What Psychiatry, Developmental Psychology, and Neuroscience Can Teach Us About At-Risk Students†

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I am usually asked to speak on the topic of psychosocial development and brain immaturity in the context of adolescent culpability, particularly around the issue of adolescents charged as adults for serious crimes. I am very happy to be discussing these important issues as they may relate to youth suicide, and appreciate Professor Massie’s attention to the convergence of psychiatric illness, developmental maturity, and suicidal behavior in youth.

Let me begin by acknowledging that functional neuroimaging and neuroscience is in its infancy.† Much of the developmental psychology literature on adolescent immaturity and culpability appears to have been a

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1. See Rebecca Saxe et al., Understanding Our Minds: Linking Developmental Psychology and Functional Neuroimaging, 55 ANN. REV. PSYCHOL. 87, 88 (2004) (acknowledging that neuroimaging has recently joined other theories, such as psychology and ethology, as a mode for understanding the human capacity for reasoning).
response to public policy decisions and responses to juvenile crime that
were not only unfounded scientifically, but also ran counter to what every
parent and grandparent knows—children and teenagers are immature. 2 We
have all made decisions in our youth that we may recall fondly if they did
not result in significantly negative consequences, but realize that on some
level, good fortune was a critical factor in remaining unscathed, which is
one reason why we cringe at the thought of our children making similar
decisions. A "learning" or "growth" experience can just as easily become a
disaster from which it is hard to rebound. 3 An example is the question on
the Common Application for college entrance as to whether an applicant
has ever been found guilty of a felony or a misdemeanor (pertaining to
juvenile as well as adult court). 4

A problem in medicine, including psychiatry, is making
generalizations about one group based on data pertaining to a different
group. 5 We have heard the justifiable criticism of translating data obtained
from research on male heart disease and resulting treatment

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2. See, e.g., Elizabeth S. Scott & Laurence Steinberg, Adolescent Development and the Regulation of Youth Crime, 18 FUTURE CHILD. 15, 16 (2008) (discussing the legal and policy transformation in treatment of juvenile offenders at the end of the twentieth century). The article posits that, at the end of the 1990s, state legislatures began altering their justice systems so as to disregard age and immaturity in criminal sentencing. Id. The authors attribute this phenomenon to public pressure in the wake of violent juvenile crime. Id. at 16. 18. See also Stephen J. Morse, Immaturity and Responsibility, 88 J. CRIM. L. & CRIMINOLOGY 15, 53–59 (2008) (attempting to assign degrees of responsibility to adolescents who commit severe crimes but are nonetheless lacking developmentally).


5. See, e.g., Karla J. Gingerich, Diversity and Attention Deficit Hyperactivity Disorder, 54 J. CLINICAL PSYCHOL. 415, 416 (1998) (criticizing the cross-application of data obtained from white males with ADHD to other, more diverse groups).
recommendations to heart disease in women. Similarly, conclusions based on research, however methodologically sound, with mood disorders in adults cannot be generalized to children, and research findings on mood disorders in children cannot be assumed to accurately reflect the condition in adolescents.

Our topic today is focused on "campus" suicide. Technically, that group is comprised almost exclusively of individuals who are legal adults, but developmentally, the eighteen-year-olds to twenty-year-olds are probably much closer to adolescents, and even the twenty-one–year-olds to twenty-two-year-olds have probably not achieved the level of myelination and neuronal pruning that will have occurred by the time they are in their mid-twenties.

The databases MEDLINE and PubMed were searched for studies on suicide among college students using the following terms: "college or university students" and "suicide." The search yielded seventy-three relevant publications in the past twenty years. None of the articles or studies was related to neuroscientific developments or findings in that population, and only two focused on cognitive or developmental influences.

Suicide is the second leading cause of death among college students, and the third leading cause of death among fifteen-year-olds to twenty-four-year-olds.

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6. See, e.g., Proceedings from the Scientific Symposium: Sex Differences in Cardiovascular Disease and Implications for Therapies, 19 J. WOMEN’S HEALTH 1059, 1063 (2010) (describing the adverse effects incurred by women taking heart medication tested solely on male patients).

7. See Konstantinos N. Fountoulakis, The Emerging Modern Face of Mood Disorders: A Didactic Editorial with a Detailed Presentation of Data and Definitions, 9 ANNALS OF PSYCHIATRY (REVIEW ISSUE) 1, 14 (2010) ("Although the core features of mood disorders are essentially the same across a lifetime, traditionally children and older patients are considered somewhat separately because of the special features their phases of life include.").


