13 Reactive attachment disorder in adolescence

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Abstract

Reactive attachment disorder (RAD) has received increasing attention as a possible explanation of severe behavioral disturbances in children and adolescents. Its etiology is hypothesized as related to failure of attachment beginning in infancy. Although the diagnosis of reactive attachment disorder (RAD) is usually made in early childhood, the diagnosis may be carried over into adolescence. In some cases, the diagnosis may be made for the first time in adolescence if there is sufficient information in the history to make the diagnosis retrospectively. It is unlikely that the diagnosis of RAD can be made in the absence of comorbid diagnoses in adolescence because these children usually have symptoms which meet the criteria for other diagnoses, such as attention deficit disorder (ADHD), post-traumatic stress disorder (PTSD), oppositional defiant disorder (ODD), mood disorder, or conduct disorder (CD) by the time they become early or mid-adolescent ages. During development, additional diagnostic criteria for other DSM-IV diagnoses may be observed. Although a comorbid diagnosis of ADHD, ODD, and/or CD might appear to take precedence over RAD, with the burgeoning information in genetics it may be useful to know that RAD was present or may still be present in the symptom complex of an individual patient. This chapter presents an overview of the issues involved in nosology and possible etiology, with particular emphasis on neurobiology and genetics. Case vignettes are used to illustrate the challenges to treatment that these patients present.

Definition and diagnosis

The diagnostic criteria for RAD are primarily “a markedly disturbed and developmentally inappropriate social relatedness, in most contexts beginning before 5 years” of age, which is associated with pathogenic care (American Psychiatric Association, 2000, p. 130). Two types of RAD are described: (1) inhibited and (2) disinhibited. In the literature on RAD there are many descriptions and definitions. It seems appropriate, although possibly oversimplified, to state that the basic problem is a disturbance in the child-parent relationship, i.e., in social relatedness.

The disturbance in social relatedness continues to be the defining feature of the disorder, despite evolution of the diagnostic criteria. Diagnostic criteria for RAD have changed across various editions of the Diagnostic and Statistical Manual of
Mental Disorders of the American Psychiatric Association. For decades “attachment” was synonymous with the infant-caregiver relationship. Subsequently, the diagnosis of RAD has come to apply to the child’s appearing to have a disturbance in social relatedness to others. The term “reactive” is used in the sense that the condition is considered to be a reaction to “pathogenic care,” which is defined as characterized by “persistent disregard for the child’s basic emotional needs for comfort, stimulation and affection.” It is sometimes also associated with “a prolonged disregard for the child’s physical needs” (American Psychiatric Association, 2000, p. 130). The constellation of behavioral and physical signs seen in infants with RAD include lack of a smiling response and lack of an auditory alerting response with head-turning towards the caregiver’s voice, coupled with abnormal physical development such as failure to thrive with no apparent physical cause.

Changes in successive editions of the DSM reflected a broadening of the diagnostic criteria and the age groups to which RAD could be applied. In DSM-III (American Psychiatric Association, 1980) the diagnosis basically applied to infants aged 8 months or less and, therefore, was limited in its application to older children. In the DSM-III-R (American Psychiatric Association, 1987) the age of onset was extended up to less than 5 years of age. Also, instead of a detailed list of symptoms, the criteria consisted of the presence of either of two patterns of social relatedness: (1) excessively inhibited, ambivalent interactions with others, and (2) indiscriminate social behaviors. A history of “grossly pathogenic care” was still a required criterion. DSM-IV (American Psychiatric Association, 1994) employed a more detailed description which took into consideration research findings which indicated that individual children respond in different ways to pathogenic care. Some may form selective attachments, while others may develop RAD in situations in which the care is not “grossly pathogenic.” Therefore, the term “grossly” was eliminated from the DSM-IV description of diagnostic criteria. There was no change in the RAD diagnostic criteria in DSM-IV-TR (American Psychiatric Association, 2000), and the two subtypes designated “inhibited” and “disinhibited” remained.

**Contributions from attachment research**

Early investigators observed infants who had been neglected, abused, or both, and developed hypotheses to account for the profound disturbances in development they saw. Spitz (1946) called the condition he observed “anaclitic depression in infants.” Bowlby (1982) considered the disorder a reaction to attachment and loss. Provence and Lipton (1962) made further observations on infants in institutions. Ainsworth, studying attachment in normal children, developed the “strange situation” procedure which assessed the child’s response to a change involving the caretaker (1978). In the strange situation, the baby is exposed to two brief separations from its mother and a brief exposure to a stranger. Ainsworth observed “coherent” and “incoherent” patterns of response to this stressful situation. Infants with “coherent” responses fell into three subtypes: “secure type”
infants communicated interactively with their mothers and were able to use the mother as a secure base for exploration. The other two coherent subtypes were described as “insecure avoidant” and “insecure resistant.” Infants manifesting an “incoherent response” showed evidence of disorganized attachment, defined as freezing, appearing fearful in the presence of the mother, engaging in stereotypy and “contradictory behavior.” Subsequent research has shown that attachment patterns formed in infancy tend to be stable over time, even into adulthood (Waters et al., 2000), although they are subject to change in response to the vicissitudes of development. The relationship between various types of attachment and psychopathology is complex, and empirical research in this area is still in its early stages. Disorganized attachment has been associated with aggression and disruptive behavior later in development (Lyons-Ruth, 1996) and with dissociative symptoms (Ogawa, Stroufe, Weinfield, Carlson and Egeland, 1997). While youngsters who do not have attachment disorders are likely to be securely attached, those who have disorganized attachments do not necessarily develop attachment disorders (Boris et al., 2004).

