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Familial Transmission of Suicidal Behavior

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Suicide and suicidal behavior is highly familial, and appears to be familially transmitted independently from the familial transmission of psychiatric disorder *per se* (1). Adoption, twin, and family studies support the view that the etiology of the familial transmission of suicidal behavior is at least in part genetic, and may be mediated by the transmission of intermediate phenotypes, such as impulsive aggression. In addition, there may be environmental causes for familial transmission, including imitation, and the intergenerational transmission of family adversity. In this review, we cover the evidence supporting the familial transmission of suicidal behavior, possible genetic and environmental explanations for this phenomenom, describe putative intermediate phenotypes, and discuss the contributory roles of early child-rearing and concurrent familial environmental stressors to suicidal risk. A better understanding of the mechanisms for the familial transmission of suicidal behavior can help to shed light on etiology, identify individuals at high risk for the development of incident suicidal behavior, and frame targets for intervention and prevention.

Adoption studies (see Table 1)

Three adoption studies have been conducted, all using the same Danish adoption registry. Kety et al., in a study designed to examine the genetics of schizophrenia and mood disorders, found a non-significant trend towards higher concordance for suicide in biological, compared to adoptive relatives of adoptees who committed suicide (2). Subsequently, a second study compared the rates of suicide among the biological and adoptive relatives of adoptees who committed suicide vs. biological and adoptive relatives of a matched living adoptee control group in Denmark (3). This study found a six-fold higher rate of suicide in the biological relatives of the suicide vs. those of the control adoptees, and an absence of suicide among the adopted relatives of the suicide vs. control adoptees supporting a genetic rather than environmental etiology (see Table 1). The rate of suicide was higher in the biologic relatives of suicide adoptees regardless of whether the adoptees were psychiatric patients or not. However, it was not possible to determine if the genetic liability to suicide was attributable to the transmission of major psychiatric disorders or to a suicide diathesis *per se*.

In a third adoption study using this registry, a comparison of biological and adoptive relatives of adult adoptees with mood disorder and matched unaffected adoptees were examined (4), revealed a 15-fold increase in suicide among the biological relatives of the mood-disordered adoptees vs. those of the unaffected adoptees (4). This finding supports the role of mood disorder in the genetics of suicide. However, the greatest increased risk for suicidal behavior was found in the relatives of those probands with "affect reaction," a diagnosis akin to

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borderline personality disorder, suggesting that impulsive-aggressive personality traits may play a role in familial aggregation of suicidal behavior (see Table 2).

Taken together, these studies support a strong role for genetics in explaining the familial concordance of completed suicide. Limitations of these studies include restriction to data gathered through routine medical records, and lack of systematic assessment of suicide attempts as well as completions. Thus, while these studies show there are genetic factors explaining the familial aggregation of suicide, they do not shed a great deal of light on *what factors* might be involved in familial transmission.

Twin studies (see Tables 3 and 4)

In their review of twin case reports for suicide, Roy and Segal found an increased concordance for suicide in monogyzotic (MZ) vs. dizygotic twins (DZ) (14.9% vs. 0.7%), consistent with Tsuang's original observations (5). Roy et al. found an even higher concordance rate for *suicide attempt* in the surviving monozygotic twin of the co-twin's suicide in MZ vs. DZ twins (38% vs. 0%), supporting the view that the clinical phenotype for concordance included *both completed suicide and suicide attempts* (6;7). Because these meta-analyses use reported case series, they are not necessarily representative of all twin pairs affected by suicide. The differential concordance rate for suicide for MZ vs. DZ twins does not appear to be due to greater bereavement reactions in MZ twins (8), since the risk of suicide attempt after the non-suicide death of a co-twin is similar in MZ vs. DZ twins (1.4% vs. 3.3%).

Three twin studies demonstrate familial transmission for suicidal behavior that cannot be explained by the transmission of other psychopathology (9–11). The heritability of suicidal behavior ranging from ideation to attempts ranged between 38% and 55%. While there appears to be overlap between the heritability of suicidal ideation and of actual suicidal behavior, there is a distinct heritable component of suicide attempts demonstrated in two of these studies (9; 10). In one study, the heritability of suicidal behavior was demonstrated, even after controlling for the heritability of psychiatric disorders (10). Twin studies generally provide more detailed assessment than adoption studies, and allow for an assessment of environmental and genetic contributors to concordance. However, unless twin studies are combined with adoption studies (i.e., comparison of twins adopted away to different parents), it is difficult to definitively differentiate shared environmental from genetic effects. For example, in a twins-adopted away design, components of maternal behavior previously considered "environment" were explained by genetic concordance of MZ twins eliciting similar maternal responses from unrelated mothers (12). A second limitation is that MZ vs. DZ concordance may be differentially affected by shared or distinct perinatal experiences (13).