10. Id. The search, using the referenced terms, yielded the reported results as of September 5, 2010.

year-olds. In a large study in ten Midwestern university campuses, Silverman and colleagues found an overall suicide rate of 7.5 per 100,000 among college students, compared to 15 per 100,000 in a national sample matched for age, ethnicity, and sex. While fears of a suicide epidemic among college students are unfounded, with the most recent statistics indicating a suicide rate half that of non-student peers, there remains a fascination, particularly within the media and press with "preventing" campus suicide. Concern regarding suicidality in college students is not a new phenomenon. It was recognized almost a century ago by college administrators who raised concerns about suicide in this population when it ranked as the third or fourth highest cause of death among students. However, there is a growing perception among the public and the lay press that colleges should prevent student suicide. The reality is that suicide is a phenomenon with such a low base rate (and campus homicide is even rarer) that predicting with any reasonable precision who will kill himself or herself is impossible. The best that we can do, and this is no insignificant accomplishment, is to identify scientifically validated risk factors for the behavior in question. Those risk factors, which include the presence of mental illness, especially untreated mental illness, and the potential impingement of developmental factors, including cognitive and second leading cause of death among students at American colleges and universities.


14. See Schwartz, supra note 11, at 344 (noting that the suicide rate among the general U.S. population, aged twenty to twenty-four, is 52% greater than the student population).


16. See Schwartz, supra note 11, at 341 (discussing the scholarship of several studies, beginning in the 1920s, that have attempted to account for suicide among college students).

17. See Harold S. Diehl & Charles E. Shepard, The Health of College Students 100 (1939) (reporting suicide as the third leading cause of death from data provided by nine universities for 327 student deaths during a ten-year period, 1925–35).

18. See Arenson, supra note 15 (describing schools’ efforts to curb suicide among its students by intervening at the outset of suicidal tendencies).

19. See Schwartz, supra note 11, at 344 (reporting that only 6.5 students per 100,000 per year committed suicide during the years of 1991–2004).
psychosocial maturity, as well as the findings of neuroscience and genetic research, is what I will be talking to you about today.

I. Neuroscience

Neuroscience received a great deal of interest from the legal community around the *Roper v. Simmons* Supreme Court case. Many professional associations (including the American Medical Association, the American Academy of Psychiatry and the Law, and the American Academy of Child and Adolescent Psychiatry) signed onto an amicus brief urging the Supreme Court to rely on neuroimaging data that reveals unequivocally that the human brain continues to mature until the middle to late twenties. The Supreme Court did not cite this neuroscience evidence in their opinion, at best referring to it obliquely, but they did cite the behavioral science that demonstrated on average that adolescents are less rational than adults.

I share the opinion of others, notably Steven Morse, JD, PhD, that the Supreme Court was right to not rely on neuroscientific data. Rationality and impulsivity are behavioral characteristics. Behavioral science research confirms what every parent knows: adolescents (and I might add by extension college students) are less rational, more impulsive, and more prone to risk-taking than adults. Functional neuroimaging only provides a

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20. *See Roper v. Simmons*, 543 U.S. 551, 578 (2005) (finding that the Eighth and Fourteenth Amendments preclude the imposition of the death penalty on offenders who were under eighteen when they committed the crime).


23. *See Roper*, 543 U.S. at 569–70 (distinguishing juveniles from adults based on inherent differences reflected in sociological and behavioral studies).

24. *See Stephen J. Morse, The Ethics of Forensic Practice: Reclaiming the Wasteland, 36 J. ACAD. PSYCHIATRY & L. 206, 211 (2008) (discussing that the Supreme Court did not need to rely on neurological data, a mere partial explanation for an individual’s action, once it acknowledged that minors are insufficiently rational to warrant capital punishment).

25. *See id.* (concurring with the Court’s acceptance of rationality, or lack thereof, as a behavioral characteristic).

26. *See id.* (noting that the Court accepted that adolescents are less rational than adults).
partial explanation of the causal mechanism for why this is so. 27 And I think that similar cautions are important with respect to the interpretation of neuroscience, especially neuroimaging, in the oversimplification of suicidal behavior.

II. Development

Ellis and Trumpower studied 318 college students who completed surveys on health risk behaviors, depression, suicidal ideation, and health-related attitudes. 28 They hypothesized that unhealthy (risky) behaviors such as cigarette smoking and problem-drinking may be subtle forms of suicidal behavior. 29 Contrary to their hypothesis, the association between suicidality and "health-compromising behaviors" was limited largely to substance-related behaviors, and furthermore, the association between suicidal behavior and health-related attitudes was mediated by depression. 30 Their results were not so much compatible with the notion of unhealthy (risky) behaviors as subtle suicidality (with suicidality on a continuum with risk-taking among college students in general), as a model in which suicidality is associated specifically with psychopathology, such as depression and substance abuse. 31

Currier and colleagues, in an article discussing the potential link between genetics and suicidal behavior, noted that "[e]nvironment, particularly during critical childhood developmental periods, can influence the effect of genetic variants on neurobiologic function." 32 Caspi and colleagues found that life events predicted the onset of clinical depression.

27. See id. (distinguishing neurological data, which provides partial explanation as to why adolescents are less rational than adults, from behavioral data, which provides a full explanation).


29. See id. (operating under the presumption that negative attitudes, possibly developed through adverse childhood experiences, could help explain the link between suicide and unhealthy behaviors); see also id. at 254–55 (reporting that smoking and problem-drinking ranked among the highest health risk behaviors between suicidal and non-suicidal individuals).