There have been few studies on the reliability of RAD diagnoses. Using their own diagnostic criteria, which differ slightly from those of the DSM, researchers in infant psychiatry have been able to demonstrate that attachment disorders can be reliably diagnosed in high-risk samples of young children (Boris et al., 2004).

Overlap with other disorders

RAD can be confused with other disorders. Some children with disturbances in social relatedness have communication problems that can be classified as a language disorder. Presumably the longer the child is deprived of normal language stimulation, the more severe the communication problem becomes. Richters and Volkmar (1994) suggest that, when communication problems are present, the diagnosis should be considered one of atypical development rather than a disorder of attachment, per se.

Children with RAD may become disruptive and disorganized with poor affect regulation and poor frustration tolerance, as well as inattention, impulsivity, and hyperactivity. By the time these children reach adolescence, they have often accumulated numerous comorbid diagnoses such as ADHD, and/or ODD, and/or CD, and/or PTSD. Also, one of the several mood-disorder diagnoses may be associated with RAD.

The following two case vignettes are examples of adolescents with RAD.

Case #1

A 14-year-old girl was brought, by her adoptive parents, to an outpatient psychiatric clinic because of their concern about recent changes in her behavior. She had been adopted at 7 years of age by a middle-aged couple after their own children had grown up. This couple felt that they were ready to accept
the challenge of raising a problem child. This child had been neglected and
abused by her natural parents, and she had behaved aggressively and destructively in several foster homes. Initially these adoptive parents had taken this child into their home as a foster child. They had been given the history of her previous pathogenic care and difficult behavior and her diagnosis of RAD. They were instructed to provide a warm and loving environment, as this was considered her greatest need at that time. The couple was successful in providing a supportive environment in spite of the child’s testing the limits of their patience periodically, and they proceeded to adopt her. After the reassurance provided by the adoption, the relationship between the child and parents continued to improve until some typical adolescent peer interactions occurred. Several other girls in her school, with whom she had become acquainted, formed a clique and rejected her. At the same time, because she had blossomed into an attractive young girl, boys showed her increased attention. Eventually she started dating the boys and became sexually promiscuous. These behaviors prompted her parents to seek help at an outpatient clinic, where they were provided with counseling from a social worker and medical care for the girl from a psychiatrist. She was given the comorbid diagnoses of RAD, ADHD, ODD, and mood disorder, not otherwise specified. The parents were supported in their attempts to set limits on these behaviors, and the child was given therapy that was aimed to improve self esteem and impulse control. She was also given several trials of psychotropic medicines. The therapeutic program provided by the clinic and the parental intervention were not successful in controlling her sexual acting out. She became more oppositional and refused to see both her therapist and her psychiatrist. Her behaviors became more dangerous to her health. She ultimately appeared to have some of the characteristics of borderline personality disorder and eventually was placed in a residential program for adolescents with borderline personality disorder.

Case #2

A 15-year-old girl was referred by the school because of symptoms of truancy and refusal to cooperate. Both the patient and the mother agreed that the mother had neglected her children. Her father had deserted the family when the patient was an infant. Her mother suffered from severe recurrent major depressive episodes during which she was unable to care for her children. The mother refused therapy. Although the patient was in an outpatient treatment program, she continued to refuse to attend school. She was admitted to an adolescent unit in a psychiatric hospital for an intensive evaluation which included an inpatient behavioral assessment, a complete psychiatric and psychological workup, and a neurological assessment. Her admitting diagnoses were RAD and ODD. The results of the intensive evaluation indicated that she had never developed an attachment to her mother (RAD) and later had never developed
any deep investment in her peers. Her reality testing was usually good, but occasionally she became very unrealistic and her judgment was often poor. She was angry and depressed much of the time in the hospital and she was given the diagnosis of borderline personality disorder. The neurologist who consulted on the case had some concern that she might have evidence of prefrontal executive function deficits, which have been reported to be associated with borderline personality disorder (Zelkowitz, Paris, Guzder et al., 2001).

In both of these cases, the adolescents had received pathogenic care as infants and, in subsequent developmental years, they did not form relationships with either adults or peers that might foster attachment. In the first case, the opportunity for attachment was there—her adoptive parents had provided loving care—but the child had been unable to incorporate the investment that the parents had provided. She was not able to form the identification necessary to internalize those characteristics that are needed to accept parental guidance. She was unable to reciprocate, either showing appreciation for the parental effort, or by attempting to meet some of the parental expectations.