Family Studies

Family studies compare the rate of suicide or suicidal behavior in the relatives of a proband with suicidality to the rate of suicide or suicidal behavior in the relatives of probands without suicidality. Studies have varied in outcome (family history of completed suicide, attempted suicide, or both), choice of proband (either completed or attempted suicide), choice of comparison group (community or psychiatric control), and method of assessment of family loading (record review, family history, or direct interview) (14–40). Among the most convincing of these studies have been those based on large population registries, which have shown concordance in death by suicide between parents and children, even after controlling for psychiatric diagnosis and treatment (37;38;41).

Despite variations in methodology, the results are remarkably similar across studies, consistently showing that suicidal behavior aggregates within families. Those studies that adjusted statistically for the familial transmission of psychiatric disorder and other risk factors

generally found a familial effect for suicidal behavior that still persisted even after statistical adjustment with effects ranging from a 2- to 12-fold elevation in rates after adjustment (23; 24;26;28). These studies support the view that the clinical phenotype of suicidal behavior that is familially transmitted includes both suicide attempt and suicide completion, since the rate of suicide is elevated in the families of attempters, and the rate of attempted suicide is elevated in the families of suicide completers.

Studies of the Risk of Suicide in Probands with Completed Suicide (see Table 5)

In studies that examined the familial rates of completed suicide in the relatives of probands who committed suicide, all show an elevated rate of completed suicide in the relatives of completers vs. relatives of a comparison group, regardless of whether that comparison group consists of psychiatric, general medical, and community controls. Also, these findings are consistent, regardless of whether the probands were drawn from large community pedigrees (14), diagnostically heterogenous inpatients (29;42), community samples (27), or bipolar suicides vs. living bipolar controls (36). Two of the studies showed a significant association between family history of suicide and familial suicide after controlling for other risk factors, stressing the unique contribution of the familial transmission of suicidal behavior to suicidal risk.

Population Registry Studies (see Table 6)

Four studies using Scandinavian registries report a increased risk of suicide conveyed to a first-degree relative, even after controlling for parental and personal history of inpatient psychiatric treatment (35;37;38;41). In one study, family history of suicide was associated with an increased rate of suicide even compared to those who have had a first-degree relative die from either accidents or homicides, supporting the view that the familial transmission of suicidal behavior is not strongly mediated by bereavement (38). One study found an impact of parental suicide on children aged 10–21 for both maternal and paternal suicide, with an increased risk for suicide in offspring even for maternal loss from qother causes; however, the effect of maternal suicide was greater than maternal loss due to other causes (AOR's 4.8 vs. 2.06). While such studies have the advantage of large, representative databases, they are limited to the information available in medical records, and assessment of psychiatric disorder is limited to those who received treatment. However, in Scandinavian countries, where access to health care has fewer barriers than in the United States, a treated sample is likely to be more representative than it would be in an American study.

Family studies of suicide probands and familial rates of suicidal behavior (See Table 7)

Four studies have examined rates of attempted and completed suicide in the families of suicide probands vs. the relatives of community controls (23;24;28;40). Two studies focused on adolescents (23;24), and two on adults (28), one of which focused exclusively on males (40). All found an increased rate of suicidal behavior in the relatives of completers compared to relatives of community controls, even after controlling for differences in rates of psychiatric disorder in probands (23;28;40), parent-child discord (24), and rates of psychiatric disorder in family members (23;24;40). Two studies found that the rates of familial suicidal behavior were most significantly increased in the relatives of the probands with increased levels of aggression or Cluster B personality disorder in probands (23;40), supporting a relationship between the familial transmission of aggression and of suicidal behavior. An increased rate of suicide attempts in the relatives of suicide probands supports the definition of a clinical phenotype of suicidal behavior that includes both attempts and completions. In contrast, suicidal ideation

was not increased in relatives of completers after adjusting for rates of psychiatric disorder in relatives (23;40), indicating that suicidal ideation is transmitted along with psychiatric disorder, whereas the tendency to translate that ideation into an actual attempt is co-transmitted with impulsivity and aggression.

Family History of Suicidal Behavior in Suicide Attempt Probands (see Table 8)

Table 8 lists 12 studies that have examined the rate of suicidal behavior in the families of suicide attempter probands, using a family history method. The findings are very consistent across studies, finding an increased rate of both completed and attempted suicide in the relatives of suicide attempters compared to the family members of controls. These findings are robust across a wide range of conditions: age of attempters (adolescents and adults), sampling frame (community samples, inpatients, outpatients), and diagnostic category (mixed, depression, bipolar, alcohol abuse, substance abuse). Greater lethality and violence of the attempt was associated with increased family loading in two studies (15;18). Loss of parent in childhood (under age of 11) either due to suicide (43) or due to any cause (22) was associated with an increased risk of attempt. Greater familial loading for suicidal behavior was associated with proband neuroticism, history of abuse or neglect, increased lifetime aggression, and, in those probands with mood disorder, an earlier age of onset of mood disorder (32–34;44;45). Moreover, a history of abuse, increased lifetime aggression, and earlier age of onset of mood disorder were interrelated (44). In one population study, significant relationships between parental and offspring ideation and attempt were reported (46). However, after adjustment for comorbidity, the strongest relationships were between parental and offspring attempt.