30. Id. at 251

31. Id.

only in those with the low expressing 5-HTTLPR short (s) allele. For example, it has been shown that child maltreatment predicted adult depression that seemed to be triggered by stress, but more so in individuals with the low expressing 5-HTTLPR s allele.

Several studies have reported a relationship between early life stress and abnormal hypothalamus-pituitary-adrenal (HPA) function in adulthood, but no studies have examined the relationship between early life stress, genes, and suicidal behavior with respect to the HPA axis. An early life-stress gene interaction of the CRH-R1 gene and child abuse on the severity of depression has been reported.

III. Risk Factors for Completed and Attempted Suicide

A variety of risk factors have been empirically validated for attempted and completed suicide in this population and have been well summarized by Bridge and colleagues. The risk factors are divided into six main

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33. See Avshalom Caspi et al., Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5–HTT Gene, 301 SCI. 386, 387 (2003) (substantiating the study’s hypothesis that genetic composition can affect how an individual reacts to stress). According to this study, an s allele in a 5–HTTLPR, a gene-linked polymorphic region, has an indeterminable effect on life stress and the onset of depression. Id. Those carrying the gene react worse to stress than those with different genetic makeups. Id. Accordingly, the study surmises, albeit inconclusively, that gene-environment interaction plays a critical role in determining whether certain individuals are genetically predisposed to depression. Id. at 388.

34. See Rudolf Uher & Peter McGuffin, The Moderation by the Serotonin Transporter Gene of Environmental Adversity in the Aetiology of Mental Illness: Review and Methodological Analysis, 13 MOLECULAR PSYCHIATRY 131, 131, 140 (2008) (confirming previous studies that suggest carriers of the s allele in 5–HTTLPR regions are more amenable to depression following stressful events, such as childhood abuse).

35. See Sonia J. Lupien et al., Effects of Stress Throughout the Lifespan on the Brain, Behaviour, and Cognition, 10 NATURE REV. NEUROSCIENCE 434, 434 (discussing several tests and studies that measured the effects of stress at different stages of life—including prenatal life, infancy, adolescence, and adulthood—on the brain, behavior, and cognition). More specifically, this study, conducted on animals and humans, measured how stress triggers the HPA axis, subsequently triggering the production of glucocorticoids (steroids) by the adrenal glands. Id. The study, however, did not address the relationship among stress, the HPA axis, and suicidal behavior. See generally id.

36. See Rebekah G. Bradley et al., Influence of Child Abuse on Adult Depression: Moderation by the Corticotropin-Releasing Hormone Receptor Gene, 65 ARCHIVES GEN. PSYCHIATRY 190, 195–96 (concluding that genetic polymorphisms in the CRHR1 gene, the type 1 receptor of the corticotrophin-releasing hormone, moderate the effects of child abuse on adult depression).

37. See Jeffery A. Bridge et al., Adolescent Suicide and Suicidal Behavior, 43 J. CHILD
categories: individual risk factors, familial factors, family-environment factors, biological factors, suicide exposure, and availability of lethal agents. Bridge and associates subsequently identified specific components within each risk category, such as suicidal ideation and previous suicidal behavior under "individual risk factors." The full list as follows:

A. Individual Risk Factors
   1. Suicidal ideation
   2. Previous suicidal behavior
   3. Lethality of the suicide attempt
   4. Intent and motivation
   5. Precipitant
   6. Mental illness
      a. Mood disorders
      b. Substance abuse (including alcohol) disorders*
      c. Conduct disorder and antisocial behavior
      d. Anxiety disorder
      e. PTSD
      f. Psychosis
      g. Eating disorders
      h. Psychiatric co-morbidity
   7. Poor physical health and chronic disability
   8. Interrelated health risk behaviors
   9. Personality and psychological factors
      a. Personality disorder/impulsive aggression
      b. Impulsivity
      c. Neuroticism
      d. Self-esteem
      e. Hopelessness
      f. Perfectionism
      g. Sexual orientation

B. Familial Factors
   1. Parental psychopathology
   2. Family history of suicidal behavior

38. Id. at 374–81.
39. Id.
C. Family-Environmental Factors
   1. Family constellation
   2. Loss
   3. Family relationships
   4. Maltreatment
   5. Alienation or "drifting"

D. Biological Factors

E. Suicide Exposure

F. Availability of Lethal Agents

IV. Psychiatric Disorders

A study conducted in North Carolina found that by age sixteen, 12% of girls and 7% of boys have had a depressive disorder at some time in their lives. At least 40% of cases of depression in adolescence are treatment resistant. We also know that depression is strongly associated with suicidality. A prior suicide attempt is one of the best predictors of completed suicide. Lecompte and colleagues studied the socio-demographic, clinical characteristics, autopsy, and toxicological findings in 392 youth suicides (ages fourteen to twenty-four) in Paris, between 1989 and 1996. During the eight-year study period 392 suicides involving young people were investigated. Two hundred and sixty victims (66%)

