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PROMETEO: Project on Metacognition in Borderline Personality Disorder

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ABSTRACT

Borderline Personality Disorder (BPD) is characterized by Metacognition/Mentalization deficits and Emotion Dysregulation (ED). BPD's first-choice treatment is psychotherapy, but a comprehensive model for this disorder has not yet been formulated, consequently also treatments result controversial.

Study 1:
Aims: to examine the relationships between Metacognitive Functions and ED and other clinical features in a BPD sample.
Methods: Seventy patients were assessed for the inclusion and 45 BPD patients were included. Metacognitive functions were evaluated with Metacognition Assessment Interview (MAI). Specific self-reports measured respectively: ED (Difficulties in Emotion Regulation Scale, DERS), Alexithymia (Toronto Alexithymia Scale, TAS), Impulsiveness (Barratt Impulsiveness Scale, BIS), Mood (Beck Depression Inventory; BDI), Interpersonal Sensitivity (Inventory of Interpersonal Problems, IIP) and general psychopathology (Global Severity Index (GSI) of SCL-90).
A Structural Equation Model (SEM) was used to evaluate the relations between variables.
Results: SEM showed that TAS score resulted a mediator between MAI total score and DERS score and DERS significantly predicted BIS, BDI, IIP and GSI scores.
Conclusions: The general level of psychopathology and the other clinical variables seemed directly linked to ED. ED didn't seem to correlate directly to Metacognition, but indirectly through Alexithymia.

Study 2:
Aims: to compare the effect of 1-year Metacognitive Interpersonal Therapy (MIT) and Mentalization Based Therapy (MBT) vs TAU (Treatment as usual) on Metacognition functions, ED and other clinical features in a BPD sample.
Methods: Forty-five patients were divided in 3 groups: MIT (N=14), MBT (N=16) and TAU (N=15). MAI scores were the primary outcome, DERS, TAS, BIS, BDI, IIP and GSI of SCL-90 scores were the secondary outcomes.
Linear Mixed model were used for the longitudinal evaluation of the results.
Results: MAI total score improve in both experimental groups, but only MIT group statistically differ from TAU, probably due to the small sample size. Between Metacognition sub-scales Differentiation and Integration played a central role. Secondary outcomes improved, but the effect wasn't statistically significant.
Conclusions: Differentiation and Integration played a central role both in MIT and MBT.

PART 1: GENERAL INTRODUCTION

Chapter 1: Borderline Personality Disorder (BPD)

1.1 A brief history of the definition and epidemiology

The term 'borderline personality' was proposed for the first time in the United States by Adolph Stern in 1938. Stern described a group of patients who 'fit frankly neither into the psychotic nor into the psychoneurotic group' and introduced the term 'borderline' to describe what he observed because it 'bordered' on other conditions (Stern, 1938). Afterwards Otto Kernberg (1975) introduced the term "borderline personality organization" to refer to a consistent pattern of functioning and behavior characterized by instability and reflecting a disturbed psychological self-organization. From these first conceptualizations to nowadays the study of the Borderline Personality Disorder (BPD) has been characterized by a great debate. Whatever the purported underlying psychological structures, the cluster of symptoms and behavior associated with borderline personality were becoming more widely recognized (Clarkin, et al. 2007), and included striking fluctuations from periods of confidence to times of absolute despair, markedly unstable self-image, rapid changes in mood, with fears of abandonment and rejection, and a strong tendency towards suicidal thinking and self-harm (APA, 2000). Although BPD is a condition that is thought to occur globally (Gunderson, et al. 2011), there has been little epidemiological research into the disorder outside the western world.

In primary care, the prevalence of Borderline Personality Disorder ranges from 4 to 6% of primary attenders (Lenzenweger, et al. 2007). Compared with those without personality disorder, people with BPD are more likely to visit their GP frequently and to report psychosocial impairment (Grant, et al., 2008). In spite of this, BPD appears to be under-recognized by general psychiatrist (Paris, 2010). In mental healthcare settings, the prevalence of all personality disorder subtypes is high, with many studies reporting 30-60 % of BPD between patients

diagnosed with personality disorders (Torgersen, 2009). Borderline personality disorder is generally the most prevalent category of personality disorder in mental healthcare settings. In community samples the prevalence of the disorder is roughly equal male to female, whereas in clinical services there is a clear preponderance of women, who are more likely to seek treatment. It follows that the majority of people diagnosed with personality disorder, most of whom will have borderline personality disorder, will be women (Banzhaf, et al, 2012).

Historically, BPD has been viewed as a disorder, which is notoriously difficult to treat, evidenced by high levels of patient drop-out during therapeutic interventions, high number of comorbidity with other personality disorders, severe symptom disorders (depression, PTSD and anxiety disorders), alcohol / drug abuse and behavioral disorders (eating disorders, self-destructive behavior) (Barnicot, 2011), often showing chronic self-harming behaviors (Linehan, et al. 1991; Oumaya, et al. 2008), and present a lifetime risk of suicide estimated to be up to 10% (Jørgensen, 2009).

1.2 Diagnostic criteria of BPD

The course of borderline personality disorder is very variable. Most people show symptoms in late adolescence or early adult life, although some may not come to the attention of psychiatric services until much later (Zanarini, et al., 2003). Diagnosis itself represent a problem (Clarkin, et al, 2007) due to its definition and because it's not always diagnosed accurately or separated from primary mood disorders (Paris, 2013). Diagnostic criteria of BPD is described in axis II of DSM-IV-TR (APA, 2000), that state that at least five criteria on the nine is necessary to make a diagnosis, so that there are more than 200 combination to get a diagnosis and at the same time it is possible for two people to satisfy the criteria and yet have very different personalities (see fig. 1 in Appendix for DSM-IV diagnostic criteria). Since its introduction in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (APA, 1980), the hypothesis of a possible overlap between BPD and mood disorders, in particular

bipolar disorder (Gunderson & Phillips, 1991), has been highly controversial. Furthermore there's still nowadays a great problem of overlap between criteria belonging to different personality disorder, in fact patients meeting criteria for a specific personality disorder frequently also meet criteria for other personality disorder. This heterogeneity and the clinical features described above make it also difficult to be investigated. Diagnosis and etiology remain still nowadays a central theme of investigation with repercussions also on treatment research, in fact to manage these patients effectively, one first has to recognize the disorder (Paris, 2013), that results still underdiagnosed. The new version of DSM-5 (APA, 2013), published in may 2013, suggests an alternative model for personality disorder. This new approach, located in section III as alternative and not substitute to preserve continuity with current clinical practice, consider personality disorder characterized by impairments in personality functioning and pathological personality traits. Each disorder is defined by a specific pattern of impairments and traits (see the diagnostic criteria for BPD in Appendix, Fig. 2).

In the categorical approach, mostly used, the diagnosis is based on symptoms that have been present since adolescence or early adulthood and appear in multiple contexts (APA, 2013), and there are no laboratory or imaging tests that can help with the diagnosis (Paris J, 2008). A number of structured and semi-structured interviews can assist in making the diagnosis and the most frequently used is the SCID II (First, et al., 1996), based on DSM-IV (APA, 2000) criteria. When interviewing patients, four domains of symptoms must be explored: affectivity, impulse control, interpersonal functioning and cognitive domain, that can help to distinguish BPD from other disorder.

1. Three criteria refers to the "affectivity domain" and they are the presence of "affective instability due to a marked reactivity of mood ... that lasts hours to rarely more than a few days"; "inappropriate and intense anger" and "a chronic feeling of emptiness" (APA, 2000). These frequent mood changes may appear to overlap with bipolar disorder, but there are several clear distinctions. First, the duration of the fluctuations is shorter than in bipolar disorder.

The second difference is the persistence of affective instability throughout life, rather than during a discrete mood episode. The third difference is reactivity of mood. The mood symptoms of patients with BPD are triggered by external events and are particularly sensitive to perceived rejection, failure and abandonment (Zanarini, at al, 2008). Mood usually shifts between depression and anger, and euphoria is transient. Shifts between depression and euphoria are more frequently seen in bipolar disorder (Henry C, et, 2001). Moreover several study suggest that negative emotions, such as anger, may persist for longer and be more intense in patients with the disorder than in healthy controls (Lobbestael&McNally, 2015).

2. The impulsive symptoms of borderline personality disorder may be more recognizable to clinicians, but they can still pose diagnostic challenges. This domain encompass self-harm and suicidality, but also many other behaviors, including gambling, spending, binge eating, sexual promiscuity and substance abuse, that are associated with an increased risk of completed suicide (McGirr, et al, 2007).

3. A pattern of unstable relationships, marked by extremes of idealization and devaluation and "to make frantic efforts to avoid abandonment" are characteristic of the interpersonal domain and they are two of the most important symptoms in making an accurate diagnosis of BPD, with studies reporting high level of sensitivity and peculiarity (Johansen, et al, 2004; Fossati, et. 1999). Identity disturbance is the other interpersonal symptom and it included a lack of consistently invested goals, values, ideals, and relationships; a tendency to make temporary hyper-investments in roles, value systems, world views, and relationships that ultimately break down and lead to a sense of emptiness and meaninglessness; gross inconsistencies in behavior over time and across situations that lead to a relatively accurate perception of the self as lacking coherence; difficulty integrating multiple representations of self at any given time; a lack of a coherent life narrative or sense of continuity over time (Westen&Cohen, 1993).

4. Finally the more common symptoms in “Cognitive domain” are depersonalization and dissociation, but also psychotic symptoms could be present and we can distinguish from schizophrenia because usually they are much more likely to be short, circumscribed, and either based in reality or totally fantastic (Zanarini & Frankenburg, 2007).

1.3 Models of the disorder

Beyond the diagnostic difficulties, the causes of BPD are complex and remain partly uncertain. No current model has been advanced that is able to integrate all of the available evidence. Different factors contribute to its development: genetics and constitutional vulnerabilities; neurophysiological and neurobiological dysfunctions of emotional regulation and stress (Linneahn, 1993); psychosocial histories of childhood maltreatment and abuse; and disorganization of aspects of the affiliative behavioral system, most particularly the attachment system (Morse et al, 2009). Summarizing contributions from different branches of research, individuals constitutionally vulnerable and/or exposed to influences that undermine the development of social cognitive capacities, such as neglect in early relationships, develop with an impaired ability both to represent and to modulate affect and effortful control attentional capacity. These factors, with or without further trauma, exemplified by severe neglect, abuse and other forms of maltreatment, may cause changes in the neural mechanisms of arousal and lead to structural and functional changes in the developing brain (O’Neill & Frodl, 2012). So the biological and psychosocial pathways to BPD are extremely complex (Fonagy&Bateman, 2008) and so far no model has been advanced that is able to integrate all the available data. Consideration has to be given to the role of genetics and constitutional vulnerabilities, neurophysiological dysfunctions of affect regulation and the stress response (Martin-Blanco, et al, 2015), evidence concerning the limbic system, executive control and frontal cortex dysfunction, psychosocial histories of childhood maltreatment and abuse (Reed et al, 2015) found in a significant proportion of cases, and the disorganization of aspects of the affiliative behavioral sys-

tem, most particularly the attachment system, found in almost all individuals with a diagnosis of BPD.

1.3.1 Mentalization, Metacognition and Emotion Dysregulation

An interesting model considering all these areas it's the model that focuses on the development of mentalization by Bateman&Fonagy (2004). The model suggests that disruption of the attachment relationship early in development in combination with later traumatic experiences in an attachment context interacts with neurobiological development. The combination leads to hyper-responsiveness of the attachment system which makes mentalizing, the capacity to make sense of ourselves and others in terms of mental states, unstable during emotional arousal. This unstable or reduced mentalizing capacity is the core feature of BPD in this model, and the emergence of earlier modes of psychological function at these times accounts for the symptoms of BPD (Fonagy&Bateman, 2008). Mentalization is the capacity to make sense of each other and ourselves, implicitly and explicitly, in terms of subjective states and mental processes. Understanding other people's behavior in terms of their likely thoughts, feelings, wishes, and desires is a major developmental achievement that, probably, biologically originates in the context of the attachment relationship. The capacity to understand self and others as being guided by aims and intentions is considered to be a key developmental achievement and the disruption of this is seen to be a major aspect in the psychopathology of BPD. The most important cause of such disruption is psychological trauma early or late in childhood which undermines the capacity to think about mental states or the ability to give narrative accounts of one's past relationships. Even the capacity to identify the mental states associated with specific facial expressions may be impaired. This reduced capacity for mentalizing may be speculatively attributed to one or more of at least four processes: (1) the vulnerable child's defensive inhibition of the capacity to think about others' thoughts and feelings in the face of the experience of the genuine malevolent intent of others; (2) early excessive stress which dis-

torts the functioning of arousal mechanisms, resulting in the inhibition of orbitofrontal cortical activity (arguably the location of one of the neural systems involved in mentalizing); (3) the fact that any trauma arouses the attachment system, leading to an intensified search for attachment security and a deactivation of reflective capacity. Where the attachment relationship is itself traumatizing such arousal is exacerbated because, in seeking proximity to the traumatizing attachment figure, the child may be further traumatized. Such prolonged activation of the attachment system may have specific inhibitory consequences for mentalization; (4) the child, in "identifying with the aggressor" as a way of gaining illusory control over the abuser may internalize the intent of the aggressor in an alien (dissociated) part of the self. While this might offer temporary relief, the destructive intent of the abuser will in this way come to be experienced from within rather than outside of the self, leading to unbearable self-hatred.

Brain abnormalities identified in borderline patients are consistent with the suggestion that a failure of representation of self-states is a key dysfunction in BPD. Some evidence suggests that the anterior cingulate cortex plays a key role in mentalizing the self (Frith & Frith, 2003) but also the prefrontal cortex, the mesial prefrontal cortex, the parieto-temporal junction, and the temporal poles constitute a network of areas that are invariably active when mentalizing activity is taking place (Gallagher & Frith, 2003). Moreover current evidence suggests that genes have both main effects (Torgersen, 2000; White, et al, 2003) and interactive effects with anomalous environmental influences (Caspi et al., 2002, 2003). Moreover the mentalization theory of BPD suggests that individuals either constitutionally vulnerable and/or exposed to influences that undermine the development of cognitive capacities necessary for mentalization such as neglect in early relationships (Battle et al., 2004) where the contingency between their emotional experience and the caregiver's mirroring is not congruent (Crandell et al, 2003), develop with an enfeebled ability both to represent affect and effortful control attentional capacity (Posner et al., 2002). Early trauma may also cause changes in the neural mech-

anisms of arousal leading to a relatively ready triggering of the arousal system underpinning posterior cortical activation in response to relatively mild emotional stimuli.

In the MBT model, it's not attribute a central role to trauma, but it's expected that in individuals made vulnerable by early inadequate mirroring and disorganized attachment to highly stressful psychosocial experiences in an attachment context, trauma will play a key role in shaping the pathology of BPD and will contribute to directly causing it by undermining the capacity for mentalization. The impact of trauma is most likely to be felt as part of a more general failure of consideration of the child's perspective through neglect, rejection, excessive control, unsupportive relationship, incoherence, and confusion. These can devastate the experiential world of the developing child and leave deep scars which are evident in their social-cognitive functioning and behavior (Fonagy&Bateman, 2008). This aspect of the MBT formulation therefore converges with that advanced by Marsha Linehan concerning the assumption of invalidating family environments and creatively developed further by Fruzzetti et al. (2005). According to Linehan (2006), BPD is primarily a disorder of emotion dysregulation and emerges from transactions between individuals with biological vulnerabilities and specific environmental influences. The dysfunction proposed by Linehan is one of broad dysregulation across all aspects of emotional responding. As a consequence, individuals with BPD have (a) heightened emotional sensitivity, (b) inability to regulate intense emotional responses, and (c) slow return to emotional baseline. Furthermore, from Linehan's perspective, the construct of emotion (and thus of emotion dyregulation) is very broad and includes emotion-linked cognitive process, biochemistry and physiology, facial and muscle reactions, action urges, and emotion-linked actions. Emotion dysregulation subsequently leads to dysfunctional response patterns during emotionally challenging events. Linehan suggested a number of possible biological substrates of emotional dysregulation (e.g., limbic dysfunction). However, the literature on the biology of psychological disorders was extremely limited when Linehan first articulated her theory.

In addition, Linehan proposed that the development of BPD occurs within an invalidating developmental context. This invalidating environment is characterized by intolerance toward the expression of private emotional experiences, in particular emotions that are not supported by observable events. Furthermore, although invalidating environments intermittently reinforce extreme expressions of emotion, they simultaneously communicate to the child that such emotional displays are unwarranted and that emotions should be coped with internally and without parental support. Consequently, the child does not learn how to understand, label, regulate, or tolerate emotional responses and instead learns to oscillate between emotional inhibition and extreme emotional lability. The child also fails to learn how to solve the problems contributing to these emotional reactions.

In Italy the "Terzo Centro di Terapia Cognitiva", located in Rome, has developed an another model that combines the cognitive approach with the concept of metacognition. This approach is called Metacognitive Interpersonal Therapy (MIT) and it's a cognitive behavior-based psychotherapeutic approach that works to increase metacognitive abilities and to improve interpersonal relationships (Dimaggio, Semerari, Carcione et al 2006; Dimaggio, Carcione, Salvatore, et al. 2010). Metacognition, as formulated by Semerari (Semerari, et al. 2003; Carcione, et al. 2008), refers to a broad set of cognitive and affective skills which allow people to identify mental states, reasoning about them, and ascribing them to themselves and others. These skills allow us to recognize the reason why a person reacts psychologically according to some regularities and constructs personal meaning over their lifespan (Semerari et al, 2012). Metacognition (Semerari et al., 2003) partially overlaps with similar constructs such as mentalization (Bateman & Fonagy, 2004; Allen, et al., 2008) and Theory of Mind (ToM) (Baron-Cohen, Leslie, Frith, 1985), but with some differences. Compared to ToM, metacognition usually includes more complex mental functions. Additionally, metacognition also refers to emotional understanding, while ToM mainly focuses on cognitive attribution (Semerari et al, 2012). Compared to the general definition of mentalization given by Bateman

and Fonagy (2004), Semerari's concept differs since it considers mind-reading to be a general ability created by different sub-functions that interact with each other and that can be selectively impaired (Semerari, et al. 2003). Dysfunctions in metacognition are associated with low social functioning, low quality of life, psychopathology and symptoms of several psychiatric and personality disorders seem to predict worst treatment response (Semerari et al., 2007; Lysaker, et al., 2010a, Lysaker, et al, 2010b; Carcione, et al., 2011; Lysaker, et al., 2011; Ogrodniczuk, et al., 2011). Moreover recently Semerari et al. (2012) showed that PDs presented a high correlation between metacognitive dysfunctions and the general severity of personality pathology. However, the data also show that when the severity of personalities' pathology was controlled, patients with different personality styles still present specific difficulties in metacognitive skills. In particular, the mindreading profile of BPD seems to be defined by two specific disabilities. Bateman and Fonagy (2004) suggested that these patients have problems distinguishing between internal mental representations and external reality, oscillating between a state where every representation is experienced as real and a state where the outside world seems imaginary and unreal. Clarkin et al. (1999) emphasized the BPD patient's inability to consider multiple and contradictory representations of himself/herself and of others. Consistently with these clinical observations, Semerari et al. (2005), using the Metacognitive Assessment Scale (MAS) to analyze therapy sessions of patients with BPD, found that the most impaired metacognitive sub-functions were the ability to differentiate between representation and reality (differentiation) and the ability to reflect on varied and contradictory mental representations to construct a unified and coherent narrative (integration). In a later study, Semerari et al. (2015) showed that patients with BPD typically presented an "instability" personality style, which correlated to a specific profile of metacognitive dysfunctions characterized by poor differentiation and poor integration. Therefore, poor differentiation and poor integration seem to be the "typically borderline" metacognitive profile. This indication was also supported by the logistic regression analysis in their study which confirmed that in-

tegration and differentiation, along with global severity, were the main features which predict and identify participants of the BPD group. This result is consistent with previous studies that highlighted the difficulty of patients with BPD to distinguish between mental representations and reality and to integrate contradictory internal representations (Semerari et al., 2005, 2014). These results are also consistent with several clinical observations (Bateman and Fonagy, 2004). Poor differentiation implies that the individual perceives his/her own representations not as subjective and hypothetical scenarios but as objective, unquestionable fact, concrete realities that call for direct action (Bateman and Fonagy, 2004). Borderline patients are impulsive and they have a tendency to act out; it is plausible that the specific metacognitive dysfunction in differentiation plays a role in generating their behavioral dyscontrol. Dysfunctional integration, on the other hand, means that the individual finds it difficult to reflect on the contradictions inherent in his own thoughts and feelings. A specific impairment of integration is consistent with the characteristic difficulties encountered by these pa- tients in forming a stable self-image and stable representations of interpersonal relations. Additionally, comparisons of other metacognitive sub-functions, such as monitoring and decentering, in the BPD and PD groups produced further interesting insights. Monitoring scores in the two groups were very similar in mean scores, both before and after controlling for general severity. This indicates that difficulty in recognizing thoughts and emotions, which constitute mental states, could not be considered a defining characteristic of borderline patients in particular, but rather of PDs in general. In contrast, when decentering was assessed, the borderline group performance emerged as weaker than that of the control group. This difference remained constant even after general severity was taken into account, although it became no longer statistically significant. This impairment in decentering in the BPD group is comparable to the lack of cognitive empathy observed in other studies (New et al., 2012; Hengartner et al., 2014). Cognitive empathy involves the ability to consider other people's mental states, while discounting one's own viewpoint and degree of personal involvement (perspective taking).

