What family studies teach us about suicidal behavior: Implications for research, treatment, and prevention

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1. Introduction

Family studies are designed to assess the extent to which a given condition is transmitted within families. The rate of a disorder in the relatives of affected individuals (“proband”) is compared to the rate of this disorder in the relatives of unaffected individuals. There are two types of classic family studies, “bottom-up,” in which the parents, siblings and other relatives of an affected proband are assessed; and “top-down,” in which the offspring of affected probands are assessed and followed forward to demonstrate familial transmission and identify precursors of a given disorder (Fig. 1). These types of studies, in contrast to adoption and twin studies, cannot disentangle that which is familial from that which is heritable. However, these approaches can: (a) demonstrate that a condition is familial; (b) delineate the boundaries of a familial phenotype; (c) clarify patterns of co-transmission and possible endophenotypes; (d) identify precursors of a condition; and (e) detect important environmental and gene by environmental sources of familial risk. Family studies of suicide and suicidal behavior are reviewed with respect to these five issues.

2. Familial aggregation of suicidal behavior

Family studies have conclusively shown that suicidal behavior runs in families. Moreover, these studies have helped to clarify that the familial suicidal phenotype includes both completed and attempted suicide, whereas some family studies in which the proband is a suicide attempter, an increased familial rate of suicide is reported [15,20,24] (Table 2). For example, in a large population-registry study, Mittendorfer-Rutz et al. found that both familial suicide completion (odds ratio [OR]: 1.9–3.4) and familial suicide attempt (OR: 1.8–1.9) contributed to an increased risk for a suicide attempt among youth [19].

3. Boundaries of the familial transmitted suicidal phenotype

Family studies have demonstrated that, while the familial phenotype for suicidal behavior includes both completed and attempted suicide, it does not include suicidal ideation. In one “bottom-up” family study, the rate of suicidal behavior was assessed in the relatives of 58 adolescent suicide completers and the relatives of 55 non-suicide attempting adolescent community controls [1]. The rate of suicidal behavior (attempt or completion) was much higher in the relatives of the suicide victims (11.6% vs. 2.4%, p < .001, OR = 5.3). There was a more modest increase in the risk of clinically significant suicidal ideation (lifetime history of ideation with a plan) in the first and second degree relatives of suicide completers (OR: 1.9 and 1.8, respectively), which was no longer statistically significant after controlling for the increased rate of familial psychopathology in the relatives of the suicide victims [1].

In a community prospective study, Lieber et al. compared 933 offspring classified by whether their mother had a history of depression and a history of either an attempt, suicidal ideation, or neither ideation or an attempt. The risk of suicide attempt was increased 7-fold in the offspring of depressed mothers who had
phenotypes

4. Co-transmission of psychiatric disorder and intermediate phenotypes

Family studies have shown that the familial transmission of suicidal behavior is distinct from the familial transmission of psychiatric disorder. Egeland & Sussex described four large pedigrees in the Old-order Amish [8] all of which were loaded for mood disorders, but only two of which had high rates of suicide. Many family studies have found an increased risk of suicidal behavior in relatives of attempter or completer probands, even after controlling for the increased rates of psychiatric disorder in the relatives of the suicidal probands [1,12,13]. Conversely, psychiatric outpatients with a family history of suicidal behavior show higher levels of hostility, impulsivity, and impulsive aggression than those patients without such a family history [7].

The mediation of the familial transmission of suicidal behavior by the familial transmission of impulsive aggression has been demonstrated in one top-down study of the offspring of mood disorders parents, some of whom had attempted suicide [3]. In this study, the greater the family loading for suicidal behavior, the higher the levels of impulsive aggression, both in probands and their offspring. Those parents who had made an attempt and also had a sibling concordant for suicide attempt had higher levels of impulsive aggression than did parental attempters without a concordant sibling, whose ratings of impulsive aggression were, in turn, higher than those mood-disordered parents without a history of an attempt. Parallel findings with respect to impulsive aggression were found in the offspring of these three groups, with the highest levels of impulsive aggression found in those with the greatest family loading for suicidal behavior. Those offspring with the highest family loading for suicidal behavior showed the greatest morbid risk for suicidal behavior and had a median age of onset for an attempt that was 8 years earlier than the age of onset of attempt in the offspring of attempters without a concordant sibling [Fig. 3]. However, this group difference in morbid risk disappeared after controlling for levels of impulsive aggression in parent and offspring, meaning that the familial transmission of suicidal behavior was mediated by the transmission of impulsive aggression.
5. Age of onset of suicidal behavior