In the second case, the diagnosis of RAD was made retrospectively during outpatient care by a child psychiatrist and was substantiated in the course of an intensive inpatient evaluation and treatment effort. During treatment, both patients demonstrated projective identification in which they projected a transferred identity on the therapist. In the opinion of the staff, this provided them with a justification for their inability to form an emotionally close relationship.

**Etiological factors in RAD**

**Longitudinal studies on the impact of early deprivation**

Longitudinal studies on brain function, cognition, and social behaviors of children, raised under conditions of extreme deprivation, have also provided further information about the impact of severe early deprivation on later development (Chisholm, 1998; Chugani, Behen, Muzik, et al., 2001; Kaler and Freeman, 1994; Rutter, Anderson-Wood, Beckett, et al., 1999). The unfortunate "experiment of nature" in Romanian orphanages has provided a rich source of data about the response of infants to defective maternal care. As infants, children in these orphanages were exposed to severe deprivation—some for as long as 42 months—and were then adopted and raised by families in the U.K. They have been extensively studied longitudinally by Rutter and colleagues, and many publications appeared on their findings. The highly pathogenic nature of this environment has been well documented. There is a linear relationship between the intensity of care (that is, the caretaker to child ratio), the duration of deprivation, and the child's subsequent behavior. Low intensity of care and prolonged duration of exposure to social deprivation were found to be associated with higher levels of disturbed attachment, delays in physical growth and cognitive development, and later psychopathology.
At age 6 years, some of these children manifested normal social and cognitive development, whereas others did not (Rutter and O'Connor, 2004). This finding suggests that some children are constitutionally more vulnerable than others to early pathogenic environments and that their pathological behaviors may persist, despite later nurturing environments and treatments. Thus, although early pathogenic care is an important factor, it is not the only one. The interaction between the child, the caregiver, and the child's developmental trajectory depends on a number of factors, particularly the child's resilience and ability to respond to later appropriate care.

Disruption of normal brain development by intrauterine or perinatal encephalopathic factors (e.g., maternal illness, exposure to drugs and toxins, prematurity, hypoxia, or malnutrition) is likely to increase the negative impact of environmental factors on later development and the infant's ability to respond to its caretaker. This is particularly true when the neural systems that underlie social relatedness and autonomic function are affected. Infants who are extremely irritable and inconsolable, on one hand, or those who are lethargic and unresponsive, on the other, pose a formidable challenge to even the most caring and experienced mother. In some infants, the neural network underlying social-emotional behaviors may be impaired to the extent that the infants cannot develop appropriate attachment, even in the most optimal situation (Pipp-Siegel, Siegel, and Dean, 1999).

A second, obviously important factor involves the mother's ability to relate to and nurture the infant. Poor mothering appears to be, at least in part, the result of the mother's own early experience, as well as being the result of cognitive, emotional, and environmental factors (Wilson, Kuebli, and Hughes, 2005). There are relatively few studies about the effect of poor mothering on a mother's own behavior, but there is a large research literature indicating that nonhuman primate mothers who were abused as infants have a high likelihood of being abusive to their own children. This is observed in infants raised by their biological as well as nonbiological abusive mothers (Maestripieri, 2005). Another factor is the mother's emotional state and ability to regulate her own behavior in response to the child, particularly if the child is hard to manage. In one large longitudinal study, maternal anxiety during pregnancy and postpartum maternal depression constituted independent and additive risks for emotional and behavioral problems in the child at age 4 years. This was true even after controlling for factors such as maternal smoking, alcohol use, the child's birth weight relative to gestational age, maternal age, gender, and socioeconomic status (O'Connor, Heron, and Glover, 2002).

There is also the matter of "goodness of fit" in the mother-child dyad. Mothers who cannot adapt their interactive styles to a quiet, relatively unresponsive infant or to one who is irritable and demanding will also enhance the child's risk of developing RAD. The more the mother is able to provide external regulation of the infant's level of arousal, the less likely the environment will be a pathogenic trigger.
However, even in this highly pathogenic situation there is some variability in the child’s response. Somatic growth appears to be one factor that has a bearing on the child’s response to deprivation in an institutional setting. Although growth retardation occurs in most of these children (the mean stature of the children in Romanian orphanages fell 1.6 standard deviations below the mean), there is a difference in the behavior of large and small children. In the study reported by Ellis, Fisher, and Zaharie (2004), smaller children manifested more anxiety/affective symptoms, whereas large physical size was associated with higher levels of disruptive behavior and aggression. The authors speculated that, in an institutional setting, aggression might be adaptive because the more aggressive the behavior, the more likely the child would receive both food and attention.