Nonetheless, New et al. (2012) highlighted that difficulties in cognitive empathy in BPD do not necessarily imply a similar difficulty in emotional empathy; borderline patients are, indeed, well able to understand other people's emotions quickly and intuitively.

In the last years literature has grown on this topic and focused on difficulties in emotion regulation, in addition to scarce mentalization/metacognitive abilities, as core features of BPD (Sharp, Pane, Ha, et al. 2011). Emotion dysregulation is the inability to flexibly respond to and manage emotions. Although this definition may appear straightforward, there is considerable variation in the phenomena studied under the heading of emotion dysregulation in BPD. Some researchers have focused on emotion sensitivity, others on affective intensity or affective lability, still others on emotional vulnerability, and so on (Carpenter & Trull, 2013). This is not surprising, given the complexity of the construct. One way to understand these disparate approaches is to view emotion dysregulation as a process, incorporating multiple interactive components, and not as an end-state (Werner & Gross, 2010).

Studies involving the use of magnetic resonance imaging or positron-emission tomography in patients with BPD have shown a hyperesponsive amygdala and impaired inhibition from the prefrontal cortex during tasks involving exposure to facial expressions, reactions to emotionally charged words, and interpersonal cooperation (King-Casas, Sharp, Lomax-Bream et al, 2008). There is evidence that neuro-hormones, such as oxytocin and opioids, mediate the exaggerated fears of rejection and abandonment that are characteristic of BPD (Stanley & Siever 2010). Emotion dysregulation (ED) has been conceptualized in different ways, however, alternative conceptualizations vary in the importance they attribute to the interpersonal context in which emotions are regulated. At one end of the spectrum is the view that interpersonal relationships and ED are closely and inevitably intertwined. The exemplar is attachment theory, which some proponents argue is "fundamentally about emotional experiences and their regulation" (Tidwell, et al., 1996). In this view, insecure attachment styles (especially preoccupied, unresolved, and disorganized variants) are likely to be associated with ED

(Levy, et al 2005). At the opposite pole is the view that negative emotionality or neuroticism shapes both subjective experience and expressive style and permeates both social and nonsocial contexts uniformly. In this view, a predisposition to intense, negative affect and limited capacity for executive control of such affect is fundamental to ED (Tidwell, et al, 1996). A third view, which also credits the reciprocal relationship between interpersonal functioning and ED, asserts that ED occurs in relation to the contrasting demands of different kinds of social interaction. We refer to difficulties regulating behavior and emotions in a way that is consistent with the expectations for different kinds of social interaction as domain disorganization (Morse, et al, 2009).

Beyond the ED is conceptualized, environmental influences also appear to be important in the pathogenesis of the disorder; insecure attachment, childhood neglect or trauma, and family psychiatric problems are recognized as risk markers, with the impossibility for the child to build a clear ideas of self and other. Ability of mentalization is in fact strictly connected with ED (Choi-Kain & Gunderson, 2008) and several evidence suggests that BPD patients experience core deficits in mentalizing (Bateman & Fonagy, 2004) or metacognition (Semerari, Carcione, Dimaggio et al 2007).

Metacognition is the general capacity to think about thinking (Semerari, et al., 2003); it involves a wide range of semi-independent faculties that allow an individual to manage complex mental states and to cope with interpersonal problems. A deficit in metacognition would limit someone’s ability to perform discrete tasks, such as recognizing what triggers one's emotions, taking a critical distance from one's ideas or forming a mature theory of the another person’s mental states (Semerari et al., 2012). Individuals with personality disorders (PD) have difficulty modulating their mental states and cope with interpersonal problems according to a mentalistic formulation of the problem (Carcione et al 2011). Patients with BPD show mentalization problems including deficits in monitoring and identifying emotions, inability to integrate different mental states, or failure to distinguish between one’s inner world and ex-

ternal reality; these dysfunctions, and emotion dysregulation can account for many of the clinical phenomena commonly observed in BPD (Fonagy, 2012; Semerari et al., 2005). Furthermore, poor metacognitive abilities have been directly linked with an inability to cope with problems that arise from living with others, and difficulty employing effective problem-solving strategies and adaptive behaviours (Carcione et al., 2011).

In conclusion, although growing evidence in the field of BPD, the conceptualization of the disorder remains very complex and a comprehensive model has not yet been formulated; consequently also treatments result controversial.

Chapter 2: Treatment for BPD

2.1 Pharmacologic and not-pharmacologic treatment

As reported in APA guidelines (APA, 2001), NICE guidelines (2009) and in the systematic review of the Cochrane collaboration (Stoffers, et al, 2010; Stoffers, et al 2012) core feature of BPD as the ones described in the introduction, and avoidance of abandonment, chronic feelings of emptiness, identity disturbance, and dissociation were not found to be affected significantly by any drug.

Drugs are useful to improve specific target symptoms but currently, there is no RCT evidence-based "gold standard" for the pharmacological treatment of BPD (Stoffens, et al, 2010).

Principles for choosing specific medications most used and recognized as guideline for the treatment are reported by the American Psychiatry Association (APA, 2001) and include the following:

_ Treatment is symptom specific, directed at particular behavioral dimensions.

_ Affective dysregulation and impulsivity/aggression are risk factors for suicidal behavior, self-injury, and are given high priority in selecting pharmacological agents.

_ Medication targets both acute symptoms (e.g., anger treated with dopamine-blocking agents) and chronic vulnerabilities (e.g., temperamental impulsivity treated with serotonergic agents).

Symptoms to be targeted are divided in three groups: Affective dysregulation symptoms, Impulsive behavioral symptoms and Cognitive-perceptual symptoms and each of this has specific recommendation (see Fig. 6.3, 6.4, 6.5 in Appendix).

Otherwise in the last decade, psychotherapy has been identified as the treatment of first choice for patients with BPD (Zanarini, 2009), although the mechanism of change remains partly unknown (Fonagy & Bateman, 2006).

2.2 Psychotherapy for BPD

Controlled trials provide support for the effectiveness of various forms of psychotherapeutic treatments, such as Dialectical Behavior Therapy (DBT; Linehan et al., 2006), Schema-Focused Therapy (SFT; Giesen-Bloo et al., 2006), Transference-Focused Psychotherapy (TFP; Clarkin, et al, 2007), Systems Training for Emotional Predictability and Problem Solving (STEPPS; Blum et al., 2008), and Cognitive Behavior Therapy (CBT; Davidson et al., 2006). However, no single treatment model has been established as the primary treatment of choice and few study has been conducted outside the sites of the development of the respective BPD treatment model, consequently, replication by independent groups is urgently required (Jorgensen, et al., 2012). To date, only eight randomized outcome studies have been conducted outside the sites of the development of the respective BPD treatment models. Koons et al. (Koons et al., 2001) and Verheul et al. (Verheul, et al., 2003.) compared DBT (6 and 12 months respectively) with treatment as usual. Carter et al. (Carter et al. 2010) compared 6 months DBT with TAU and waiting list. All three studies found that DBT was superior to TAU on some but not all outcome measures. McMain et al. (2009) compared 1-year DBT with a manualized version of general psychiatric management as described in the APA practice guidelines for BPD treatment (Oldham et al., 2001). They found no significant differences between the two groups. Similarly, Feigenbaum et al. (2012) found practically no significant differences in outcome between 1 year of DBT and TAU. In a comparison of the effectiveness of 3 years of TFP and SFT, Giesen-Bloo et al. (2006) found that significantly more patients in SFT recovered or showed reliable clinical improvement on a BPD severity index compared with patients in TFP. However, this study has been criticized for insufficient

integrity checks (indicating inadequate therapist adherence) of the delivered TFP treatment (Yeomans F, 2007). Pribe et al. (2012) studied the effectiveness of DBT in a randomized controlled design. Finally, in a comparison of 1-year TFP with psychotherapy in the community, (Doering, et al., 2010) it was found that TFP was superior on selected outcome measures like BPD symptomatology, psychosocial functioning and personality organization.

Overall, the results indicate that intensive therapeutic interventions are more effective than treatment as usual for patients with BPD (Carter, et al, 2010); however, the question of whether any one therapeutic intervention model provides greater clinical advantage to BPD patients than the other intervention models remains unclear.

2.3 Mentalization Based Treatment and Metacognitive Iinterpersonal Treatment

As mentioned before, In Italy the "Terzo Centro di Terapia Cognitiva", located in Rome, has developed an original model that combines the cognitive approach with the concept of metacognition. This approach is called Metacognitive Interpersonal Therapy (MIT) and it's a cognitive behavior-based psychotherapeutic approach that works to increase metacognitive abilities and to improve interpersonal relationships (Dimaggio, et al 2006; Dimaggio, et al. 2010). Metacognition, as formulated by Semerari (Semerari, et al. 2003; Carcione, et al. 2008), refers to abroad set of cognitive and affective skills which allow people to identify mental states, reasoning about them, and ascribing them to themselves and others. These skills allow us to recognize the reason why a person reacts psychologically according to some regularities and constructs personal meaning over their lifespan (Semerari et al, 2012).

Although the differences of theorizing the construct of mentalization/metacognition the aim of the MIT is similar to the MBT one, that is to improve these functions through the therapeutic relationship. The aim of Metacognitive Interpersonal Therapy (MIT) should be to interrupt the circuits arising between metacognitive malfunctioning, problematic states of mind and interpersonal cycles (Dimaggio, et al, 2007). In particular, to improve life quality requires pa-

tients to create new narrative scenarios with which to master wider areas of their relational lives (Livesly, 2012) and improve their metacognitive skills (Semerari, et al. 2003), so as to have a greater choice of possible future and acquire new tools for understanding their preference and desires creating and maintaining intimacy and a sense of belonging to groups, steering the carrying out of tasks and correcting forecast (Dimaggio, et al, 2007).

In MIT's formulation of the disorder metacognitive problems, problematic states of mind and interpersonal cycles, and impoverished narratives give rise to pathogenic cycles; treatment should aim at interrupting them and stimulating the virtuous ones. Therapist should create conditions necessary for technical intervention, first of all regulating emotional atmosphere and favor condition in which metacognition skills could be improved through discussion about own inner states and the patient's ones. Working on the therapeutic relationship constitutes the main intervention tool with these patients, aimed to getting away from pathological interpersonal cycles, regulating emotional one and improving metacognition (Safran & Muran, 2000). Therapist should focus first on their inner states and try to pinpoint their own feelings and states of mind and then asked themselves what in their own experience is similar or complementary to their patients. Achieving good inner self-discipline interrupts a cycle, as it blocks antiterapeutic actions and transport therapists to an empathetic position. This operation occurs in a therapist's mind (Dimaggio, et al, 2007). Disrupting pathological cycles therapist could help patients to work on his inner states, improving consciousness and metacognitive skills.

In a similar way Mentalization Based Therapy (MBT, Bateman&Fonagy, 2004) aims to create a "good environment" to allow the patients to enhance mentalization. The therapist uses largely unconscious techniques to activate the attachment system, through: 1. the discussion of current attachment relationship, 2. the discussion of past attachment relationship and 3. the therapist's encouragement and regulation of the patient's attachment bond to him/her by the creation of an environment that promotes the patient's regulation affect. Starting with rela-

tionship that have relatively low levels of involvement and only gradually to focus the patient's thinking on relationship closer to the patient's core self, therapists promote self-reflection and metacognition functions (Bateman & Fonagy, 2006). Albeit implicit, mentalization/metacognition is basis of different psychotherapeutic approach for Borderline Personality Disorder, the choice to focus on and compare just MIT and MBT rise from the fact that these two approach have as their primary and explicit outcome precisely the improvement of these functions. To our knowledge no study has been conducted on a direct comparison of different approach with the same primary outcome on metacognition functions. This feature represents the originality of this project.

PART 2. EXPERIMENTAL PART

Chapter 3:
STUDY 1: CROSS-SECTIONAL STUDY

3.1 Introduction to the cross-sectional study and aims

As mentioned before, the conceptualization of BPD remains very complex and a comprehensive model has not yet been formulated. In the last years literature has grown on this topic and focused on difficulties in emotion regulation (ED) and scarce mentalization abilities as core features of BPD (Sharp, Pane, Ha, et al. 2011), but the relationship between these variables and with the other clinical features remains unclear.

Emotion dysregulation plays a central role in the etiology and development of BPD (Werner et al, 2010), giving rise to affective instability (defined as marked intensity, reactivity, and variability of moods) as well as other symptoms of the disorder such as identity disturbance, interpersonal dysfunction, and self-harm (Carlson et al, 2009). On the other hand to regulate effectively our own emotions, we must first recognize them with mentalization abilities (Fonagy&Bateman, 2006). Similarly, to be able to build a coherent self-image and a stable view of the people we relate to, we have to form realistic representations of the emotions, ideas, aims, values, and intentions which underpin behavior and shape our own mental states and those of others (Semerari et al, 2015) These skills are called metacognitive abilities. So, difficulties in emotion regulation (ED) and scarce mentalization/mentalization abilities are linked, but the relationship between them and in which way they influence the other clinical variables remains still unclear. Few studies assessed all these variables at the same time and there's no agreement on the relationship between them.

For these reasons in this cross-sectional study we collected data in order to examine the relationships between Metacognitive Functions and Emotion Dysregulation (ED) and other clini-

cal features as Alexithymia, Impulsiveness, Mood and the General level psychopathology in a BPD sample.

3.2 Methods

3.2.1 Study population

BPD patients were recruited in 3 different psychiatric clinic: the hospital IRCCS San Giovanni di Dio, located in Brescia, the Mental Health Service of Savona and the CIRDIP, located in Pavia. The first one is a clinical and research center dedicated to the Mental Health, the second one is a community mental health service and the last one is an outpatient service, specialized in Personality Disorder treatment.

Inclusion criteria were:

_ Meet DSM-IV-TR (APA, 2000) criteria for BPD (see Fig. 6.1 of the appendix);

_ Age at baseline between 18 and 45 years;

_ Able to provide informed consent.

Exclusion criteria:

_ Lifetime diagnosis of schizophrenia, schizoaffective disorder, major depressive disorder with psychotic symptoms, organic mental syndromes;

_ Active substance abuse or dependence during the 3 months prior to entry into the study;

_ Ongoing psychotherapy,

_ Cognitive impairment or dementia (Mini Mental State Exam score <26) or relevant neurological signs.

3.2.2 Cross-sectional Study Protocol

Patients with a possible diagnosis of BPD and meeting the inclusion criteria were evaluated. Structured Clinical Interview for DSM disorder (I and II) (First et al., 1994; 1995) was administered to confirm the diagnoses of BPD and evaluate comorbidity. After this screening phase patients who accepted to participate to the study was included. Socio-demographical and clinical information were collected by a specific form, investigating history of the disorder, substance abuse/dependency history, trauma, suicide attempts, self-harm, aggressions and previous treatments, both pharmacologic and non-pharmacologic (see fig. 6.7 in Appendix).

Clinical evaluation included the primary outcomes measures on Metacognition Functions and secondary outcomes measures on the other clinical variables.

3.2.3 Outcome Measure on Metacognition:

Total scores on MAI (Semerari, et al., 2008) were collected as the primary outcome measure after the inclusion in the study. MAI were administered by an independent assessor, trained directly by MAI's authors on administration and scoring of the interview.

The MAI refers to the description of emotions and cognitions, and assesses how people are able to identify their own and others' recurrent patterns of thinking, feeling and dealing with social problems (see Fig. 6.6 in Appendix) . The interview evaluates two main functional skill domains of metacognition, 'the Self' and 'the Other', each one composed of two dimensions: Monitoring and Integration for the Self, Differentiation and Decentering for the Other. To identify the 16 basic facets of which the dimensions are composed (four facets for each dimension) the authors took into account the clinical literature that describes deficits in the ability to know and regulate mental states, theoretically based on the literature on mentalization and attachment theories (Fonagy&Moran 1991; Fonagy&Target, 2006; Allen et al., 2008), theory of mind (Baron-Cohen et al., 1985; Premack&Woodruff, 1978), metacognition

(Wellman, 1990; Wells, 2000) and, more generally, metarepresentation (Frith, 1992; Sperber, 2000).

The Self domain comprises the 'monitoring' and 'integrating' dimensions and describes the way in which a person has explicit access to his own mental states (cognitive and emotional) in relation to behavior.

1. 'Monitoring' (MON) is referred to the ability to distinguish, recognize and define one's own inner states (emotions and cognitions) and following behaviors during the 'here and now' of the described real-life episode.

MON is composed of four facets:

(a) the ability to recognize one's own representations (thoughts and beliefs);

(b) the ability to recognize and verbalize one's own emotions;

(c) the ability to establish relations among the separate components of a mental state; and

(d) the ability to establish relations between the components of mental states and behavior.

MON evaluates how a subject explains his/her own behavior in terms of causes and/or motivations. If there is a deficit, he/she is unable to discern the reasons for his/ her behavior, and he/she cannot recognize or verbalize emotions or other mental states. Examples of questions stimulating MON are 'What do you feel?', 'What do you think?' and 'What was your aim?'.

2. 'Integrating' (INT) is the second dimension of Self domain and involves the ability to produce coherent descriptions of people's mental processes and states over time. INT refers to the ability to reflect on mental states and contents, putting them in a logical order and ranking them by relevance. Using INT abilities the subject is able to understand the link between his/her own mental states and different behaviors in different situations, decoding his/her mental, functional and dysfunctional habits and forming a consistent account of how his/her mental life has changed over his/her lifespan.

INT includes four skills:

(a) the ability to describe understandable and coherent links among thoughts, events, actions and behaviors;

(b) the ability to describe transitions among different mental states and explain the reasons why;

(c) the ability to form generalized representations of his/her mental functioning, taking into account continuity over time of patterns of thinking and feeling;

(d) the ability to reconstruct and describe to the interviewer one's own mental functioning, providing enough information, without giving irrelevant and out-of-focus details, and giving a sense of order and coherence to the discourse. Examples of questions stimulating INT are 'So, you have found yourself reacting by [the interviewer refers to the described behavior], and feelings [the interviewer refers to the mentioned emotion]. Does feeling/thinking and behaving like this happen frequently to you?' 'You might also react in a different way, with different emotions or thoughts, in circumstances like the one described. Can you remember a specific episode?'

Other metacognition domain comprises the 'differentiating' and the 'decentering' dimensions.

3. 'Differentiating' (DIF) concerns the ability to recognize the representational nature of one's own and other individuals' thoughts, the ability to differentiate between classes of representations, such as imagination, evaluation and expectation, and to distinguish between representation and reality. Using DIF abilities, the interviewee is able to consider his/her own opinion as a hypothesis and not as a matter of fact; DIF abilities allow one to consider representations as mental phenomena, separate from but related to reality. Good DIF functioning makes people flexible in formulating opinions and points of view, and causes mental states to change depending on the communicative acts and on the availability of salient information.

DIF comprises four skills:

(a) the ability to consider one's own representation of the world as subjective and questionable;

(b) the ability to give plausible interpretations of events;

(c) the ability to reflect on and evaluate events (as opposed to a tendency to act impulsively);

(d) the ability to distinguish between different modes of thoughts such as dreaming, fantasizing and imagining. Examples of questions stimulating DIF are ‘You said you have though that [the interview refers to the reported episode]. In that moment, how did you subjectively believe it and how did you consider other options?’ ‘Did you take into consideration alternative interpretations of the events?’ ‘During the episode how much did you feel confused or clear-headed?’ Have you ever experienced such levels of confusion, or not been able to remember whether something really happened, or felt dreamy, unreal, like brain fog?’.

4. ‘Decentering’ (DEC) refers to the ability to infer others’ mental states in a plausible manner and adopt their perspective, recognizing that it is distinct from our own. DEC leads to the realization that other people’s behaviors are understandable on the basis of their own aims, beliefs, values and principles, which could be different from ours and independent of the relationship a person has with the subject. It involves the ability to describe others’ psychology in a plausible, clear way, without using stereotypes or cliché. DEC also includes the ability to realize that basically we are not the center of others’ intentions and goals.