42. See Boris Birmaher et al., Practice Parameter for the Assessment and Treatment of Children and Adolescents with Depressive Disorders, 46 J. AM. ACAD. CHILD ADOLESCENT PSYCHIATRY 1503, 1503 (2007) (noting that early identification and treatment of depression may reduce the risk of suicide).
43. See Dominique Lecomte & Paul Fornes, Suicide Among Youth and Young Adults, 15 Through 24 Years of Age: A Report of 392 Cases from Paris, 1989–1996, 43 J. FORENSIC SCI. 964, 967 (1998) (reporting that one-third of suicide victims had previously attempted suicide). The study further notes that an additional one-third had previously verbalized intent to kill themselves or, similarly, wished to die. Id.
44. See id. at 964–65 (dividing the study into two parts: first, accounting for suicide rates among the studied population; then, second, focusing on the socio-demographic and psychological patterns in conjunction with the autopsy and toxicology reports).
45. Id. at 965.
were males.\textsuperscript{46} The mean age was twenty-two years in both sexes.\textsuperscript{47} Fifteen percent of the victims were below twenty years of age.\textsuperscript{48} Ninety-two percent of the subjects were single.\textsuperscript{49} Forty percent of the victims were students, 25\% were unemployed.\textsuperscript{50} One-third of the victims had previously attempted suicide.\textsuperscript{51} Sixty-six percent of the subjects used to take psychoactive prescription drugs and some of them had been under the care of a mental health professional at the time of the suicide.\textsuperscript{52} In forty percent of the cases a suicide note was found near the body.\textsuperscript{53} Depression (70\% of victims), schizophrenia (10\%), affective disorders, parent-child relational problems, partner relational problems, adolescent antisocial behavior, and borderline personality were found to be the most frequent diseases and stressors involved in the suicides.\textsuperscript{54} The suicide was rarely an accidental reaction to stress.\textsuperscript{55} It was constantly preceded by situational distress, which led to suicidal ideas if the adolescent failed to cope with problems.\textsuperscript{56} Ten percent were known as heroin users.\textsuperscript{57} In 25\% of the cases, the victim’s parents were divorced or separated.\textsuperscript{58} The most frequent method of suicide was poisoning, followed by jumping from a height, gunshot, subway death, and hanging/asphyxia.\textsuperscript{59} Among firearms, a handgun was more likely to be used than shotguns or rifles (85\% versus 15\%).\textsuperscript{60} Tranquilizers were the most frequent psychoactive drugs used for suicide

\begin{itemize}
\item[46.] Id.
\item[47.] Id.
\item[48.] Id.
\item[49.] Id.
\item[50.] Id.
\item[51.] Id.
\item[52.] Id.
\item[53.] Id. at 966.
\item[54.] See id. at 967 (confirming past studies that suggest familial strife and psychiatric disorders are common characteristics among suicide victims). The percentages for depression (70\%) and schizophrenia (10\%) represent the 60\% of victims who suffered from mental disorders at the time of death—not the population writ large. Id. at 965.
\item[55.] See id. at 967 (discussing the overwhelming presence of domestic discord, psychiatric disorders, and interpersonal conflicts among suicide victims).
\item[56.] See id. ("[W]e found the suicide to be embedded in a situation of not just the problems every adolescent has to deal with but turmoil in family life already rooted in childhood and not stabilizing during adolescence, in combination with . . . social instability in the year or month preceding the suicide.").
\item[57.] Id. at 965.
\item[58.] Id.
\item[59.] Id.
\item[60.] Id. at 966.
\end{itemize}
followed by antipsychotic drugs and antidepressants. Bridge and colleagues examined changes in suicide rates among ten-year-olds to twenty-four-year-olds in the United States from 1992 to 2006. The overall suicide rate and the rate by firearms, poisoning, and other methods declined markedly, whereas the hanging/suffocation rate increased significantly from 1992 to 2006. This increase occurred across every major demographic subgroup, but was most dramatic for females.

"[S]ubthreshold depressive disorder is one of the best-established risk factors for the development of full-syndrome depressive disorders," with "the lifetime prevalence [of subthreshold depression] through late adolescence being as high as 26%." A recent study estimated the risk for escalation of subthreshold depression into full-syndrome depression to be 67%, with five variables accounting for the variance in predicting escalation—severity of depressive symptoms, medical conditions or symptoms, history of suicidal ideation, history of anxiety disorder, and familial loading for depression. "Adolescents with three or more risk factors had an estimated 90.1% chance of escalating to full-syndrome depressive disorder, compared with 46.6% of adolescents with fewer than three risk factors." In light of these findings, identification of students with mood disorders, and especially those with mood disorders comorbid with alcohol and/or substance abuse, and referring those students for

61. Id.
63. See id. at 504 (reporting that suicide rates by firearms, poisoning, and other methods decreased by 45% and 20%, respectively, while suicide rates by intentional hanging and/or suffocation increased by 47%). This study collected data in which suicide was the underlying cause of death among ten-year-olds to twenty-four-year-olds. Id. at 503. Furthermore, the percentages are quantified based on rates per 10,000. Id.
64. Id. at 504.
65. Subthreshold depression is defined in a variety of ways and there are a number of potential categories in the DSM-IV for diagnosis, including dysthymia, depressive disorder, NOS, brief recurrent depression, and minor depressive disorder. Daniel N. Klein et al., Subthreshold Depressive Disorder in Adolescents: Predictors of Escalation to Full-Syndrome Depressive Disorders, 48 J. AM. ACAD. CHILD ADOLESCENT PSYCHIATRY 703, 703 (2009).
66. Id.
67. Id.
68. Id. at 708.
69. Id. at 710.
appropriate and adequate treatment is critical in decreasing the risk of completed suicide.