Impulsive aggression appears to be a characteristic most closely associated with adolescent and young adult suicide. In a large series of psychological autopsies conducted across the life span, the earlier the age of completed suicide, the higher the levels of impulsivity, aggression, and novelty seeking [17]. Conversely, the role of harm-avoidance, which roughly corresponds to “neuroticism,” and is thought to be an important endophenotype for depression and anxiety, becomes more prominent with increasing age. Greater family loading for suicidal behavior is associated with an earlier onset of suicidal behavior [3,25].

6. Precursors of suicidal behavior

Top-down family studies can also help to identify precursors of suicidal behavior in high-risk youth. In a 1- to 6-year prospective follow-up of 365 offspring of 203 mood-disordered probands, 110 of whom had a history of a suicide attempt, the risk of new-onset suicide attempts in the offspring was 6.5 times higher in the offspring of attempters (4.1% vs. 0.6%, p = .04) [5,18]. Moreover, three important precursors of suicidal behavior were identified: early-onset of a mood disorder, impulsive aggression, and sexual abuse of the proband. The latter was an unexpected finding that opened up an examination of possible environmental factors that predispose to the familial transmission of suicidal behavior.

7. Possible gene–environment interactions

A history of parental sexual abuse conferred as much of an increased risk for a suicide attempt in an offspring as did a family history of an attempt. Moreover, these two risk factors were additive [17]. Path analytic models showed that proband sexual abuse contributed to offspring attempt via two pathways: (a) proband abuse increased the risk of abuse in offspring; and (b) proband sexual abuse was associated with higher impulsive aggression, which in turn increased the liability for high impulsive aggression in the offspring, with both pathways increasing the likelihood of an attempt [4] (Fig. 4). A history of abuse in a parent is related to greater familial loading for mood disorder and suicidal behavior, higher offspring aggression, and higher offspring risk of abuse, all leading to early-onset attempts [5,16,18].

8. Summary

Suicidal behavior is transmitted within families, independently from the transmission of psychiatric disorder. The familial phenotype of suicidal behavior includes suicide completion and attempts, but not suicidal ideation, the latter of which is transmitted along with depression. The familial transmission of early-onset suicidal behavior is co-transmitted with, and appears to be mediated by the transmission of impulsive aggression. In part, the familial transmission of suicidal behavior is mediated by the familial transmission of abuse. Moreover, high family loading for mood disorder and suicidal behavior are related to multigenerational abuse, impulsive aggression, and early-onset of mood disorder and of suicidal behavior.

9. Implications for research

Genetic studies of suicidal behavior must include the assessment of early childhood adversity. Age of onset of both mood disorder and of suicidal behavior are important areas of inquiry, because genetic and familial risk factors for suicidal behavior appear to vary across the life span. Current assessments of impulsive aggression using interview and paper-and-pencil measures should be supplemented by laboratory-based measures.

10. Implications for treatment and prevention

These findings suggest that treatment targets for suicidal youth should include not only depression, but also the liability to impulsive aggression, since the latter is an independent contributor to suicidal risk. A careful assessment, and when appropriate, treatment of intergenerational trauma is indicated, in light of its prominent role in the onset and familial transmission of suicidal behavior. Finally, given the strong relationships between parental and offspring disorders, and between the treatment of parental psychiatric illness and child outcome [10,27,29], assessment and treatment of parental disorder is important. In addition to treatment of parental depression, we currently possess interventions that effectively reduce the risk for abuse in offspring and prevent the onset of depression in high-risk offspring of depressed parents [10,21]. An adaptation of these interventions to families in which children are at high risk for the onset of suicidal behavior could translate extant findings in family studies of suicidal behavior into viable public health efforts to reduce the toll of early-onset suicidal behavior.
References