DEC comprises four skills:

(a) the ability to recognize, define and verbalize other people’s emotional inner state;

(b) the ability to recognize, define and verbalize other people’s cognitive inner state;

(c) the ability to establish relations among the separate components of others’ mental state; and

(d) the ability to establish relations between the components of others’ mental state and their behavior.

Examples of questions stimulating DEC are ‘How did you think the other person would react emotionally during the episode?’ ‘What did you think he/she thought?’ ‘Why did you think he/she thought that?’ and ‘What reasons did he/ she have?’.

The MAI begins with the description of an autobiographical episode about the worst psychological situation that he/she has experienced in the last six months. In order to evaluate the comprehension of others' mental state, the episode has to include interaction with another person. MAI is focused on the worst episode of the last six months in order to be able to evaluate metacognitive function in critical circumstances with the prospect of applying it to clinical populations. The MAI continues with four modules, each specific to the evaluation of one metacognitive dimension as described before. For each dimension of the metacognitive construct, the interviewer has to ask a structured list of questions; the duration of MAI depends on the richness and how detailed the episode is been reported by the patient (Semerari et al., 2008). For each skill of each ability the score is measured on a likert scale from 1 to 5 (See Fig. 6.6 in Appendix)

In particular authors provide these guidelines to assess the scoring:

1. Insufficient ability. The subject can't use the ability spontaneously, even with the help of the interviewer. The ability is rarely present during the interview, the description of the mental state is always unclear. Helps from the interviewers never help the subject to use correctly the ability.

2. Partial ability. The ability is never used spontaneously, but the subject sometimes can use the ability partially with the help of the interviewer. The description of internal states is superficial and never spontaneous, but with the helps of the interviewer there is some sporadic improvement in the use of the ability, only in some specific question of the interview.

3. Moderate ability. Occasionally the subject can use the ability spontaneously and correctly, but it happens rarely, despite of the helps from interviewer. Mental states is clearly descripted, even if the descriptions are simple and not well-structured. Sometimes during the interview the subject try to use spontaneously the ability, but his ability still depends on the interviewer's support.

4. Good ability. Often the subject uses spontaneously the ability, but rarely he still needs some support from the interviewer. Mental states are clearly descripted. The subject can use the specific metacognition ability, but sometimes he would fail without the interviewer's helps.

5***. Excellent ability: The subject succeeds in using the ability spontaneously and constantly, without any help.*** During the interview the subject can describe mental state, without fall in the use of the ability. The subject is able to refer to his mental state in a detailed and comprehensive way. The answers to the questions of the interview tend to go beyond the questions.

The MAI provided good inter-rater reliability, factorial validity and internal consistency (Semerari, et al, 2012).

3.2.4 Other Clinical Outcome Measures:

Patients were also assessed on the following clinical features:

- **Emotional dysregulation:** it' s a key feature of patients with borderline personality disorder (BPD; Gratz et al., 2006). Compared with healthy subjects, patients with BPD report more affective instability, increased affect intensity and reactivity, and a rather negative affectivity (Rosenthal et al., 2008). Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004) is the most used self-report questionnaire designed to assess emotion dysregulation and it's based on 36-items. The measure yields a total score as well as scores on six scales: non-acceptance of emotional responses, difficulties engaging in goal directed behaviour, impulse control difficulties, lack of emotional awareness, limited access to emotion regulation strategies, and lack of emotional clarity. Emotion regulation is conceptualize as involving: a) awareness and understanding of emotions, b) acceptance of emotions, c) ability to control impulsive behaviors and behave in accordance with desired goals, d) ability to use appropriate emotion regulation strategies flexibly to modulate emotional responses in order to meet indi-

vidual goals and situational demands. The scale has high internal consistency, good test–retest reliability, and adequate construct and predictive validity. (Gratz&Roemer, 2004).

- **Alexithymia** it's a multifaceted personality construct defined as (a) a difficulty in identifying feelings (DIF), (b) a difficulty in describing feelings (DDF), and (c) externally oriented thinking (EOT). Studies have reported an association between alexithymia and primitive and immature ego defense styles, which implies a relatively primitive way of dealing with emotional problems (Parker, 1998). Manifestation of alexithymic features might be a transitory reaction evoked by stressful situations and accompanying depression and anxiety, which is called secondary alexithymia (Parker et al, 1991). The relationship between alexithymia and BPD suggests that difficulty identifying, differentiating, understanding, and communicating emotions and feelings impairs the ability to regulate their emotions in these patients (Webb&McMuran, 2008). In other studies alexithymia is described as another strategy that has been put forward as a coping mechanism to alleviate painful emotions (Elzinga BM, et al, 2002) and so can be linked to difficulties in emotion regulation. The Toronto Alexithymia Scale (TAS-20, Bagby, et al, 1994) is the most used self-report scale to assess this concept and comprised of 20 items. Each item is rated on a five-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree); five items are negatively keyed. The first factor (F1) in the three-factor model consists of seven items assessing the ability to identify feelings and to distinguish them from the somatic sensations that accompany emotional arousal. Factor 2 (F2) consists of five items assessing the ability to describe feelings to other people and Factor 3 (F3) consists of eight items assessing externally oriented thinking. In this study we used the total score to classify persons as having alexithimya (score>61), possibile Alexithymia (score between 52 and 60) and no alexithymia (score<51). Authors reported good factorial validity, concurrent validity and reliability for TAS (Bagby, et al., 1994).

- **Impulsiveness:** it has been defined as a tendency for rapid and unplanned behaviors (Critchfield, Levy, & Clarkin, 2004) and a tendency to act on urges without regard for the possible

consequences (Hochhausen, N. M., Lorenz, A. R., & Newman, 2002). These definitions point to the role of behavioral disinhibition in facilitating impulsive behaviors in BPD, and this has received empirical support (Rentrop et al., 2008). Impulsive behaviors in BPD have also been conceptualized as attempts to manage negative emotions (Brown, Comtois, & Linehan, 2002; Trull et al., 2000). In this way, impulsive behaviors are chosen to provide immediate distraction or relief from intense negative affects and it could be linked with the other clinical features of BPD. Barratt Impulsiveness Scale (BIS; Patton, et al, 1995) is a questionnaire designed to assess the personality/behavioral construct of impulsiveness. The BIS-11 identifies three factors that express three different constructs of impulsivity: Motor impulsiveness, Impulsivity without planning and Cognitive impulsivity. These scales have shown a good reliability and validity with other measures of the same dimension and the total score of the BIS-11 is an internally consistent measure of impulsiveness.

- **Depressive mood**: Depression and BPD frequently coexist (Zanarini et al., 1998) and research suggests that the presence of BPD in depression influences the course as well as treatment response in depression in negative ways (Stringer et al., 2013). Beck Depression Inventory (Beck, Steer, Garbin 1988) is a 21-question multiple-choice self-report inventory and it's one of the most widely used instruments for measuring the severity of depression. Each response is assigned a score ranging from zero to three, indicating the severity of the symptom, the sum of each item provides a total score that correspond to a depression severity level, from mild to severe.
- **Interpersonal Sensitivity**: Interpersonal instability has been recognized as an essential feature of BPD, as reported in the diagnostic criteria (APA; 2000). This kind of instability seems due to the a specific vulnerability in BPD patients, for which they are more sensitive in the interpersonal relationship (Linnehan, 1993). Their 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 ge-

neric 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 (Gunderson&Lyons-Ruth, 2008). The Inventory of Interpersonal Problems (Pilkonis, et al., 1996) it's a 57 items self-report, assessing different aspects of interpersonal features (interpersonal sensitivity, interpersonal ambivalence, aggression, need for social approval, and lack of sociability). Between this subscale the Interpersonal Sensitivity has been recognized as an essential feature of BPD (Trull, et al, 2001) that predispose subjects to over-react to other people's comment.

- **General psychopathology**: in order to obtain a general index of psychopathology the Symptoms Check-list 90 Revised (SCL-90, Derogatis, 1994) was used. It's a psychiatric self-report inventory assessing the psychological symptom status and it has been used in numerous studies as a brief indicator of mental health (Preston et al. 2002). The 90 items in the questionnaire are scored on a five-point Likert scale, indicating the rate of occurrence of the symptom during the time reference. It is intended to measure symptoms intensity on nine different subscales and on a global indices that provide a means of communicating an individual's pathology with a single number. This index is called Global Severity Index (GSI) and it' s suggested to be a good single indicator of the current level of the disorder (Derogatis 2000). The SCL-90 has been used as a central outcome measure in numerous clinical trials, both psychopharmacological trials as well as in psychotherapy trials (Pani et al. 2000) and showed good psychometric qualities (Derogatis, 1994).

3.2.5 Statistical analyses

Descriptive statistics (mean and standard deviation for continuous variables, frequency and percentage for categorical variables) were used to summarize demographics and clinical features of the study sample. Parametric and non-parametric tests (Chi-square and Kruskal Wallis test) were used to assess absence of differences in demographic and clinical variables among the three recruitment center. Rank correlation between scores of the primary and secondary outcomes was calculated with Spearman rho coefficients.

Finally, a path analysis via Structural Equation Model was performed for analyzing the interrelations between principal outcome (MAI total score) and other variables resulted associated/correlated with it. The main advantage of using SEM is the flexibility to model complex relationships between one or more independent (exogenous) variables (MAI score, TAS score) and one or more dependent (endogenous) variables (BIS score, BDI scores, IIP score and GSI score) simultaneously (Bollen, 2014). The goodness of fit of the model, to test if the hypothesized model is a plausible explanatory model for the empirical data, was checked by several measures (Hancock GR, et al 201): χ^2 test, relative χ^2 test (less than 2.5 indicate a good fit) and comparative fit index (CFI -close to 1 for good fit-), root mean square error of approximation (RMSEA –less than 0.05 indicate a good fit-) and Tucker–Lewis coefficient (TLI - higher than 0.9 indicate a good fit).

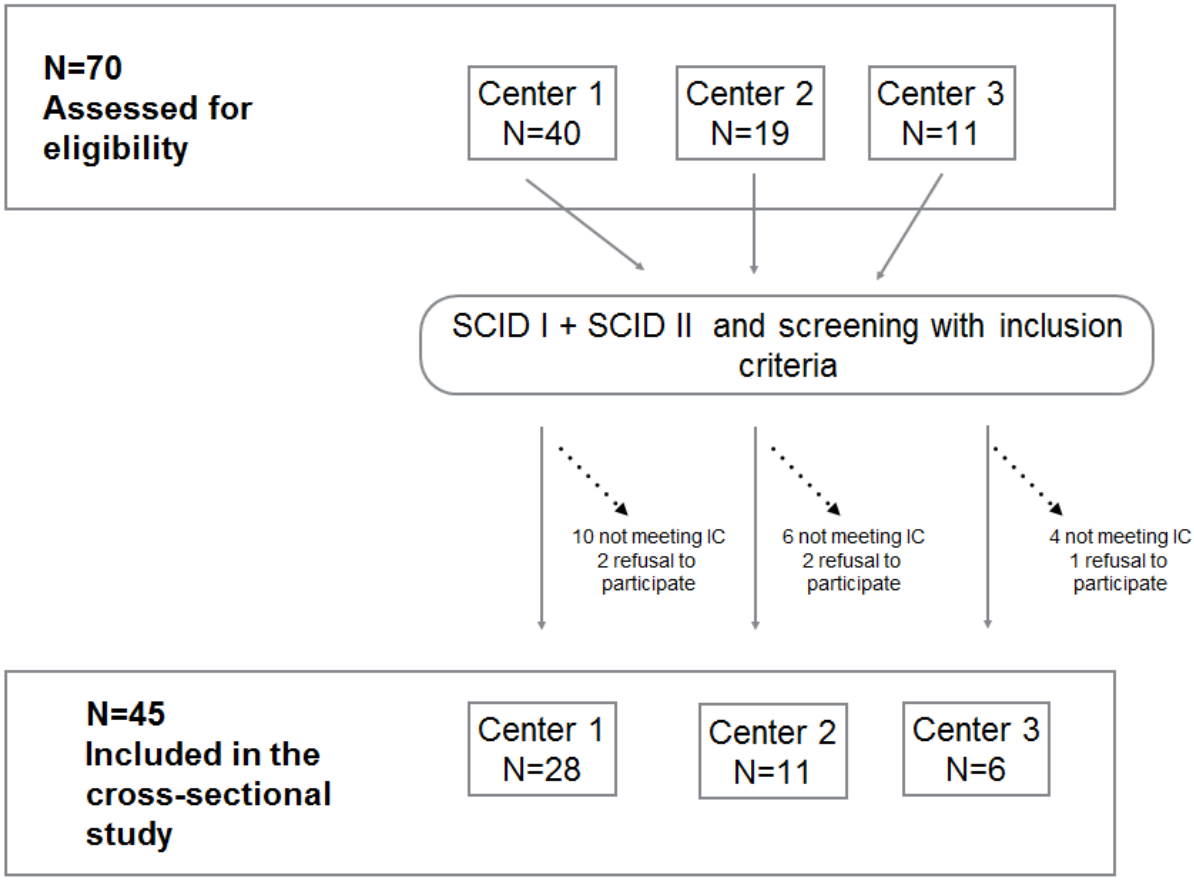
Missing data (less than 15%) of variables included in SEM were handled by stochastic regression imputation (Enders, 2010). Moreover, the presence of indirect mediator effect was evaluated by Sobe, Aroian and Goodman tests (Preacher&Hayes, 2004).

All statistical analysis were carried out by using SPSS 21.0; SEM was implemented by package AMOS 21.0. Statistical significance was set at $p<0.05$.

3.3 Cross-Sectional study results

Seventy patients were assessed for the inclusion and 45 met the inclusion criteria. Twenty-five patients were excluded from the study: n=20 for different principal diagnosis and n=5 patients refused to participate. In particular 12 in the Center 1, 8 in the Center 2 and 5 in the Center 3 were included (see Fig. 3.1).

Figure 3. 1: Flow diagram of the sample selection.



Socio-demographic and clinical characteristics of the patients recruited were similar among sites (p of Anova and Kruskal-Wallis test larger than 0.05 for all variables) (see Tab. 3.2).

Table 3.2 Comparison of socio-demographic and clinical characteristic of the three groups

	Center 1 N=28 Mean (DS)	**Center 2 N=11 Mean (DS)**	**Center 3 N=6 Mean (DS)**	**ANOVA F statistic #**	**p-value**
Age	34.5 (7.9)	27.6 (4.9)	36.9 (6.2)	3.163	0.053
Education (years)	11.3 (3.1)	12.5 (2.5)	10.5 (2.7)	1.001	0.376
Age at onset (years)	21.6 (7.9)	16.7 (3.6)	20.8 (7.6)	1.771	0.183
Duration of illness	12.3 (7.5)	10.0 (5.5)	13.2 (8.7)	0.478	0.624
Age at first contact with Psych Services	24.8 (7.9)	21.2 (5.9)	23.0 (11.4)	0.807	0.453
Number of DSM-IV BPD's criteria (mean)	6.5 (0.9)	7,0 (1.2)	6.7 (2.5)	0.663	0.521
	N (%)	**N (%)**	**N (%)**	**Chi Square test**	**p-value**
Sex (%F)	20 (71.4%)	8 (72.7%)	4 (66.7%)	4.012	0.135
Alcohol Abu-se/Addiction lifetime	15 (53.6%)	6 (60.0%)	4 (66.7%)	0.819	0.399
Substance Abu-se/Addiction lifetime	14 (50.0%)	5 (50.0%)	4 (66.7%)	0.329	0.848
Attenpted suicide	17 (60.7%)	4 (40.0%)	1 (16.7%)	4.352	0.113
Self-harm	9 (64.3%)	10 (62.5%)	7 (46.7%)	3.999	0.819
At least one relative with psych. disorder	25 (92.6%)	8 (80.0%)	3 (60.0%)	4.010	0.135

Considering the groups sample size, differences among groups were evaluated also with non-parametric Kruskal-Wallis test, obtaining consistent results with respect to ANOVA test.

Tables 3.3 shows comparisons on principal and secondary outcomes between the groups. All the variables, both the total and subscale scores, resulted not statistically different so we can consider all the subjects as a whole sample (p-value larger than 0.05 for all variables).

Table 3.3 Comparison of primary and secondary outcomes of the three groups

		Center 1 N=28 Mean (DS)	**Center 2 N=11 Mean (DS)**	**Center 3 N=6 Mean (DS)**	**F #**	**p-value**
MAI	Total Score	41.6 (5.5)	40.6 (8.2)	45.8 (6.1)	1.168	0.322
Sub-scale	Monitoring	10.9 (2.3)	11.0 (2.3)	12.0(1.7)	0.473	0.627
	Differentiation	10.3 (1.3)	9.8 (1.9)	11.0 (1.4)	1.071	0.353
	Integration	10.3 (1.4)	9.7 (2.4)	11.6 (0.9)	2.105	0.136
	Decentering	10.0 (1.4)	10.1 (2.0)	11.2 (2.4)	0.940	0.400
TAS	Total Score	52.9 (15.1)	51.7 (15.5)	55.5 (14.7)	0.078	0.925
DERS	Total Score	119.1 (19.1)	115.0 (23.0)	108.5 (36.6)	0.433	0.653
BIS	Total Score	76.7 (10.5)	78.8 (16.7)	72.8 (15.3)	0.472	0.628
SCL 90	GSI (Global Severity Index)	1.3 (0.7)	2.0 (0.6)	2.0 (0.8)	3.171	0.066
IIP	Interpersonal Sensitivity	2.0 (0.8)	1.8 (1.0)	1.8 (1.0)	0.205	0.816
BDI	Total Score	26.2 (11.6)	26.3 (13.4)	25.5 (14.1)	0.006	0.995

Considering the groups sample size, differences among groups were evaluated also with non-parametric Kruskal-Wallis test, obtaining consistent results with respect to ANOVA test.

3.3.1 Demographical and clinical characteristic of the sample

Demographical data of the whole sample (N=45) are shown in Tables 3.4 and 3.5. Mean age was 32 years and the mean age at onset was 20 years, so the mean duration of illness was around 12 years. The age at first contact was 24, so the gap between the beginning of symptoms and the first contact to psychiatric services was around 3 years.

Table 3.4 Socio-demographic and clinical characteristic of the sample

	Cross-Sectional Study's Sample N=45		
	Mean	**SD**	**Range**
Age	32.6	8.0	18-45
Education (years)	11.4	3.0	8-19
Age at onset (years)	20.4	7.2	10-44
Duration of illness (years)	11.8	7.1	1-30
Age at first contact with Psych Services	23.8	7.9	12-44
Number of DSM-IV BPD's criteria	6.6	1.1	5-9

The female in the sample was the majority and more than an half of the patients was unemployed (Table 3.5). The presence of SUD, Substance Use Disorder, was around 50%, and a similar percentage of the patients attempted suicide lifetime. Finally almost the 60% experienced self-harming behavior and the most common Axis I comorbidity was depression and anxiety disorders. Finally the 85% of the family of the patients had at last one familiar with psychiatric disorders.

Table 3.5 Socio-demographic and clinical characteristic of the sample

	N	**Percentage**
Sex (F)	32	71.1%
Occupation unemployed employed other (student/housewife)	 23 13 9	 52.3% 29.5% 18,2%
Alcohol Abuse/Addiction (lifetime)	25	55.6%
Substance Abuse/Addiction (lifetime)	23	51.1%
Attempted suicide (lifetime)	22	48.9%
Self-harm (lifetime)	26	57.8%
At least one relative with psych. disorder	39	85.7%
Axis I comorbidities (lifetime) Depression Anxiety Disorders	 22 17	 48.9% 37.8%

The metacognition functions (see Table 3.6), measured by Total score on MAI, corresponded to a moderate deficit in metacognition. The mean score in sub-scale “monitoring” was higher than in the other subscales, indicating a better ability to recognize emotions than to manage them. The medium level of this sub-scale correspond to “moderate ability”, while the other functions was in “partial ability” range. The medium score on DERS was 2DS over the mean score of the sample validation of the scale. The TAS Total score indicate the presence of “Alexithymia” in a quarter of the sample and “possible Alexithymia” in another quarter, referring to the cut-off given by author (Bagby, et al, 1994). The sample was characterized by a

high level of impulsivity, as indicate by BIS total score and the level of depression, measured by BDI mean score, revealed a score in the range of "moderate depression".

