we analyzed siblings of a group of adoptees which was divided into two: those attempting suicide before age 60 years and those surviving to age 60 years. The survival analysis targets survival times of the siblings, therefore covariates relating to the adoptee cannot be time dependent.

2.3. Assessment of attempted suicide and psychiatric admissions

2.3.1. Attempted suicide

We extracted information from the national hospitalization registers (including somatic and psychiatric records) about suicide attempts between 1977 and 2010 based upon diagnoses E950.0–E959.9 (ICD 8), or a contract with “suicide attempt” as the reason for contact or main diagnoses F00–F99.9 (ICD 10) together with auxiliary diagnoses T36–T50, T52–T60, S51, S55, S59, S61, S65 or S69, or with main diagnoses T39, T42, T43 or T58 (ICD 10), or with a diagnose of X60–X84 (ICD 9 was not used in Denmark). Actual suicides were not included.

2.3.2. Psychiatric admission

Information on psychiatric admissions defined as discharges, available between 1st January 1970 and 31st December 2010, was obtained by record linkage.

2.4. Comparison of two cohorts

The rates of suicide attempts in two cohorts of siblings were compared: one cohort included siblings of adoptees who attempted suicide, the other cohort included siblings of adoptees who had not attempted suicide. When comparing the two cohorts, the interpretation differs between biological and adoptive

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