Running head: attachment, mentalization, and BPD

TITLE: Attachment and reflective functioning in women with borderline personality disorder

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Insecure attachment and impairments in reflective functioning (RF) are thought to play a critical role in borderline personality disorder (BPD). In particular, the mentalization-based model argues that insecure attachment indirectly accounts for increased BPD features, notably via disruption of RF capacities. Although the mediation relationship between attachment, RF and BPD is supported by previous evidence, it remains to be directly tested in adults with BPD. In the current study, a sample of 55 female adult BPD patients and 105 female healthy controls completed a battery of self-report measures to investigate the interplay between attachment, RF capacities, and BPD clinical status. Overall, the results showed that BPD patients predominantly reported insecure attachment, characterized by negative internal working models of the self as unlovable and unimportant to others, and decreased RF abilities. Our findings further indicated that actual RF capacities mediated the relationships between adult insecure attachment and BPD clinical status.

Keywords: Borderline Personality Disorder, Mentalization, Reflective Functioning, Attachment, Internal working model
Mentalization, or the processes sustaining our understanding of human action as driven by mental states, has been operationalized in terms of reflective functioning (RF; Fonagy, Gergely, Jurist, & Target, 2002). Genuine RF implies to acknowledge the opaqueness of mental states, in combination with the capacity to form relatively accurate models of the mind of self and others (Fonagy et al., 2016). Reflectively thinking about behaviors and interpersonal interactions helps us to experience oneself and others as predictable, manageable, and meaningful, rather than puzzling and unreliable. RF is therefore one of the cornerstones of one’s sense of agency, and sustains self-coherence and continuity over time and across situations (Fonagy & Target, 1997). At the same time, RF significantly contributes to the adaptive management of distressing feelings when one is facing difficult interpersonal events (e.g. conflicts, losses), and previous studies have demonstrated how trauma and neglect may significantly interfere in its development (e.g. Fonagy & Target, 1997). These different lines of research thus frame RF as a psychological mechanism central to the consolidation of coherent identity and self-regulation during development. Consequently, it has been assumed that disrupted RF processes might be one crucial variable for understanding the core features of borderline personality disorder (BPD), namely affective dysregulation, impulsivity and social dysfunctions. Impairments in RF can manifest themselves in two ways, namely hypomentalizing and hypermentalizing. Hypomentalizing describes the inability to consider complex models of one’s own mind and/or those of others implying high uncertainty about self and other mental states. The opposite tendency, namely hypermentalizing, refers to the generation of highly certain mentalistic representations of actions without appropriate evidence available to support them (Fonagy et al., 2016). Specifically, the mentalization-based model for BPD argues that RF dysfunction during
adulthood critically mediates the relationship between feelings of insecurity in close relationships and BPD psychopathology in adulthood (Fonagy & Luyten, 2009).

Although RF might constitute an innate human ability, its degree of maturation, and its robustness in the face of high emotional interactions appears to be critically influenced by primary attachment relationships (Fonagy et al., 2002, Luyten, Fonagy, Lowyck, & Vermote, 2012). Indeed, the attachment context supplies the setting in which the infant can be sensitized to inner self-states, through his interactions with caregivers, whom strive to make sense of his signals (e.g., figuring out whether a cry means the infant is sad or angry). A secure environment may reflect caregiving that is consistently attuned to baby’s mental states, thereby favoring the development of RF and self-regulation processes (e.g., Gergely & Unoka, 2008). Conversely, an insecure attachment may suggest difficulties in the infant-parent dyad, which can undermine the development of RF and self-regulation and confer an increased risk for expressing early features of BPD (Fonagy et al., 2002).

One basic premise of attachment theory stipulates that over repeated interaction patterns with his caregivers, the child develops cognitive representations of self and others in relationships (i.e., internal working models; Bowlby, 1973) that remain relatively stable and influential across the lifespan (Bowlby, 1979). Attachment research has provided evidence that infant attachment insecurity can later translate into insecure attachment patterns in close relationships during adulthood (e.g. Fraley, 2002). Research on adult attachment further sustains that RF is associated to the way people consciously manage actual significant relationships. Adults securely attached to their significant others (i.e., reporting positive and soothing working models of oneself and other in close relationships) benefit from a robust capacity to explicitly consider the mental states that lie behind oneself and others’ behaviors, which helps them adaptively manage interpersonal stress. Conversely, adults with insecure anxious or avoidant bonds with close ones (reporting negative and dysregulating working
models of self and others) tend to exhibit fragile reflective functioning that with maladaptive fluctuations in response to attachment arousal (e.g. Luyten et al., 2012).

