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Citation

Gunderson, John G., and Karlen Lyons-Ruth. 2008. "BPD's Interpersonal Hypersensitivity Phenotype: A Gene-Environment-Developmental Model." *Journal of Personality Disorders* 22 (1) (February): 22–41. doi:10.1521/pedi.2008.22.1.22.

Published Version

doi:10.1521/pedi.2008.22.1.22

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Published in final edited form as:

J Pers Disord. 2008 February ; 22(1): 22–41. doi:10.1521/pedi.2008.22.1.22.

BPD'S INTERPERSONAL HYPERSENSITIVITY PHENOTYPE: A GENE-ENVIRONMENT-DEVELOPMENTAL MODEL

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Abstract

This paper explores the development of BPD as it might emerge in the child's early interpersonal reactions and how such reactions might evolve into the interpersonal pattern that typifies BPD. It begins to bridge the relevant bodies of clinical literature on the borderline's prototypic interpersonal problems with the concurrently expanding relevant literature on early child development. We will start by considering how a psychobiological disposition to BPD is likely to include a constitutional diathesis for relational reactivity, that is, for hypersensitivity to interpersonal stressors. Data relevant to this disposition's manifestations in adult clinical samples and to its heritability and neurobiology will be reviewed. We then consider how such a psychobiological disposition for interpersonal reactivity might contribute to the development of a *disorganized-ambivalent* form of attachment, noting especially the likely contributions of both the predisposed child and of parents who are themselves predisposed to maladaptive responses, leading to an escalation of problematic transactions. Evidence concerning both the genetics and the developmental pathways associated with *disorganized attachments* will be considered. Emerging links between such developmental pathways and adult BPD will be described, in particular the potential appearance by early- to middle-childhood of *controlling-caregiving* or *controlling-punitive* interpersonal strategies. Some implications from this gene-environment interactional theory for a better developmental understanding of BPD's etiology are discussed.

Borderline Personality Disorder (BPD), like other major psychiatric disorders, evolves from the interaction between a genetic diathesis and environmental stressors. This paper offers a theory with supporting evidence that the preborderline child has a genetically based hypersensitivity to interpersonal interactions that interacts with adverse early caretaking experiences and later stressors to become elaborated into disorganized and controlling interpersonal strategies. These interpersonal strategies then provide the soil from which the borderline patient's prototypically contradictory (i.e., needy and fearful) interpersonal features arise.

BPD AND AN INTERPERSONAL HYPERSENSITIVITY PHENOTYPE

Existing evidence supports the idea of three sectors of borderline psychopathology: *Affective Instability*, *Impulsivity* and *Disturbed Relationships* (Skodol, Siever et al., 2002). *Affective Instability* and *Impulsivity* have been described and accepted as basic psychobiological dispositions (phenotypes) for BPD since Siever and Davis's seminal article in 1991 (Siever & Davis, 1991). Yet the disturbed relationship sector has been the most central to clinical theories (Kernberg, 1967; Masterson & Rinsley, 1975; Adler, 1986; Benjamin, 1993; Gunderson, 1996). Evidence that the interpersonal sector of BPD psychopathology has a comparable level

of familiarity (Zanarini et al., 2004) and heritability (Jang, Livesley, Vernon, & Jackson, 1996) to the Affective Instability and Impulsivity sectors indicates it should also be conceptualized as a phenotype (Gunderson, 2007).

The adult borderline patients' interpersonal style is characterized by a paradoxical, seemingly contradictory combination of intense needs for closeness and attention with equally intense fears of rejection or abandonment. Given the obvious and generic evolutionary value of needing others, it is the fearful or highly reactive component of this interpersonal style that is probably the more distinctive and pathogenic component. In any event, it is this fearful component, combining abandonment fears, rejection sensitivity, and intolerance of aloneness that Jang et al. (1996) have shown to demonstrate a heritability of 0.48 (Jang et al., 1996). We hereafter refer to this as the *interpersonal hypersensitivity* phenotype. While the magnitude of this heritability coefficient may include some gene-environment interactions and replications are needed, we are left with the fact that genetic vulnerability plays an important role.

