Pathways to Suicide-Related Behavior in Offspring of Mothers With Depression: The Role of Offspring Psychopathology

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Objective: Offspring of mothers with depression are a high-risk group for the development of suicide-related behavior. These offspring are therefore a priority for preventive interventions; however, pathways contributing to risk, including specific aspects of offspring psychopathology, remain unclear. The aim of this study was to examine whether offspring symptoms of major depressive disorder (MDD), generalized anxiety disorder (GAD), disruptive behavior disorder (DBD), attention-deficit/hyperactivity disorder (ADHD), and alcohol abuse independently mediate the association between maternal depression and offspring suicide-related behavior.

Method: Data were used from a population-based birth cohort, the Avon Longitudinal Study of Parents and Children (ALSPAC). Three distinct classes of depression symptoms across the mothers' first 11 years of their child's life were identified (minimal, moderate, chronic-severe). Offspring psychopathology was assessed at age 15 years and suicide-related behavior at age 16 years. Data were analyzed using structural equation modeling.

Results: There was evidence for increased risk of suicidal ideation in offspring of mothers with chronic-severe depression symptoms in comparison to offspring of mothers with minimal symptoms (odds ratio = 3.04, 95% CI = 2.19, 4.21). This association was independently mediated by offspring MDD, GAD, and DBD symptoms. The same mechanisms were found for offspring of mothers with moderate depression symptoms over time. Results were similar for offspring suicide attempt except for additional evidence of an indirect effect through offspring ADHD symptoms.

Conclusion: Findings highlight that suicide prevention efforts in offspring of mothers with depression should not only be targeted at offspring with MDD; it is also important to consider offspring with other forms of psychopathology.

Key Words: suicide-related behavior, ALSPAC, maternal depression, psychopathology

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It is well established that offspring of mothers with depression are at increased risk for the development of suicide-related behavior[1] and are therefore a priority for preventive interventions. However, the reasons why they are at increased risk, including the role of specific aspects of offspring psychopathology, remain unclear. Offspring of mothers with depression are at increased risk for a range of mental health problems (including depression, anxiety, disruptive behavior disorders, attention-deficit/hyperactivity disorder (ADHD), and alcohol abuse),[2,3] and there is some evidence that each of these disorders is associated with both suicidal ideation and suicide attempt in adolescence.[4-7] Studies have consistently shown that depressive disorder is associated with suicide-related behavior when taking account of other psychopathology[5,6]; however, findings as to whether the effects of other disorders are independent of depression and each other have been inconsistent. A recent national survey of US adolescents[6] found no independent effect of generalized anxiety disorder (GAD), assessed retrospectively, on suicide-related behavior in adolescents. However, a longitudinal sample of adolescents[7] found that GAD was associated with later suicide-related behavior after adjusting for the presence of other psychopathology. Findings for substance abuse have also been inconsistent, with some studies showing an association with suicidal ideation[6] and others only with suicide attempt.[4,5] ADHD has generally been combined with other disruptive behavior disorders,[4,5] meaning that it is difficult to draw conclusions about the independent effects; however, the national survey of US adolescents[6] examined the disorders separately and found an independent effect of oppositional defiant disorder (ODD) on later suicidal ideation but that ADHD was associated only with the transition from ideation to attempt.[6] Previous studies, however, have not fully taken account of the co-occurrence of offspring psychopathology by examining the effects of each disorder while adjusting for covariance between them. Given the evidence that disorders tend to co-occur in adolescents[8] and that high levels of comorbidity are associated with suicide,[9] taking account of this co-occurrence is


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important to examine the independent effects of specific aspects of offspring psychopathology.

Longitudinal studies examining the influence of maternal depression on offspring suicidal ideation have found that adjustment for offspring depression symptoms did not fully account for risk effects[10,11]; however, the mediating role of other types of offspring psychopathology has rarely been investigated. One longitudinal case-control study using Swedish inpatient care registers found that the association between maternal affective disorder and offspring suicide attempt was attenuated, although still present, when adjusted for whether offspring had been hospitalized because of psychiatric disorder.[12] A cross-sectional study found a similar pattern of results when examining suicidal ideation and suicide attempt in adult offspring of parents with depression, with adjustment for the presence of lifetime offspring psychiatric disorder.[13] However, more research is needed to examine the relative or differential importance of specific types of offspring psychopathology in explaining the association between maternal depression and subsequent offspring suicidal ideation and suicide attempt in adolescence. This is important, given that offspring of mothers with depression show a broad range of psychopathology. In addition, it is an essential first step to establishing whether treating specific symptoms in offspring of mothers with depression is likely to lead to a reduction in suicide-related behavior. There is evidence that more chronic and severe symptoms of maternal depression have a greater impact on offspring development,[14] highlighting the importance of testing mechanisms for this group. However, it is not known whether risk mechanisms' underlying links with offspring suicide-related behavior vary by maternal depression severity.