To date, several studies have reported associations between BPD and adult insecure attachment models (e.g. Agrawal, Gunderson, Holmes, & Lyons-Ruth, 2004 for a review) as well as between BPD and RF dysfunctions (e.g., Fonagy et al., 1996; Gullestad et al., 2012; Harari, Shamay-Tsoory, Ravid, & Levkovitz, 2010; Preissler, Dziobek, Ritter, Heekeren, & Roepke, 2010). These studies underline the relevance of adult attachment patterns sustained by negative self internal working model while other findings have also highlighted the importance of negative internal working model of others. As a whole, these results lead many to consider that BPD patients may fluctuate in the valence of internal working models of self and others (for a review see Agrawal et al., 2004)

In terms of mentalization, BPD patients are typically described as struggling to effortfully engage cognitive resources when attributing mental states (e.g., Fonagy et al., 1996; Gullestad et al., 2012; Harari et al., 2010; Preissler et al., 2010). This feature in their mentalization profile may bias the interpretation of mental states that motivate self and other’s action, towards automatic and affectively-based reasoning, which strongly reduces their emotion regulation success (Fonagy & Luyten, 2009).

Recently, several studies have also started to examine the RF’s putative mediation role linking insecure adolescent or adult attachment to BPD symptom expression (Carlson, Egeland, & Sroufe, 2009; Fossati et al., 2009; Fossati, Feeney, Maffei, & Borroni, 2011, 2014; Sharp, Venta, et al., 2016). Fossati and colleagues provided three cross-sectional studies carried on community samples, examining the relationships between avoidant and anxious attachment dimensions and conceptual cousins of RF processes (i.e. alexythymia; mindfulness; mental state attribution and awareness of one's own emotional states; respectively in Fossati et al., 2009, 2011, 2014). They specifically examined the degree to
which expressions of nonclinical borderline personality features were associated with these processes. Their results suggest that insecure adolescent or adult relationship styles, and particularly attachment patterns involving predominantly anxious (Fossati et al., 2011, 2014) or poorly organized strategies (Fossati et al., 2009) contribute to higher expression of borderline personality features through their negative (i.e. decreasing) associations with mediating RF processes (Fossati et al., 2011, 2014). In another study involving a sample of 54 adolescents with a diagnosis of BPD and 50 matched healthy controls, Deborde et al. (2012) show that insecure attachment, and particularly attachment patterns that imply negative internal representation of oneself (i.e. preoccupied and fearful), is related to BPD diagnosis via alexithymia features, namely difficulties in describing and being aware of one’s own feelings, thereby hinting to impairments in RF. Finally, based on a multiple mediational approach, Sharp et al. (2016) investigated the cross-sectional interplay between attachment, objective performance to a socio-cognitive task, self-reported emotion regulation and borderline features in a sample of 259 adolescent inpatients. They observed that, unlike emotion dysregulation, excessive RF capacities independently mediated the relation between attachment insecurity and level of BPD features in adolescence. Together, the six studies reported above provide supporting evidence concerning the mediating role of RF as conceptualized by mentalization-based model of BPD. The available literature further motivates an examination of Fonagy and colleagues’ hypothesis in a clinical sample of adults BPD patients, using a direct measurement of RF, rather than variables measuring its “conceptual cousins” (i.e. mindfulness, alexythimia, Choi-Kain & Gunderson, 2008).

In this context, the present study aims to further the examination of the relationships between RF, attachment and BPD symptoms, and address the limitations of previous work by testing the mediation model between current attachment relationship models, RF, and BPD diagnosis in a sample of outpatient women with BPD and healthy controls. Using a valid
questionnaire designed to assess the ability to conceive behaviour as motivated by mental states (i.e. the Reflective Functioning Questionnaire; RFQ; Badoud, Luyten, Fonseca-Pedrero, Eliez, Fonagy, & Debbané, 2015; Fonagy et al., 2016) the current investigation examined the following hypotheses. As a premise, in line with previous studies, we first postulate that, in comparison with nonclinical controls, a higher proportion of BPD patients will report insecure attachment, particularly of the anxious-preoccupied prototype; we further expect that these patients will report a higher degree of negative internal working models of the self. Second, we expect BPD patients will report lower mean level of RF in comparison to healthy controls. Finally, in order to reach beyond current available literature, we predict that RF will significantly mediate the relationship between attachment insecurity and BPD clinical status. More specifically, we hypothesize that the relationship between negative working models of self and the likelihood of having received a diagnosis of BPD will me significantly mediated by decreased RF capacities.

