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An Attachment Perspective on Borderline Personality Disorder: Advances in Gene–Environment Considerations

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Abstract Accumulating evidence points to severe relationship dysfunction as the core epigenetic expression of borderline personality disorder (BPD). In adulthood, BPD is typified by disorganization within and across interpersonal domains of functioning. When interacting with their infants, mothers with BPD show marked withdrawal and frightening or frightened behavior, leading to disorganized infant–mother attachments. Linked to both infant disorganization and BPD is a maternal state of mind typified by unresolved mourning regarding past loss or trauma. Early risk factors for BPD in adulthood include maternal withdrawal in infancy and separation of 1 month or more from mother in the first 5 years of life. Likely contributing biological factors include genes linked to dopamine, serotonin, the hypothalamic-pituitary-adrenal axis, and neuropeptides. The complex gene-environment picture emerging confers risk or protection against BPD pathology in ways consistent with infants varying biological sensitivity to context. This line of research may refine early risk assessment and preventive mental health services.

Keywords Attachment · Disorganization · BPD · Gene-environment interactions · Risk assessment

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Introduction

Compelling convergent evidence from multiple investigations of personality disorders in adult samples indicates that severe relationship dysfunction is the endophenotypic expression of borderline personality disorder (BPD), with an increasing understanding of the extent to which genetic factors influence this complex set of emotional and social dysfunctions [1•, 2••, 3–5]. Clinical theories and retrospective data have long suggested that experiences of severe relationship adversity and maltreatment typify the childhood backgrounds of adults with BPD [6, 7]. However, only recently have prospective longitudinal investigations begun to document the early relationship difficulties that may predispose an individual to develop along a trajectory toward adult borderline pathology [8]. Notably, the most serious early attachment relationship disturbance is infant–caregiver attachment disorganization, which was first documented by Main and Solomon [9, 10]. They described infants showing multiple indications of apprehension and fear in the presence of their mother during the classic Strange Situation procedure [11]. For disorganized infant–mother pairs, the indices of fear appear often in the low-stress pre-separation episodes, suggesting a heightened sensitivity to stress in these infants [12]. The fearful disorganized behaviors also typically appear following one of the brief separations, during that moment of reunion when the securely attached child approaches readily and is comforted promptly. Attachment disorganization in the early infant–mother relationship has been associated prospectively in longitudinal work and meta-analytic summaries of the findings with later childhood problem behaviors, especially aggression [13], post-traumatic stress disorder (PTSD) symptoms in the school years [14], and dissociation problems in adolescence [15].

The recently suggested link between extreme interpersonal sensitivity, disorganized-ambivalent attachment, and borderline pathology [1•] in adolescence and adulthood seems like a most relevant natural extension of the extant findings. Such findings were in many ways anticipated by Liotti [16] based on his clinical observations of links among personality disorder, PTSD, dissociation, unresolved grief, and profound early attachment disturbances. Thus, Liotti [17] has described BPD as prototypically an attachment disorder of the disorganized type.

This report aims to not only point out the contribution attachment theory and research has to make to understanding BPD, but also to draw attention to some of the most likely genetic polymorphisms linked to disorganization and BPD and speculate on gene–environment interactions, making it more or less likely that an infant will 1) develop a disorganized attachment and 2) that an infant with disorganization will later develop borderline pathology [1•]. Toward this end, we distinguish between two methods of assessing attachment in adulthood [18], one being self-report concerning current romantic partnerships and the other more probing in the form of an interview (the Adult Attachment Interview [AAI]) concerning thoughts, feelings, and meaning derived from one's childhood attachment history [19••]. In the case of the former self-report measure, yielding scores for avoidance and anxiety, recent evidence suggests that they are in part heritable [20]. In contrast, environmental—not genetic—effects are highlighted in sibling studies [21] and adoption studies [22] relying on the AAI. Furthermore, robust meta-analytic evidence from 10,000 respondents linking AAI responses to mental health outcomes [23•] underscores the value of the AAI as an indicator of psychotherapeutic treatment progress and outcome [3, 24•].

Severe Relationship Dysfunctions Transmitted Across Generations

Intrapersonal processes, most notably affective instability and impulsivity [25], have long been recognized as phenotypic markers of BPD, yet most current reports on BPD have focused on the profound interpersonal deficits evident for people with borderline psychopathology [2••, 3]. Scott et al. [5] posited a model in which the link between attachment anxiety and BPD features—in their self-report study of more than 1,400 undergraduates—was fully mediated by temperamental factors, namely trait-negative affect and impulsivity in line with the findings of Siever and Davis [25]. This suggests that broad adult relationship dysfunction (high anxiety, high avoidance, or both) in the absence of temperamental or genetic biases does not lead to borderline pathology.