Family Studies of Suicide Attempting Probands (see Table 9)

Three family studies of child or adolescent suicide attempting probands have been conducted, finding an increased risk of suicide attempt in the relatives of suicide attempting probands (21;25;26). These studies also support a definition of the clinical phenotype that includes suicidal behavior, but does not include suicidal ideation, insofar as Pfeffer and colleagues found that a family history of attempts was increased only in the relatives of proband attempters but not in the relatives of proband ideators (21). A relationship between familial transmission of suicidal behavior and of impulsive aggression was also supported, since a higher rate of assaultive behavior was reported in the relatives of proband suicide attempters (21), and conversely, a higher rate of suicidal behavior in relatives was reported in the relatives of those proband attempters with higher levels of impulsive aggression (26).

High risk studies

A variant of the family study, the high risk study, has been used to prospectively examine the risks and processes associated with the familial transmission of suicidal behavior. In three studies that have taken this strategy, results are consistent—offspring of adult mood disordered suicide attempters have a much higher risk of suicide attempt than offspring of mood disordered probands who have never made a suicide attempt (see Figure 1). Greater familial loading for suicidal behavior is associated with a higher risk and earlier age of onset of suicidal behavior in offspring (see Figure 2), as well as higher levels of impulsive aggression in both parent and offspring (46–50). In one study, it was demonstrated that the familial transmission of suicidal behavior was in part mediated by the familial transmission of impulsive aggression (48). Furthermore, in prospective follow-up of high risk offspring, high levels of impulsive aggression, along with early-onset depression, predicted earlier onset and higher risk of suicidal behavior (49).

High risk, family-genetic studies may also shed some light on some family-environmental factors that may contribute to the familial transmission of suicidal behavior. Most notably, the risk of suicide attempt in offspring of adult suicide attempters was greatly heightened if the parent themselves had a reported history of sexual abuse (47;49). Using a high-risk design (top-down), this relationship between parental sexual abuse and offspring attempt appears to be mediated through two pathways: (1) parental history of abuse that leads to an increased risk of offspring abuse, which in turn increases the risk for mood and anxiety disorder and suicide attempt; and (2) parental history of abuse that is associated with higher offspring impulsive aggression, which in turn increases the risk for early onset mood disorder and suicide attempt (51;52). Similar inter-relationships among parental history of abuse, offspring early-onset mood disorder and impulsive aggression, and suicide attempt were found in a "bottom-up" family history study (44). Taken together, these studies suggest that early abuse in childhood could account for some, but not all of the familial clustering of suicidal behavior because of the familial transmission of liability to abuse.

Possible mechanisms by which familial transmission of suicidal behavior may occur

Some possible intermediate phenotypes have emerged from family genetic studies. An intermediate phenotype according to Gottesman and Gould (53), must be related to the clinical phenotype, must be heritable, must predict the onset of the condition in offspring, and show evidence of mediation when controlling for the relationship between parent and offspring transmission of the overall clinical phenotype. The intermediate phenotype with the most convergent evidence is impulsive aggression, i.e., the propensity to react with aggression or hostility to frustration or provocation. This construct has been shown to be related to risk for suicide attempt (54), to predict onset of suicide attempt (49), to be heritable (55), and to mediate the transmission of suicidal behavior (48). Other possible intermediate phenotypes include neuroticism, which is heritable, and is related both to onset of attempt, and to family loading for suicidal behavior (56). Impaired working memory and executive function, which may form the neurocognitive substrate for impulsive aggression and for poor interpersonal problem-solving, has been shown to be altered in adult attempters, offspring of adult attempters, and to be heritable (57;58).

In addition to genetic transmission, familial transmission of suicidal behavior could be explained in a number of other ways, such as familial transmission of adverse family environment, imitation, or bereavement.

Intergenerational transmission of adverse family rearing environments

As noted above, the familial transmission of suicidal behavior is confounded by the familial transmission of abuse. The inter-relationship between the transmission of abuse and of suicidal behavior is complex, in part because parents who abuse their children are also at higher risk for psychiatric conditions that predispose to suicidal behavior, including depression, substance abuse, and suicidal behavior (59;60). Furthermore, impulsive aggression in a parent may predispose that parent to be abusive, but also may be transmitted to that child as a heritable trait. In fact, the relationship between parental abuse and offspring suicidal behavior is mediated in part by the transmission of impulsivity and aggression (51;52). Further complicating an understanding of this interrelationship between the child abuse and impulsive aggression are the longstanding neurobiological changes that have been reported in maltreated children that may account for increased impulsivity and aggression (61).