**Mechanisms by which deprivation of care may alter brain function**

Early deprivation of maternal care results in a series of somatic, emotional, and neurocognitive sequelae, which reflects a complex interplay between environmental input and brain development. A prominent aspect of the impact on brain function, with significant downstream effects on emotional regulation, is the dysfunction of the hypothalamic–pituitary–adrenal (HPA) axis that occurs in RAD. This dysfunction is characterized by elevated cortisol release in response to stressful events. Adults who experienced childhood abuse and neglect manifest hyperreactivity of the hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system in response to stress, compared to adults who did not have this history. This effect is particularly striking in women who are also depressed (Heim et al., 2002). These observations in adults are echoed in the finding that children, who spent over eight months of their first year of life in a Romanian orphanage, had daytime cortisol levels that were significantly higher than controls. The longer they remained in the orphanage, the higher the levels (Gunnar, Morison, Chisholm, and Schuder, 2001).

In response to stress, corticotrophin release factor (CRF) is secreted by the hypothalamus, stimulating the release of ACTH from the pituitary, which in turn stimulates the release of cortisol from the adrenals. CRF is regulated through negative feedback by glucocorticoid receptors which are located in the hippocampus as well as several other areas of the brain. Thus, highly sensitive glucocorticoid receptors will down-regulate CRF. Of particular interest, given the role of serotonin in depression and hippocampal function, is the fact that serotonin increases the expression of hippocampal glucocorticoid receptor expression as well as expression of nerve-growth-factor-inducible factor A (NGFI-A) gene. This gene is a member of the family of zinc-finger transcription factors encoded by immediate-early genes, and induced by a wide variety of extra cellular stimuli. NGFI is involved in cell proliferation, synaptic activation, and long-term potentiation, and is distributed in several brain regions, including the hippocampus. This aspect of RAD has been the focus of considerable preclinical research and is likely to be of considerable importance to the clinician.
To explain these persisting effects of maternal deprivation on the HPA axis, Meaney and Szyf (2005) have proposed an intriguing theory which ties the impact of poor maternal care to experience-dependent chromatin plasticity. In other words, experience in the neonatal period results in long-lasting changes in the system regulating CRF in response to stress. The experimental animal model involved the newborn rat. (However, similar effects of early maternal deprivation have also been demonstrated in male rhesus monkeys: see Winslow, 2005.) Adult rats raised by mother rats that are devoted lickers-and-groomers showed reduced ACTH and corticosterone responses to acute stress, in comparison to rats raised by less attentive rat mothers (Liu et al., 1997). Good maternal care is associated with a significant increase in hippocampal glucocorticoid receptor messenger RNA and protein expression, as a result of increased binding NGFI-A to the glucocorticoid receptor, which results in increased sensitivity of hippocampal glucocorticoid receptors and results in the down-regulation of CRF. This effect appears to be directly related to the effect of early maternal care, as switching rat pups born to low-intensity lickers and groomers to mothers who are intense lickers and groomers results in more stress-resistant adult rats. (Reversing this switch also has the opposite effect.) The mechanism involves the demethylation of the NGFI-A gene. Immediately after birth, the NGFI-A gene is methylated and therefore silenced. Intense licking and grooming activates serotonin receptor-7 (5-HT7 receptor), which in turn demethylates NGFI-A, and increases NGFI-A transcription. The resulting increased sensitivity to CRF by the hippocampal glucocorticoid receptor down-regulates cortisol secretion. Meaney and Szyf (2005) note that since DNA methyltransferases and demethylases are present in neurons and repetitive stimulation can alter the methylation status of neuronal genes, this is a more general model explaining how early environmental impacts can alter the brain's genetic programming.

This theory is particularly exciting because it integrates the clinical data which demonstrates the marked hyperreactivity of the HPA axis in response to stress in individuals who suffered neglect and abuse in early childhood. It also provides a model that explains how early experience affects genetic programming, and in turn results in persistent patterns of brain function which become “organic” (Kemph, 1964). Moreover, although these effects remain through life if not treated, there are manipulations in the laboratory setting that can reverse the genetic effects. The theory also suggests a number of approaches to therapy as it may be possible to demethylate some genes that have been silenced.

The infant’s genetic constitution

There are other components of the way poor maternal care affects the infant. Infants are born with different genetic profiles, and recent clinical and animal studies have provided strong evidence that the infant’s genetic make-up is an important factor in the response to pathogenic environments. Genes that regulate the neuronal systems which underlie the infant’s ability to relate to its mother and
the infant's resilience in the face of adversity will affect response to pathogenic rearing conditions. It is likely that some infants are genetically more susceptible to develop disturbed attachment. Genes involving the dopaminergic, vasopressin, serotonergic, and μ-opoid systems have been implicated.

**Dopaminergic system** Dopamine is involved in social relatedness through the mesolimbic system. Mesolimbic dopamine plays an important role in motivation, attention, and response to rewards. At this point it is not clear whether dopamine may be involved in the hedonic aspect of social bonding or in enhancing the relevance of social signals (Insel, 2003). However, in one study young adults who were exposed to poor maternal care and did not bond well with their mothers displayed a significant increase in ventral striatal dopamine release (as well as cortisol) in response to a stressor (Pruessner, Champagne, Mesney, et al. 2004). This, as well as other studies, would suggest that poor maternal care affects the dopaminergic system (Liu et al., 1997).