Methods

Participants

Fifty-five women diagnosed with BPD ($M_{age} = 30.63$, $SD_{age} = 9.02$) were recruited from the University Hospitals of Geneva outpatient psychiatric service specializing in the treatment of BPD. Participants were referred by their physician or other medical services due to severe suicidal or self-damaging behaviors and/or emotional dysregulation. Patients were interviewed by a trained psychologist using the Structured Interview for Axis II Disorder (SCID-II; First, Gibbon, Spitzer, Williams, & Smith Benjamin, 1994) BPD part; only those fulfilling DSM-IV/5 criteria for BPD were accepted into the program. Studies have shown that the SCID-II 2.0 has adequate inter-rater and internal consistency reliability for diagnosing BPD (Maffei et al., 1997). In addition, the French version of the Diagnostic Interview for Genetic Studies (DIGS; Preisig, Fenton, Matthey, Berney, & Ferrero, 1999)
was used to assess Axis I disorders. If needed, participants received psychopharmacological treatment such as, for instance, antidepressant medication for a depressive episode, as previously described (Perroud, Nicastro, Jermann, & Huguelet, 2012). Those with severe cognitive impairments, severe depressive episodes, mania and hypomania, and/or psychotic symptoms that required more intensive care or hospitalization were not taken into the center’s program.

The control group of 161 non-referred women was recruited from the community of Geneva through written advertisements and word of mouth. The sole inclusion criterion was age (at least 18 years); exclusion criteria comprised a clinical level of psychopathology, assessed by standardized scores (t-score of 63 and above) on the French version of the Symptom Checklist-90-Revised (SCL-90-R; Pariente & Guelfi, 1990) and Adult Self-Report scales (ASR; Achenbach & Rescorla, 2003) Participants who reported a clinical score on the internalizing ASR subscale, on the externalizing ASR subscale, on the global severity index of the SCL-90-R were excluded from the control group. Following these criteria, 56 participants were excluded.

The final sample encompassed 55 patients with BPD ($M_{age} = 30.63, SD_{age} = 9.02$) and 105 healthy controls ($M_{age} = 23.26, SD_{age} = 2.47$). The cantonal ethics committee for human research of Geneva and the ethics committee of the psychology and educational sciences department of the University of Geneva approved the study. All participants gave written informed consent before participating.

**Measures**

All participants completed the following self-report questionnaires. To ensure that all subjects understood the items, trained clinical psychologists supervised the process.
The *Relationship Questionnaire* (RQ; Bartholomew & Horowitz, 1991) was used to obtain a categorical and dimensional evaluation of the four attachment patterns (i.e., secure, preoccupied, fearful, and dismissing).

The categorical ascription of attachment relies upon the RQ, a single-item measure consisting of four short paragraphs corresponding to four prototypical attachment patterns: secure, fearful, preoccupied and dismissing. The participants were instructed to rate the four attachment descriptions on a 6-point scale (1 = “This is not at all like me” to 6 = “This is absolutely like me”) and to choose the one that best captured their individual attachment style. The single choice provided the categorical value, while the continuous ratings were used to derive the two dimensional values, namely, the valence of internal working models of self and other. The two internal working models were chosen because they fit with the predominant view of attachment as a dimensional construct and specifically account for the fact the individual may correspond to a greater or lesser degree to different prototypical descriptions. Moreover, the internal working models are believed to capture the mechanisms behind the categories that are stable with age and may consist in measures suitable for adult participants (see Shaver & Mikulincer, 2010 for an exhaustive view on attachment in adulthood).