Imitation

The familial transmission of suicidal behavior could in theory be explained by imitation. This is plausible given evidence that youth suicide occurs in time-space clusters, and that exposure to print and electronic media publicity about suicidal behavior has been consistently been shown to be associated with an increase in suicidal behavior (62). However, in youth exposed to a sibling's or a friend's suicide, there is no evidence of imitation (63;64). In both high risk and twin studies that have examined the temporal relationship between attempts in relatives, no relationship consistent with imitation could be found (9;47). While imitation is difficult to disprove, these prospective case-control studies, taken with those of adoption studies, suggest that imitation is not a clinically significant contributor to the familial transmission of suicidal behavior.

Interestingly, exposure to a friend's suicide *attempt*, but not to a friend's *completed* suicide, appears to be associated with an increased risk for suicidal behavior (64;65). Knowing a person who has attempted suicide, whether a relative or not, has also been reported to be a risk factor for suicidal behavior in mid-life (66). It is possible, though, that exposure to suicidal behavior is the result of "assortative friendships," insofar as friends of individuals with psychological difficulties are more likely to have mental disorder themselves. Peers with health risk behaviors, including suicidal behavior, are much more likely to have friends with increased rates of these behaviors (67). Moreover, the concordance among peers' health risk behaviors is much higher in the face of family dysfunction (67). Conversely, the deleterious impact of an adverse rearing environment can be buffered by a pro-social peer group (68).

Parental bereavement

Retrospective, record linkage and prospective longitudinal studies have found that bereavement conveys an increased risk for depression and suicide.(69–73). There seems to be a more deleterious effect of parental bereavement when the child who has lost a parent is younger than the age of 12 (33;65;74). Record linkage studies indicate that parental loss by suicide is most strongly associated with suicide risk in offspring, but that so is maternal loss from any cause (41). The relationship between early parental loss and suicidal behavior may be mediated by an increased risk for depression (71;72). Other factors that may contribute further to suicidal risk are pre-morbid parental psychopathology (49), traumatic exposure predisposing to post-traumatic stress disorder (PTSD), and the development of complicated grief (prolonged negative affect and rumination about the loss), which in turn has been shown to predispose to suicidal ideation in young adults (75). However, empirical data does not support a specific relationship between parent loss due to suicide and suicidal behavior in the child, compared to parent loss due to other causes (76–79). Moreover, the association between child completed suicide and parental attempted suicide suggests that, while bereavement and loss may play a small role in the overall effect of familial transmission, the majority of the familial effect is due to some other mechanism.

Other family-environmental factors that may interact with genetic risk factors for suicidal behavior

Parental divorce and separation

There is a large literature documenting a higher risk for suicidal behavior and suicide in children from non-intact families. However, divorce *per se* is unlikely to lead to suicidal behavior (41;80;81). For example, marital disruption is more common in parents with psychiatric disorder. In studies that have examined the three-way relationships between divorce, parental and child psychiatric disorder, and child suicidal behavior, the relationship between divorce and child suicidal behavior is markedly attenuated after controlling for higher rates of parental

psychiatric disorder (82–84). Young maternal age is another correlate of divorce that also predicts onset of suicidal behavior in adolescents (65). It is likely that the processes that ensue subsequent to the divorce that predict child adjustment. For example, Tousignant showed a dose response relationship between the number of parental figures (and subsequent disruptions) and the risk for adolescent suicidal behavior (85). A cascade of processes and predisposing factors mediate the relationship between divorce and eventual suicidal behavior (86). The relationship between parental divorce and child mental health disorders is mediated by the quality of the child's relationship with the caretaking parent, the caretaking parent's mental health, and the degree to which the child engages in active and problem-based coping.

Marital break-up and conjugal bereavement in adult life

Marital break-up is a frequent precipitant for suicide attempts and completed suicide, particularly in those with alcohol and substance abuse problems (87). There is evidence that the relationship rupture in alcoholics often follows domestic violence (88). In midlife and older individuals, particular males, conjugal bereavement is a risk factor for suicidal ideation and behavior, especially in concert with other psychiatric risk factors (89;90) Among women, having a child was protective against conjugal bereavement's impact on suicide risk (91). Complicated grief has been shows to increase the risk for suicidal ideation above and beyond psychiatric disorder (75). Conversely, suicide, particularly in the geriatric age group is less likely to occur in those with a strong support network, e.g., confiding friendships, children nearby, or living with children (92;93).

Quality of family relationships

Family discord, including high expressed emotion have consistently been shown to be both correlates and predictors of adolescent suicidal behavior (94), although the relationship between discord and suicide attempt is somewhat attenuated after controlling for parental and child psychiatric disorder (84). Parent-child discord is the single most common precipitant for completed suicide in adolescents under the age of 16 (95). Other characteristics of parent-child relationships that have characterized suicidal adolescents have been lack of perceived support, and poor communication, particularly between children and fathers (24;85;96). In older individuals, marital conflict is often associated with depression and substance abuse, although it is difficult to disentangle the extent to which the psychiatric illness is a source of the discord, or a consequence. Nevertheless, marital therapy aimed at reducing discord and increasing support has been shown to relieve depression when discord is a prominent part of the presentation (97–100). Moral objections to suicide have also been shown to protect against suicidal behavior, and such attitudes can also be familially transmitted (101;102).