The dopamine D4 receptor (DRD4) has a number of polymorphisms which are related to effective dopaminergic signaling. One polymorphism involves a 48-base pair-variable number of tandem repeats in exon III. The number of repeats is associated with differential sensitivity to dopamine. Thrill-seeking, novelty-seeking (Benjamin, Patterson, Greenberg, Murphy, et al. 1996), drug addiction, (Kotler et al., 1997), and impulsive/compulsive behavior (Comings et al., 1999) in various adult populations around the world have been linked to the DRD4 gene polymorphisms. There are numerous studies reporting an association of the dopamine receptor D4 gene with ADHD, but these associations have certainly not been universally replicated in all samples and in all ethnic populations.

Some studies have reported that behavior in infancy is influenced by various DRD4 polymorphisms. In a sample of 122 Italian infants, those infants with the long DRD4 receptor polymorphism scored more poorly on adaptability, in contrast to those with the short allele. At five months of age these differences were no longer observed (De Luca, Rizziardi, Buccino, et al., 2001). However, at 3 years of age, toddlers with a long DRD4 7-repeat allele were more reactive than those who were homozygous for the short DRD4 (4/4) alleles. No relationship to adaptability, extraversion, or exploratory behaviors was noted (De Luca et al., 2003).

Lakatos and colleagues (2002) described a study on a cohort of 12- to 13-month-old infants that employed Ainsworth's strange situation paradigm described above (Ainsworth et al., 1985). They noted that 71 percent of the infants with a pattern of disorganized behavior in the strange situation had at least one 7-repeat DRD4 allele, compared to 29 percent of children who did not manifest this type of disorganized response.

In a subsequent study by the same group, it was found that when the 7-repeat DRD4 allele as well as a C → T substitution in the 5'-promoter region of the DRD4 gene (resulting in reduced transcriptional efficiency) (Okuyama et al., 2000) were present, the odds ratio for disorganized behavior increased tenfold (Lakatos et al., 2002). Gervai, Nemoda, Lakatos et al. (2005) have subsequently
replicated this finding and noted that the absence of the 7-repeat haplotypes and the C → T substitution in the promoter region enhanced optimal development of early attachment. However, these findings have not been replicated in all populations (Bakermans-Kranenburg & Van Ijzendoom, 2004).

It would be simplistic to assume that the infant’s genetic constitution is the only factor in this equation. However, a given genotype may increase an infant’s vulnerability to a pathogenic environment. Support for this notion comes from a 14-year longitudinal study of Finnish children followed into adulthood. Keltikangas-Jarvinen and colleagues, (2004) noted that when the parents were strict disciplinarians, had little tolerance for the normal activity of young children, and were emotionally remote, the offspring who had 2- or 5-repeat alleles of the DRD4 gene were much more likely to manifest the novelty-seeking profile (above the 10th percentile compared to Finnish norms) than those who did not have those alleles. In a more accepting child-rearing environment, the DRD4 genotype did not appear to have an effect.

Moreover, it is also likely that it is not just one set of genes but rather the interaction of multiple genes that contributes to the infant’s response to its environment. There is a complex relationship between serotonin and dopamine. Auerbach and colleagues (2001) reported that 12-month old infants with the DRD4 7-repeat allele manifested a higher level of activity in a free play situation and were less interested in structured block play and had greater difficulty sustaining attention to a task than infants who did not have the 7-repeat allele. They also examined the relation of the serotonin transporter promoter (5-HTTLPR) gene in this situation and noted that infants with two short 5-HTTLPR alleles appeared less fearful when approached by a stranger and were also less involved in the structured block play. They also noted a significant interaction between DRD4 7-repeat allele and the serotonin transporter promoter (5-HTTLPR) gene in relation to sustained attention.

**Monoamine Oxidase-A (MAO-A)** Monoamine oxidase-A is one of the enzymes involved in the metabolism of monoamine neurotransmitters. A variable number tandem repeat polymorphism at the promoter of the MAO-A gene (mapped to Xp11.23–11.4) results in enhanced enzymatic activity and, thus, would be expected to moderate increased catecholamine levels, which occur in response to pathogenic care. Testing the hypothesis that enhanced MAO-A activity would result in less psychiatric pathology in children raised in pathogenic environments, Caspi et al., (2002) observed, in a large longitudinal study, that boys raised in pathogenic environments who had a genotype conferring high levels of MAO–A expression were less likely to develop antisocial problems. Of the sample, only 12 percent of the males had the low-activity MAO–A genotype combined with early maltreatment. However, 85 percent of them developed some form of antisocial behavior and they accounted for 44 percent of the cohort’s violent convictions.
The Vasopression System  Arginine vasopressin has also been shown to play an important role in social behaviors, including affiliation and attachment, via the arginine vasopressin receptor 1A, by mediating the relationship between social stimuli and brain reward circuits (Winslow and Insel, 2002; Insel, 2003). The arginine-vasopressin (AVP) system also plays an important role in linking social signals to the mesocorticolimbic circuit. The AVP receptor 1A gene (AVPR1A) has been identified as an autism-susceptibility gene (Wassink, Piven, Vieland et al., 2004). Male monkeys with social deficits also show reduced binding of AVP to limbic structures. CRF binding is reduced in these monkeys as well (Winslow, 2005).