According to Griffin and Bartholomew (1994), the self internal working model was computed as followed: the rating score of patterns characterized by a negative view of self (i.e., fearful and preoccupied) minus the rating score of patterns characterized by positive self-models (i.e., secure and dismissing). Higher scores indicate consideration of the self as not deserving of help or love from close others. The internal working model of others also consisted in a difference score: the rating score for patterns characterized by positive models of others (i.e., secure and preoccupied) minus the rating score for patterns characterized by negative models of others (i.e., fearful and dismissing). Higher scores designate a
representation of significant others as being helpful and reliable. Because this study was part of a larger study, the RQ was used for time and feasibility concerns.

The Reflective Functioning Questionnaire (Badoud, Luyten, et al., 2015; Fonagy et al., 2016) provides a valid self-reported measure of RF, which strives to make RF assessment more readily accessible (i.e. less time-consuming than clinical interview such as the adult attachment interview; George, Kaplan, & Main, 1985) and more straightforward than instruments developed for related constructs such as mindfulness (Choi-Kain & Gunderson, 2008). The validation studies of the RFQ showed that the factorial structure that best accounted for the data is a two-dimension model, which translates the nature of minds (opacity) and the possible pitfalls in thinking about minds: uncertainty about the value of information about minds and rigid certainty about mentalistic attributes. They further supported the good psychometric properties of the two subscale scores within different samples of participants (Badoud et al., 2015; Fonagy et al., 2016). The Certainty about Mental States (α=.74 and .70 in the control and BPD samples respectively) subscale consists of 6 items focusing on the extent to which individuals disagree with statements such as “I don’t always know why I do what I do”. All items are scored by participants on a 7-point Likert type scale, ranging from “completely disagree” to “completely agree”. Items are subsequently rescored to capture more extreme levels of certainty, so that very low agreements on this scale reflect excessive RF while some agreement reflects adaptive levels of certainty about mental states. The Uncertainty about mental states subscale (α=.65 and .75 in the control and BPD samples respectively), which in the extreme captures deficits of RF, also consists of 6 items scored on the same 7-point Likert type scale; high scores reflecting a stance characterized by an almost complete lack of knowledge about mental states, while lower scores reflect acknowledgment of the opaqueness of one’s own mental states and that of others, typical of genuine RF.
In the current study, we then computed a difference score (i.e. certainty minus uncertainty scores) to bring greater clarity around the construct of mentalization. The difference/total score merges the two subscale scores in one dimension, which indeed would reflect “calibrated mentalization”. This “total score” can be interpreted as follows: negative values (i.e. individuals for whom the uncertainty score is higher than the certainty score) characterize individuals who mostly poorly recognize that self and other actions are driven by mind states. On the other hand, values in the positive range (i.e. individuals for whom the certainty score is higher than the uncertainty score) designate people who are predominantly confident that behaviors originate from intentional mental states.

**Statistical analysis**

Z-tests were calculated to compare the percentage of answers reported for each attachment pattern (RQ_{choice}) in the BPD and healthy control groups.

Analysis of variance (ANOVA) was performed to analyse the dimensional attachment scores (RQ self/other internal working models) and level of RF.

Based on the ANOVA results, variables that significantly differed between our two groups were introduced in the mediation analysis. Direct, indirect, and total effects of dimensional attachment and level of RF on clinical status (BPD vs. healthy control served as the dependent variable) were concurrently estimated with an implemented script for SPSS (Preacher & Hayes, 2008). An alternative model that switches the mediator from the independent variable was also tested. A bootstrap test for the indirect effect (5000 samples, confidence intervals set at 95%) was performed according to Preacher and Hayes (2008) recommendations. Because the patient group was significantly older than the control group ($t = -6.12, p < .001$), all statistical analyses included age as a covariate.

**Results**
Attachment in BPD

Sixteen patients with BPD had missing data on the RQ questionnaire and were thus excluded from the following analyses.

First, with regard to the forced choice of the prototypical attachment category that best described participants in the two groups, 68.2% of the control group could be categorized as secure, 11.2% as fearful, 7.5% as preoccupied, and 13.1% as dismissing. In the BPD group, 25% could be categorized as secure, 35% as fearful, 30% as preoccupied, and 10% as dismissing. Percentage comparisons indicated significant differences between the two groups for fearful, preoccupied (both higher in the BPD group) and secure attachment (lower in the BPD group; all \( p < .05 \)). No between-group differences were found for the dismissing style (\( p > .05 \); Table 1).