CLINICAL EVIDENCE OF INTERPERSONAL HYPERSENSITIVITY IN BPD

The clinical significance of an interpersonal relationship phenotype can be found in studies showing that the states of intense aversive tension (i.e., dysphoric negative emotional states) that characterize BPD patients (Stiglmayr, Shapiro, Stieglitz, Limberger, & Bohus, 2001; Zanarini et al., 1998), and which frequently prompt dissociation and self-injurious behaviors (Philipsen et al., 2004; Coid, 1993), are often prompted by interpersonal events such as rejecting criticisms or aloneness (Herpertz, 1995; Stiglmayr et al., 2005; Rafaeli, Howland, Vorus, Skodol, & Gunderson, 2007). Other research has demonstrated that borderline patients are hypersensitive to the feeling states perceived in other's faces (Levine, Marziali, & Hood, 1997; Wagner & Linehan, 1999; Rosenthal, Cheavens, Kosson, Lejuez, & Lynch, 2005; Donegan et al., 2003), and are particularly sensitive (and physiologically reactive) to angry faces (Lynch, 2004), abandonment scripts (Herpertz, Sass, & Favazza, 1997; Schmahl et al., 2004), and interpersonal events (Jovev & Jackson, 2006). Longitudinal data show that when borderline patients symptoms remit, it is in response to positive interpersonal events (Links & Hesgrave 2000), and their typically negative emotional responses to interpersonal interactions convert to positive responses (Rafaeli et al., 2007). When they relapse, it is typically (and specifically) in response to negative love/relationship events (Shea, 2007). All of these studies show that the sensitivity and highly negative meaning associated with real or imagined interpersonal slights, particularly in important attachment relationships, is an essential psychological vulnerability in borderline patients.

INTERPERSONAL HYPERSENSITIVITY AND BPD'S ATTACHMENT TYPES

Multiple studies with adult borderline samples have documented a high prevalence (more than 90%) of insecure attachment (Agrawal, Gunderson, Holmes, & Lyons-Ruth, 2004; Levy & Clarkin, 2005). These studies have found that borderline patients are characterized by having the *preoccupied* (60–100%) or *unresolved* (50–88%) types. As shown in Table 1, the preoccupied type captures the needy quality and the unresolved type captures the fearful and contradictory qualities. The unresolved form of attachment is a form of adult attachment whose relationship to BPD is supported by its association with trauma (Stalker & Davies, 1995) and suicidality (Adam, Sheldon-Keller, & West, 1996). While neither of these types is specific to BPD, when they are combined, the specificity rises considerably and their estimated prevalence in the general population, i.e., 3%, comes closer to that estimated for BPD.

In addition to the evidence for unresolved and preoccupied attachments found in borderline patients more recent approaches have also identified a high prevalence of what Lyons-Ruth, Melnick, Patrick, and Hobson (2006) and Lyons-Ruth, Yellin, Melnick, and Atwood (2005) call hostile-helpless attachments. These results suggest that representations of attachment

figures as hostile, untrustworthy, or abdicating of a parental role are consistent features of the syndrome, a portrait confirmed by other evidence, such as the self-endorsed relational beliefs of patients with BPD (Butler, Brown, Beck, & Grisham, 2002) and their observed-and-reported experiences of other people in videotaped clinical interviews (Hobson, Patrick, & Valentine, 1998).

Table 1 also identifies the types of attachment observed in children in the Strange Situation (Ainsworth & Witting, 1969) that have shown strong to moderate levels of association with the adult forms (van IJzendoorn, 1995; van IJzendoorn, Schnengal, & Bakermans-Kranenburg, 1999). The descriptions of these corresponding types, i.e. the ambivalent (preoccupied) and disorganized types, offer plausible signals of risk for the later development of the borderline's interpersonal phenotype. More will be said about these.

NEUROBIOLOGICAL (ENDOPHENOTYPIC) CONSIDERATIONS FOR INTERPERSONAL HYPERSENSITIVITY

In this section we identify neurobiological and candidate gene research that might be expected to be related to the development of the interpersonal hypersensitivity of the type that characterizes BPD.

THE SEROTONERGIC SYSTEM

Several types of evidence suggest that serotonin neurotransmitter system disturbance is a potential contributor to the increased interpersonal stress reactivity seen in BPD. The serotonin transporter linked polymorphic region (5HTTLPR) is located in the promoter region of the serotonin transporter gene (SLC6A4) and the short (44 base pair deletion) variant showed reduced transcription activity in reporter gene systems (Heils, Mossner, & Lesch, 1997). Therefore, this risk allele may account for reduced serotonin uptake in the serotonergic synapses. The presence of the short allele has been linked to augmented response in the amygdala (Hairiri & Holmes, 2006) and increased release of the stress hormone cortisol in response to separation in animal studies (Barr et al., 2004). Insofar as interpersonal events are the laboratory stressor most evocative of cortisol responses (Dickerson & Kemeny, 2004), this abnormality of the serotonergic system could be directly accountable for the interpersonal hypersensitivity found in borderline patients.