However, there may be a specific relationship dysfunction in adults with BPD, as suggested recently by Hill and colleagues [2••, 4], who, borrowing from the attachment lexicon, wrote about "domain disorganization." By this, they mean profound failures in functioning in an organized adaptive way within and across domains of interpersonal experience, including work, love, and parenting. Their interview-based assessment of personality functioning is highly revealing as to the severe interpersonal difficulties experienced by adults with BPD. A focus on disorganization in this work is consonant with an attachment perspective in which disoriented/disorganized feelings, thoughts, and behavior are seen as the normal response to loss or trauma [26]. The problem for people with BPD from this perspective is that they are trapped in an ongoing and unrelenting grief response, one that appears too easily transmitted to the next generation [13] insofar as unresolved loss responses to the AAI are significantly predictive of disorganized infant–mother attachments.

This transgenerational theme is evident in the work of Hobson and colleagues [27, 28], who have explored in detail the dysfunctional behavior seen in parenting behaviors by mothers with BPD [27, 28]. This group studied video-filmed behavior of 10 mothers with BPD and 22 mothers free of psychopathology during the Strange Situation separation–reunion paradigm [11]. They found not only a significantly elevated level of attachment disorganization among the infants of BPD mothers (80% vs 27% in the control group) but also that BPD mothers were significantly different from the comparison group mothers in terms of their atypically frightening and disoriented behavior. While this work highlights how disorganized attachment is highly common among infants of mothers with BPD, this intergenerational pattern (frightening/frightened parenting and disorganized infant–parent attachment) is also evident in a minority of community sample infants [29]. Thus, neither disorganized attachment nor frightening/frightened parenting is uniquely related to BPD or psychopathology generally. However, longitudinal prospective work has found disorganization to be linked forward in time to disturbed forms of social relating and merits being seen as a risk factor for aggressive [13] and dissociation-related problems in later life [15].

Early Attachment Disturbances Linked to Borderline Personality Disorder

Lyons-Ruth and colleagues [30] recently highlighted the probable toxic influence of severe maternal withdrawal, leading to controlling (punitive or solicitous) interpersonal behavior in middle childhood and borderline features, if not BPD diagnosis itself, in adolescence. Along the dimension

of maternal withdrawal, at the high end is complete maternal absence. This construct—prolonged separations from mother lasting 1 month or more at 5 years of age or younger—recently has been studied prospectively and linked to later borderline pathology in adolescence and adulthood [8]. Crawford et al. [8] reported on more than 750 families selected in the early-1980s for their representativeness of the full US population who were studied longitudinally from infancy through adulthood. According to their index of early maternal separation experiences, 35 children (4%) of the sample were thus exposed. For this group, elevated levels of BPD symptoms were repeatedly observed from early adolescence into middle adulthood. Long-term effects of early separations were largely independent of childhood temperament, child abuse, maternal problems, and parenting risks. Although 11 children experienced the death of a mother or father before 5 years of age and considerably more experienced parental divorce before 10 years of age, these relationship disruptions were not predictive of later BPD symptoms. The mechanism of influence that may explain the observed unique link between early separations and later borderline symptoms is open to speculation. We would suggest that the first 5 years of life are a highly sensitive period with respect to the development of emotion regulation skills, effortful control, theory of mind, and executive functioning such that a prolonged separation from the mother during these years may skew a child's development in the direction of impulse-control difficulties, affective instability, and mistrust in the domain of close relationships. It would thus contribute to higher scores on subsequent indices of BPD symptoms.

From the domain of treatment research for people with BPD [6, 7], it is widely assumed that adults with BPD suffered during early childhood extreme lacks in validating experiences that would normally engender positive self-regard and trust in others, as well as theory-of-mind or mentalization skills. Teaching these skills to adults with BPD has led to significant documented decreases in symptoms and increases in adaptive functioning in work and relationship domains [31]. Accordingly, an industry has developed that aims to teach adults with BPD basic lessons in how relationships work, the ordinary call for trust in others, and the ongoing need to guess with more or less accuracy what others are thinking and feeling in order to negotiate the interpersonal process on which we all depend. Enthusiasm for training in mentalization-based treatments [7] and dialectical behavior therapy [6] far outstrips the available developmental evidence linking early relationship deficits to BPD symptoms per se. The principles of equifinality (multiple pathways to the same outcome) and multifinality (diverse outcomes arising from the same source) are requisite models to begin explaining the diverse developmental pathways to BPD, as well as the diverse outcomes of early relationship deficits, including risk and resilience profiles. Notwithstanding the compelling evidence from the longitudinal work by Lyons-Ruth et al. [30], the controlled sensitive observations of Hobson et al. [28] concerning the ominously insensitive maternal behaviors of mothers with BPD, and the blunt survey data of Crawford et al. [8] isolating the pernicious consequences of separations from mother in the first 5 years of life, much further work is needed to establish the developmental precursors to BPD.