Depression is different from sadness, and stress does not fully explain the development of a disorder.\textsuperscript{70} 

"[D]isorder results from the interaction of stress and vulnerability."\textsuperscript{71} The diathesis-stress model stresses the relationship between potential causes of depression, and the degree to which people may be vulnerable to react to those causes.\textsuperscript{72} The diathesis-stress model suggests that people have, to varying degrees, vulnerabilities or predispositions for developing depression.\textsuperscript{73} Diathesis is a fancy word for vulnerability.\textsuperscript{74} Diatheses include biological, psychological, and social factors.\textsuperscript{75} Biological factors relate to the fact that we know that individuals with depression have disturbed immune, hormonal, and neurotransmitter system functioning. "Postmortem and neuroimaging studies of the brains of individuals who have completed or attempted suicide reveal changes in the number and functions of serotonin receptors in the regions of the prefrontal cortex, areas of the brain involved in the regulation of emotions and behavioral inhibition."\textsuperscript{76} Depression can increase one’s vulnerability to a range of physical disorders, and an individual with a physical disorder is more vulnerable to developing depression.\textsuperscript{77} As we will discuss, recent research advances indicate that genes can influence the transmission of depression from generation to generation.

Psychological factors that influence depression include negative patterns of thinking, called cognitive distortions, poor coping skills, and deficits in perceiving, understanding, and expressing emotions.\textsuperscript{78}

\textsuperscript{70} See David A. Brent, \textit{Medicalize Depression, Not Sadness}, 48 J. AM. ACAD. CHILD ADOLESCENT PSYCHIATRY 681, 681 (2009) (reviewing the difference between sadness due to life stressors and the diagnosis of depression).

\textsuperscript{71} Id.

\textsuperscript{72} See David A. Brent & J. John Mann, \textit{Familial Pathways to Suicidal Behavior—Understanding and Preventing Suicide Among Adolescents}, 355 NEW ENG. J. MED. 2719, 2720 (2006) (analyzing the relationship between the spread of vulnerabilities from family members to suicidal behavior and outside stressors).

\textsuperscript{73} See id. (explaining that the cause of suicidal behavior is a combination of both stress and inherited vulnerabilities).

\textsuperscript{74} See id. (explaining how the diathesis-stress model works, in that an inherited vulnerability to depression is clarified in the model through use of the word "diathesis").

\textsuperscript{75} See id. (describing the factors included in diathesis in terms of the diathesis-stress model).

\textsuperscript{76} Id. at 2720–21.

\textsuperscript{77} See Bridge et al., \textit{supra} note 37, at 378 ("Poor physical health and physical disability were associated with suicidal ideation or behavior.").

\textsuperscript{78} See P. Marton et al., \textit{Cognitive Distortion in Depressed Adolescents}, 18 J.
Psychological factors to some extent may be influenced by innate biological characteristics, such as temperament, as well as by social factors such as coping skills modeled for us by our families of origin, teachers, and peer groups.\textsuperscript{79} Social factors that contribute to depression include early separation from attachment figures, trauma, neglect, and bullying, and physical, sexual, and emotional abuse.\textsuperscript{80} Recent research has shown social stressors can serve as switches for turning genes on and off, causing changes in brain functioning.\textsuperscript{81} Children exposed to chronic stress including abuse are more likely to manifest clinical depression if they are genetically at risk.\textsuperscript{82} "Neglect and abuse during early childhood seem to contribute to the familial transmission of suicidal behavior by compounding genetic vulnerability."\textsuperscript{83}

The diathesis-stress model acknowledges that some individuals have more of these diatheses/vulnerabilities for developing depression.\textsuperscript{84} This model proposes that a propensity for developing depression is not sufficient to actually develop depression.\textsuperscript{85} Rather, a person’s diathesis must interact with stressful life events (of a social, psychological, or biological nature) in order to precipitate the onset of the illness.\textsuperscript{86}

According to the diathesis-stress model, the greater a person’s inherent vulnerability for developing depression, the less environmental stress will


\textsuperscript{80.} See \textit{id.} at 675 (describing the maltreatment history of the study subjects including the major subtypes of abuse).

\textsuperscript{81.} See \textit{id.} at 673 (showing that children with certain gene interactions had a higher vulnerability for depression but abused children were more likely to actually be depressed).

\textsuperscript{82.} See \textit{id.} ("Children with the met allele of the BDNF gene and two short alleles of 5-HTTLPR had the highest depression scores, but the vulnerability associated with these two genotypes was only evident in the maltreated children.").

\textsuperscript{83.} Brent & Mann, \textit{supra} note 72, at 2719.