The μ-Opioid System  This system plays a critical role in the development of positive affective states linked to the mother. Since social contact provides opioid-mediated comfort, and social separation typically causes distress similar to opiate withdrawal (Panksepp, Sivily and Normansell, 1985), mouse pups lacking the μ-opioid gene would not experience either state because of the absence of the receptors which regulate the responses to social isolation or comfort. This is supported by studies on μ-opioid “knockout” mouse pups (those in whom the gene has been inactivated). In contrast to normal pups, those lacking the μ-opioid gene do not emit distress signals when removed from their mothers, although they do express distress in the presence of other cues (Moles, Kieffer & D’Amato, 2004). The implication of these findings is that infants with atypical μ-opioid genetic profiles might tolerate absence of a mother figure to a greater extent than those with intact μ-opioid systems.

The Serotonergic System  This system is also likely to be involved in the way children respond to abuse and neglect. As noted above, serotonin plays a crucial role in the hippocampal NGFI-A/glucocortical receptor transcription. There is a large literature on the relationship of serotonin to mood, social anxiety, and obsessive-compulsive behaviors, and both age and gender appear to be important variables in this relationship. There are two common polymorphisms in a variable repeat sequence of the serotonin transporter promoter (5-HTT—also known as SLC6A4) gene (on chromosome 17q11.1-q12). The long variant has more than twice the activity of the short variant, which is associated with reduced transcription and lower transporter activity. A number of studies have described an association between one or two copies of the short allele of the 5-HTT promoter polymorphism and depression and suicidality in response to stressful life events (Caspi et al., 2003) although this has not been replicated in all populations (Gillespie, Whitfield, Williams, et al. 2005). The short 5-HTT promoter polymorphism has also been associated with increased activation of the amygdala and increased fear and anxiety-related behaviors (Hariri, Mathay, Tessitore et al., 2002). Children with one or two copies of the short allele manifested higher levels of shyness and behavioral inhibition (antecedents of social anxiety disorder). There are also differences in patterns of cortical activation in these children in response to angry and neutral faces (Battaglia, Ogliari, Zanoni et al., 2005).
Implications for treatment

The previous section provides a neurobiological explanation for the mechanisms by which environmental factors program patterns of brain function, and in turn set up long-lasting behaviors. Once a pattern of behavior is established over a long period of time in a human being at any age, it is embedded in the genetic patterns that regulate neuronal activity, and in turn lead to behavioral patterns and identity (Kemph, 1964). The longer the pattern exists the more difficult it is to change, but change should nonetheless still be possible. A rational approach to treatment in these cases would likely involve both pharmacologic as well as persistent behavioral interventions. In addition to generating new nerve cells in the hippocampus, enhancing the development of new patterns of neuronal connectivity should encourage the development of more adaptive ideas and behavior patterns to replace old patterns.

With appropriate care, in our experience, some children with RAD show remarkable improvement. For example, an adopted 6-year-old boy with typical autistic behavior improved over the course of a year with once-a-week therapy for the boy and counseling for the adoptive parents, and with the supportive environment of his new family. After one year he was able to function in a regular classroom and interact well with his adoptive family. Although the developmental history was not available, this child had probably not been genuinely autistic, but rather was "quasi-autistic" as suggested by Rutter et al. (1999).

Another case is that of a 15-year-old boy who was treated in a children's psychiatric hospital for more than a year. Although he initially appeared to be only minimally responsive to this intensive treatment, he subsequently showed evidence of having benefited from it through having made an attachment to the therapist. This boy had a stormy history of failure to form an attachment to his mother, other adults, peers, or therapists. He had frequent rages and dangerous behavior directed toward peers and adults, including therapists. He was considered to have RAD and conduct disorder. Although some progress was made in forming an attachment to his therapist in the hospital (they met for daily therapy sessions for one year), his behavior did not improve to the point that it could be tolerated. The episode that triggered his transfer occurred when, in a rage, he had produced eight knives that he had obtained, and twirled in a dangerous fashion, attempting to cut the staff. He was eventually talked into going into the quiet room with his therapist, where he relinquished the knives and quickly settled down when he realized he had gone too far. Shorty thereafter he was transferred to a high-security state hospital. Eventually, after discharge from that hospital, he returned for a visit with his former therapist at the children's psychiatric hospital. He told his former therapist that while he was alone in the secure hospital he began to recall many of the discussions he had had with his therapist, and began to determine what he had to do to work his way out of the hospital. He stated that he now realized that the work with his former therapist was helpful. Apparently he had internalized enough of the relationship with his former therapist, possibly through identification, for him to use to his advantage in the state hospital.
The management of RAD children, whether by parents or therapists, requires considerable patience with very little expectation of immediate success. These children and adolescents are often aggressive and oppositional, frequently testing the limits of external controls or rules. Their caretakers must be prepared to forego any expression of appreciation from these patients for the caretaker’s efforts; they must be prepared for frequent negative testing behavior. Some people are more capable of providing this type of care than others. When these patients become aggressive and oppositional it is often helpful to wait briefly and patiently before giving any response, allowing time for the patient to become more aware of the situation which he/she is creating and then help the patient to respond more appropriately. Many repetitions will be necessary to promote the development of new, more adaptive behaviors (which in turn involves “resetting” some of the underlying neuronal pathways and, by altering transcription patterns—possibly by some of the mechanisms described above—changing some of the underlying genetic programs). The older the patient the more time and repetitions will be required. Optimistically, the younger the patient the better the chance of getting results relatively soon. Caretakers and the therapists must be capable of providing care even with negative response or little reward from patients initially, and even after many repetitions there will be only minimal reward. If we consider the biological processes that must occur in order to achieve a change in behavior, we may be less impatient with the intractable quality of the behaviors.