Second, group comparisons performed on the two dimensions that underlie the attachment prototypes (i.e., the valence of internal models of the self and significant others) revealed that the BPD group overall had a more negative self-model (\( F_{(2,144)} = 33.03, p = .00 \)). No differences were found between the groups for the internal model concerning others (\( p = .47 \); Table 1).

Reflective functioning in BPD

Mean comparisons performed on RF level indicated lower RFQ total score in the BPD group than in control participants (\( F_{(2,157)} = 69.15, p < .001 \); Table 1).

Insert Table 1

Contribution of attachment and reflective functioning to BPD

Mediation analysis showed from the bootstrap analysis a significant indirect effect (\( M = .25, SE = .08 \)), with a 95% bias corrected confidence interval excluding zero (\( .14–.43 \)).
indicating that the association between the valence of the internal working model of self and BPD diagnosis acts through the level of RFQ total score. The direct effect and the other coefficient paths of the model were also significant (see figure 1 for path coefficients and p-values).

Concerning the alternative reverse model (self-model as mediator, RFQ as independent variable), the results revealed a significant indirect effect of the RFQ in the relationship between the attachment measure and the clinical status ($M =-.08, SE=.07, CI 95\% =-.21--.02$). The other coefficient paths of the model were also all significant as summarized in the figure 2.

INSERT FIGURE 1 AND 2

**Discussion**

In the present study attachment, RF, and their relationship were investigated in a clinical sample of women with BPD and a healthy control group. Our results replicate prior studies showing an increased prevalence of insecure attachment and impaired RF in BPD patients compared to the control group. We provide first direct evidence for the RF capacity as a mediator in the relationship between attachment insecurity (internal working model of self) and BPD diagnosis in a clinical sample. We will discuss the results sequentially in light of the evidence concerning the different associations between insecure attachment, RF, and BPD.

Consistent with our first hypothesis, the present results highlight the prevalence of preoccupied-anxious attachment in BPD and underlie that BPD might not be characterized by a unitary attachment style. Indeed, as reported by previous studies based on the RQ (Brennan & Shaver, 1998; Choi-Kain, Fitzmaurice, Zanarini, Laverdiere, & Gunderson, 2009; Dutton, Saunders, & Starzomski, 1994; Hoermann, Clarkin, Hull, & Fertuck, 2004), our data supports
the fact that a fearful attachment pattern is also relevant to BPD. Preoccupied and fearful patterns both imply negative working models of self, namely a representation of oneself as being unworthy and unacceptable that goes along with excessive anxiety and dependency in close relationships. Nevertheless preoccupied and fearful patterns are different in terms of internal working models of others. Preoccupied adults maintain positive working models of others and actively seek approval to validate their own fragile sense of self-worth, while fearful individuals exhibit a pervasive sense of interpersonal distrust (Bartholomew, 1990; see Mikulincer & Shaver, 2010 for an exhaustive view on attachment in adulthood). As a consequence, fearfully attached individuals exhibit approach/avoidance conflicts in relation to significant others (Dutton et al., 1994; Pietromonaco & Feldman Barret, 2000). Unsurprisingly these categorical results prelude our dimensional investigation of attachment; whereas no difference between groups in terms of working models of others was found, the BPD sample reported negative working models of self in comparison to the controls, implying views of oneself as unimportant and undesirable in the eyes of significant others. Interestingly, these results might be coherent with recent literature about shame-proneness in BPD (Gratz, Rosenthal, Tull, Lejuez, & Gunderson, 2010). Indeed, shame-proneness refers to the individual tendency to easily feel ashamed due to a global sense of self as being a ‘bad’ person (Lewis, 1971). This description echoes the negative internal working model of the self observed in the current BPD sample. Shame is a predominant emotion in BPD and has been linked to the most serious symptoms of BPD (e.g., suicidal behaviors or nonsuicidal self-injury), lower quality of life and self-esteem, and increased hostility (Rüsch et al., 2007). Specifically, we might speculate that one path to exaggerated shame-proneness in BPD arises from negative internalized expectations about oneself in relationships. This hypothesis could potentially be a fruitful avenue of research in BPD psychopathology.
Second, the observed RF impairments in our sample of women with BPD suggest that these participants might experience the inherent relationship between actions and mental states more tenuously than control participants. The present data contributes to previous work on RF capacities in two ways. First, it provides a direct investigation of subjective (self-reported) RF capacities in individuals with BPD. So far studies about RF in BPD have mostly relied upon proxy measures, such as experimental tasks and/or self-reports primarily designed to assess constructs overlapping with RF (Choi-Kain & Gunderson, 2008). Secondly, it adds compelling evidence for the existence of significant impairments in RF in BPD. The current scientific and clinical literature reports impairments in RF processes that may express themselves through seemingly reduced (notably in the present study) or over-active mentalization (e.g. Fertuck et al., 2009; Franzen et al., 2011; Frick et al., 2012; Krohn, 1974; Preissler et al., 2010; Sharp, 2014; Sharp et al., 2011). A number of variables may moderate the relationship between BPD and RF dysfunction, such as measurement methods (subjective self-report versus objective experimental task), level of participant’s arousal (high versus low) or the developmental period (adolescent versus adult sample). For instance, a recent study carried out in a community sample showed higher mean levels of self-reported RF capacities in the adult group compared to the adolescent group (Badoud, Menghetti, Eliez, & Debbané, 2016). The current results suggest that women with BPD, when filling a self-report in non-arousing conditions, conserve a degree of awareness of their difficulties to link behaviours with mental states. However, the relative influence of within-individual and situational variables on RF functioning in BPD should be systematically examined in future assessments to bridge the potentially contradictory perspectives on RF processes (hypo versus hyper functioning) in BPD