In relation to BPD specifically, low levels of the serotonin metabolite (5-hydroxyindoleacetic acid, 5HIAA) have been detected in the cerebrospinal fluid of borderline personality disorder patients (Brown et al., 1982). Using a candidate-gene approach, meta-analyses of data on serotonin-related genes supported the role of the short allele of the serotonin transporter linked polymorphic region (5HTTLPR) as a genetic risk factor for suicide, while other polymorphisms in the serotonin receptor genes were not shown to play a role (Anguelova, Benkelfar, & Turecki, 2003). Caspi et al., (2003) has further demonstrated the potential relevance of the short allele in that only if one such allele was present did stressful life events predict increased suicidal ideation or attempts. In addition, in a low-income sample Lyons-Ruth et al. (2006) found a relation between the short serotonin transporter polymorphism and two or more borderline criteria, most frequently impulsive self-damaging behavior, and, most relevant here, also intense unstable relationships. Another recent study offers evidence that a more complex genotype, also involving the short allele, was associated with the full diagnosis of BPD, suggesting that additional genetic components of the serotonin system may be needed for the full syndrome to occur (Ni et al., 2006).

THE DOPAMINERGIC SYSTEM

In relation to interpersonal sensitivity more generally, Insel (2004) has described parallels between close attachments (e.g., parent-child or romantic relationships) and addiction, where what begins as positive rewarding responses can switch into a preoccupation from which withdrawal symptoms occur. The description closely corresponds to borderline patients' relief and pleasure when given attention and their dramatic switch into angry clinging demands; i.e., "withdrawal symptoms," when separations occur. Insel notes that specific mesocortical pathways (notably the nucleus accumbens shell) mediate such close attachments in rodents and that disruptions of dopamine in these mesocortical pathways disrupt attachments. More specifically, in voles, the activation of dopamine D2 receptors (but not D1) in the mesolimbic area is necessary and sufficient for selecting and bonding with a partner. Given the role of dopamine in mediating reward, lack of activation of D2 receptors appears to remove the reward value of the partner's cues and disrupts pair bonding. Therefore, in the model to be elaborated here, we would expect that the future borderline patient would carry a genotype congruent with normal or enhanced dopamine transmission in attachment-relevant brain regions. We are positing, then, a genetic predisposition toward both increased interpersonal stress reactivity and high initial reward value of attachment-related cues.

Insel (2004), as well as others (Carter, 1998; Kendrick, 2000; Pedersen, 1997), have shown that evocative social stimuli (e.g., a child or lover) release rewarding neuropeptides (i.e., oxytocin or vasopressin) and this appears to be necessary for the onset of maternal and other loving behaviors, and possibly, even for memory of the particular evocative social stimulus (i.e., one's partner). Voles who form partnerships have a receptor system in their ventral tegmental area that is linked to the amygdala and to mesocorticolimbic areas. Ongoing stimulation of this system releases the rewarding neuropeptides (the same as released by a drug like cocaine), and this creates and perpetuates an addiction-like quality to maternal and romantic love relationships. This receptor system is distinctively different in those types of vole who do not partner.

Using fMRI, Donegan et al. (2003) showed that borderline patients' hypersensitivity to emotional faces is mediated by activation of the amygdala. Using PET, Schmahel et al. (2003) showed that borderline patients' reactions to abandonment scripts are mediated by more blood flow in the dorsolateral prefrontal cortex (an area responsible for remembering people who aren't present) and by less blood flow in the right anterior cingulate, a region that coordinates more complex responses. The evidence as a whole would lead to the hypothesis that perceived experiences of trauma and abandonment are differentially remembered, are related to heightened fearful affect, and that such prompts may interfere with the borderline patient's brain's ability to conduct complex assessments.

In summary, research has established a neurobiological basis for separations and attachments that involves the dopamine systems, is specific to mammals, and that links similar neuropeptides to mother-child and adult romantic relationships. We would propose that particular forms of this neurobiological substrate evolve in conjunction with interpersonal interactions over the course of development (as discussed below), and would eventually become specific for the interpersonal hypersensitivity observed in adult BPD. There is growing evidence that interpersonal hypersensitivity represents a trait with genetic components and a neurobiological basis in areas of the brain (i.e., the amygdala and limbic hypothalamic-pituitary-adrenal (LHPA) axis) that are closely connected to the mesolimbic areas responsible for attachment behaviors.