We earlier discussed the importance of “goodness of fit” in fostering attachment. Goodness of fit has been cited as helpful in planning which caretakers would be a good fit for which patients. Colin (1996) has noted that clinicians should be aware of the importance of goodness of fit between the child and the adoptive parent and how well they function together in their relationship. A change in that relationship, if needed, may require prolonged intensive treatment with the child and the caregiver. To demonstrate the goodness of fit, two brief case vignettes will be described. Both cases were being treated by the same child psychiatrist who provided psychotropic medicines for the child and brief counseling for the mother and child. Both of these children had been given the comorbid diagnoses of RAD, ADHD, ODD, and PTSD. One was a 10-year-old adopted girl who had previously been placed in several foster homes. The adoptive mother needed occasional reassuring responses from the child that would indicate that she was trying to become part of the family, but the child gave much more negative than positive feedback. The girl was very oppositional and the mother responded with disappointment or anger. The mother frequently requested help, in the form of increased medication, which provided only partial improvement in behavior. The mother was often in tears and became increasingly desperate and tired. Eventually she gave up custody of the child to social services.

The other child was an 11-year-old girl who had been adopted at 4 1/2 years of age from a Russian orphanage. The mother said that the first two years were horrible, with no professional support. She brought the child to an outpatient clinic when the child was 7 years old. Over time, and with the help of the therapist,
the adoptive mother became very capable of managing the child's oppositional behavior. In the psychiatrist's office at the clinic, when the child became aggressively oppositional, the mother would wait, briefly allowing the child to think about what she had done, and pleasantly, usually with a smile, teach the child how to respond more appropriately.

A much better result was obtained in the second of these two examples, which illustrate different expectations and reactions to the child on the part of the adoptive parent. In the second case, the adoptive mother was more realistic in her expectations. She was not seeking personal gratification from her interventions with the child and was not reacting immediately or intensely in a negative way to the child's behavior. There are obviously many issues involved in the treatment of these children, but, considering the potential reactivity of these children to stressors, the lack of heightened negative emotional responses from the caretakers may be an important factor.

Because of the extreme difficulties these children present for caregivers, not to mention social agencies and therapists who deal with them, various outpatient and inpatient programs have appeared in the United States specializing in treating patients with RAD. The examples described by Wilson (2001) utilize stimulation therapy, parental counseling, psychiatric consultation, and "holding therapy." Control via coercive techniques is heavily emphasized in some of these programs. According to Wilson, holding therapy attempts to recreate the bonding cycle that an infant may have experienced with a parent by the following procedure: the therapist holds the child's head in his/her lap to maintain eye contact while others restrain the arms and the legs. The therapist confronts the child with questions such as "Who has control now?" and "I know you hate, but who ends up suffering?" Thirty hours in 10 days is devoted to this procedure. Wilson concludes, given the complexity of the factors underlying the development of RAD, and the fact that there are no peer-reviewed outcome studies, "until such time as holding techniques can be empirically validated to improve the condition of RAD without excessive stress to the child, parents may be well advised to consider other options in the treatment of a child with RAD" (Wilson, 2001, p. 49). Holding therapy and an even more extreme form of restraint and noxious stimulation known as "rebirthing therapy" are quite controversial and have been condemned by the American Psychiatric Association (2002), which stated, "there is no scientific evidence to support the effectiveness of such interventions," and cited "a strong clinical consensus that coercive therapies are contraindicated in this disorder." The American Academy of Child and Adolescent Psychiatry (AACAP) has issued a similar statement (2003), noting that at least six documented child fatalities have occurred related to the use of these methods. The AACAP also notes "these techniques also violate the fundamental human rights of the children subjected to them. The AACAP therefore urges that these coercive, dangerous and ineffective practices be discontinued." Nonetheless, these techniques continue to have their supporters, and persist in some programs as a treatment in both outpatient and inpatient settings.
Reactive attachment disorder in adolescence

As noted previously, some children raised in pathogenic environments develop symptoms resembling borderline personality disorder. These patients often manifest prefrontal executive dysfunction (Zelkowitz et al., 2001). Further support for frontal dysfunction is supported by the finding of hypometabolism in orbitofrontal cortex on positron emission tomography scans (Soloff et al., 2003). These observations are consistent with the disruption of dopaminergic transmission observed following exposure to maternal deprivation (Liu et al., 1997; Preussner et al., 2004). If these symptoms develop in adolescence the APA guidelines for treatment of patients with borderline personality disorder (American Psychiatric Association, 2001) may be helpful in therapy.