Our final analysis examined how attachment insecurity and RF are associated with BPD diagnosis in women. Consistent with our hypothesis, we observed that the
representation of the self as undesirable and insignificant to others significantly relates to the
degree of uncertainty when inferring mental states to understand self and other behaviours. In
turn, uncertainty in the value of mental state knowledge increased the probability of
belonging to the BPD group. The present results are in line with previous studies that
emphasize the mediating role of RF in the specific relationship between attachment
disturbances and BPD features expression (Carlson et al., 2009; Deborde et al., 2012; Fossati
et al., 2009, 2011) as well as those reporting on the role of RF in the more general association
between childhood adversity and adult functioning (e.g. RF as mediating the relation between
childhood maltreatment and personality disorder; Bouchard et al., 2008; Chiesa & Fonagy,
2014; for other examples see also McIntosh, 2013 for a review or Stein, Fonagy, Wheat,
Kipp, & Gerber, 2004; Taubner & Curth, 2013 for specific examples).

Developmental studies suggest a prospective link between early attachment,
adolescent RF, and adult BPD symptoms (Carlson et al., 2009). Our results further suggest
that negative views of the self in actual relationship with close persons contributes to the
clinical status of someone, through one’s prevailing level of RF. Put another way, our results
may critically lead to the belief that impaired RF processes are not only involved in the BPD
developmental path but also in the maintenance of adult BPD difficulties of clinical
significance. Of note, the present study also emphasized that the reverse indirect model (i.e.
with attachment as mediator) is equally significant than the original developmental model.
This emphasizes the need for longitudinal prospective design to illuminate the directionality
of the link.

Some limitations to this study warrant consideration. First, like most studies in the
field of BPD, the sample consisted exclusively of females, which constrains the
generalization of the results. The SCID-II interviews were not subjected to inter-rater
reliability procedures; however to guarantee the reliability of the assessment the SCID-II was
only administered by researchers who were also trained as clinical psychologists and with several years of practice in the assessment and care of BPD patients. We further need to mention that the mediation analyses were performed on a subsample of participants, as a part of the BPD patients did not report attachment data. The current study offers preliminary results that need to be longitudinally replicated in integrating other measurement methods (e.g. using objective reflective functioning performances) to assess the role of RF as a maintenance factor. It should also include additional clinical samples to test the specificity of the relationships highlighted here to BPD, as compared to regular community controls (i.e. including a group from the general population, wider than students).

Despite these limitations, the current investigation opens promising empirical questions that can be summed up as follows. The study of RF and attachment in adults with BPD might benefit from studies that aim to specify the role of RF in the maintenance of BPD across adulthood. BPD symptomatology is thought to decrease over time, with a much higher percentage of remission than was previously expected (Gunderson et al., 2011). A better understanding of the factors involved in the persistence of BPD and how these factors participate in chronic self-image disturbance, interpersonal relationships instability or emotion dysregulation may be potential mechanisms of change and therefore clinically relevant.

Reference