Family protective factors

High parent-child warmth, parental monitoring, consistent parental discipline, and family cohesion have been shown to be protective against youthful suicidal behavior (103). High levels of protective factors lower the risk for suicide attempt in adolescents even in the presence of other high risk behaviors and predisposing factors (67;103)

Adult suicide attempters, in general, report lower perceived family support, and concern about the impact on family is one of the most common reasons given by depressed individuals for not engaging in suicidal behavior (104;105). A much lower proportion of adults who commit suicide are in a stable relationship compared to living controls (76), suggesting that the continuation of a strong pair-bond is protective. As noted above, other factors protective against suicide in older individuals are a strong network of support, including living with children (if the individual is female) or having them nearby.

Childhood experience of abuse

Physical and sexual abuse, particularly sexual abuse that involves genital or anal penetration, are strongly associated with suicide attempts and completions. According to some epidemiological studies, sexual abuse has a population attributable risk of nearly 20%, meaning that the rate of suicidal behavior in adolescents could be decreased by 20% if sexual abuse could be eliminated (106–108). The mechanism by which abuse increases risk for suicidal behavior is complex, as child maltreatment usually takes place against a background of family discord, parental psychopathology, including a parental history of suicidal behavior, all of which can also increase the risk for suicidal behavior in children (59;60). However, while it is clear that abuse increases the risk for a wide array of psychiatric disorders, some studies show that even after controlling for the increased risk of psychiatric disorder, abuse increases the risk and decreases the age of onset for suicidal behavior (109;110).

Sexual abuse in parent and child appear to increase the risk for transmission of suicidal behavior through several possible mechanisms. As noted above, sexual abuse in a parent increases the likelihood of sexual abuse in the child, which in turn increases the likelihood for a mood or anxiety disorder, and for suicide attempt (33;48;51;111). Second, parents who abuse their children are more likely to also attempt suicide as well as have mood and substance disorders, so that the liability for suicide attempt in the child may come from both genetic and environmental manifestations of a common diathesis (59;60). Third, sexual abuse may increase the likelihood of expression of traits related to suicidal risk, like neuroticism, anxiety, depression, and impulsive aggression (32;47;51;110;112–114). Also, abuse and other adverse circumstances could be familially transmitted by shared environmental rather than by genetic mechanisms. Fu et al. found that shared environment explained as much of the variance in suicide attempts as did heritability (10). Dinwiddie et al., in an analysis of the Australian twin registry reported in Statham et al. (9), found that the negative impact of sexual abuse on mental health outcomes was explained by shared environment, rather than genetic factors (115).

There is growing evidence of long-lasting neurobiological changes as a result of neglectful or abusive rearing environments. In mice, pups who are exposed to low levels of maternal grooming show changes in cortisol response to stress, cognitive impairment, and lower persistence in the face of frustrating tasks than those exposed to high levels of grooming (116–118). Moreover, the specific maternal behavior (grooming) appears to be familially transmitted from mother to daughter. However, this transmission is not due to genetic factors because cross-fostering experiments show that it is exposure to grooming rather than the grooming style of the biological mother that determines grooming behavior in the offspring (116). Neuroendocrine studies of children with a history of maltreatment show alternations in the hypothalamic pituitary adrenal axis (HPA), although some studies have reported lower than expected response to stress, and some, higher than expected response (119). Neuroimaging studies in children exposed to maltreatment also show changes in corpus collusum and hippocampus volume that may account for some of the cognitive findings associated with a history of maltreatment (61). Abuse and adverse rearing environments result in a decrease in central serotonergic function, a biological system that has been linked to impulsive aggression and suicidal behavior (120–124).

Interactions between genes and environment

In the debate between about the relative contributions of nature and nurture, there is a “nature to nurture,” (125) meaning that adverse family environments do not occur at random, and may arise due to parental or child genetic contributors to these adverse environments. Parental psychiatric illness is a risk factor for premature parental death, which in turn puts their offspring at higher risk for psychiatric disorder (49). Parents who abuse their children are more likely to have psychiatric disorders such as depression, substance abuse, and a history of suicidal

behavior, so that their children are at risk because of their genetic diathesis as well as because of the exposure to abuse (60;126). Children who are risk for depression may follow a stochastic pathway: (1) genes that predispose to anxiety also predispose to the occurrence of certain depressogenic life events, that, in the face of a genetic diathesis to anxiety, lead to depression (127). Finally, studies of twins reared apart show that dimensions of maternal behavior such as parental warmth are actually heritable, being induced by the behavior of the twin offspring (12).