\textsuperscript{84.} See \textit{id.} at 2720 (explaining that inherited factors that lead to vulnerability for depression occur at different levels depending on genetics).

\textsuperscript{85.} See \textit{id.} (explaining that vulnerability combined with outside stressors can lead to depression).

\textsuperscript{86.} See \textit{id.} ("In combination with such stressors, the inherited diathesis predisposes people to suicidal behavior.").
be necessary to cause him or her to become depressed. By the same token, if someone has a smaller amount of vulnerability for becoming depressed, it will take greater levels of environmental stress in order to produce the disorder. Until this critical threshold of stress is reached, vulnerable individuals typically function normally. Their vulnerabilities are considered to be "latent" or hidden. The presence of one or more psychiatric disorders, a family history of suicide and psychopathology, stressful life events, and access to firearms are key risk factors for youth and young adult suicide.

While interesting and exciting findings have emerged on the biology of suicide in adults, these are yet to be replicated in youths. Of major concern is that among adolescent suicide victims, only 7% to 15% were seen in a mental health clinic in the month prior to their deaths. In a study of college students who participated in the American Foundation for Suicide Prevention-sponsored College Screening Project at Emory University, 729 students were screened and 11.1% endorsed current suicidal ideation and 16.5% had a lifetime suicide attempt. Of note, "[t]he vast majority of students with moderately severe to severe depression

87. See Caspi et al., supra note 33, at 387 ("Diathesis-stress theories of depression predict that individuals’ sensitivity to stressful events depends on their genetic makeup.").
88. See id. ("[T]he risk of depression after a stressful event is elevated among people who are at high genetic risk and diminished among those at low genetic risk.").
89. See id. (explaining how without additional stressors, vulnerability to depression is not enough to bring about depression, on its own).
90. See id. (clarifying that absent outside stress factors, genetic vulnerabilities alone do not lead to depression).
91. See Brent & Mann, supra note 72, at 2720 ("Although psychiatric disorders also run in families, suicidal behavior appears to be familially transmitted independently of these disorders."); see also Bridge, supra note 37, at 381 (2006) ("A series of case–control studies has demonstrated a clear and consistent association between firearms in the home and completed suicides."); J. John Mann, Neurobiology of Suicidal Behavior, 4 Neuroscience 819, 819 (2003) ("Suicide is not simply a response to stress, but generally a complication of a psychiatric disorder.").
92. See Brent & Mann, supra note 72, at 2720 ("We have proposed a stress-diathesis model for adults that, along with the familial transmission of vulnerabilities to suicidal behavior, may help to explain and predict suicide among young people.").
93. See Brent, supra note 70, at 682 ("Only an estimated 7% to 15% of adolescent suicide victims have been seen in a mental health setting in the month before their suicide.").
94. Steven J. Garlow et al., Depression, Desperation, and Suicidal Ideation in College Students: Results from the American Foundation for Suicide Prevention College Screening Project at Emory University, 25 Depression & Anxiety 482, 482 (2008) ("Seven hundred and twenty-nine students participated over a 3-school year interval (2002–2005). Most notably, 11.1% of the students endorsed current (past 4 weeks) suicidal ideation and 16.5% had a lifetime suicide attempt or self-injurious episode.").
(85%) or current suicidal ideation (84%) were not receiving any psychiatric treatment at the time of assessment. 95 The National College Health Assessment Survey (NCHA) sponsored by the American College Health Association, measured depression, suicidal ideation, and suicide attempts among 15,977 college students in the academic year 1999–2000. 96 The survey found that "9.5% of students reported that they had seriously considered attempting suicide" within the past 1999–2000 school year, and 1.5% of students reported actually attempting suicide. 97 The findings revealed that depressed mood, sexual identity and orientation issues, and problematic relationships increased the likelihood of vulnerability to suicidal behavior. 98 The authors noted that "not all students who report depressive symptoms have considered suicide, but that among students who had contemplated or attempted suicide, depressive symptoms were almost always present." 99 Among students who had considered or attempted suicide, 94.9% reported feeling hopeless and so depressed that it was difficult to function at least once during the previous 12 months. 100 Only 20% of students who reported considering or attempting suicide were receiving treatment. 101

Thus it is critical to identify depressive disorders in college students, to identify additional vulnerabilities for suicide, and to intervene appropriately. A reality that needs to be considered is that frequently adolescents and young adults, particularly males, do not identify themselves as being "sad" or depressed. 102 Anger resulting in behavior that brings a student in front of a college disciplinary board (for example, assault against a peer or a romantic partner), especially if it is in combination with alcohol