A CHILD'S CONTRIBUTIONS TO DISTURBED EARLY ATTACHMENT AND INTERPERSONAL HYPERSENSITIVITY

In considering how the borderline patients' relationship style develops, it is important to recognize that caregivers do not shape passive children, and that the child's behaviors will affect parental behaviors. A child's temperament affects parenting both by way of passively evoking parental behaviors and by virtue of actively soliciting particular types of parental interactions (Reiss, Neiderhiser, Hetherington, & Plomin, 2000; Bell & Chapman, 1986; Gc et al., 1996). A dramatic example is twin data showing that the elicitation of parental warmth, especially maternal, is substantially controlled by a child's temperament (Kendler, 1996).

SEPARATION DISTRESS AS A TEMPERAMENT AND AMBIVALENT/DISORGANIZED ATTACHMENT

Distress proneness and the related phenomenon of distress at separation are forms of temperament that can be connected to the child attachment patterns (i.e., ambivalent and disorganized) that are counterparts to the adult BPD attachment problems (as noted above and in Table 1). Among insecurely attached infants, those who are more distress-prone and irritable are more likely to display the ambivalent form of attachment (Vaughn, Lefever, & Seifer, 1989). Ambivalent infants display combinations of clinging, anger, resistance to contact, and failure to soothe in the presence of their parents (Ainsworth, Blehar, Waters, & Wall, 1978). Ambivalent infants are viewed as exhibiting a "hyperactivating" strategy by augmenting their expressions of anger and distress to assure the involvement of an inconsistently attentive caregiver (Cassidy & Berlin, 1990). A high proportion of ambivalently attached children are also likely to be cross-classified as disorganized (van IJzendoorn, Schuengel, & Bakermans-Kranenburg, 1999). Conversely, of the infants who display disorganized attachments, a subgroup also display the exaggerated distress and difficulty to soothe associated with ambivalent attachment (Main & Solomon, 1986). It is this group of infants, with classifications of disorganized and/or ambivalent attachment that we are suggesting may have an increased vulnerability for later development of BPD. We suggest this with two significant reservations. First, these forms of child attachment should not be construed as a diathesis sufficient in itself to predict only adult BPD, but simply as early risk factors that increase the likelihood of BPD as well as other adult disorders. Second, evidence has failed to show a connection of distress proneness to development of disorganized attachment (see Vaughn et al., 1989; Spangler & Grossmann, 1993; Grossmann, Grossman, Spangler, Suess, & Unzner, 1985; Carlson, 1998). We suggest only that a temperament involving high distress-proneness in infancy constitutes a vulnerability factor, which, under conditions of nonoptimal care, may evolve into ambivalent/disorganized attachment and later BPD.

DISORGANIZED ATTACHMENT

As noted in Table 1, disorganized attachment is of special importance to development of BPD because of its association with one of the two adult forms of attachment; i.e., unresolved, that characterize adult BPD patients. It also warrants special attention because, again as described in Table 1, this form of attachment involves the contradictory approach and avoidant and dissociative responses to caregivers that clinically resemble the borderline's prototypic relational style. As a result, several developmentalists have elaborated theories connecting this form of infant attachment to adult BPD (Fonagy et al., 1995; Holmes, 2004; Lyons-Ruth, & Jacobvitz, 1999). Disorganized patterns of attachment are seen in about 15% of infants by one year of age (van IJzendoorn & Bakermans-Kranenburg, 1996), predict the emergence of controlling patterns of attachment relations by 3 to 6 years of age (discussed further below), and are associated with increased behavior problems by school age (Lyons-Ruth & Jacobvitz, 1999). The prevalence of disorganized attachment strategies becomes much higher among low

socio-economic status groups (24%), infants of parents with psychopathology (30–60%), and in maltreated samples (60–70%) (van IJzendoorn, Goldberg, Kroonenberg, & Frenkel, 1992; van IJzendoorn & Sagi, 1999). Importantly, infants with disorganized attachments exhibit higher cortisol stress responses than do infants with organized attachment strategies following a brief laboratory separation-reunion procedure (Spangler, Fremmer-Bombik, & Grossmann, 1996). This is consistent with the genetic basis for the serotonergic abnormalities and high cortisol responses to separations found in borderline patients (and described above).