Second, it is important to recognize that environmental factors are most likely to affect those with a genetic diathesis. This was most elegantly demonstrated by Caspi and colleagues, who showed that the likelihood of depression and suicidal behavior was greatest when there was a history of stressful life events (including abuse) and a less function allelic form of the serotonin transporter promoter gene (112). This finding has been replicated several times (71;128–130). Kaufman et al. found that the risk for depression was greatest in abused children who also had a family history of depression (124).

Third, these different family-environmental stressors rarely occur in isolation. For example, it is more common for a child with a background of maltreatment to have been also exposed to multiple parental figures, parental criminality and psychiatric disorder, witnessing domestic violence, and economic instability (96;131;132). Nevertheless, there is evidence that there are factors that are protective against suicidal behavior even in the face of substantial other risk factors (103).

Summary

It is well-recognized that suicidal behavior runs in families. Adoption and twin studies together make a compelling case that familial transmission of suicidal behavior is in part attributable to genetic factors. There is some evidence that the transmission of suicidal behavior is mediated by the transmission of impulsive aggression. Other, less thoroughly investigated possible mediators include neuroticism and neurocognitive deficits. However, given that at best, around 50% of the variance is explained by genes, there is a significant role for environmental factors as well. The most plausible explanations for non-genetic familial transmission are the intergenerational transmission of abuse and of adverse familial environments. Bereavement and relationship disruption may make a specific contribution to suicidal risk via the development of complicated grief although the long-term effects are likely to be mediated by complex chain of inter-related events. Imitation may also make a contribution to suicidal risk, at least with regard to attempted suicide. However, so-called family environmental factors often are related to risk factors that are heritable. Conversely, and most genetic factors exert their impact on depression and suicidal behavior via an interaction with a stressful environment.

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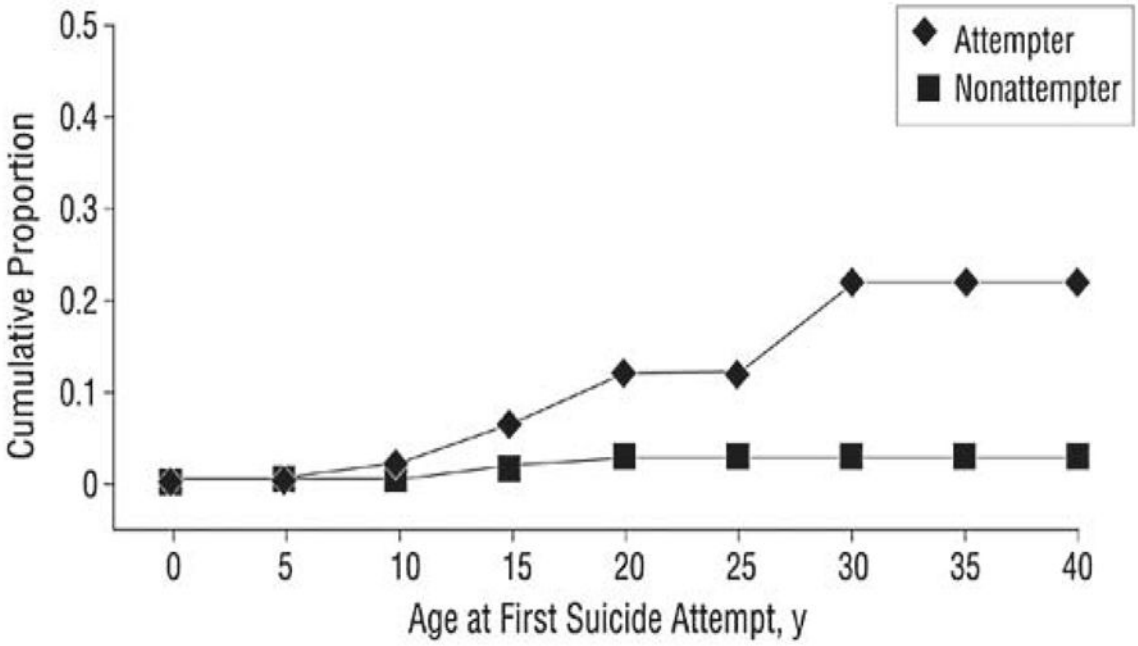

Figure 1. Risk of Suicide Attempt in the Offspring of Attempters Compared to Offspring of Non-Attempters.*

Diamond = Attempter

Square = Nonattempter

*From Brent et al. Familial pathways to early-onset suicide attempt: Risk for suicidal behavior in offspring of mood-disordered suicide attempters. Arch Gen Psychiatry 2002; 59:801–807, with permission.