Table 3.6 Primary and secondary outcomes of the sample

		Cross-Sectional Study's Sample N=45		
		Mean	**SD**	**Range**
MAI	Total Score	41.8	6.4	32-54
Sub-scale	Monitoring	11.1	2.2	8-17
	Differentiation	10,2	1,5	7-13
	Integration	10.3	1.7	6-13
	Decentering	10.2	1.7	7-14
DERS	Total Score	117.2	21.7	73-154
BIS	Total Score	74.5	12,1	52-109
SCL 90	GSI (Global Severity Index)	2.1	0.7	0.5-3.3
IIP	Interpersonal Sensitivity	1.9	0.8	0-3
BDI	Total Score	26.1	11.8	0-50
TAS	Total Score	22 (48.9%) No Alexithymia 12 (26.7%) Possible Alexithymia 11 (24.4) Alexithymia		

3.3.2 Correlation between clinical variables

Correlations between the principal and secondary outcomes are shown in Table 3.7. MAI Total score showed a negative correlation only with TAS Total score. The major part of the secondary outcome measures resulted correlated. In particular DERS Total scores was associated with all the other measures and TAS score with all, except IIP Interpersonal Sensitivity score. GSI score didn't correlate to BIS and IIP scores.

Table 3.7 Correlation Matrix on primary and secondary outcomes. *=p<0.05; **=p<0.01

	TAS Total Score	**DERS Total Score**	**BIS Total Score**	**SCL-90 Global Severity Index**	**IIP Inter-personal Sensitiv-ity**	**BDI**
MAI Total Score	-.415* .031	-.291 .100	-.311 .083	-0.011 0.952	-.154 .393	-.113 .567
TAS Total Score	1	-.599** .002	.479** .009	0.460* 0.014	.262 .170	.414* .026
DERS Total Score		1	.613** .000	0.384* 0.027	.759** .000	.529** .003
BIS Total Score			1	0.284 0.109	.536** .001	.281 .133
SCL 90 Global Severity Index				1	.348* .044	.659** .000
IIP Interpersonal Sensitivity					1	.618** .000
BDI						1

3.3.3 Structural Equation Model

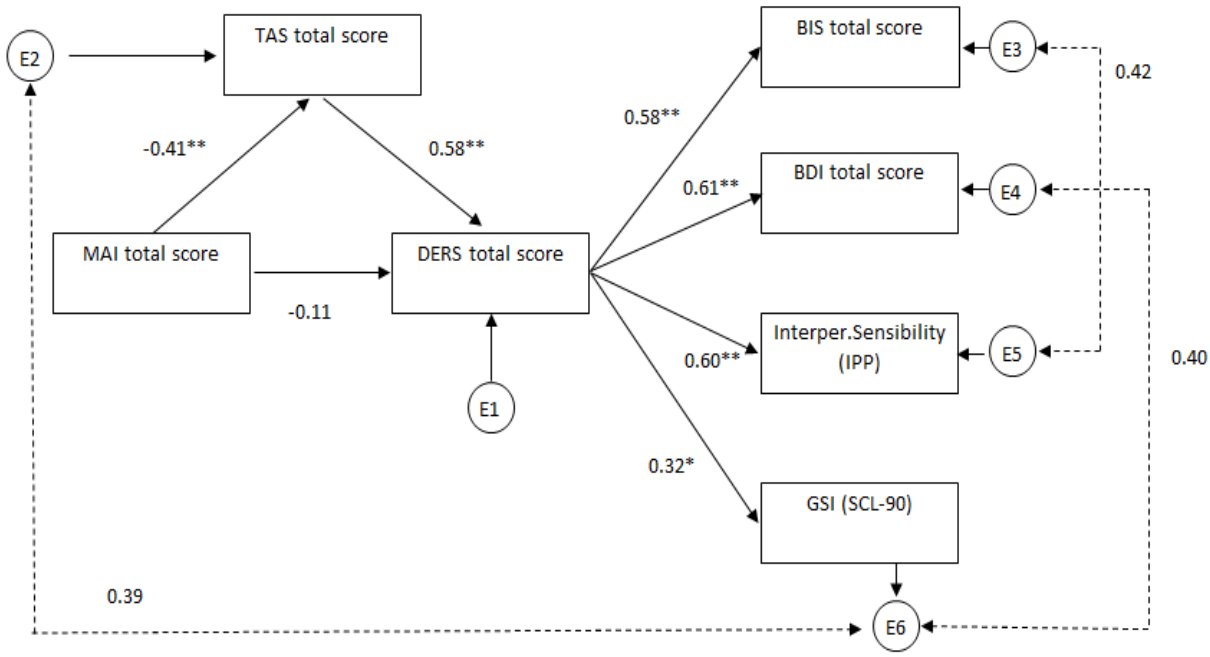
All variables significantly associated to the main outcome (MAI Total score) and DERS Total score were included in SEM. Although MAI Total score and DERS Total score weren't correlated directly, we tested the hypothesis to evaluate the indirect relation of TAS Total Score as a mediator of the relation between MAI and DERS. Finally, we evaluated the relationship between DERS, as predictor, and symptomatic scale, BIS, SCL-90, BDI and IIP.

The final model is displayed in Figure 3.8 in the next page. The number of estimated parameters was 35, including covariance parameters between exogenous variables for improving the model fit. Model fit indices showed a good fit of the model to the data (χ^2 = 18.82, df= 13, p=0.129, relative χ^2= 1.45, CFI= 0.95, TLI = 0.92, RSMEA= 0.1 [90%CI 0.000-0.147]).

TAS resulted a mediator between MAI total score and DERS score (Sobel, Aroian and Goodman p-values were 0.012,0.013,0.011 respectively)

Finally, DERS significantly predicted the clinical variables, BIS Total score (beta standardized regression coefficient= 0.58, p<0.001); BDI total score (beta=0.61, p<0.001); Interpersonal sensitivity score, a sub-scale of IIP (beta= 0.60, p<0.001); GSI, Global Severity Index of SCL-90 (beta=0.32, p=0.023).

Figure 3.8. Structural Equation Model: standardized estimates. In black dotted line the correlation (standardized covariance) parameters between variables are depicted. The number of different parameters to be estimated was 35, including covariance parameters for improving the model fit. **=p<.05, **=p<.001*



3.4 Discussion of the cross-sectional study

The present study shows that metacognition and emotion regulation deficits play a central role in the conceptualization on BPD. Since 1980, till some years ago, BPD was unequivocally reported as more common in women than men (APA, 2004), but a recent and well-executed study by Grant et al. (2011) found that BPD is equally prevalent among men and women. Nonetheless samples of BPD studies continues to show a disproportion between gender (Sansone&Sansone, 2011). The reasons of these bias could be found in the traditional settings for studies, i.e., psychiatric settings, that may not reflect the true gender distribution of BPD, in which women with BPD are more likely to be over-represented, instead of men with BPD that are more likely to be over-represented in substance-abuse treatment programs (Goodman, 2010). Probably for the same reason, also in our sample females were the majority, and the setting of recruiting could have influenced also the duration of the illness, that results similar to studies included in a metanalysis on this topic (Stoffers et al, 2012). In fact, symptoms of BPD usually begin in late adolescence (Chanen, et al., 2004; Miller, et al., 2007), even though treatment typically begins in early adulthood (Zanarini, et al., 2001) and often BPD patients present for evaluation or treatment with one or more comorbid axis I disorders. Initially, these symptomatic disorders may mask the underlying borderline psychopathology, impeding accurate diagnosis and making treatment planning difficult (Zanarini, 1998). In our sample the 50% of the sample had suffered of a Depressive Episode and 40% of an Anxiety Disorder lifetime, in line with the percentage reported by other studies in which Mood and Anxiety Disorders remains the most common lifetime Axis I comorbidity disorders in BPD (Zanarini et al., 1989, Marino&Zanarini, 2001, Zanarini et al., 2014). Even the alcohol or substance abuse/dependence resulted frequent in our sample, around 50%, as reported also in cross-sectional studies in which 23.8–66% of borderline patients report meeting crite-

ria for alcohol abuse or dependence and 19–87% report meeting criteria for drug abuse or dependence (McGlashan et al., 2000).

Beyond the comorbidities that get more difficult the treatment of the disorder, also the presence of attempted suicide and self-harm had contributed historically to earn the reputation to be one of the hardest psychiatric disorder to manage. In our sample the prevalence of the attempted suicide or self-harm is around 60% lifetime and usually this behavior is the dysfunctional way that patients found to manage negative emotions, as shown in cross-sectional studies reporting that self-mutilation help to gain relief from negative emotions (Hulbert&Thomas, 2010).

Factors pertaining to traumatic experiences throughout the lifespan are associated with self-mutilation over time (Zanarini et al., 2011), and also our sample reported violence, abuse or an invalidating family environments during childhood in the 70% of cases. A key role is in fact played by the family, cause it could represent both a genetic and environmental risk factor for the disorder with a heightened prevalence of psychiatric disorders in the first-degree relatives of borderline patients (Zanarini, et al., 2004), as reported in our sample too. Difficulties in familiar environmental, in adjunction to an individual vulnerability, could be considered also the principal obstacle to develop a secure attachment with parents and consequently to develop good mentalization abilities. Fonagy emphasized a developmental model, contextualizing the formation of mentalization in the setting of secure early attachment relationships (Fonagy, 1991). More specifically, the author argued that the primary caretaker's marked and contingent mirroring of a child's internal states within a secure attachment facilitates the child's development of a capacity to mentalize (Choi-Kain&Gunderson, 2008). Problematic family context, trauma, and even innate biological factors may cause a dysfunction and hypersensitivity in the stress-response system, leading to a cascade of hyperarousal, affective dysregulation, and inhibition of the orbitofrontal cortex, a brain region associated with mentalizing activity (Fonagy&Bateman, 2007). In this conceptualization BPD is formulated as a

syndrome organized around an unstable capacity for mentalization. Similarly, in Semerari et al. (2014) theory, metacognitive dysfunctions is characteristic of personality disorder and in particular BPD patients show lower score in two metacognitive area: differentiating and integration (Semerari et al, 2015), as reported in our sample too. Studies focused on "mind reading", that is the ability to recognize and name emotions (Gullestad et al., 2013; Mc Main et al, 2013) or, vice versa, on the ability to interpret other people's mental states by reading facial expressions, instead show contrasting results (Semerari, et al, 2015). Some studies on alexithymia, which is defined as the difficulty to recognize and label our own emotions (Bagby et al., 1994), show that this was a characteristic difficulty of patients with BPD (McMain et al., 2013), whereas in other studies alexithymia is observed in a sub-sample of patients, mostly suffering from avoidant, dependent, passive–aggressive and depressive PD, and less frequently in patients with BPD traits (Nicolò et al., 2011). In our sample the distribution of the total score on TAS is perfectly assailable to what found in this study, (Nicolò et al., 2011) and in particular an half of the sample didn't not show Alexithymia, while the other half of the sample is equally divided between a quarter in the range of "possible Alexithymia" and the other quarter over the cut off, indicating the presence of Alexithymia. The construct of Alexithymia, as mentioned before, is referred to the difficulty in recognizing and naming emotions, and partially overlap with the concept of Monitoring, measured by the first sub-score of MAI. In our sample Monitoring score is higher than the score on the other Metacognition sub-functions, according to the literature in which BPD patients showed less severe deficits on this skill (Semerari, et al, 2015). These results are also consistent with several clinical observations (Bateman and Fonagy, 2004). The impairments in other metacognitive sub-functions instead was linked to the BPD conceptualization itself. Difficulties of these patients to distinguish between reality and mental representation, called Differentiation in Semerari's model, resulted impaired in several previous studies, both in MIT field and MBT's one (Semerari et al., 2005, 2014; Bateman and Fonagy, 2006). Poor differentation implies that subjects per-

ceived their representation as objective, not an hypothetical scenario, but as concrete facts calling for reactions, and this could play a role in generating their behavioral dyscontrol. The other sub-function "typically impaired" in these patients is Integration that reflect their difficulties to integrate different emotions and thoughts and can contribute to their difficulties to form a stable self-imagine and a stable representation of other people (Semerari et al., 2015). Finally difficulties in Decentering could be comparable to the lack of cognitive empathy observed in other studies (New et al, 2012; Hengartner, et al, 2014).

In our sample the score on TAS (Toronto Alexithymia Scale) was associated with the metacognitive functions but also with the inability to regulate emotions, measured by DERS Total score, and in particular the score on TAS seemed to mediate between MAI and DERS scores. Alexithymia is a construct which includes different facets, namely difficulties identifying feelings and distinguishing them from somatic sensations; difficulties describing feelings to others; constricted imaginal processes; and a concrete, externally oriented style of thinking (Bagby et al., 1994). The construct of alexithymia has been linked to heightened levels of psychiatric symptoms (Parker et al., 2008), to poor regulation of impulses (Fossati et al., 2009) and interpersonal dysfunctions (Vanheule, et al, 2007), all typical signs of Personality Disorder. Therefore it could be hypothesized that alexithymia is a typical construct of many personality disorders (Nicolò et al, 2011), and it could be reflect a failure to adequately develop purely mental constructs to process and modulate emotions (Joyce et al., 2013). In our sample the TAS score was associated to DERS score, so we can suppose that the difficulties in emotion regulation is linked to the construct of alexithymia. Although there is no consensus on the definition, emotion dysregulation could be considered as a deficit in the ability to modulate the experience and expression of emotions and to maintain goal directed behavior in the presence of intense negative affect (Gratz et al., 2006). Many criteria for BPD in the DSM-IV reflect abnormalities in emotional functioning, and emotion dysregulation is hypothesized to play a central role in the etiology and development of BPD (Put-

nam&Silk, 2005; McLaughlin et al., 2011), giving rise to affective instability as well as other symptoms of the disorder such as identity disturbance, interpersonal dysfunction, and self-harm (Gleen&Klonsky 2009).

Moreover emotion dysregulation (ED) may sustain BPD symptoms and associated problematic behaviors, which is consistent with several studies illustrating a link between ED and behavior (Selby&Joiner, 2012). The transaction between an individual's innate biological disposition toward an emotional over-reaction and an invalidating environment leads to deficit in skill to regulate intense emotions (Adrian, et al., 2011). At the same time these deficits to cope with and modulate affect contribute to even more intense and variable affects, maintaining this features over time (Selby et al., 2009). In an interesting study by Steep et al. (2014) they showed that the overall level of emotion dysregulation difficulties mediate the association between BPD symptoms and BPD features at 1-year follow-up, demonstrating that ED was a maintance mechanism for BPD symptoms. In our study ED was associated to general symptomatology, measured by GSI (General Severity Index of SCL-90 scale, Derogatis, 1994), impulsivity (BIS score), level of depression (BDI score) and interpersonal sensitivity (IIP Interpersonal Sensitivity score). Studies on BPD suggest that ED exhibits a robust and unique relationship with symptomatology (Glenn et al., 2009), measured either by self-report or semistructured interview. The inability to regulate emotion when experiencing heightened emotional arousal, both negative and positive, lead to the tendency to act impulsively (Jacob et al., 2010), that may serve to reduce negative affect (Traggeser&Robinson, 2009). In addition emotion dysregulation and some dimensions of impulsivity are robustly related to BPD features (Fossati et al., 2014) and to their interpersonal problems (Werner, et al., 2010). Our findings support the idea that the inability to manage emotion is an important contributor to BPD, as reported by Carpenter and Trull (2013) and by other studies, even if these are only preliminary results that have to be examined more in depth and replicated in a larger sample.

3.5 Strengths and limitations

This study has both strengths and limitations. It's the first study using a SEM Model to link together Metacognition, Emotion Dysregulation and symptoms of BPD. The principal limitation of this study is due to the use of self-report to test psychopathology, and clinical rating only for assessing Metacognition functions. The other main limitation is due to the small sample size that can affect the generalization of our results. However these results can contribute to an area in which empirical findings are still scarce and inconsistent (Gulestad&Wilberg, 2011).

Chapter 4:
LONGITUDINAL STUDY

4.1 Introduction to the longitudinal study and aims

Most patients with BPD are treated with non-specialist standard psychiatric services, including inpatient treatment, partial hospitalization, and outpatient services as necessary (Bateman and Fonagy, 2006). However, specific psychological interventions have been developed and actually structured psychotherapy is the "gold standard" treatment for this disorder (Stoffers et al, 2012), because the dysfunctional characteristics of the disorder cannot change with pharmacotherapy. Efficacy studies demonstrated that different psychotherapy approaches improve specific target of the disorder and actually the supported psychosocial treatments for BPD are dialectical behavior therapy (DBT) (Linneahn, 1993), mentalization-based psychotherapy (MBT) (Bateman&Fonagy, 2006) transference-focused psychotherapy (TFP), schema-focused psychotherapy (SFT) (Clarkin et al, 2006), general psychiatric management (GPM) (Links et al., 2010), and systems training for emotional predictability and problem solving (STEPPS) (Young et al, 2003). All these therapies share non-specific therapeutic aspects, but they differ in other aspects that can improve specific features of the disorder, as demonstrated by their specific RCT outcomes. On these premises, it could be speculated that in the future treatments may be tailored to specific clinical constellations presented by BPD patients (Gabbard, 2007), but far more research is needed to test this hypothesis.

So far only few studies are present in literature that compare different approaches for BPD and regarding outcomes as number of admission, suicide attempts and other unspecific clinical features. This is mainly due to the difficulty to find a single outcome for such a complex disorder. All the study on depression, for example, obviously has the same measurable outcome, the level of depression, but for Personality Disorder it's difficult to find a specific outcome. Although a comprehensive model has not yet been formulated, in the last years litera-

ture focused on scarce mentalization abilities and difficulties in emotion regulation, as core features of BPD (Sharp, Pane, Ha, et al. 2011). So with the aim to evaluate how these dimensions change during psychotherapeutic treatment we choose to compare the two specific approaches explicitly focused on metacognition/mentalization, Mentalization Based Treatment (MBT, Bateman&Fonagy, 2004) and the Metacognitive Interpersonal Therapy (MIT). The study addresses the following questions: do metacognitive abilities improve after 1 year of MIT/MBT vs TAU? And do MIT and MBT influence metacognition abilities in a different way?

Finally we investigate if emotion dysregulation, and other clinical variables, such as impulsivity, alexithymia, depressed mood, interpersonal sensitivity, and the general level of psychopathology change in 1 year therapy and if changes in these variables are associate with changes in Metacognitive functions.

4.2 Methods

4.2.1 study population

BPD patients were recruited in 3 different psychiatric clinic: the hospital IRCCS San Giovanni di Dio, located in Brescia, the Mental Health Service of Savona and the CIRDIP, located in Pavia. The first one is a clinical and research center dedicated to the mental health, the second one is a community mental health service and the last one is an outpatient service, specialized in personality disorder treatment. Clinical approaches to personality disorders of these services are different and one of the aims of the study is to compare the outcomes of their approaches.

Inclusion criteria were:

_ Meet DSM-IV-TR (APA, 2000) criteria for BPD;

_ Age at baseline between 18 and 45 years;

_ Able to provide informed consent.

Exclusion criteria were:

_ Lifetime diagnosis of schizophrenia, schizoaffective disorder, major depressive disorder with psychotic symptoms, organic mental syndromes;

_ Active substance abuse or dependence during the 3 months prior to entry into the study;

_ Ongoing psychotherapy,

_ Cognitive impairment (Mini Mental State Exam score <26) or relevant neurological signs.

4.2.2 Protocol and design of the study

Structured Clinical Interview for DSM disorder (I and II) (First et al., 1994; 1995) was administered to confirm the diagnoses of BPD and evaluate comorbidities. At baseline socio-demographical and clinical information were collected by a specific form, investigating history of the illness, substance abuse/dependency history, trauma, suicide attempts, self-harm, aggressions and previous treatments, both pharmacologic and non-pharmacologic ones (see Fig. 6.7). After 12 months these information were updated, in particular number and length of hospitalizations, suicide attempts, substance abuse, self-harm and aggressions were investigated. Primary outcome interview and the other self-report scales too were administered at baseline and after 12months.

Patients were divided into 3 different groups:

1. BPD patients treated with Metacognitive Interpersonal Therapy (Dimaggio&Semerari, 2006);

2. BPD patients treated with Mentalization Based Therapy (Bateman&Fonagy, 2006);

3. BPD patients treated as usual (TAU): general psychiatric care, but no specialist psychotherapy.

Patients were classified as having completed treatment if the time between the first and last sessions was at least 12 months. Patients who missed four consecutive sessions, with no ascertained reasons to justify this, were considered as dropouts.

4.2.3 Treatment and Therapist

Patients were treated by two kinds of active interventions: MIT (Dimaggio, et al., 2007) and MBT (Bateman&Fonagy, 2006); or belong to a control group (TAU). Unfortunately the sample couldn't be randomized because we couldn't find a center provided both MIT and MBT treatments.

- MIT consisted of a 50-minute weekly individual session. MIT is designed to achieve a hierarchy of goals: (a) assessment of problematic mental states and interpersonal processes; (b) management of maladaptive behaviors, (c) intervention on symptoms that cause emotional distress; (d) to increase the ability (integration) to construct an integrated representation of self and others; (e) to increase the ability to recognize her/his role in interpersonal processes and to promote more adaptive behaviors (Dimaggio, et al., 2007).