Although children and adolescents with RAD may improve in cognitive function, language, and motor development, changes in social relatedness may be more difficult to achieve. The following is a brief example of improved social relatedness in an adolescent:

A 13 1/2-year-old boy had been adopted by his great aunt when he was 10 years old. When the boy was just 8 months of age, the aunt was surprised to learn that her niece had an infant son about whom she had never heard. When the aunt visited the child she was appalled at the poor physical condition of this tiny infant. The mother told her aunt that she had been on several illicit drugs while she was pregnant with this child. She was addicted to several drugs, including methamphetamine and cocaine, and had not cared for the child properly. The infant’s great aunt tried repeatedly to get her niece to give the child to her and let her take the child into her home. Her own children had been raised well and were out of the home. Finally, when the child was 10 years old, the mother of the child allowed her aunt to adopt him. At that time the aunt took the child to a children’s psychiatric clinic where he was diagnosed as having ADHD, ODD, and, by history, RAD. The child and caretaker were seen in counseling by a social worker and by a psychiatrist who provided medicine. During three years of treatment as an outpatient, the patient developed an attachment to his adoptive mother and his oppositional and aggressive behavior were largely diminished. However, he continued to give a negative initial response to most questions, albeit with a pleasant demeanor. Then he would use his adoptive mother’s knowledge and support to formulate a plan for further responses, reminiscent of the infant using its attachment to its caretaker when a secure attachment has been established. He made friends among peers and the adoptive mother’s grownup children. When a new child psychiatrist interviewed the dyad the adoptive mother was asked if there was any mental illness in the family, the boy said immediately, “My mom.” The adoptive mother then explained that his mother had been diagnosed as having schizophrenia in addition to substance abuse. Although this boy lags behind academically and has symptoms of inattentiveness and distractibility, which require medication, he has formed a secure attachment to his adoptive mother during puberty and early adolescence and this provides a basis for trust and for him to further his development in the future.
Effective pharmacotherapy

The fact that various genetic features appear to play a role in RAD, as we have discussed above, suggests that carefully conceptualized approaches to medication might be helpful. When more information is available about a specific child's genotype, particularly as it relates to neurotransmitters and drug metabolism, this should provide a rational approach, utilizing pharmacogenomic information, to managing some of the behaviors that characterize RAD. However, even in the absence of such information, systematically targeting the oxytocin, μ-opioid, serotonin, and dopaminergic systems may be helpful in combination with persistent behavioral interventions.

Summary

Although the examples of patients with RAD described in this article are anecdotal and not conclusive proof that some adolescents with RAD can develop an attachment when this has not occurred at a younger age, they offer the possibility that such behavioral changes may occur in an appropriate setting. The recent advances in knowledge of genetics and neuroscience are reassuring, because there is evidence that brain function and some of the genetic factors underlying brain-function structure can be modified to allow for changes in behavior.

RAD is a useful diagnosis for some adolescents who present with "markedly disturbed and inappropriate social relatedness in most contexts," when the problem in relatedness can be demonstrated to have begun in early childhood and there is a history of "pathogenic care," or at least profound disturbance in the parent-child relationship. RAD places children at risk for other psychopathology as they grow older, so that by the time a child with RAD becomes an adolescent other diagnoses have been added, such as ADHD, ODD, PTSD, mood disorder, or CD. When a diagnosis of RAD is first made during childhood, it may be carried over into adolescence. A diagnosis of RAD may be made in older children or adolescents retrospectively from history. Although the DSM criteria associate RAD with pathogenic care, research in infant psychiatry has led to a revision of thinking about this disorder, positing that the nature of the parent-child relationship may be critical. Irritability or uncontrolled negative-affective responses on one end of the spectrum, as well as indifferent, apathetic responses on the other—on the part of either the parent or the child — may interfere with the development of normal attachment, particularly if there is a "poor fit." The caretaker's ability to regulate the infant's arousal level may be one important factor. Another factor may involve the influence of different genotypes which will determine, in part, the sensitivity of the child to the pathogenic situation. Treatment of RAD requires many repetitions of appropriate thoughts and behaviors over a prolonged period of time to foster the changes necessary to form new neuronal patterns, which may enable the adolescent to develop socially acceptable relationships with other people. Skillful use of medication may also be helpful.
References