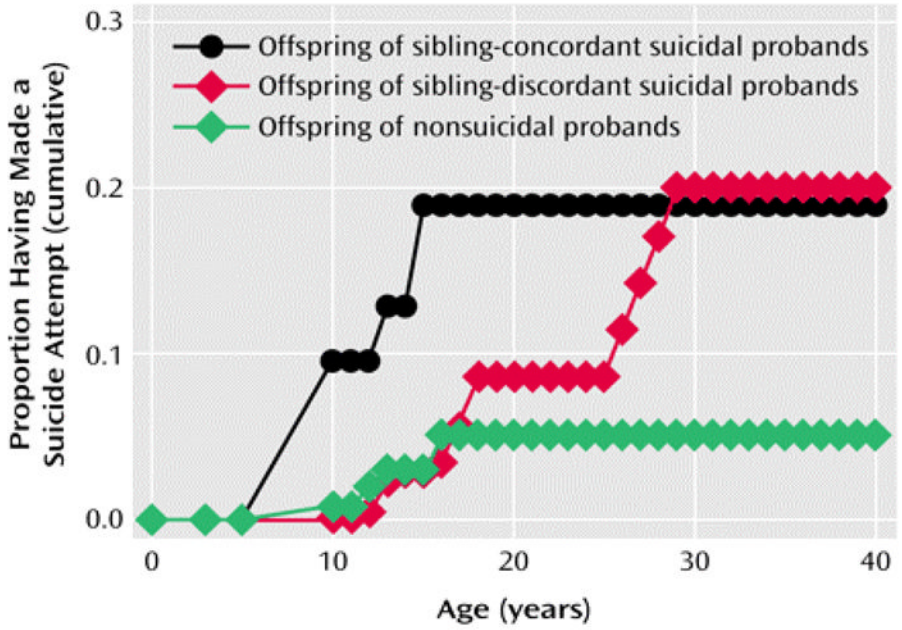

Figure 2. Suicide Attempts Over Time Among Offspring of Mood Disorder Probands From Sibling Pairs Concordant or Discordant for Suicidal Behavior*

Black Circle = Offspring of sibling-concordant suicidal probands
Red Diamond = Offspring of sibling-discordant suicidal probands
Green Diamond = Offspring of nonsuicidal probands
*From Brent et al. Peripubertal suicide attempts in offspring of suicide attempters with siblings concordant for suicidal behavior. Am J Psychiatry 2003; 160:1486–1493, with permission.

Table 1

Schulsinger et al. (1979): Adoption Study: Rates of Suicide in Biological Versus Adoptive Relatives of Adoptees who Committed Suicide and of Live Adoptee Controls*

Adopted	Index cases	Suicide/biological relatives	Suicide/adopted relatives
Suicide	57	12/269*	0/148
Controls	57	2/269	0/150

* $P < 0.01$.

* From Schulsinger et al. A family study of suicide. In: Schou M, Stromgren E, eds. *Origin, Prevention and Treatment of Affective Disorders*. London: Academic Press 1979: 277–287, with permission.

Table 2

Incidence of Suicide in Biological Relatives of Depressive and Control Adoptees*

Diagnosis in adoptee	Incidence of suicide in biological relative (%)	OR	*P*
Affective reaction	5/62 (8.1)	30.3	< 0.0001
Bipolar depression	4/71 (5.6)	20.6	0.003
Neurotic depression	3/122 (2.5)	8.7	0.056
Unipolar depression	3/132 (2.3)	8.0	0.066
No mental illness	1/346 (0.3)	-	-

* From Wender et al. Psychiatric disorders in the biological and adoptive families of adopted individuals with affective disorders. Arch Gen Psychiatry 1986;43:923–929, with permission.

Table 3

Twins Studies in Which one Twin has Committed Suicide*

Study	No. of twins (%) concordant for suicide behavior		
	MZ	**DZ**	***P***
Haberlandt [1967]	14/51 (17.6)[a]	0/98 (0)	< 0.001
Juel-Nielsen [1970]	4/19 (21.1)	0/58 (0)	< 0.003
Zair [1981]	1/1 (100)	0/0 (0)	NS
Roy et al. [1991]	7/62 (11.3)	2/114 (0)	< 0.01
Roy et al. [1995]	10/26 (38.5)[b]	0/9 (1.7)	< 0.04
Roy and Segal [2001]	4/13 (30.7)[c]	0/15 (0)	< 0.04
Total	40/172 (23.0)	2/294 (0.7)	< 0.00001

[a] Five pairs, co-twin attempted suicide.

[b] Ten pairs, co-twin attempted suicide.

[c] Three pairs, co-twin attempted suicide.

* From Brent and Mann. Family genetic studies, suicide, and suicidal behavior. Am J Psychiatry 2005;133C:13–24, with permission.