GENETICS OF DISORGANIZED ATTACHMENT

There is little convincing evidence to date that patterns of attachment behavior are heritable. Of the three major twin studies conducted, two found no evidence of heritability of attachment security (O'Connor & Craft, 2001; Bokhorst et al., 2003) and one found modest heritability (Finkel, Willie, & Matheny, 1998). However, the number of disorganized or ambivalent infants in these normative samples were too small to provide a separate heritability estimate for this pattern. The failure of childhood attachment patterns to demonstrate much heritability contrasts with the overall relatively strong heritability found for adult BPD by Torgersen et al. (2000) and for the fearful abandonment and rejection sensitive traits (interpersonal hypersensitivity) identified by Jang et al. (1996). This may be because the childhood forms are quite transitory (discussed below) or because they only weakly capture the specific interpersonal manifestations of risk associated with BPD.

Molecular genetic data have also been inconclusive in showing a main effect of genes on attachment strategies. Among a low-risk sample of infants, the Budapest Infant-Parent Study found that infants carrying the 7-repeat allele of the DRD4 gene were four times more likely to be classified disorganized (OR = 4.15) (Lakatos et al., 2000). However, only 36% of infants carrying this allele were classified disorganized, compared to 9% without the allele. Of note, the 7-repeat allele is associated with subsensitivity of the postsynaptic dopamine receptor (Swanson et al., 2000), which, as described earlier, might disrupt bonding. Further analyses revealed that the association between disorganized attachment and the 7-repeat allele may depend upon the presence of the -521 T allele of the C/T single nucleotide polymorphism (SNP); (Lakatos et al., 2002). Such evidence, while provocative, has not been replicated (Bakermans-Kranenburg & van IJzendoorn, 2004; Sangler and Zimmerman, 2007).

In further work combining data from the normative Budapest sample with Lyons-Ruth, Bronfman, and Parsons (1999) socially-at-risk sample, a particular form of gene-environment interaction effect on disorganized attachment was found (Gervai et al., 2007). There was a strong relation between quality of maternal affective communication and infant disorganization ($r = .56$) when the infant carried the more common (4-repeat) variant of the DRD4 allele. Among infants with the less common 7-repeat variant, there was no relation between maternal affective communication and infant disorganization. This study suggests that for infants with the 4-repeat allele (and more efficient dopamine function), the reward value of maternal attachment cues may be enhanced, resulting in greater potential for regulation or deregulation based on the quality of parental cues.

PARENTAL CONTRIBUTIONS TO DISTURBED EARLY ATTACHMENT AND INTERPERSONAL HYPERSENSITIVITY

Having already noted evidence that a child's genetic code is likely to effect their distress proneness, separation fears, and their responsiveness to maternal affective communication, this section identifies four bodies of literature that suggest early caretakers have a significant effect on development of the borderline's disturbed early attachments and their enduring interpersonal hypersensitivity.

RETROSPECTIVE REPORTS

One highly influential body of literature has been the reports by borderline patients' themselves. BPD patients typically report very difficult childhood experiences in primary attachment relationships. Individuals with BPD report early family environments in which they experienced emotional neglect from both parents, and portray caregivers who denied the validity of their thoughts and feelings, were emotionally withdrawn, inconsistent, and either failed to protect them or were overcontrolling (Zanarini et al., 1997; Zweig-Frank & Paris, 1991). Early separations are also reported as part of this caregiving constellation (Bandelow et al., 2005; Reich & Zanarini, 2001). On the other hand, when parents are also asked to assess their families, they are often less damning (Young & Gunderson, 1995; Gunderson & Lyoo, 1997), and, indeed, siblings frequently can have much better adjustments. In any event, the retrospective accounts by borderline patients cannot be discounted, though they need to be accepted with caution.

CAREGIVER EFFECTS ON INFANT ATTACHMENTS

Any viable developmental model must recognize types of evidence that caretaker behaviors influence the development of an infant's attachment pattern. One type of evidence is that the attachment strategies displayed toward primary caregivers are more predictive of later social adaptation than are strategies shown toward other caregivers (Main, Kaplan, & Cassidy, 1985; Suess, Grossmann, & Sroufe, 1992), even when the primary caregiver is not biologically related (Oppenheim, Sagi, & Lamb, 1988). A second type of evidence is that in 70% of cases an infant's attachment pattern with the primary caregiver is predictable from that caregiver's attachment style assessed prior to the birth of the infant (van Ijzendoorn et al., 1999). Moreover, those same twin studies that have failed to establish heritability for attachments, have shown that while caretaking behaviors are insufficient to explain child attachments, they are nonetheless very important (O'Connor & Craft, 2001; Finkel et al., 1998; Brussoni, Jang, Livesley, & MacBeth, 2000; Bokhorst et al., 2003).