95. Id.
97. Id.
98. Id.
99. Id. at 8.
100. See id. ("Among those students who considered suicide, 94.9% reported that they experienced feeling SDDF [So Depressed it was Difficult to Function] at least once during the previous 12 months.").
101. See id. at 3 ("Less than 20% of students reporting suicidal ideation or attempts were receiving treatment.").
102. See Renee D. Goodwin, Association Between Coping with Anger and Feelings of Depression Among Youths, 96 AM. J. PUB. HEALTH 664, 666 (2006) ("Male youths were less likely to report feeling depressed in the past year than female youths . . . . Female youths were more likely to report feelings of depression.").
or other substance abuse, should be thoroughly evaluated by a clinician experienced in psychiatric illness and treatment.\textsuperscript{103} To refer that individual for "anger management" without a thorough investigation of potential etiologies would be a mistake. Anger is a nonspecific sign or symptom in much the same way as fever is nonspecific. Fever is a symptom of a myriad of infectious and noninfectious disorders, and anger is a symptom observed in a variety of psychiatric and neurological disorders. However, there is increasing research indicating that impulsivity and aggression are important targets for treatment in depression and confer increased risk for completed suicide.\textsuperscript{104} "Studies in nonhuman primates show that early neglect by parents results in alterations in brain serotonin function, with attendant increases in impulsivity and aggression, especially in those who are genetically vulnerable."\textsuperscript{105}

We have discussed that completed suicide is almost always associated with a mental illness, but that most persons with a mental illness neither attempt, nor commit suicide. The pivotal question that will greatly enhance our assessment and treatment of patients at risk for suicide is to discover what differentiates depressed individuals (including depressed college students).

\section*{V. Genetic Links}

The first evidence that genes moderate the ability of an environmental risk to precipitate mental disorders was reported in 2002.\textsuperscript{106} Caspi and colleagues found that abused children with genotypes that conferred low levels of the neurotransmitter-metabolizing enzyme monoamine oxidase A (MAOA) more often developed conduct disorder, antisocial personality disorder, and adult violent crime than children with a high-activity MAOA genotype.\textsuperscript{107}

\begin{footnotesize}
\begin{enumerate}
\item See Bridge et al., supra note 37, at 375 ("In youth with conduct disorder and substance abuse, legal and disciplinary problems are common precipitants for suicidal behavior and suicide, reflecting in part contributions that impulsivity, aggression, and substance use make to suicidal risk.").
\item See Brent & Mann, supra note 72, at 2720 ("Impulsive aggression is strongly associated with suicidal behavior.").
\item Mann, supra note 91, at 820.
\item See Avshalom Caspi et al., \textit{Role of Genotype in the Cycle of Violence in Maltreated Children}, 297 S.Ct. 851 (2002) [hereinafter \textit{Role of Genotype}] (arguing that functional polymorphism in certain genes helps to curb the product of child abuse).
\item See id. at 851 ("Maltreated children with a genotype conferring high levels of
\end{enumerate}
\end{footnotesize}
Another study found that "individuals with one or two copies of the 5-HTT ‘short’ allele evidenced more depression and suicidality following stressful life events than those with two copies of the ‘long’ allele."108 "Twin, adoption, and family studies have established the heritability of suicide attempts and suicide."109 "Identifying specific ‘suicide-related’ genes has proven to be a more difficult task."110

Endophenotype is a psychiatric concept and refers to a type of biological marker.111 "Endophenotypes are measurable components unseen by the unaided eye along the pathway between disease and distal genotype."112 "[An] endophenotype may be neuophysiological, biochemical, endocrinological, . . . cognitive, or neuropsychological."113 The purpose of the concept was to bridge the gap between the gene and the puzzling disease process.114 A phenotype is any observable characteristic or trait of an organism such as its biochemical or physiological properties, or behavior.115 Phenotypes result from the expression of an organism’s genes (genotype) as well as the influence of environmental factors and possible interactions between the two.116 The genotype of an organism is the inherited instructions it carries within its genetic code.117 There are

MAOA expression were less likely to develop antisocial problems.

108. Caspi et al., supra note 33, at 386 ("Individuals with one or two copies of the short allele of the 5-HTT promoter polymorphism exhibited more depressive symptoms, diagnosable depression, and suicidality in relation to stressful life events than individuals homozygous for the long allele.").
109. J. John Mann et al., Candidate Endophenotypes for Genetic Studies of Suicidal Behavior, 65 BIOLOGICAL PSYCHIATRY 556, 556 (2009) [hereinafter Candidate Endophenotypes].
110. Id.
111. See generally id.
113. Id.
114. See id. ("Endophenotypes represent simpler clues to genetic underpinnings than the disease syndrome itself, promoting the view that psychiatric diagnoses can be decomposed or deconstructed, which can result in more straightforward—and successful—genetic analysis.").
115. See Mann, supra note 91, at 825 (linking genetics with physical and mental traits).
116. See id. (describing the biological basis for diathesis, linking genetics with vulnerabilities towards depression).
117. See id. at 824 (describing the genetic variations that lead to vulnerability for depression).
several criteria that a biomarker or cognitive marker must fulfill to be called an endophenotype.118

1. The endophenotype is associated with illness in the population.
2. The endophenotype is heritable.
3. The endophenotype is state-independent (manifests in an individual whether or not illness is active).
4. Within families, endophenotype and illness co-segregate.
5. The endophenotype found in affected family members is found in nonaffected family members at a higher rate than in the general population.119