Relevance of Attachment-Based Research Tools in Studies of Personality Disorder

In charting an agenda for how this developmental work may proceed, we can point to certain attachment research methods that arguably measure features of development that are predominantly outcomes of the shared or nonshared environment [32–34] that should be included in the battery of assessments deployed in this vital future work. Pregnancy risk assessments and infant developmental assessments could profitably include two attachment research tools, namely the AAI (for parents) [19••] and the Strange Situation procedure (for observing the infant/toddler–parent relationship) [11].

Twin and adoption studies [21, 22] using the AAI have robustly suggested that the AAI assesses the unique meaning the adult has given to his or her attachment history and further, that this meaning is likely to reflect the environment (shared and nonshared) within families. A rather different, more genetic-driven set of findings has been suggested by questionnaire or self-report measures of adult romantic attachment styles operationalized on the dimensions of avoidance or anxiety, in which the suggestion emerges that these attachment constructs overlap with the Big Five personality traits in ways that point to shared genetic influences [20]. Given the relative absence of overlap between adults' responses to the AAI and adults' responses to romantic attachment style questionnaires [35], it is difficult to know what to make of the flurry of studies reporting that 30–40% of the variance in adults' attachment anxiety and avoidance is accounted for by genetic factors [36]. However, low scores on avoidance and anxiety on attachment self-report measures cannot simply be equated with security in response to the AAI. This conclusion is supported by the work of Roisman and colleagues [35], who carried out a meta-analysis of 10 studies (combined N=961) in which AAIs and self-reported attachment styles were collected. AAI security versus insecurity and self-reported attachment was equivalent to an r of 0.09 (range, 0.02–0.17), suggesting trivial to small empiric overlap between these measures using the criteria established by Cohen [37]. Similarly, self-reported anxiety did not dis-

criminate between AAI preoccupied and dismissing states of mind (r=0.06, a trivial effect). In contrast, self-reported avoidance was linked to AAI dismissing (vs preoccupied) states of mind (r=0.15, a small effect). With respect to the important AAI consideration of whether the adult speaker is unresolved with respect to past experiences of loss or abuse, there was a small but significant effect of self-reported anxiety linked to unresolved mourning [35]. Taken together, these findings must serve as a caution to those seeking a quick self-report alternative to the AAI.

The clinical relevance of the AAI for understanding and treating a range of adult psychopathology has been detailed recently in an edited book on the clinical applications of the AAI [38]. The AAI is a 45- to 60-minute interview that probes in detail about past attachment experiences and current thoughts and feelings regarding one's relationship past. Most notable among the clinical uses of the AAI is the remarkable capacity this structured interview has to reliably identify adults with loss or trauma experiences that are unresolved in their minds [19••]. This phenomenon of unresolved grief or mourning regarding the past, together with an insecure-preoccupied state of mind regarding attachment in general, has been repeatedly observed in studies of BPD [23•]. Gunderson and Lyons-Ruth [1•] remarked on how this profile of preoccupying anxiety and anger on the one hand, with fearful absorption regarding past hurts, is prototypically indicative of BPD symptomatology. Interestingly, unresolved mourning regarding past loss or trauma in a parent has been systematically linked in several studies to infant–parent attachment disorganization, as Main and Hesse [39] first posited and has been confirmed in multiple studies [40]. The highly significant correlation from an early meta-analytic summary [13] was 0.31 across generations, linking lapses in the monitoring of speech and reason about loss or trauma in a parent to a composite of anomalous infant behaviors (e.g., hand on mouth, head banging, freezing, hiding) indicating fear and disorganization in the presence of the parent. For children who look this way with the mother at the end of the first year of life, the developmental journey includes multiple mental health risks [40, 41]. This may be because attachment disorganization in infancy is a marker of psychosocial problems (in the family context) present from pregnancy and likely to remain stable and/or because disorganization is a phenotypic marker of genetic risk [40].

Advances in Relevant Gene–Environment Considerations

Investigators have explored a number of genes in relation to attachment behavior based on genetic polymorphisms identified in adults in relation to temperamental characteristics related to mood, anxiety, affiliation, and anger [42]. These have included genes related to dopamine, serotonin, the hypothalamic-pituitary-adrenal (HPA) axis, and neuropeptides.