- MBT consisted of a 50-minute weekly individual session. The principal aim of MBT approach is to improve mentalization, activating the attachment system through the discussion of current attachment relationship, past ones and regulating the patient's attachment bond to therapist (Bateman&Fonagy, 2006).

- TAU (Treatment as usual) consisted of general psychiatric care with medication prescribed by the consultant psychiatrist, and periods of partial hospital and inpatient treatment as necessary but no specialist psychotherapy.

Psychotherapies were delivered by “expert therapists”, with a minimum of 2 years of clinical experience and a minimum of 1 year of experience treating BPD patients (as defined in McMain 2009). Six psychotherapists were involved, three for each treatment (MIT and MBT). Pharmacotherapy in all groups used a symptom-targeted approach as suggested in the APA guidelines (APA, 2001). See Fig. 6.3-6.4-6.5 in Appendix.

4.2.4 Primary outcome measures on metacognition

Total scores on Metacognition Assessment Interview (MAI, Semerari, et al., 2012) were collected as the primary outcome measure at baseline and after 12 months. MAI were administered by an independent assessor, not involved in the psychotherapeutic treatment and trained directly by MAI’s authors on administration and scoring of the interview.

The MAI refers to the description of emotions and cognitions, and assesses how people are able to identify their own and others’ recurrent patterns of thinking, feeling and dealing with social problems (see Fig.6.6). The interview evaluates two main functional skill domains of metacognition, ‘the Self’ and ‘the Other’, each one composed of two dimensions: Monitoring and Integration for the Self, Differentiation and Decentering for the Other. To identify the 16 basic facets of which the dimensions are composed (four facets for each dimension) the authors took into account the clinical literature that describes deficits in the ability to know and regulate mental states, theoretically based on the literature on mentalization and attachment theories (Fonagy&Moran 1991; Fonagy&Target, 2006; Allen et al., 2008), theory of mind (Baron-Cohen et al., 1985; Premack&Woodruff, 1978), metacognition (Wellman, 1990; Wells, 2000) and, more generally, meta- representation (Frith, 1992; Sperber, 2000).

The Self domain comprises the ‘monitoring’ and ‘integrating’ dimensions and describes the way in which a person has explicit access to his own mental states (cognitive and emotional) in relation to behavior.

1. ‘Monitoring’ (MON) is referred to as the ability to distinguish, recognize and define one’s own inner states (emotions and cognitions) and following behaviors during the ‘here and now’ of the described real-life episode.

MON is composed of four facets:

(a) the ability to recognize one’s own representations (thoughts and beliefs);

(b) the ability to recognize and verbalize one’s own emotions;

(c) the ability to establish relations among the separate components of a mental state; and

(d) the ability to establish relations between the components of mental states and behavior.

MON evaluates how a subject explains his/her own behavior in terms of causes and/or motivations. If there is a deficit, he/she is unable to discern the reasons for his/ her behavior, and he/she cannot recognize or verbalize emotions or other mental states. Examples of questions stimulating MON are ‘What do you feel?’, ‘What do you think?’ and ‘What was your aim?’.

2. ‘Integrating’ (INT) is the second dimension of Self domain and involves the ability to produce coherent descriptions of people’s mental processes and states over time. INT refers to the ability to reflect on mental states and contents, putting them in a logical order and ranking them by relevance. Using INT abilities the subject is able to understand the link between his/her own mental states and different behaviors in different situations, decoding his/her mental, functional and dysfunctional habits and forming a consistent account of how his/her mental life has changed over his/her lifespan.

INT comprises four skills:

(a) the ability to describe understandable and coherent links among thoughts, events, actions and behaviors;

(b) the ability to describe transitions among different mental states and explain the reasons why;

(c) the ability to form generalized representations of his/her mental functioning, taking into account continuity over time of patterns of thinking and feeling;

(d) the ability to reconstruct and describe to the interviewer one's own mental functioning, providing enough information, without giving irrelevant and out-of-focus details, and giving a sense of order and coherence to the discourse. Examples of questions stimulating INT are 'So, you have found yourself reacting by [the interviewer refers to the described behavior], and feelings [the interviewer refers to the mentioned emotion]. Does feeling/thinking and behaving like this happen frequently to you?' 'You might also react in a different way, with different emotions or thoughts, in circumstances like the one described. Can you remember a specific episode?'

Other metacognition domain comprises the 'differentiating' and the 'decentering' dimensions.

3. 'Differentiating' (DIF) concerns the ability to recognize the representational nature of one's own and other individuals' thoughts, the ability to differentiate between classes of representations, such as imagination, evaluation and expectation, and to distinguish between representation and reality. Using DIF abilities, the interviewee is able to consider his/her own opinion as a hypothesis and not as a matter of fact; DIF abilities allow one to consider representations as mental phenomena, separate from but related to reality. Good DIF functioning makes people flexible in formulating opinions and points of view, and causes mental states to change depending on the communicative acts and on the availability of salient information.

DIF comprises four skills:

(a) the ability to consider one's own representation of the world as subjective and questionable;

(b) the ability to give plausible interpretations of events;

(c) the ability to reflect on and evaluate events (as opposed to a tendency to act impulsively);

(d) the ability to distinguish between different modes of thoughts such as dreaming, fantasizing and imagining. Examples of questions stimulating DIF are 'You said you have though that [the interview refers to the reported episode]. In that moment, how did you subjectively believe it and how did you consider other options?' 'Did you take into consideration alternative

interpretations of the events?' 'During the episode how much did you feel confused or clear-headed?' Have you ever experienced such levels of confusion, or not been able to remember whether something really happened, or felt dreamy, unreal, like brain fog?'.

4. 'Decentering' (DEC) refers to the ability to infer others' mental states in a plausible manner and adopt their perspective, recognizing that it is distinct from our own. DEC leads to the realization that other people's behaviors are understandable on the basis of their own aims, beliefs, values and principles, which could be different from ours and independent of the relationship a person has with the subject. It involves the ability to describe others' psychology in a plausible, clear way, without using stereotypes or cliché. DEC also includes the ability to realize that basically we are not the center of others' intentions and goals.

DEC includes four skills:

(a) the ability to recognize, define and verbalize other people's emotional inner state;

(b) the ability to recognize, define and verbalize other people's cognitive inner state;

(c) the ability to establish relations among the separate components of others' mental state; and

(d) the ability to establish relations between the components of others' mental state and their behavior.

Examples of questions stimulating DEC are 'How did you think the other person would react emotionally during the episode?' 'What did you think he/she thought?' 'Why did you think he/she thought that?' and 'What reasons did he/ she have?'.

The MAI begins with the description of an autobiographical episode about the worst psychological situation that he/she has experienced in the last six months. In order to evaluate the comprehension of others' mental state, the episode has to include interaction with another person. MAI is focused on the worst episode of the last six months in order to be able to evaluate metacognitive function in critical circumstances with the prospect of applying it to clinical populations. The MAI continues with four modules, each specific to the evaluation of one

metacognitive dimension as described before. For each dimension of the metacognitive construct, the interviewer has to ask a structured list of questions; the duration of MAI depends on the richness and how detailed the episode is been reported by the patient (Semerari et al., 2008). For each skill of each ability the score is measured on a likert scale from 1 to 5 (see Fig.6.6 in Appendix).

In particular authors provide these guidelines to assess the scoring:

1. Insufficient ability. The subject can't use the ability spontaneously, even with the help of the interviewer. The ability is rarely present during the interview, the description of the mental state is always unclear. Helps from the interviewers never help the subject to use correctly the ability.

2. Partial ability. The ability is never used spontaneously, but the subject sometimes can use the ability partially with the help of the interviewer. The description of internal states is superficial and never spontaneous, but with the helps from the interviewer there is some sporadic improvement in the use of the ability, only in some specific question of the interview.

3. Moderate ability. Occasionally the subject can use the ability spontaneously and correctly, but it happens rarely, despite of the helps from interviewer. Mental states is clearly descripted, even if the descriptions are simple and not well-structured. Sometimes during the interview the subject try to use spontaneously the ability, but his ability still depends on the interviewer's support.

4. Good ability. Often the subject uses spontaneously the ability, but rarely he still needs some support from the interviewer. Mental states are clearly descripted. The subject can use the specific metacognition ability, but sometimes he would fail without the interviewer's helps.

5. ***Excellent ability: The subject succeeds in using the ability spontaneously and constantly, without any help.*** During the interview the subject can describe mental state, without fall in

the use of the ability. The subject is able to refer to his mental state in a detailed and comprehensive way. The answers to the questions of the interview tend to go beyond the questions.

The MAI provided good inter-rater reliability, factorial validity and internal consistency (Semerari, et al, 2012).

4.2.5 Secondary outcome measures

Patients were also assessed by the following self-report questionnaire, administered at baseline and after 1 year:

- Difficulties in Emotion Regulation Scale (DERS): it's a 36-item, self-report questionnaire designed to assess emotion dysregulation. The scale has high internal consistency, good test–retest reliability, and adequate construct and predictive validity (Gratz&Roemer, 2004).
- Toronto Alexithymia Scale (TAS) aims to assesses alexithymia, that refers to inability to identify and describe feelings. The TAS-20 is a self-report scale comprised of 20 items, rated on a five-point Likert scale. In this study we used the total score to classify persons as showing alexithymia (score>61), possible Alexithymia (score between 52 and 60) and no alexithymia (score<51). Authors reported good factorial validity, concurrent validity and reliability for TAS (Bagby, et al., 1994).

- Barratt Impulsiveness Scale (BIS) is a questionnaire designed to assess the personality/behavioral construct of impulsiveness. The BIS-11 identifies three factors that express three different constructs of impulsivity: Motor impulsiveness, Impulsivity without planning and Cognitive impulsivity. These scales have shown a good reliability and validity with other measures of the same dimension and the total score of the BIS-11 is an internally consistent measure of impulsiveness (Patton, et al., 1995).

- Beck Depression Inventory (BDI) it's a 21-question multiple-choice self-report inventory and it's one of the most widely used instruments for measuring the severity of depression. Each response is assigned a score ranging from zero to three, indicating the severity of the symptom, the sum of each item provides a total score that correspond to a depression severity level, from mild to severe (Beck, et al., 1988).

- Inventory of Interpersonal Problems (IIP) it's a 57 items self-report, assessing different aspects of interpersonal features: interpersonal sensitivity, interpersonal ambivalence, aggression, need for social approval, and lack of sociability (Pilkonis, et al., 1996). Within this subscales the Interpersonal Sensitivity as recognized as an essential feature of BPD (Trull, et al, 2001) that predispose subjects to over-react to other people's comment.

- Symptom Checklist-90 (SCL-90) it's the most used psychiatric self-report inventory assessing the psychological symptom status with good psychometric qualities (Derogatis, 1994). The Global Severity Index (GSI) of this self-report has been used in numerous studies as a brief indicator of mental health (Preston et al. 2002)

4.2.5 Statistical analyses

Sample size

In the original study protocol, the sample size should be N=60 and it was calculated on primary outcome (MAI), assuming a change in score of 16 points on the total raw score (range 16-80), as a significant improvement and considering a test power of 0.8 and a level of significance of alpha of 0.05. MAI has been validated (Semerari, et al, 2012) but cut-off scores for clinical sample do not yet exist. A change of 16 points has been hypothesized on clinical considerations, assuming that a change of 1 point (Likert scale) in a descriptor corresponds to an improvement in the ability manifested by the subject. Furthermore, considering drop-out rates reported in psychotherapy trial on BPD patients, sample size in study protocol was modified

in N=72, assuming a possible drop-out rate of 20%, in order to ensure at least 60 patients even in case of drop-out equal to 20%. Psychotherapy trial on BPD reported in fact drop-out rate between 10% and 45% (Bales, et al., 2013; Bateman, et al., 2009; Sempertengui, et al., 2012). Unfortunately, due to a delay and problems with a recruiting center, it was not possible to respect this sample size and this thesis reports only data so far collected.

Statistical Analyses

Descriptive statistics (mean and standard deviation for continuous variables, frequency and percentage for categorical variables) were used to summarize demographics and clinical features of the study sample. Parametric and non-parametric tests (Chi-square, ANOVA and Kruskal Wallis test) were used to assess any differences in demographic and clinical variables among the three groups at baseline (Table 1). Parametric and non-parametric tests (paired T-test and Wilcoxon tests) were used to describe the score change from baseline to follow-up.

For the evaluation of the treatment groups (MIT, MTB) vs TAU group along the time, a series of linear mixed models (LMM) with time (pre and after 12-months intervention) as repeated factor within patients (repeated measures), group as between factor and Bonferroni correction for post-hoc were performed.

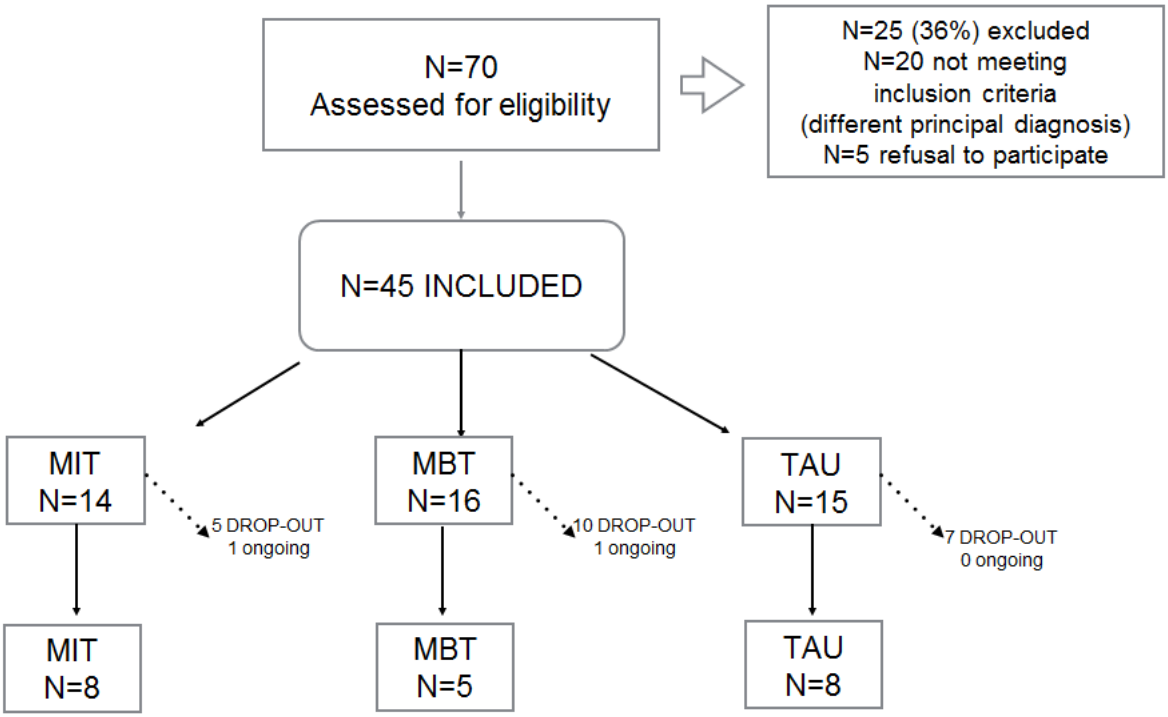
All statistical analysis were carried out by using SPSS 21.0. Statistical significance was set at $p<0.05$.

4.3 Results of the longitudinal study

4.3.1 Socio-demographic and clinical characteristic of the sample

Seventy patients were assessed for the inclusion and 45 met the inclusion criteria (see Fig. 4.1). Twenty-five patients were excluded from the study: n=20 for different principal diagnosis and n=5 patients refused to participate.

Fig. 4.1 Flow chart diagram of the longitudinal study.



Fourteen patients started a MIT therapy, 16 an MBT therapy and the other 15 patients belonged to the TAU group. Unfortunately randomization wasn't possible because it's very hard to find in Italy clinic specialized in psychotherapy for personality disorder and usually they have a specific approach and are located in different cities, and none offered to patients both MIT and MBT.

The drop-out rate after 6 months was around 35% in the MIT group, 46% in TAU and 31% in the MBT group (in this group, five patients were not evaluated at T1 due to administrative problems of one involved center that avoided the prosecution of the treatment within the protocol). Differently, the drop-out rate between 6 and 12 months was zero.

Comparison between groups (MIT, MBT and TAU) at baseline showed that only the age and the age of onset resulted higher in the TAU group, but the duration of illness, that could be linked to some clinical variables, didn't differ between groups (Tables 4.2-4.3). The other socio-demographical variables didn't differ, so we can compare the groups.

Tab. 4.2 Comparison of socio-demographic and clinical characteristic of the three groups at baseline.

	MIT (N=14) Mean (SD)	**MBT (N=16)** Mean (SD)	**TAU (N=15)** Mean (SD)	**ANOVA # F-statistic**	**p-value**
Age	31.6 (8.3)	29.2 (7.5) *	36.9 (6.2) *	4.55	0.016 *
Education (years)	12.6 (3.4)	12.0 (2.6)	10.7 (2.2)	4.57	0.116
Age at onset (years)	18.3 (4.8) *	18.3 (5.4)	24.2 (9.1) *	3.64	0.035 *
Duration of illness	12.4 (8.2)	10.4 (6.3)	12.7 (7.0)	0.43	0.654
Age at first contact with Psych Services	22.1 (7.1)	22.3 (7.8)	26.7 (8.4)	1.64	0.206
Number of DSM-IV BPD's criteria (mean)	6.5 (0.8)	6.9 (1.5)	6.5 (1.1)	0.56	0.574

Considering the groups sample size, differences among groups were evaluated also with non-parametric Kruskal-Wallis test, obtaining consistent results with respect to ANOVA test.
* Post-hoc significant difference

The majority of the sample was female (see Tab. 4.3). Half of the sample showed comorbidity with a SUD, Substance Abuse Disorder, lifetime and high percentage of the sample attempted suicide or experienced self-harm behaviors lifetime. Between 62% and 92% of the sample reported to have at least one relative with a psychiatric disorder.

Tab. 4.3 Comparison of socio-demographic and clinical characteristic of the three groups at baseline.

	MIT (N=14) N (%)	**MBT (N=16)** N (%)	**TAU (N=15)** N (%)	**Chi-square test**	**p-value**
Sex (F)	10 (71.4%)	12 (75.0%)	10 (66.7%)	0.26	0.877
Lifetime alcohol Abuse/Addiction	7 (50%)	10 (62.5%)	8 (53.3%)	0.93	0.627
Lifetime substance Abuse/Addiction	8 (57.1%)	8 (53.3%)	7 (46.7%)	0.33	0.848
Lifetime attempted suicide	7 (50%)	5 (33.3%)	10 (66.7%)	3.33	0.189
Lifetime self-harm	9 (64.3%)	10 (62.5%)	7 (46.7%)	1.47	0.479
At least one relative with psych. disorder	13 (92.9%)	10 (62.5%)	13 (86.7%)	3.50	0.174

Table 4.4 shows comparisons on principal and secondary outcomes between the groups at baseline. For all the variables, both the total and sub-scale scores, resulted not statistically different, except for GSI of the SCL-90 scale that resulted lower in MBT group.

Tab. 4.4 Comparison of clinical outcomes in the three groups at baseline.

		MIT (N=14) Mean (DS)	**MBT (N=16)** Mean (DS)	**TAU (N=15)** Mean (DS)	**ANOVA # F-statistic**	**p-value**
MAI	Total Score	40.5 (7.5)	42.7 (7.9)	42.1 (3.2)	0.40	0.672
Subscales	Monitoring	11.2 (3.1)	11.5 (2.1)	10.6 (1.2)	0.51	0.605
	Differiantiation	9.8 (1.6)	10.3 (1.8)	10.6 (1.2)	0.76	0.474
	Integration	9.9 (1.6)	10.3 (1.8)	10.6 (1.0)	0.55	0.580
	Decentering	9.6 (1.7)	10.7 (2.0)	10.6 (1.0)	1.30	0.285
TAS	Total Score	53.6 (16.2)	53.2 (14.5)	51.5 (13.5)	0.04	0.960
DERS	Total Score	125.3 (17.4)	112.4 (27.4)	111.8 (19.2)	1.54	0.229
BIS	Total Score	76.3 (10.2)	76.4 (15.6)	70.6 (10.6)	0.82	0.452
SCL 90	GSI (Global Severity Index)	1.8 * (0.7)	2.5 * (0.5)	2.0 (0.6)	3.47	0.044*
IIP	Interpersonal Sensitivity	2.7 (0.7)	2.7 (1.0)	2.3 (0.8)	0.70	0.505
BDI	Total Score	22.8 (11.3)	26.0 (12.9)	32.4 (9.9)	1.56	0.229

Considering the groups sample size, differences among groups were evaluated also with non-parametric Kruskal-Wallis test, obtaining consistent results with respect to ANOVA test.
* Post-hoc significant differences

4.3.2 Longitudinal evaluation of the primary outcomes

Table 4.5 shows the score changes between baseline and 1-year follow up on primary and secondary outcomes within the experimental groups. MAI total score improved in MIT group, while worsened in the MBT group. In particular in MIT group all the subscale of the MAI, Monitoring, Differentiation, Integration and Decentering improved. In this group even the secondary outcome improved after 1 year of MIT. In particular TAS mean score decreased from 53.6 (sd=16.2) to 51.1 (sd=20.5), DERS score from 125.3 (sd=17.4) to 109.1 (sd=8.6), BIS score from 76.3 (sd=10.2) to 63.6 (sd=10.3), SCL-90 Total Score from 1.8 (sd=0.7) to 0.7 (sd=0.9) and BDI from 22.8 (sd=11.3) to 15.7 (sd=12.4). Differently in the MBT group the secondary outcome didn't improve after therapy, but the small number of the patients in this group could have influenced this result.