PARENTAL CONTRIBUTIONS TO DISORGANIZED ATTACHMENT

Main and Solomon (1986) interpreted disorganized responses to the parent as indicating an approach-avoidance dilemma, or fear without solution, wherein the caregiver is both a source of fearful arousal for the child and the only source of comfort for such arousal. Lyons-Ruth et al. (Lyons-Ruth, Bronfman, & Parsons, 1999) have questioned whether the parent herself needs to be a source of threat or, more simply, unable to provide adequate comfort for the child's arousal due to a variety of aversive responses to the infant's attachment bids—aversive responses that include withdrawal, fearful disorientation, role-reversal, negative-intrusion, or contradictory responses. This repertoire of maternal responses is similar to the accounts by adult borderline patients noted above. Faced with this dilemma, the infant, in turn exhibits contradictory attachment responses, such as crawling toward mother crying, then collapsing on the floor midway; or calling at the door during separation, then backing away at reunion. These contradictory responses dramatically mirror the contradictory need/fear components of the adult borderline's prototypic interpersonal behaviors. Providing support for this general thesis is the evidence from metaanalyses that disorganized attachment is strongly associated with these atypical parental caretaking behaviors ($r = 0.35$) (Madigan et al., 2006) and, equally impressively that parental unresolved status when assessed before the child's birth is strongly associated with a child's subsequent development of disorganized attachment ($r = 0.31$) (van Ijzendoorn et al., 1999).

A prospective study showed that the presence of disrupted affective communication—especially emotional withdrawal—by mothers of 18-month-old infants, predicted borderline traits in young adulthood, particularly unstable relationships and self-damaging behavior (Lyons-Ruth, Holmes, & Hennighausen, 2005). A recent metaanalysis of 384 mother-infant

dyads showed that disrupted maternal affective communication was linked to both infant disorganization ($r = .35$) and to maternal unresolved attachment ($r = .20$) (Madigan et al., 2006). Such early disrupted communication continued to be associated with later BPD traits after controlling for gender, socioeconomic risk, extent of abuse, and with the presence of the serotonin transporter short allele (Lyons-Ruth, Bronfman, & Parsons, 1999). Disorganized attachments in these 18-month-old infants did not, however, in itself predict later BPD traits. These prospective data suggest that quality of early (and perhaps continued) parent-child affective communication, independent of abuse history, may be an important and independent factor in contributing to later development of adult BPD.

PARENTAL PSYCHOPATHOLOGY

An extensive literature shows a high frequency of psychopathology in the parents of patients with BPD (White, Gunderson, Zanarini, & Hudson, 2003). While this literature does not confirm Masterson and Rinsley's (1975) thesis that the mothers of borderline patients are themselves borderline, it does show that such psychopathology will be found in perhaps as many as 10–15%. And, relevant to this fraction, is evidence that those mothers with BPD are more insensitive to their infants at two months (Crandell, Patrick, & Hobson, 2003) and that by one year their children are more apt to show disorganized attachments (Hobson, Patrick, Crandell, Garcia-Perez, & Lee, 2005). In addition to elevated rates of BPD, the family history literature also shows high rates of substance abuse, depressive disorders, eating disorders, and antisocial or other personality disorders in both parents (White et al., 2003). We would estimate that only about 30% are without psychiatric disorders.

Perhaps more significant than the prevalence of psychiatric disorders found in relatives of BPD probands, are studies showing the prevalence of the affective, impulsive, and interpersonal phenotypes (Silverman et al., 1991; Zanarini et al., 2004). Zanarini et al. found that 50% of the relatives have affective instability, 33% have impulsivity, and 28% have the disturbed relationship style of their borderline offspring. Presumably assortative mating accounts for these high prevalences of illness or phenotypes in families, but for purposes of this paper it translates into a family context which will offer highly variable but often highly adverse caretaking experiences.

Given the high frequency of psychiatric illness and the demonstrated familiarity of the borderline phenotypes, it seems safe to conclude that many, if not most of the parents of pre-BPD individuals are themselves predisposed to be either underreactive or hypersensitive to their temperamentally predisposed infant's distress proneness and interpersonal hypersensitivity. Moreover, as noted already in Table 1, the presence of insecure attachment in children predicts the presence of insecure attachment style in parents. A metaanalysis of 34 clinical studies showed that mental illness in mothers is strongly related to insecure—and specifically disorganized—attachments in children (van IJzendoorn, Goldberg, Kroonenberg, & Frenkel, 1992). This is consistent with the likely pathogenic effect on preborderline children who are raised by parents who are themselves often mentally disturbed.