Investigations of genetic risk for disorganization have centered on the dopamine D_4-receptor (*DRD4*) polymorphism, perhaps because of the earlier literature linking the dopamine receptor genes to addictive and problem behavior outcomes [3]. The attachment disorganization and *DRD4* work was recently summarized well by Bernier and Meins [43], who posited a threshold approach to disorganization, arguing that when enough risk factors are encountered (genetic and environmental), disorganization results. A sample of Hungarian infants reported on by Gervai et al. [44] and Lakatos et al. [45, 46] suggested that the 7-repeat *DRD4* gene polymorphism could be a risk factor for disorganized attachment; specifically, the 7-repeat allele was observed in 71% of disorganized children in this sample, compared with only 29% of nondisorganized children. Further examination of the same sample revealed that this association was substantially enhanced when children also carried the -521T allele in the promoter region of the *DRD4* gene [46]. Children carrying both the 7-repeat allele and the -521T allele were 10 times more likely to present with disorganized attachment than their counterparts who carried neither risk allele. Thus far, two Dutch reports have attempted to replicate the findings of Lakatos et al. [46], and both failed to find a direct link between the *DRD4* gene and disorganized attachment, whether with twin infants [47] or singletons [48]. However, van IJzendoorn and Bakermans-Kranenburg [48] reported provocative findings showing how parental features measured via the AAI can interact with genetic risk in a child to make disorganization much more likely. They observed this gene–environment interaction in the development of disorganized attachment. In their sample of 85 singletons, the 7-repeat *DRD4* polymorphism made infants more likely to develop a disorganized relationship with their mother when she presented with an unresolved state of mind with respect to past loss or trauma. The presence of both risk factors (maternal unresolved loss and 7-repeat *DRD4* polymorphism) increased by 18.8-fold the odds of disorganization compared with cases in which neither risk factor was present.

Interestingly, this Dutch group recently demonstrated how this same *DRD4* polymorphism that seems to represent a risk for attachment disorganization can also be seen as a marker of high responsiveness to a therapeutic intervention designed for toddlers with aggressive behavior problems [49]. Thus, we arrive at the paradoxical conclusion for which there is an increasing range of evidence that the same genetic polymorphism that confers risk may also confer protection [50]. Consistent with the evolutionary and biological model of Boyce and Ellis [12], the 7-repeat

DRD4 allele may indicate an increased biological sensitivity to context with potential for negative health effects under conditions of adversity (e.g., unresolved mourning regarding past loss or trauma in the mother) and positive effects under conditions of support and protection (e.g., a therapeutic intervention on how to provide sensitive discipline).

Aside from *DRD4*, other genes may mediate differences in attachment through influence on temperamental characteristics such as aggression, which has been associated with allelic variation in the *MAO-A* gene, particularly in relation to child maltreatment [51]. Anxiety and inhibition—linked to the serotonin transporter—may determine in part responsiveness to parental demands and engagements [52]. Heightened behavioral inhibition has been seen in children with the short allele of the serotonin transporter promoter (low activity), particularly when mothers have low social support [53, 54]. Children who carried the short form of the serotonin transporter promoter and were insecurely attached developed poor self-regulatory capacity, whereas those who were securely attached developed normal regulatory capacity comparable to children who were homozygous for the long allele of the transporter. Homozygotes for the long allele displayed no effect of security of attachment. In this work, an example of a polymorphism in the gene of interest interacting with the quality of attachment can be observed.

Genes in the HPA axis may modulate stress reactivity and response to novelty [55], suggesting that the genes related to HPA reactivity may also be of interest in relation to attachment behavior. Polymorphisms in the arginine vasopressin receptor-1a and oxytocin receptor [56] may mediate social and affiliative behaviors and variability in the μ-opioid receptor, which can increase the intensity of attachment in primates [55]. Thus, the variability in these neuropeptides' activity through polymorphisms affecting their receptor or release properties may modulate attachment and social behavior [57, 58•]. Indeed, in adults, variability in the oxytocin receptor and the μ-opioid receptor has been related to anger dyscontrol and identity disturbance [58•]. Epigenetic mechanisms may also modulate stress responsiveness through methylation of relevant genes. For example, prenatal exposure to depression in the mother may modify the methylation and expression in glucocorticoid receptors and infant stress responses that may ultimately affect attachment [59, 60].

Conclusions

These examples provide suggestive evidence that genes influencing critical aspects of temperament, including anxiety regulation, stress reactivity, and affiliation, may directly modulate attachment, whereas alleles in other genes may interact with security of attachment to prevent adverse developmental outcomes. Furthermore, epigenetic effects of stress or maternal state of mind (especially anxiety and unresolved mourning regarding past loss or trauma) may modulate the expression of relevant genotypes to influence attachment as seen in behavioral outcomes indicative of risk for borderline psychopathology.

As these findings of gene–environment interactions are replicated and extended, we will draw nearer to a comprehensive understanding of interacting biological and social mechanisms that make more or less likely the development of disorganized (or organized) attachment, and with it the ensuing risks for (or protection against) later psychopathology, including borderline pathology in adolescence and adulthood. This holds out the hope for improvements in evidence-based risk assessment and clinical practice across mental health settings from the prenatal period, in infancy, and beyond.

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••Of major importance

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