The endophenotype concept has also been used in suicide studies.120 A tentative endophenotype between the phenotype of completed suicide and the genetic basis is impulsive aggression.127 The genetic basis of the trait has been suggested to be the gene coding for the serotonin receptor 5-HT1B, known to be relevant in aggressive behaviors.122

More recently, some of the most compelling evidence implicating impulsive aggression as an endophenotype for suicidal behavior was described in a study of "718 first-degree relatives from 120 families: 296 relatives of 51 depressed probands who committed suicide, 185 relatives of 34 nonsuicidal depressed probands, and 237 relatives of 35 community comparison subjects."123 "Testing cluster B traits as intermediate phenotypes of suicide showed that the relatives of depressed probands who committed suicide had elevated levels of

118. See Gottesman & Gould, supra note 112, at 4 ("E]ndophenotypes for psychiatric disorders must meet certain criteria, including association with a candidate gene or gene region.").
119. See Candidate Endophenotypes, supra note 109, at 557 (listing the criteria for defining the endophenotypes of suicidal behavior).
120. See generally Hana Zouk et al., The Effect of Genetic Variation of the Serotonin 1B Receptor Gene on Impulsive Aggressive Behavior and Suicide, 144B AM. J. MED. GENETICS PART B (NEUROPSYCHIATRIC GENETICS) 996 (2007).
121. See id. at 996 ("Impulsive-aggressive behaviors (IABS) are regarded as possible suicide intermediate phenotypes, mediating the relationship between genes and suicide outcome.").
122. See id. (studying the 5-HT1B gene because in animals this gene is a part of aggressive behavior and impulses).
123. Alexander McGirr et al., Familial Aggregation of Suicide Explained by Cluster B Traits: A Three-Group Family Study of Suicide Controlling for Major Depressive Disorder, 166 AM. J. PSYCHIATRY 1124, 1124 (2009).
cluster B traits.” 124 Furthermore, impulsive and aggressive traits may further contribute to the risk of suicide attempts in alcoholics. 125

As with psychiatric disorders in general, methodological difficulties include complexity of the phenotype for suicidal behavior and distinguishing suicide diathesis-related genes from genes associated with mood disorders and other suicide-associated psychiatric illness. 126

A workshop convened by the American Foundation for Suicide Prevention, the Department of Psychiatry at Columbia University, and the National Institute of Mental Health sought to identify potential target endophenotypes for genetic studies of suicidal behavior. 127 “The most promising endophenotypes were trait aggression/impulsivity, early-onset major depression, neurocognitive function, and cortisol social stress response.” 128

A variety of postmortem studies, in vivo biological studies of individuals who have attempted suicide, and family genetic studies have revealed that depressed suicide attempters show clinical and biological profiles of characteristics distinct from depressed individuals who do not attempt suicide. 129 They include decreased central serotonin activity in the ventromedial prefrontal cortex, higher levels of impulsive aggression, and familial aggregation of suicidal behavior that is not explained by the transmission of mental illnesses such as depression. 130

VI. Conclusion

Child abuse and neglect at critical developmental periods, mental illness, familial factors, and availability of lethal agents all contribute to

124. Id.
125. See G. Koller et al., Impulsivity and Aggression as Predictors of Suicide Attempts in Alcoholics, 252 EUR. ARCHIVES PSYCHIATRY & CLINICAL NEUROSCIENCE 155, 155 (2002) (assessing how impulsive and aggressive tendencies in alcoholics affect the likelihood that they will attempt suicide).
126. See Candidate Endophenotypes, supra note 109, at 560 (addressing the methodological issues within the study).
127. See id. at 556 (discussing the various vulnerabilities among people who attempt suicide and finding the related phenotypes in gene studies).
128. Id.
129. See Brent, supra note 70, at 681 (explaining the physical differences between passing feelings of sadness and the diagnosis of depression).
130. See Mann, supra note 91, at 819 (describing the neurobiological basis for genetic vulnerabilities underlying depression and suicide).
The diathesis-stress model suggests that individuals have underlying vulnerabilities or propensities to developing depression, as well as other mental illnesses. The search for biological factors pertaining to suicide risk has led to exciting research findings pertaining to adults, which have not yet been replicated in youth. However, the concept of endophenotype (especially that of impulsive aggression in suicide) holds promise for extending our understanding of differences between those who do and do not attempt suicide, even when other risk factors are present.

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131. See Role of Genotype, supra note 106, at 851 (explaining how certain genes mediate the effects of child abuse); see also Brent & Mann, supra note 72, at 2720 (studying how tendencies towards psychiatric disorders are inherited familialy); Bridge et al., supra note 37, at 381 (2006) (noting that guns and firearm availability are a factor in completed suicides).

132. See Brent & Mann, supra note 72, at 2720 (describing how the diathesis-stress model combines both genetic vulnerabilities and outside stressors to explain depression and suicidal tendencies).

133. See id. (noting that the diathesis-stress model was created to explain adult behavior but may also be useful in understanding adolescent depression).

134. See Zouk et al., supra note 120, at 996 (studying how specific variations on the genes controlling aggression and impulsivity relate to suicide).