EVOLUTION OF INFANT DISORGANIZATION IN SCHOOL AGE CHILDREN

The developmental pathways evolving from early disorganized attachment are particularly complex, and our knowledge still falls far short of providing the links with adult BPD that are needed. Some links have been suggested that await further study.

CONTROLLING ATTACHMENT STRATEGIES

Sometime between 18 months of age and 6 years, about two thirds of children with disorganized attachment become organized around the apparent goal of controlling the interaction with the

attachment figure (Main, 1995; Wartner, Grossmann, Fremmer-Bombik, & Suess, 1994). The remaining third remain disorganized. This change may serve the adaptive function of increasing a dysfunctional parent's involvement with the child in the face of the parent's previous inability to meet the child's needs for comfort and security. A possible mechanism for this change is the observation that after 18 months a child with negative feelings becomes more likely to personalize this in the form of anger at the parent (Hennighausen & Lyons-Ruth, 2005). Such responses in a child will potentially be experienced as personally rejecting by a hypersensitive parent. Many of these children display the controlling patterns of behavior in relation to the caregiver as early as 3 years of age (Moss, Parent, Gosselin, Rousseau, & St. Laurent, 1996). The shift is a classic example of phenotypic discontinuity in development, in that the controlling strategies look quite different from the earlier hesitant, apprehensive, or conflicted responses characterizing disorganized attachments in infancy.

The developmental shift to controlling strategies involves two quite different forms. *Controlling-punitive* behavior involves the child's attempts to take control of the relationship with the parent through hostile, coercive, or more subtly humiliating behaviors when attachment concerns are aroused. Controlling-caregiving behavior involves the child's attempts to control by entertaining, organizing, directing, or giving approval to the parent. By 4 to 6 years of age, the association between these preschool controlling strategies with parents and teacher-reported behavior problems has been well-established (van IJzendoorn et al., 1999; Lyons-Ruth & Jacobvitz, 1999; Moss, Rousseau, Parent, St. Laurent, & Saintong 1998; Solomon, George, & DeLong, 1995). In addition, controlling behaviors toward the parent are associated with clinically diagnosed oppositional defiant disorder (Speltz, Greenberg, & DeKlyen, 1990). These two forms of controlling behavior are not mutually exclusive, and many children shift from devaluing, directive or insulting comments to solicitous behavior towards the parent.

There are as yet no prospective data to tie such controlling attachment strategies to adult BPD or other psychopathology. However, several studies have shown that adult BPD patients frequently reported parentification (i.e., caregiving) or punitive controlling behaviors towards their parents in childhood (Lyons-Ruth, Melnick, Patrick, & Hobson, 2006; Zanarini et al., 1997). We also know very little about how such controlling patterns of attachment might evolve in adolescence. In one attempt to fill this gap, Lyons-Ruth and colleagues have shown that 14–16-year-old adolescents with controlling patterns of relating to their parents were likely to later (age 25) develop unresolved attachments (Hennighausen et al., 2006).

Should these controlling forms of attachment in childhood and young adulthood prove to be related to BPD, as we propose, they contribute to a more complicated picture of the borderline patients' phenotype of interpersonal hypersensitivity. These controlling forms of childhood interaction reflect considerable capacity to inhibit one's own needs and to be hypervigilant and structuring of the interaction around the needs of the caregiver. In contrast to a picture of the BPD patient as simply too reactive, self-centered, or unable to mentalize, this developmental process suggests that some fraction of BPD patients will be maladaptively predisposed to inhibit their own needs as a result of their highly sensitive attunement to subtle cues by others. As part of a transactional developmental spiral that undermines the potential for coherent dialogue with attachment figures, however, that special sensitivity would not become articulated at a reflective and verbal level. Nor would the patient be able to identify and communicate her own interpersonal needs, which would remain to be acted out in self-damaging ways. Therefore, we would expect a particular combination of heightened sensitivity to reading the cues of others and of inhibiting one's agency to be part of a caregiving stance among a sizeable proportion of BPD patients.

A NON-LINEAR, INTERACTIVE MODEL OF CHILD-CAREGIVER INTERACTION IN TRAJECTORIES TOWARD BPD

Throughout this review, it has been evident that we cannot speak of a child's development in isolation from their caretakers or of the caretaking in isolation from the particular features of the preborderline child. Therefore, we need to consider the evidence for nonlinear moderating or potentiating relations between parental behavior and child behavior in the pathways to BPD. Given the likely differential contribution to BPD of a temperamental predisposing sensitivity to interpersonal stress, more extreme states of distress in the child may trigger frightened states in a vulnerable (i.e., depressed, anxious, ill, or traumatized) caregiver, which in turn could make that caretaker all the less available to the child. In support of this transactional model, Hrdy (2006) argues that because maternal care is more costly and therefore more conditional (less ritualized and predictable) in humans than among other primates, adequate maternal care among humans depends much more on the human infant's capacity to engage the caregiver.