Tab. 4.5 Score change (baseline - follow-up) of primary outcome (total score and sub-scales scores)

	MIT				**MBT**			
	T0 (N=14) Mean (DS)	**T1 (N=8)** Mean (DS)	**T-test**	**p-value**	**T0 (N=16)** Mean (DS)	**T1 (N=5)** Mean (DS)	**T-test**	**p-value**
MAI Total Score	40.5 (7.5)	51.6 (4.3)	-3.78	0.009	42.7 (7.9)	39.2 (6.3)	-1.32	0.258
MAI Mon	11.2 (3.1)	13.7 (0.9)	-1.06	0.329	11.5 (2.1)	10.4 (1.7)	0.00	1.000
MAI Diff	9.8 (1.6)	12.7 (0.9)	-3.55	0.012	10.3 (1.8)	9.8 (1.3)	-0.89	0.426
MAI Int	9.9 (1.6)	13.0 (1.3)	-5.16	0.002	10.3 (1.8)	9.6 (1.7)	-2.45	0.070
MAI Dec	9.6 (1.7)	12.1 (1.2)	-4.60	0.004	10.7 (2.0)	9.4 (1.7)	-1.00	0.374

Considering the groups sample size, differences across time were evaluated also with non-parametric Wilcoxon test, obtaining consistent results with respect to paired t-test.

The comparison between baseline score and follow-up score, (Tab. 4.5) showed a similar situation, in which MAI Total Score and all the subscale scores, except from Monitoring, differed statistically in the MIT group; whereas none of subscales changed in the MBT group.

The linear mixed model applied for the evaluation of change across time of the MAI scores between MIT and TAU groups (Tab. 4.6) showed that MAI Total score improved in both groups, but the interaction between group and time was statistically significant, so the improvement during time in MIT group resulted larger than in TAU. Regarding the MAI subscales instead the interaction between intervention and time wasn't significant in Monitoring, and were significant in the other 3 subscales, Differentiation, Integration and Decentering.

Tab. 4.6 Linear Mixed model for the longitudinal evaluation of MAI scores in MIT vs TAU group.

	MIT		**TAU**		**Group**		**Time**		**Interaction (time x group)**	
	T0 Mean (S.E.)	**T1** Mean (S.E.)	**T0** Mean (S.E.)	**T1** Mean (S.E.)	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
MAI Mon	11.2 (0.7)	13.7 (0.4)	10.6 (0.6)	12.2 (0.4)	3.43	0.072	14.96	<0.000	0.77	0.387
MAI Diff	9.8 (0.3)	12.7 (0.3)	10.6 (0.3)	10.8 (0.3)	2.55	0.120	21.25	<0.000	13.92	**0.001**
MAI Int	9.9 (0.4)	13.0 (0.4)	10.6 (0.4)	11.5 (0.4)	1.05	0.314	27.10	<0.000	8.65	**0.006**
MAI Dec	9.6 (0.5)	12.1 (0.5)	10.2 (0.4)	10.4 (0.5)	1.45	0.238	8.30	0.007	6.45	**0.016**
MAI Total Score	40.5 (1.6)	51.6 (1.3)	42.1 (1.5)	45.0 (1.0)	3.10	0.086	24.33	<0.000	8.23	**0.007**

Similarly, we compared MTB vs TAU score changes across time (Tab. 4.7). MAI Total score showed a tendency toward significance for the interaction (p=0.066) between time x group, while a significant interaction was observed for the subscale Monitoring.

Tab. 4.7 Linear Mixed model for the longitudinal evaluation of MAI scores in MBT vs TAU group.

	MBT		**TAU**		**Group**		**Time**		**Interaction (time x group)**	
	T0 Mean (S.E.)	**T1** Mean (S.E.)	**T0** Mean (S.E.)	**T1** Mean (S.E.)	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
MAI Mon	11.5 (0.4)	10.4 (0.6)	10.6 (0.6)	12.2 (0.4)	0.97	0.334	0.27	0.608	6.59	**0.017**
MAI Diff	10.3 (0.4)	9.8 (0.5)	10.6 (0.3)	10.8 (0.3)	2.91	0.098	0.04	0.842	0.91	0.348
MAI Int	10.3 (0.5)	9.6 (0.5)	10.6 (0.4)	11.5 (0.4)	5.41	0.027	0.02	0.897	2.81	0.104
MAI Dec	10.7 (0.4)	9.4 (0.7)	10.2 (0.4)	10.4 (0.5)	0.22	0.640	1.00	0.327	1.67	0.209
MAI Total Score	42.7 (1.6)	39.2 (2.0)	42.1 (1.5)	45.0 (1.0)	2.32	0.139	0.03	0.859	3.67	0.066

Finally the comparison between MIT and MBT groups showed a significant interaction time-intervention both in the MAI Total score and sub-scales. (Tab. 4.8).

Tab. 4.8 Linear Mixed model for the longitudinal evaluation of MAI scores in MIT vs MBT group.

	MIT		**MBT**		**Group**		**Time**		**Interaction (time x group)**	
	T0 Mean (S.E.)	**T1** Mean (S.E.)	**T0** Mean (S.E.)	**T1** Mean (S.E.)	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
MAI Mon	11.2 (0.7)	13.7 (0.4)	11.5 (0.4)	10.4 (0.6)	5.77	0.022	1.39	0.246	8.30	**0.007**
MAI Diff	9.8 (0.3)	12.7 (0.3)	10.3 (0.4)	9.8 (0.5)	7.10	0.012	6.72	0.015	12.93	**0.001**
MAI Int	9.9 (0.4)	13.0 (0.4)	10.3 (0.5)	9.6 (0.5)	6.64	0.016	4.12	0.053	10.87	**0.003**
MAI Dec	9.6 (0.5)	12.1 (0.5)	10.7 (0.4)	9.4 (0.7)	2.26	0.145	1.37	0.252	12.03	**0.002**
MAI Total Score	40.5 (1.6)	51.6 (1.3)	42.7 (1.6)	39.2 (2.0)	6.49	0.001	3.59	0.67	13.47	**0.001**

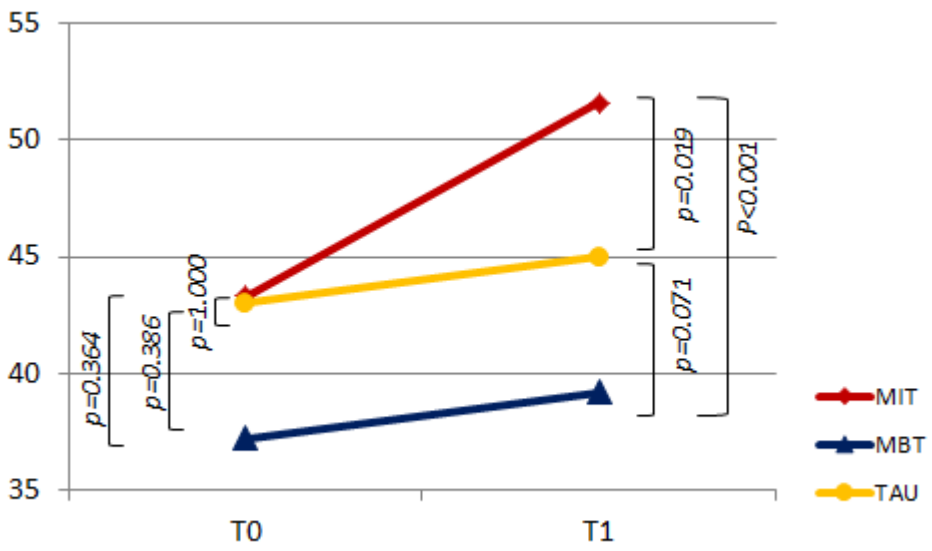
A full evaluation of MAI score changes for all the three groups was reported in Table 4.9. The within factor time for MAI total score was significant (p=0.015), as well as the interaction time x group (p=0.001). Also for all the MAI subscales the interaction factor time x group was significant (Mon: p=0.007; Diff: p<0.001; Int: p=0.001; Dec: p=0.004).

Tab. 4.9 Linear Mixed model for the longitudinal evaluation of MAI scores in the three groups.

	MIT Mean (S.E.)		**MBT** Mean (S.E.)		**TAU** Mean (S.E.)		**Group**		**Time**		**Interaction (time x group)**	
	T0 N=14	**T1 N=8**	**T0 N=16**	**T1 N=5**	**T0 N=15**	**T1 N=8**	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
MAI Mon	11.2 (0.7)	13.7 (0.4)	11.5 (0.4)	10.4 (0.6)	10.6 (0.6)	12.2 (0.4)	3.62	0.034	5.12	0.028	5.42	**0.007**
MAI Diff	9.8 (0.3)	12.7 (0.3)	10.3 (0.4)	9.8 (0.5)	10.6 (0.3)	10.8 (0.3)	4.46	0.017	7.51	0.009	9.06	**0.000**
MAI Int	9.9 (0.4)	13.0 (0.4)	10.3 (0.5)	9.6 (0.5)	10.6 (0.4)	11.5 (0.4)	4.92	0.011	7.46	0.009	7.61	**0.001**
MAI Dec	9.6 (0.5)	12.1 (0.5)	10.7 (0.4)	9.4 (0.7)	10.2 (0.4)	10.4 (0.5)	1.25	0.297	1.28	0.266	6.45	**0.004**
MAI Total Score	40.5 (1.6)	51.6 (1.3)	42.7 (1.6)	39.2 (2.0)	42.1 (1.5)	45.0 (1.0)	4.24	0.020	6.35	0.015	8.85	**0.001**

With respect to MBT, it is worth nothing that the decreasing of MAI score between baseline and follow-up was basically due to a misleading baseline data in terms of mean score of patients who completed the treatment (baseline MAI mean scores of completers was lower than the corresponding mean of the whole MBT group). The results of Mixed model carried out only for patients having both baseline and follow-up evaluations (completers) are reported in Figures from 4.10 to 4.14 and Tables from 4.10.1 to 4.14.1.

Fig. 4.10 Linear Mixed model for the longitudinal evaluation of Total MAI scores in completers (Bonferroni post-hoc comparison)



Tab. 4.10.1 Linear Mixed model output of Total MAI scores in completers

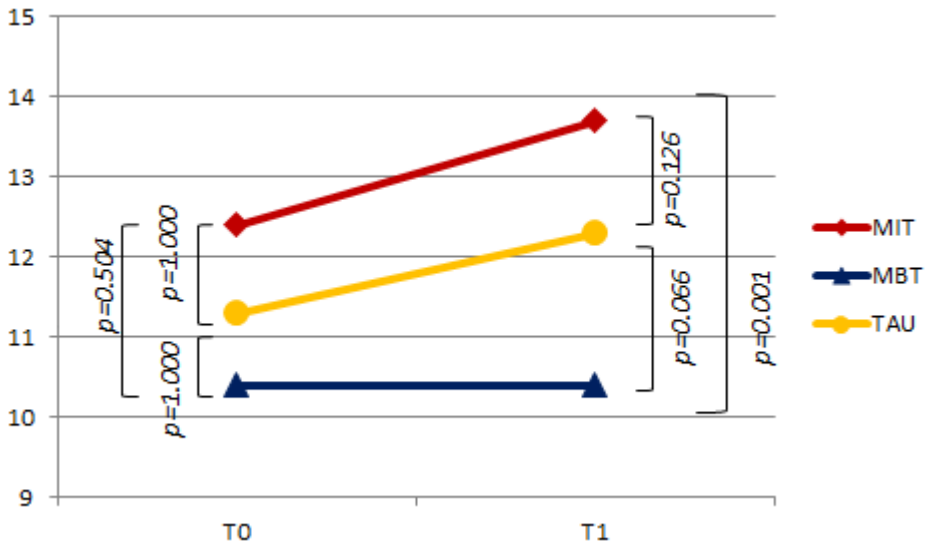
MIT Mean (SD)		**MBT** Mean (SD)		**TAU** Mean (SD)		**Group**		**Time**		**Interaction (time x group)**	
T0 N=8	**T1 N=8**	**T0 N=5**	**T1 N=5**	**T0 N=8**	**T1 N=8**	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
43.3 (8.6)	51.6 (3.5)	37.2 (7.4)	39.2 (5.7)	43.0 (2.1)	45.0 (3.4)	5.12	0.018	18.57	<0.001	5.17	**0.018**

No differences were observed for MAI Total score and sub-scales score at baseline among the three groups (p>0.05) (Fig. 410-4.14).

MAI total score improved in all the groups, but the change during time was larger in MIT than in TAU and MBT, making the interaction effect significant (p=0.018). MBT and TAU increased of the same score (2 points from T0 to T1) but corresponding to 5.4% and 4.6% of enhancing respectively (Fig. 4.10).

Considering MAI subscales, Monitoring improved in a similar way in MIT and TAU groups, while it remained stable in MBT group (Fig. 4.11- Tab. 4.11.1). MIT groups instead statistically differed from both MBT and TAU in the other Metacognitive functions: Differentiation, Integration and Decentering (Fig. 4.12-4.14; Tab. 4.12.1-4.14.1).

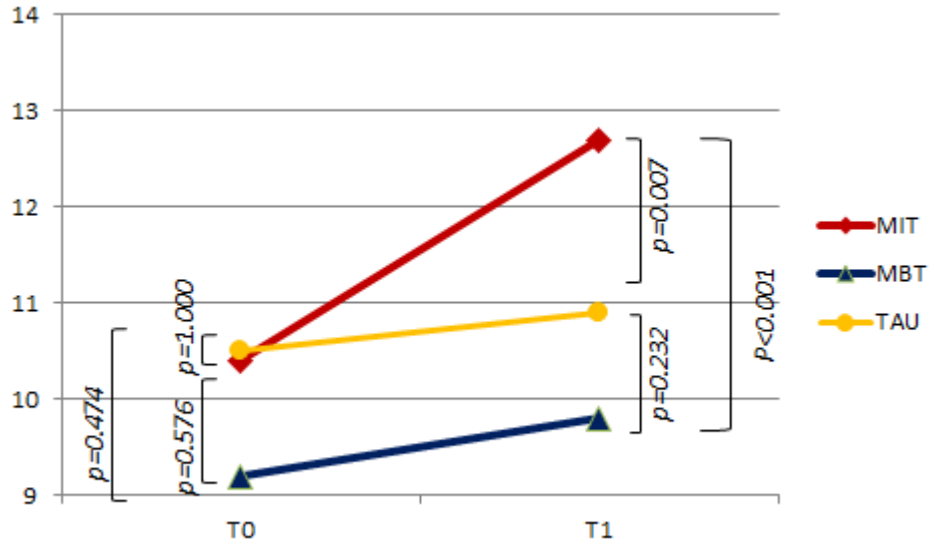
Fig. 4.11 Linear Mixed model for the longitudinal evaluation of Sub-scale Monitoring (MAI) in completers (Bonferroni post-hoc comparison)



Tab. 4.11.1 Linear Mixed model output of Sub-scale Monitoring scores in completers

MIT Mean (SD)		**MBT** Mean (SD)		**TAU** Mean (SD)		**Group**		**Time**		**Interaction (time x group)**	
T0 N=8	**T1 N=8**	**T0 N=5**	**T1 N=5**	**T0 N=8**	**T1 N=8**	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
12.4 (3.5)	13.7 (0.9)	10.4 (2.1)	10.4 (1.7)	11.3 (0.7)	12.3 (1.3)	4.12	0.035	2.39	0.141	0.55	0.588

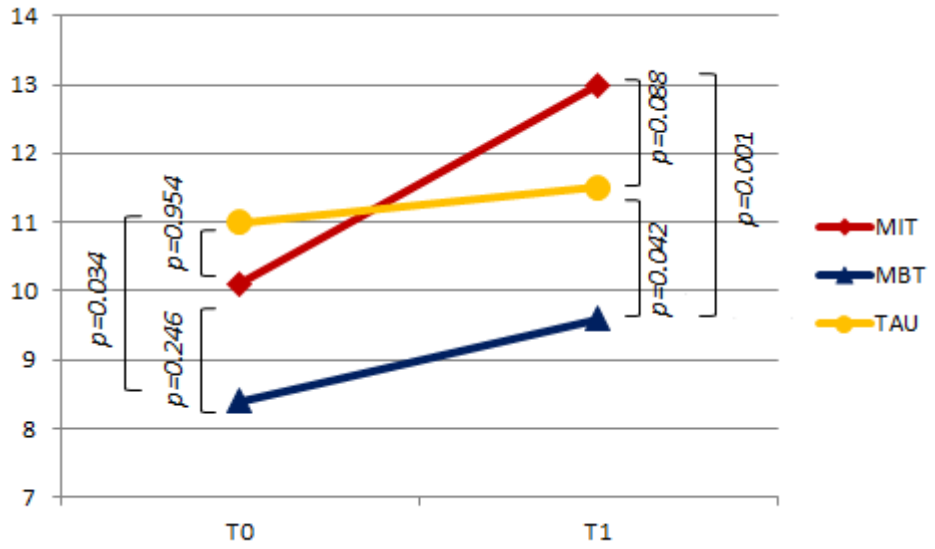
Fig. 4.12 Linear Mixed model for the longitudinal evaluation of Sub-scale Differentiating (MAI) in completers (Bonferroni post-hoc comparison)



Tab. 4.12.1 Linear Mixed model output of Sub-scale Differentiating scores in completers

MIT Mean (SD)		**MBT** Mean (SD)		**TAU** Mean (SD)		**Group**		**Time**		**Interaction (time x group)**	
T0 N=8	**T1 N=8**	**T0 N=5**	**T1 N=5**	**T0 N=8**	**T1 N=8**	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
10.4 (1.7)	12.7 (1.0)	9.2 (2.0)	9.8 (1.3)	10.5 (1.1)	10.9 (0.8)	5.70	0.013	9.54	0.007	3.21	0.066

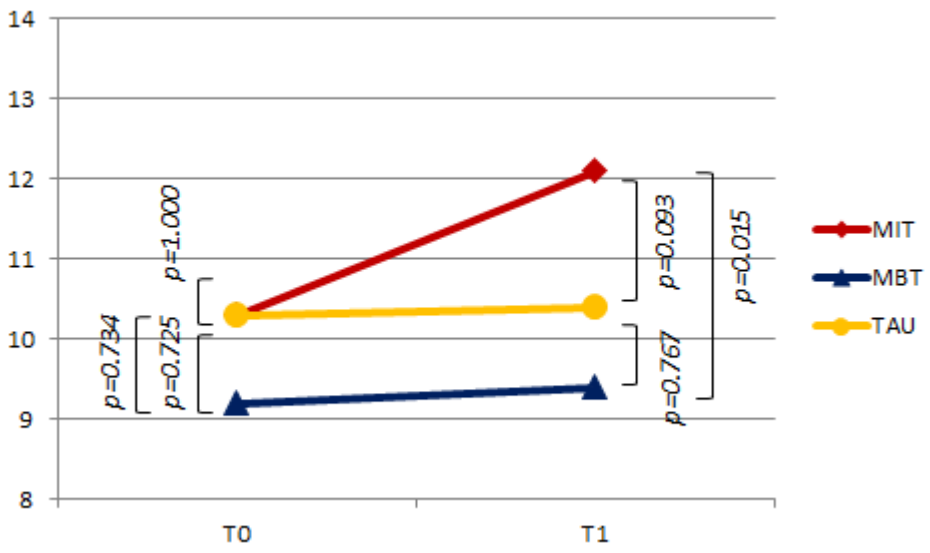
Fig. 4.13 Linear Mixed model for the longitudinal evaluation of Sub-scale Integration (MAI) in completers (Bonferroni post-hoc comparison)



Tab. 4.13.1 Linear Mixed model output of Sub-scale Integration scores in completers

MIT Mean (SD)		**MBT** Mean (SD)		**TAU** Mean (SD)		**Group**		**Time**		**Interaction (time x group)**	
T0 N=8	**T1 N=8**	**T0 N=5**	**T1 N=5**	**T0 N=8**	**T1 N=8**	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
10.1 (1.9)	13.0 (1.3)	8.4 (2.2)	9.6 (1.7)	11.0 (0.8)	11.5 (0.8)	6.62	0.007	29.411	<0.000	7.071	**0.006**

Fig. 4.14 Linear Mixed model for the longitudinal evaluation of Sub-scale Decentering (MAI) in completers (Bonferroni post-hoc comparison)



Tab. 4.14.1 Linear Mixed model output of Sub-scale Decentering scores in completers

MIT Mean (SD)		**MBT** Mean (SD)		**TAU** Mean (SD)		**Group**		**Time**		**Interaction (time x group)**	
T0 N=8	**T1 N=8**	**T0 N=5**	**T1 N=5**	**T0 N=8**	**T1 N=8**	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
10.3 (1.8)	12.1 (1.2)	9.2 (1.6)	9.4 (1.7)	10.3 (1.2)	10.4 (1.5)	2.75	0.092	9.336	0.007	6.063	**0.010**

4.3.3 Longitudinal evaluation of the secondary outcomes

Table 4.15 showed score change (baseline - follow-up) of secondary outcomes in experimental groups. In MIT group all the scales showed improvements during 1 year treatment. In MBT group only TAS score and IIP score improve, while the other variables worsen during time. However the exiguous size of the sample (due to missing data) did not allow to drive any robust conclusion about it.