Therefore, the present investigation uses a large population cohort to examine how much of the association between differing levels of maternal depression symptoms, over the first 11 years of their child's life, and later offspring suicidal ideation and suicide attempt is explained by proximal offspring psychopathology, including symptoms of major depressive disorder (MDD), GAD, disruptive behavior disorder (DBD), ADHD, and alcohol abuse.

METHOD

Study Sample

Data were used from a large UK birth cohort study: the Avon Longitudinal Study of Parents and Children (ALSPAC). The cohort was set up to examine genetic and environmental determinants of health and development.[15] The core enrolled sample consisted of 14,541 pregnant women resident in the former county of Avon, United Kingdom, who had an expected date of delivery between April 1, 1991, and December 31, 1992. Of the 14,062 live births, 13,617 were singletons and were alive at 1 year of age. The sample is broadly representative of the UK population; however, mothers enrolled in ALSPAC were more likely to live in owner-occupied accommodation and to have a car, more likely to be married, and more likely to be white.[16] Parents and children have been followed up regularly since recruitment via questionnaire and clinic assessments. All adult participants gave informed consent, and ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the local research ethics committees. Further details on the sample characteristics and methodology have been described previously,[15,16] and detailed information about ALSPAC can be found on the study website (http://www.bristol.ac.uk/alspac). Information on all available ALSPAC data is available on the fully searchable data dictionary (http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary).

Measures

Maternal Depression Symptom Trajectories. Maternal depression symptoms were assessed at 10 time points (from 18 weeks' gestation to child age 11 years) using the Edinburgh Postnatal Depression Scale (EPDS).[17] In a prior analysis using this dataset, latent class growth analysis was used to identify qualitatively distinct patterns of depression symptoms in mothers over time. Further details on the derivation and validation of classes are given in Supplement 1 and Table S1, available online. For the purposes of these analyses, 3 trajectory classes of depression are compared: mothers with chronic and severe levels of symptoms ("chronic-severe"), those with subthreshold but sustained depression symptoms over time ("moderate"), and those with very low levels of depression symptoms ("minimal"). Approximately 40% of the sample belonged to the minimal class, 55% of the sample belonged to the moderate class, and 5% of the sample belonged to the chronic-severe class. In all analyses, the minimal class is treated as the reference group. Table S2 (available online) shows mean depression symptoms at each assessment for mothers in each of the groups.

Offspring Suicide-Related Behavior. Suicide-related behavior at age 16 years was assessed via a self-report postal questionnaire.[18] Participants were classified as having a lifetime history of suicidal ideation if they responded positively to either of the following questions: Have you ever found yourself wishing you were dead and away from it all? Have you ever thought of killing yourself, even if you would not really do it? The present investigation focuses on children who reported suicidal ideation in the previous year only (78% of those who reported lifetime suicidal ideation by age 16 years) to preserve the time ordering of the analysis. History of suicidal ideation at age 11 years was assessed using the childhood interview for borderline personality disorder with the question, Have you thought about killing yourself?

Secondary analyses investigated specific associations with lifetime history of suicide attempt by age 16 years. Participants were classified as having a lifetime history of a suicide attempt if they endorsed the following question: On any of the occasions when you have hurt yourself on purpose, have you ever seriously wanted to kill yourself? Participants were also included if they reported "I wanted to die" as a reason to explain why they hurt themselves on purpose on the most recent occasion.

Possible Mediating Variables: Offspring Psychopathology. Offspring psychopathology was assessed using the Development and Well-Being Assessment (DAWBA)[19] parent and child versions. The DAWBA is a semi-structured interview consisting of questions about child mental health symptoms and their impact. Different time spans are used across the DAWBA sections to follow *DSM-IV* criteria. At age 15 years, parent versions of the DAWBA were used to assess symptoms of DBD (ODD over the past 6 months or conduct disorder over the past year) and symptoms of ADHD over the past 6 months. Child versions of the DAWBA were used to assess symptoms of MDD over the past month and symptoms of GAD over the past 6 months. Each DAWBA section consisted of 20 to 25 questions that followed the diagnostic criteria operationalized in the *DSM-IV* or *ICD-10*. Continuous symptom scores were derived from the sum of all symptom items within the relevant section of the DAWBA. Symptoms of alcohol abuse over the