To date few studies have examined interactions between qualities of the caregiving environment and genetic or temperamental qualities of the infant in developmental pathways toward BPD. The thesis of this paper is that innate psychobiological or temperamental traits in the child interact with adverse relational predispositions in the parents to create increasingly difficult interactions that culminate in the full syndrome of adult BPD. We would propose that the child's interpersonally hypersensitive and stress reactive traits would be more apt to evoke a parents' helplessness withdrawal, or fearfulness and that such reactions are apt to have more significant effects on the vulnerable child. We would in addition hypothesize that the parents of a BPD child often carry a disposition of their own towards adverse responses to a child's increasing neediness or anger that would be particularly likely to bring about an escalating series of negative interactions.

CONCLUSIONS

In this paper we have attempted to synthesize two previously separate literatures to present the current state of knowledge regarding developmental pathways that may be associated with the interpersonal style that characterizes BPD. In this integration we have hoped to expand awareness of the potential role of the interpersonal environment as an interacting component of these pathways. We are aware that by focusing on selected clinical and caretaking perspectives we are overlooking the significant contributors that derive from trauma, peer relationships, and the ongoing family environment. Further we are overlooking the role that affective instability or impulsivity may have in shaping the borderlines' interpersonal hypersensitivity. This is not meant to be comprehensive.

Current clinical and research literature would point to early disorganized attachment strategies and their later evolution into controlling patterns as one pathway likely to contribute to the development of BPD. A pathway through attachment disorganization is not expected to be the only pathway, however. Instead, disorganized parent-child relationships are likely to represent one early relational component that interacts with other temperamental predispositions of parent and child to increase the likelihood of BPD.

Relevant gaps in our knowledge include identification of risk markers in infants and children for development of disorganized or ambivalent attachments and of later BPD. We also should learn what particular forms of parenting may represent risk factors for those subgroups who are more likely to progress to the full BPD presentation. Certainly the tendency to withdraw in the face of a child's needs or protests emerges from both the current developmental and clinical literatures.

We would also argue that interpersonal psychopathology needs to be reconceptualized alongside affective instability, and impulsivity as also having significant genetic contributors and reflecting escalating transactional processes with the caregiving environment. Speculations regarding the specific genetic components for the proposed interpersonal hypersensitivity will undoubtedly need to be revised as the field of molecular genetics progresses. The more general hypothesis, however, is that genetic contributors to both stress reactivity and interpersonal sensitivity will be a part of the interacting factors that culminate in adult BPD.

This paper is necessarily highly speculative given the dearth of developmental literature on BPD and the very recent emergence of psychiatric molecular genetics as a field. Therefore, new findings are likely to alter substantially the hypotheses put forward here. However, points of convergence are clearly emerging between the body of developmental work on attachment relationships and studies of the interpersonal characteristics of adult BPD patients, so that it has seemed timely to draw this literature together and set forth some hypotheses to stimulate further work.

Acknowledgements

This work was supported by National Institute of Mental Health (NIMH) (MH400130).

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TABLE 1

BPD and its Attachment Types

Adult Types (Self Report) ¹	Corresponding Child Type ²	Correlation of Adult/Child ³
<i>Preoccupied (preoccupied)</i> Definition: In children, heightened distress and proximity seeking are combined with angry resistance to contact or passive bids for help. Adults display mental preoccupation with attachment concerns that may have either an angry or passive quality (AAI). Negative image of self is combined with positive images of others (self-report).	<i>Ambivalent (Preoccupied)</i>	.42
<i>Unresolved (fearful)</i> Definition: In children, contradictory and unintegrated approach/avoidance responses or confused, disoriented behaviors are displayed toward the parent when distressed and needing care. Adults display lapses in reasoning or narrative structure when discussing losses or traumatic experiences (AAI). A negative image of self is combined with negative expectations of others (self-report).	<i>Disorganized</i>	.31

¹Types based on Adult Attachment Interview (corresponding self report types in parenthesis). After Agrawal et al. (2004).

²Based on Strange Situation (separation and reunion of infant and caretaker) (Ainsworth & Wittig, 1969).

³From van IJzendoorn et al. (1995) and van IJzendoorn et al. (1999).