Tab. 4.15 Score change (baseline - follow-up) of secondary outcomes

	MIT				**MBT**			
	T0 N=14 Mean (SD)	**T1 N=7** Mean (SD)	**T test**	**p-value**	**T0 N=15** Mean (SD)	**T1 N=3** Mean (SD)	**T test**	**p-value**
TAS	53.6 (16.2)	51.1 (20.5)	0.95	0.377	53.2 (14.5)	51.3 (13.3)	0.23	0.837
DERS	125.3 (17.4)	109.1 (8.6)	1.15	0.295	112.4 (27.4)	125.3 (15.1)	-1.44	0.287
BIS	76.3 (10.2)	63.6 (10.3)	1.97	0.096	76.4 (15.6)	85.3 (17.9)	-033	0.776
SCL 90	1.8 (0.7)	0.7 (0.9)	4.46	**0.004**	2.5 (0.5)	2.4 (1.0)	0.00	1.000
IIP	2.7 (0.7)	1.7 (0.5)	1.00	0.356	2.7 (1.0)	1.7 (0.6)	0.00	1.000
BDI	22.8 (11.3)	15.7 (12.4)	1.94	0.101	26.0 (12.9)	27,7 (12.6)	-0.30	0.791

Considering the groups sample size, differences across time were evaluated also with non-parametric Wilcoxon test, obtaining consistent results with respect to paired t-test.

The exiguous size of the sample at 12 months didn't permit to run other analysis except the explorative ones on MIT versus TAU group for which a major number of data were collected (Tab. 4.16).

Tab. 4.16 Linear Mixed model for the longitudinal evaluation of secondary outcomes in MIT vs TAU group.

	MIT Mean (SE)		**TAU** Mean (SE)		**Group**		**Time**		**Interaction (time x group)**	
	T0	**T1**	**T0**	**T1**	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**
BIS	76.2 (2.9)	63.5 (5.0)	70.6 (3.1)	65.8 (4.7)	0.181	0.674	4.778	0.039	0.938	0.343
BDI	22.9 (3.0)	15.7 (4.4)	32.4 (4.1)	21.0 (8.3)	1.938	0.191	3.020	0.109	0.162	0.695
DERS	125.3 (5.1)	109.1 (14.7)	111.8 (5.5)	90.9 (13.7)	2.200	0.157	3.004	0.102	0.050	0.826
TAS	53.6 (4.3)	51.1 (7.6)	51.5 (6.3)	54.5 (14.2)	0.005	0.946	0.001	0,977	0.094	0.765
IIP	2.2 (0.2)	1.7 (0.3)	1.8 (0.2)	1.3 (0.3)	2.466	0.127	4.189	0.049	0.803	0.776
SCL-90	1.763 (0.2)	1.609 (0.2)	2.027 (0.3)	1.413 (0.3)	0.019	0.890	2.505	0.127	0.904	0.352

The improvement in secondary outcomes in MIT was larger than TAU in the most of the variables, anyway the differences were not statistically significant.

Finally, we verified if the relations among primary and secondary outcomes detected in the cross-sectional study (analyzed by structural equation model -SEM- and reported in Figure 3.8, pag.45) hold also across time in MIT group. The sample size at T1 for the secondary outcomes avoid us to use SEM, so that we decided to evaluate the relationships among clinical scales in two steps (Tab. 4.17- Fig. 4.18).

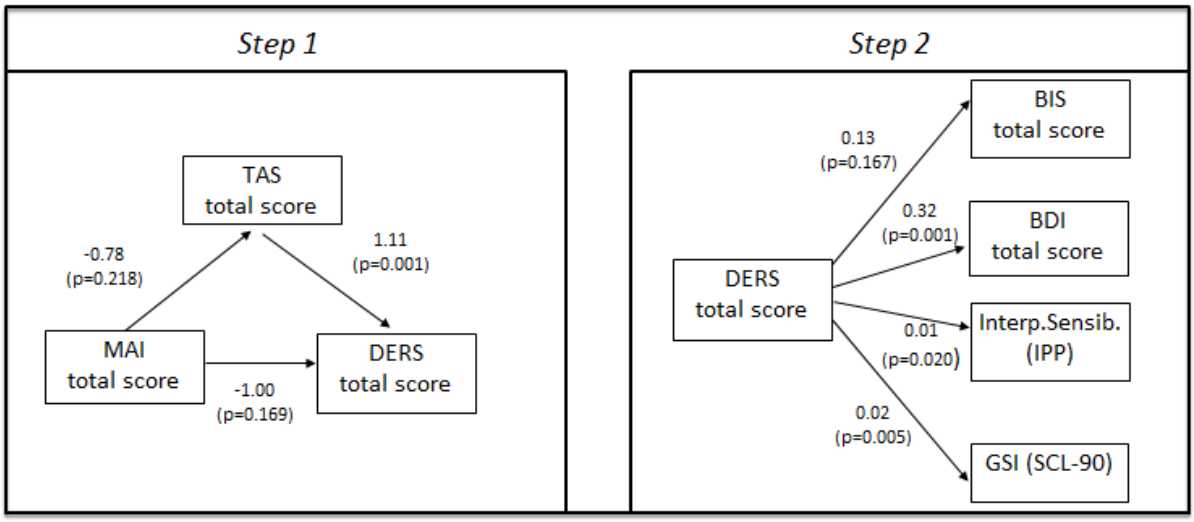
Tab. 4.17 Linear Mixed model for the longitudinal evaluation of relationships of primary and secondary outcomes in MIT group .

STEP 1 *Dependent variable* DERS	Beta	p-value
Independent variables		
MAI Total Score	- 1.00	0.169
TAS (as mediator)	1.11	0.001
Dependent variable TAS		
MAI Total Score	-0.78	0.218
STEP 2 *Independent variable* DERS		
Dependent variables		
BDI score	0.32	0.001
IIP Interpersonal Sensitivity	0.01	0.020
GSI (Global Severity Index SCL-90)	0.02	0.005
BIS Total score	0.13	0.167

In particular, we first evaluated, through linear mixed models, the relations across time among DERS (as dependent variable) and MAI and TAS (as independent and mediator variable respectively).

Then, by other four univariate mixed models (adjusted for time effect), we analyzed the relationships between BIS, BDI, IPP and GSI (as dependent variables of four different models) and DERS (as independent variable) (see Tab. 4.17).

Fig. 4.18 Graphical representation of Linear Mixed Models output for STEP 1 & STEP 2



Differently it was found for the cross-sectional study carried out on the whole sample (N=45) at baseline, the relationship between MAI TAS and DERS across time for MIT group showed a different path. Instead, the relations between DERS and the other clinical variables hold for BDI, IPP and GSI. It is worth to note that these results were affected by the small sample size (N=7) that influence the significance.

4.4 Discussion of the longitudinal study

Different psychotherapies for BPD has different specific aims but, as suggested by Gabbard in an interesting editorial (Gabbard, 2007), probably "all the roads lead to Rome" i.e. different therapies try to get the same target through different "roads". In a shortened and simplified way, DBT (Linehan, et al. 2006) works directly to reduce ED, while MBT (Bateman&Fonagy, 2006) and MIT (Dimaggio&Semerari, 2007) is focused on the improvement of metacognition/mentalization to reduce ED in an "indirect way". Conversely, a recent article concludes that mentalizing is present in some DBT technique too, even if it's not explicit (Swenson&Choi-Khan, 2015).

In our study metacognition functions were evaluated after one year of MBT and MIT in order to verify if these functions improve in a different way in these two approaches and comparing to a TAU group. Despite the international guidelines indicating psychotherapy as the "gold standard" for personality disorder, it's uncommon to find evidence-based psychotherapy in psychiatric services in Italy (Nicolò&Pompili, 2012). Moreover each service has specific approach, so it was impossible to find a single center to run this study or at least two centers in the same city, so it was impossible to randomize patients to the different experimental groups. The lack of randomization make our study less reliable and generalizable than a randomized one, but the lack of differences at baseline for the outcomes between the three groups let us compare the groups and permit to draw some consideration, even if prudent.

Furthermore the high percentage of drop-out in psychotherapy of BPD (Wnuk et al. 2013) gets more difficult to recruit a big enough sample for longitudinal study, as happened in our sample in which around 35% drop-out from treatment before 6 months. An interesting review on this topic (Barnicot et al., 2011) shows a great heterogeneity in the completion rates ranging from 36% to80%, so research on the psychological processes involved in dropping out of treatment are still needed (Goldman&Gregory, 2010). However, interestingly, in our sample the drop-out rate between 6 months and the end of treatment in the experimental group was

zero and we could presume that the development of a strong therapeutic alliance could be one predictor of drop-out. Factors predicting dropout in BPD in fact included commitment to change and a strong therapeutic relationship (Barnicot et al., 2011).

Moving from these assumptions, the complexity of the management of this disorder started on the diagnosis itself. In our study 20 patients was excluded because the principal diagnosis was different, even if they received this diagnosis incorrectly in the past. The lack of a comprehensive model can count for the diagnostic difficulties and even the new DSM-5 (APA, 2013) didn't solve definitively the discussion about BPD diagnosis. Overlap of symptoms with other psychiatric disorders and high frequency of comorbidities makes diagnosis of borderline personality disorder a challenge (Biskin, et al, 2012). Moreover BPD is a clinical diagnosis, with no supporting laboratory or imaging tests. Even the core pathological features remain in debate (Linneahn, 2006; Bateman&Fonagy, 2004) but there is a broad consensus supporting the current categorical criteria of DSM-5, the same of DSM-IV (APA, 2000), while the new DSM-5 dimensional criteria (see Fig. 6.2 in Appendix) remains only an alternative for the moment, and not a substitution (APA, 2013).

The high number of comorbidities, as reported in our sample too, beyond diagnostic difficulties, make the treatment more complicate and could change the priorities of the intervention. Moreover clinicians who treat patients with PD face more than just the symptoms of the disorder; they also are often faced with patients who have significant difficulty in describing and reflecting on mental states and are often unable to use what unique knowledge they have about themselves and others to resolve social and psychological challenges (Dimaggio et al, 2015). These difficulty are the metacognitive abilities, primary outcomes of this study.

Patients of our sample showed at baseline deficits in metacognition analogous to what reported by the author of the MAI interview in a similar BPD sample (Semerari, et al., 2015). Moreover also the score on metacognitive sub-functions were similar, and showed that poor differentiation and poor integration seem to be the "typically borderline" metacognitive pro-

file, consistent with previous studies (Semerari et al, 2014) and several clinical observations (Bateman and Fonagy, 2004). The Total scores on MAI and the sub-scales scores were very similar to what reported by Semerari (Semerari et al, 2014) and they both correspond to a moderate level of deficit in Metacognition. Poor differentiation implies that the individual perceives his/her own representations not as subjective and hypothetical scenarios but as a fact (Bateman and Fonagy, 2004). Borderline patients are impulsive and they have a tendency to act out; it is plausible that differentiation deficits plays a role in generating their behavioral dyscontrol. Dysfunctional integration, on the other hand, means that the subject finds difficult to reflect on the contradictions inherent in his own thoughts and feelings. A specific impairment of integration is consistent with the difficulties of these patients in forming a stable self-image and stable representations of interpersonal relations (Semerari et al, 2015). Finally deficits in decentering could be linked to the lack of cognitive empathy observed in other studies (New et al., 2012, Hengartner et al., 2014). So, Metacognition functions seemed to be involved both in internal and interpersonal process and they can help to explain also their impairments in social functioning. According to two famous longitudinal study on BPD, called CLPS (Gunderson et al, 2011) and MSCAD (Zanarini, et al, 2014), lasting respectively 10 and 16 years, although sustained symptomatic remission is common, only 20% of BPD patients showed good social function after 10-16 years. The reasons of these results can be found in one hand to the affective dysregulation, impulsivity and anger proneness, but on the other hand to frequent misunderstanding and experiences of being rejected and offended by others (Herpertz et al, 2014). Metacognition deficits, maladaptive attachment and invalidating environment contribute to these misunderstanding and negative experiences in complex causal ways (Fonagy&Bateman, 2016) and psychotherapy for BPD has to keep in consideration all these factors. Moreover clinicians should be aware that the development of a working alliance might feel frightening to patients early in treatment (Fonagy et al, 2016). Some patients might experience the relationship as a threat because of its potential to evoke painful reflec-

tions that may emerge. How to manage the therapy relationship to promote metacognition and mentalization are described by proponents of both approaches (Bateman & Fonagy, 2006; Dimaggio et al., 2015; Lysaker et al., 2013) and probably it's the harder part of the psychotherapeutic work with these patients. To test if one year therapy can promote improvement in metacognition and consequently in other clinical variables we assessed metacognitive functions with MAI at baseline and after 1 year. To our knowledge it's the first time that longitudinal data on MAI Interview were analyzed, so it's hard to discuss this findings, that moreover are referred to a very small sample size.

The improvement in MAI Total score in MIT seemed a promising result because is statistically and clinically different from TAU, although the small sample size and even if the change is smaller than the significant change set in the original protocol. The change in MBT group instead was not significant, but these results cannot drive to any conclusion for at least four reasons. First of all the number of completers (with both data at baseline and follow-up) in MBT were just five, and in addition these patients show lower mean score on MAI at baseline and lower GSI Index, indicating a major severity. Moreover other longitudinal study on MBT considered longer therapy period, between 18 to 36 months (Laurenssen, et al, 2014). Finally another limitation was the use of MAI as the primary outcome measure, that could have foster MIT group because the author of the interview are the same of the MIT approach too. Beyond these premises and considering as preliminary these results, we could make some hypothesis starting from longitudinal sub-scale analysis. As shown in Fig. 4.11-4.14 the so called "typically Borderline" metacognitive deficits (Semerari et al, 2014) in Differentiating and Integration improved in both MIT and MBT groups. These trends were interesting from a clinical point of view and the lack of statistically significance can be due to the very small sample size and should be replicate in a large sample. Also the smaller improvement in Monitoring in MBT vs MIT can be interestingly linked to differences in therapy, with a more explicit approach to improve monitoring emotions in MIT and a more implicit in MBT. MIT

used in fact cognitive-behavioral therapy (Semerari, et al, 2008) in which explicitly therapist and patients works together to recognize and name emotions, and therapist improve this function with psychoeducational approach. In MBT instead the change in mentalization is obtained in a implicit (unconscious) way through the therapeutic relationship, so the recognition and naming of the emotions and specific mental states is not one of the main aim of the therapy. Moreover the low metacognitive profile of the completers in MBT group could have influenced all the results, as shown in other study (Gulestag,et al, 2012) in which baseline Mentalization, measured by Reflective Function (RF), was a moderator of the therapy effect. In particular in the first phase of the therapy patients with an higher RF at baseline improved more than patients with low RF, but this effect did not endure through the second period of the treatments (i.e., from 8 to 36 months). So we could speculate that the small improvement shown by our MBT sample would be larger with a better baseline MAI score and with a longer follow-up.

The secondary clinical outcomes of the study improved after 1 year of MIT, and even if the differences were not statistically significant, these were interesting data in order to deepen the study of the effect of MIT. Unfortunately the number of data at follow-up were small because at the initial small sample size and high number of drop-out we had to add some data missing on self reports, that make impossible to run other analysis on these data. As I mentioned before, it would be very interesting to replicate these analysis on a larger sample, in which we expect that differences could be also statistically significant. The correlation between DERS and TAS, BDI e IIP during time could be studied to deepen the relationships between these variables during time. In particular it would be interesting to verify the Structured Equation Model shown in study 1 with longitudinal data, but we'd need longer follow-up and especially a larger sample. We could speculate that TAS score or maybe Monitoring function score could be a mediator between the "typically borderline" metacognitive functions and emotion dysregulation that influence directly symptoms. If this hypothesis would be confirmed we

could guess that psychotherapy focused on metacognition/mentalization works on this "roads" while it would be interesting test the same idea with a different kind of psychotherapy, for example DBT (Linnehan, 1993) to verify if to work more directly on emotion dysregulation led to change in mentalization too, as speculated by Swenson et al (2015). In this interesting paper authors compared MBT and DBT to verify that even if the two approach originate from different theories, they share common elements. In DBT the therapist, having established a secure and important attachment relationship, stays focused on behavioral targets, and brings problem-solving tools, including skills, to help the patient be able to change. Anyway during these work mentalization/metacognition is needed and probably it develop during treatment, so an RCT with larger number and comparing MIT, MBT and DBT could help to better understand the role of metacognition and emotional regulation in BPD and the mechanism of change in therapy.

4.5 Strengths and limitations

This study has both strengths and limitations. It's the first study comparing directly MIT and MBT and using such a specific outcome on metacognition. The principal limitation of this study is due to its non-randomized design and the small sample size. Although we did not reveal any differences at baseline for the outcomes, the lack of randomization make our study less reliable and generalizable than a randomized one. Nonetheless it's very hard to find in Italy clinic specialized in psychotherapy for personality disorder and usually they have a specific approach and are located in different cities so it would be impossible to randomized patients to different approaches. The other main limitation is due to the small sample size that can affect the generalization of our results. Finally outcome was tested almost exclusively by using self-report measures, except of metacognition, and it would be interesting to assess the same variables with other kind of measures.

Beyond these limitations, recent influential review reported that existing therapies for borderline personality disorder remain experimental, and more "real-world" studies are necessary (Stoffers et al, 2012).

Chapter 5: CONCLUSION

In conclusion these results showed the central role of metacognition, alexithymia and emotion dysregulation in BPD and their relationship with symptomatology. The second study focused on longitudinal results of psychotherapy could help to deepen this topic, but further studies are needed.

Structural Equation Model results shown in cross-sectional study linked together MAI score, DERS score and clinical variables, and in particular showed that alexithymia was a mediator between metacognitive functions and emotion dysregulation (ED) and ED seemed to explain symptoms. Longitudinal results seemed to confirm the central role of Metacognition functions and ED in BPD psychotherapy even if the result were not robust due to the small sample size, that can affect the generalization of our results.

It has been demonstrated that metacognition functions and emotion dysregulation play an important role in BPD. In particular metacognition skills emerges in the context of the infant-caregiver relationship through early affect mirroring and is essential to the development of inter-subjectivity (Fonagy&Bateman, 2004) and emotion regulation, and our study deepen this topic. It seemed that Alexithymia mediate between these two aspects, probably linking together aspects measured by TAS sub-scales: “Difficulties in Describing/Identifying emotions” and “Monitoring” of metacognition abilities in one hand and “Externally-Oriented Thinking” with Emotion Dysregulation on the other hand. Moreover ED seemed to predict symptoms, in accordance with the study by Glenn (2009) in which ED exhibits a robust and unique relationship with BPD symptomatology.

Between metacognitive functions, deficit in differentiating and integrating appeared as central for this disorder, in accordance with other study (Semerari et al, 2015; Bateman&Fonagy, 2004). These patients showed problems with the ability to differentiate between representation and reality (differentiation), oscillating between a state where every representation is ex-

perienced as real and a state where the outside world seems imaginary and unreal (Bateman&Fonagy, 2006; Semerari et al, 2014). Moreover BPD patients typically failed in integration, as reported already by Clarkin et al. (1999), who emphasized the BPD patient's inability to consider multiple and contradictory representations of himself/herself and of others. Results of this study showed a significant improvement in these functions after 1 year of MIT therapy and a similar trend, even if not significant, in MBT group. Changes in these functions are crucial for this disorder and the results of our study it's promising because they're significant even with the small sample size. Unfortunately we couldn't drive any conclusion about the mechanism of change of these two different psychotherapy approaches, but it would be interesting to deepen this topic and understand how "two different roads" drive to such a similar destination. Results on correlations between changes during time in Emotion Dysregulation and the other clinical variables seemed promising and they could let us to speculate about the relationships these variables.