Table 4

Twin Studies of the Genetic Epidemiology of Suicidal Behavior*

Study	N	Gender	Concordance (%)		Concordance (AOR)		Heritability (%)			
			MZ	DZ	MZ	DZ	Ideation	Attempt		
Statham	5,995	Both	23.1	0	3.8	-	43	55		
Glowinski	3,416	Female	25	12.8	5.6	4.0	-	48		
Fu	7,744	Male	-	-	12.1	7.4	43	30		
							36	17[a]		

[a] Adjusted for heritability of other risk factors.

* From Brent and Mann. Family genetic studies, suicide, and suicidal behavior. Am J Psychiatry 2005;133C:13–24, with permission.

Table 5

Studies of the Risk of Familial Suicide in the Relatives of Suicide Probands

Study	Year	Probands	Controls	Sample size proband/control	OR
Tsuang	1985	Patient suicides	Patient non-suicides	29/491	3.8
Egeland	1985	Suicides in Amish studies	Comparison pedigree	-	4.6
Foster	1999	Irish suicides	Attendees in same general practice	118/118	3.0(NS)[a]
Powell	2000	Inpatient suicides	Inpatient non-suicides	112/112	4.6[a]
Tsai	2002	Bipolar suicides	Bipolar controls	41/41	15.1[a]

[a] Adjusted OR.

[*] From Brent and Mann. Family genetic studies, suicide, and suicidal behavior. Am J Psychiatry 2005;133C:13–24, with permission.

Table 6

Studies of Suicide Based on Registries and Record Linkage*

Study	Year	Country	Proband	Control	Sample size proband/controls	AOR
Qin	2002	Denmark	Suicides, 9–45	Matched community control	4,262/80,238	2.6,[ab]
Agerbo	2002	Denmark	Suicides, 10–21	Matched community controls	496/24,800	2.3–4.8,[abc]
Qin	2003	Denmark	Suicides, all ages	Matched community controls	21,169/423,128	2.1,[ab]
Runeson	2003	Sweden	Suicides, all ages	Matched non-suicide deaths	8,396/7,568	2.0[b]

[a] Adjusted for previous psychiatric admission/care.

[b] Adjusted for relatives previous psychiatric admission.

[c] OR for suicide in father/mother.

* From Brent and Mann. Family genetic studies, suicide, and suicidal behavior. Am J Psychiatry 2005;133C:13–24, with permission.

Table 7

Family Studies of Rates of Suicidal Behavior in Relatives of Suicide Versus Control Probands*

Study	Year	Proband	Control	N proband/control	AOR,[ab]
Brent	1996	Adolescent suicides	Matched community controls	58/55	4.3
Gould	1996	Adolescent suicides	Matched community controls	120/147	5.1
Cheng	2000	Adult suicides	Matched community controls	113/226	5.2
Kim	2005	Adult male suicides	Matched community controls	217/171	10.6

[a] Chart Review.

[b] FH attempt/completion.

* Adapted from Brent and Mann. Family genetic studies, suicide, and suicidal behavior. Am J Psychiatry 2005;133C:13–24, with permission.

Table 8

Family History Studies of Attempted Suicide Probands*

Study	Year	Proband	Control	N proband/control	OR
Garfinkel[a]	1982	Adol. attempters in ER	ER non-attempters	505/505	5.4
Roy[a]	1983	Adult inpt. attempters	Adult inpt. non-attempts	243/5,602	3.4
Linkowski	1985	Adult inpt. attempters	Adult inpt. non-attempts	239/474	2.0–3.5
Mitterauer	1990	Manic-depressive attempters	Manic depressive non-attempters	342/80	3.3
Sorenson	1991	Suicide attempters	Non-attempters	93/2,211	5.8
Malone	1995	Depressed attempters	Depressed non-attempters	100/100	7.6
Roy	2002	Alcoholic attempters	Alcoholic non-attempters	124/209	2.4/4.0[b]
Roy	2001	Cocaine dependent attempters	Cocaine-defendant non-attempters	84/130	4.5/5.9[b]
Roy	2002	Opiate-dependent attempters	Opiate-dependant non-attempters	105/171	2.9/6.0[b]
Roy	2003	Substance dependent attempters	Substance dependent non-attempters	175/274	3.2/5.9[b]
Mann	2005	Mood disordered attempters	Mood-disordered non-attempters	234/223	2.0/2.1[b]
Goodwin	2004	Community sample (attempters)	Community sample (non-attempters)	165/1209	4.6

[a] Chart review.

[b] Family history of attempters/completions.

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Table 9

Family Studies of Child or Adolescent Suicide-Attempting Probands*

Study	Year	Proband	Control	N proband/control	OR
Pfeffer	1994	Prepubertal attempter	Ideator/clinica l control community controls	25/28/16/54	4.3–8.3[a]
Johnson	1998	Adol. Inpt. attempters	Adol. Inpatient non-attempters	62/70	2.1[b]
Bridge	1997	Community attempters	Community controls	3/55	12.1[b]

[a] Attempter/normal control; OR = 8.3, attempter/clinical control.

[b] Adjusted OR.

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