In conclusion, we can consider Prometeo Project as a pilot study that had highlighted some interesting sparks to be considered to plan an RCT with a larger sample on this topic in the future to confirm our results.

Chapter 6. APPENDIX

Fig. 6.1: DSM-IV criteria for Borderline Personality disorder (APA, 2000)

A pervasive pattern of instability of interpersonal relationships, self-image and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by 5 (or more) of the following:

1) Frantic efforts to avoid real or imagined abandonment. Note: Do not include suicidal or self-mutilating behaviour covered in criterion 5.
2) A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation.
3) Identity disturbance: markedly and persistently unstable self-image or sense of self.
4) Impulsivity in at least 2 areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating). Note: Do not include suicidal or self-mutilating behaviour covered in criterion 5.
5) Recurrent suicidal behaviour, gestures or threats, or self-mutilating behaviour.
6) Affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability or anxiety usually lasting a few hours and only rarely more than a few days).
7) Chronic feelings of emptiness.
8) Inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights).
9) Transient, stress-related paranoid ideation or severe dissociative symptoms.

Fig. 6. 2: DSM-5 criteria for Borderline Personality disorder (APA, 2013)

_ criteria A: moderate or greater impairment in personality functioning, manifested by characteristic difficulties in two or more of the following areas:

1. IDENTITY: markedly impoverished, poorly developed, or unstable self-image, often associated with excessive criticism; chronic feelings of emptiness, dissociative states under stress.
2. SELF-DIRECTION: instability in goals, aspiration, values or career plans.
3. EMPATHY: compromised ability to recognized the feelings and needs of other associated with interpersonal hypersensitivity; perception of others selectively biased toward negative attributes or vulnerabilities.
4. INTIMACY: intense, unstable, and conflicted close relationships, marked by mistrust, neediness, and anxious preoccupation with real or imagined abandonment; close relationship often viewed in extremes of idealization and devaluation and alternating between overinvolvement and withdrawal.

_ criteria B: four or more of the following seven pathological personality traits, at least one of which must be (5) Impulsivity, (6) Risk taking, (7) Hostility:

1. Emotional Lability (an aspect of Negative Affectivity): unstable emotional experiences and frequent mood changes; emotions that are easily aroused, intense and/or out of proportion to events and circumstances.

2. Anxiousness (an aspect of Negative Affectivity): intense feelings of nervousness, tenseness, or panic, often reaction to interpersonal stresses; worry about the negative effects of past unpleasant experiences and future negative possibilities; feeling fearful, apprehensive, or threatened by uncertainty; fears of falling apart or losing control.

3. Separation insecurity (an aspect of Negative Affectivity): fears of rejection by-and/or separation from- significant others, associated with fears of excessive dependency and complete loss of autonomy.

4. Depressivity (an aspect of Negative Affectivity): frequent feelings of being down, miserable, and/or hopeless; difficulty recovering from such moods; pessimism about the future; pervasive shame; feelings of inferior self-worth; thoughts of suicide or suicide behavior.

5. Impulsivity (an aspect of Disinhibition): acting on the spur of the moment in response to immediate stimuli; acting on a momentary basis without a plan or consideration of outcomes; difficulty establishing or following plans; a sense of urgency and shelf-harming behavior under emotional distress.

6. Risk taking (an aspect of Disinhibition): engagement in dangerous, risky, and potentially self-damaging activities, unnecessarily and without regard to consequences, lack of concern for one's limitation and denial of the reality of personal danger.

7. Hostility (an aspect of Antagonism): persistent or frequent angry feelings, anger or irritability in response to minor slights and insults.

Fig. 6.3: Pharmacological Guideline - Part 1 (APA, 2001)

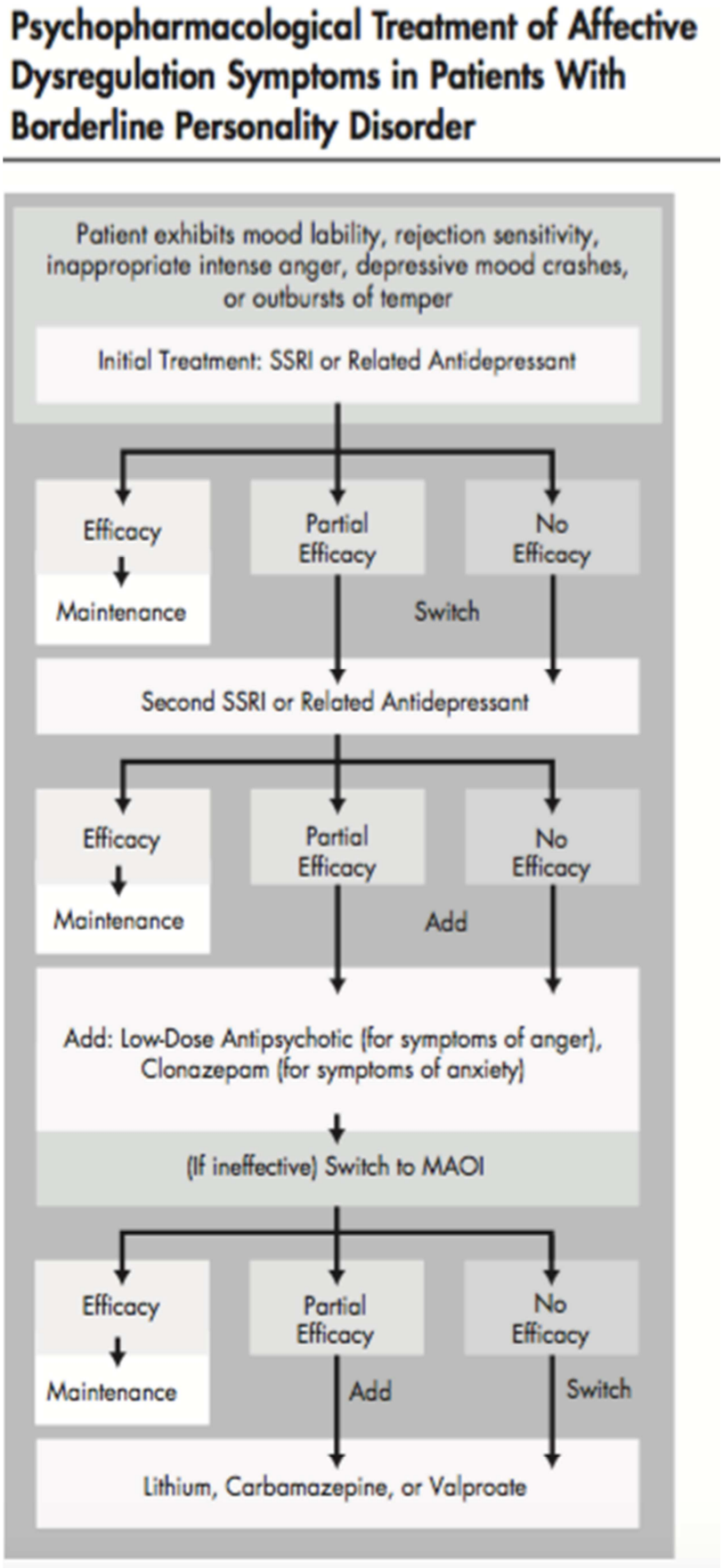
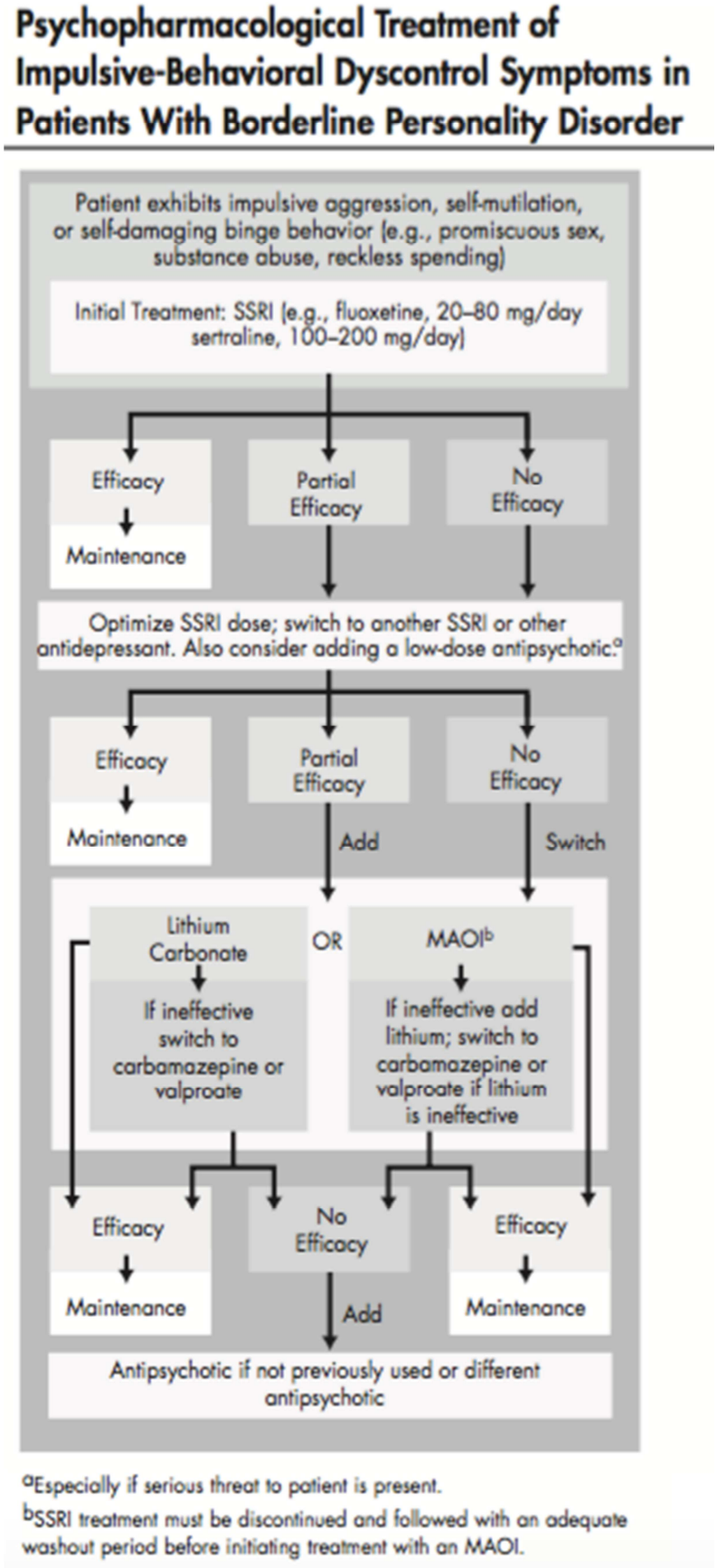


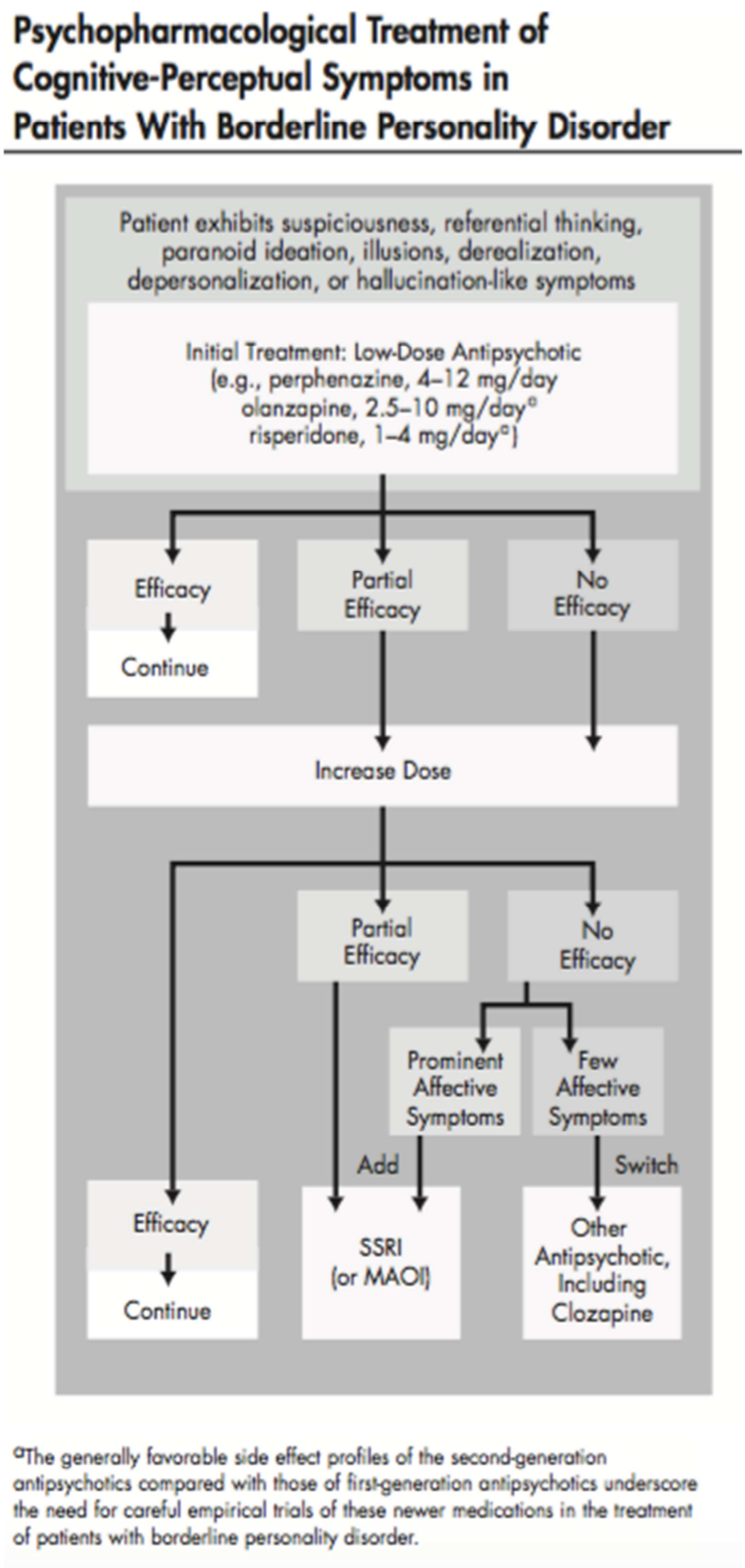
Fig. 6.4: Pharmacological Guideline - Part 2 (APA, 2001)



[a]Especially if serious threat to patient is present.

[b]SSRI treatment must be discontinued and followed with an adequate washout period before initiating treatment with an MAOI.

Fig. 6.5: Pharmacological Guideline - Part 3 (APA, 2001)



[a]The generally favorable side effect profiles of the second-generation antipsychotics compared with those of first-generation antipsychotics underscore the need for careful empirical trials of these newer medications in the treatment of patients with borderline personality disorder.

Fig. 6.6 Metacognition Assessment Interview (MAI) scoring sheet

		SCORE (range 1-5)
MONITORING (MON)	(a) the ability to recognize one's own representations (thoughts and beliefs);	
	(b) the ability to recognize and verbalize one's own emotions;	
	(c) the ability to establish relations among the separate components of a mental state; and	
	(d) the ability to establish relations between the components of mental states and behavior.	
	TOTAL MONITORING (range 4-20)	
INTEGRATION (INT)	(a) the ability to describe understandable and coherent links among thoughts, events, actions and behaviors;	
	(b) the ability to describe transitions among different mental states and explain the reasons why;	
	(c) the ability to form generalized representations of his/her mental functioning, taking into account continuity over time of patterns of thinking and feeling;	
	(d) the ability to reconstruct and describe to the interviewer one's own mental functioning, providing enough information, without giving irrelevant and out-of-focus details, and giving a sense of order and coherence to the discourse.	
	TOTAL INTEGRATION (range 4-20)	

DIFFERENTIATION (DIF)	(a) the ability to consider one's own representation of the world as subjective and questionable;	
	(b) the ability to give plausible interpretations of events;	
	(c) the ability to reflect on and evaluate events (as opposed to a tendency to act impulsively);	
	(d) the ability to distinguish between different modes of thoughts such as dreaming, fantasizing and imagining.	
	TOTAL DIFFERENTIATION (range 4-20)	
DECENTERING (DEC)	(a) the ability to recognize, define and verbalize other people's emotional inner state;	
	(b) the ability to recognize, define and verbalize other people's cognitive inner state;	
	(c) the ability to establish relations among the separate components of others' mental state; and	
	(d) the ability to establish relations between the components of others' mental state and their behavior.	
	TOTAL DECENTERING (range 4-20)	
	TOTAL MAI SCORE (range 16-80)	

Fig. 6.7 Baseline Data Sheet

Progetto ProMeTeO

PROTOCOLLO DI RILEVAZIONE DATI BASELINE pag.1/2

CODICE PAZIENTE_____

DATA RILEVAZIONE_____

DATI ANAGRAFICI

Data di nascita: _____ Sesso: [F] [M] Scolarità (anni)_____

Stato civile:

1_[nubile/celibe] 2_[coniugata/o] 3_[separata/o-divorziata/o] 4_[vedova/o] 5_[convivente]

Condizione lavorativa:

1_[disoccupato] 2_[invalido] 3_[occupazione protetta] 4_[occupazione non protetta]

5_studente

INFORMAZIONI CLINICHE

Diagnosi principale: _____

Comorbidità asse I: _____

Comorbidità asse II: _____

Età di esordio malattia psichiatrica:_____

Durata di malattia: _____

Età primo contatto con i servizi psichiatrici:_____

Numero ricoveri in SPDC nel corso della vita_____

Numero di ricoveri in altri servizi psichiatrici_____

Tipologia: [1] comunità terapeutiche [2] cliniche specialistiche [3] altro _____

Precedenti psicoterapie [SI'] [NO] Durata (mesi)_____ Tipolo-

gia_____

Familiarità psichiatrica [SI'] [NO]

Abuso di alcool [SI'] [NO]

Storia dell'abuso di alcool: [attuale] [pregresso] N° anni_____

Abuso di sostanze [SI'] [NO] **(35)** Tipologia: [Monoabuso] [Poliabuso]

Sostanza/e_____

Storia dell'abuso di sostanze: [attuale] [pregresso] N° anni_____

PROTOCOLLO DI RILEVAZIONE DATI BASELINE pag.2/2

Esperienze traumatiche/stressanti [SI'] [NO] Tipologia_____

Tentativi di suicidio [SI'] [NO] Numero di tentativi di suicidio: _____

Autolesionismo [SI'] [NO] Frequenza: [saltuaria] [abituale] Modalità_____ Eteroaggressività [SI'] [NO] Frequenza: [saltuaria] [abituale]

CRITERI DIAGNOSTICI BPD

Sforzi disperati di evitare un reale o immaginario abbandono [SI'] [NO]

Un quadro di relazioni interpersonali instabili e intense, caratterizzate dall'alternanza tra gli estremi di iperidealizzazione e svalutazione [SI'] [NO]

Disturbi dell'identità: sé instabile [SI'] [NO]

Impulsività in almeno due aree che sono potenzialmente dannose per il soggetto (quali spendere, sesso, abuso di sostanze, guida spericolata, abbuffate) [SI'] [NO]

Ricorrenti minacce, gesti, comportamenti suicidari o comportamento automutilante [SI'] [NO]

Instabilità affettiva (durata breve) [SI'] [NO]

Vuoto [SI'] [NO]

Rabbia immotivata e intensa o difficoltà a controllare la rabbia (esempio frequenti accessi di ira o rabbia costante o ricorrenti scontri fisici) [SI'] [NO]

Ideazione paranoie transitoria e legata allo stress o sintomi dissociativi [SI'] [NO]

TERAPIA FARMACOLOGICA

Antipsicotici tipici [SI'] [NO] Antipsicotici atipici [SI'] [NO]

SSRI [SI'] [NO] SNRI [SI'] [NO] Triciclici [SI'] [NO] IMAO [SI'] [NO]

Stabilizzatori dell'umore [SI'] [NO]

Benzodiazepine [SI'] [NO]

FARMACI NON PSICHIATRICI: _____

COMORBIDITA' MEDICHE:

Tiroide [SI'] [NO] Diabete [SI'] [NO] Epatite [SI'] [NO]

HIV [SI'] [NO] Trauma cranico [SI'] [NO] Ipertensione [SI'] [NO]

Anemia [SI'] [NO] Ictus/TIA [SI'] [NO] Altro, specificare_____

Chapter 7

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