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**TOWARD A NEW MODEL OF BORDERLINE
PERSONALITY DISORDER: A
PSYCHOPHYSIOLOGICAL APPROACH ON
THE LINK BETWEEN EMOTIONAL AND
BEHAVIORAL DYSREGULATION**



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Abstract

Borderline personality disorder (BPD) is one of the most studied personality disorders, given its prevalence and the severity of its symptoms. In the last years several models of the disorder were presented, however no one of this theoretical conceptualization is completely supported by literature. The aim of this thesis is to present an evidence-based alternative model of the disorder. A central core in BPD pathology is related to the connection between emotional and behavioural dysregulations that characterize these subjects. Emotional dysregulation processes in BPD subjects seem to be elicited by specific difficulties in difficulties in neuroception -the unconscious perception of dangers and threats present in the subject's surroundings- rather than being generally triggered. This could be due to differences in analyzing social contexts given by attentional and cognitive biases and to the ruminative states caused by the difficulties reported in the social environment. The studies presented in this dissertation analyzes the effect of negative affective states on executive performance, emotional response, and attentional biases, in response to socio-emotional cues, and the efficacy of a mindfulness exercise in reducing negative affective states. Self-reported, behavioural, physiological and eye-tracking data were collected and analyzed during the tasks. Finally, starting from the results obtained in these studies, and the data presented in literature a model of BPD emotional functioning will be presented.

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Acronyms and abbreviations

Amsterdam Resting State Questionnaire	ARSQ
Autonomous nervous system	ANS
Basolateral nucleus of the amygdala	BLA
Beck Depression Inventory -II	BDI-II
Berg card sortig test	BCST
Borderline Personality Disorder	BPD
BPD group that underwent the negative paradigm	BPDN
BPD group that underwent the neutral paradigm	BPDO
Central nucleus of the amygdala	CeA
Childhood Trauma Questionnaire	CTQ
Confidence interval	CI
Corticotropin-releasing hormone	CRH
Cyclic components accountable for HR variability	SDNN
Diagnostic and statistical manual of mental disorders	DSM-5
Dialectical Behavioural Therapy	DBT
Difficulties in Emotion Regulation Scale	DERS
Dorsal Motor Nucleus	DMNX
Dorsolateral periaqueductal gray matter	dIPAG
Grey Matter Volume	GMV
HC group that underwent the negative paradigm	HCN
HC group that underwent the neutral paradigm	HCO
Healthy control	HC
Heart rate variability	HRV
Heart rate variability	HR

Hypothalamic-pituitary–adrenal	HPA
Locus coeruleus	LC
Mindfulness Observing and Describing Questionnaire	MODQ
Negative affectivity	NA
Non-suicidal self-injuring	NSSI
Nucleus Ambiguus	NA
Nucleus of solitary tract	NTS
Orbitofrontal cortex	OFC
Personality Disorder	PD
Personality Inventory for DSM-5	PID-5
Positive affectivity	PA
Positive and Negative Affect Schedule	PANAS
Square root of the mean squared differences of successive NN intervals	RMSSD
Sympathetic nervous system	SNS
Theory of Mind	TOM
ventral rostromedial medulla	RVMP
Ventrolateral periaqueductal gray matter	vIPAG
Ventromedial prefrontal cortexes	VmPFC

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Introduction

The aim of this first chapter is to introduce to the reader the theoretical background that drove the research that I've conducted during my Ph.D. The final aim of this dissertation is to give new insights on Personality Disorder (BPD), one of the most studied and diagnosed personality disorder (e.g., Chou, Goldstein, Huang, Stinson, Saha et al., 2008; Zimmerman, Rothschild e Chelminski, 2005). Borderline personality disorder is particularly studied for the severity of its symptoms, which include self-injuring, suicide attempts, anxiety and aggression, depressivity and affective instability, which could be very dangerous for the patients and require immediate support and intervention (Van Asselt, Dirksen, Arntz, & Severens, 2007). In the last three decades, a huge number of studies and data have been published on BPD, leading to the creation of several models and clinical approaches of the disorder (e.g., e.g., Linehan, 1993; Fonagy, Target, & Gergely, 2000; Judd & McGlashan, 2003; Kernberg, 1967). The most used and studied model is the Biosocial model (Linehan, 1993) which provided an important clinical theory which describe the emotional dysregulation as the main dysfunction of BPD subjects. These emotional difficulties surges in the patients from a specific combination between biological vulnerabilities and specific environmental situations. A detailed description of Linehan's theory will be proposed later in the introduction chapter. A wide number of studies were conducted to empirically validate the model, however mixed and non-conclusive results were found. Given the importance of the Biosocial model in the development of clinical approaches to BPD (i.e., the Dialectical Behavioural Therapy) and the non-complete support for the theory, further studies are needed to better understand BPD emotional functioning. Moreover, giving the increasing number of studies analyzing the neurobiology of the disorder, the natural and logic evolution of theoretical model of BPD should include considerations regarding the neural functioning of the patients. A complete theoretical model should be able to describe both the mechanisms engaged at cognitive and neural levels. After an introductory chapter describing the emotional, cognitive and social functioning of BPD patients, five studies will be presented. The first study will study how negative affective

states affect the executive and attentional functioning in BPD patients. Then, two studies on social functioning will be presented, to test the hypothesis of a specific pattern of reactivity specifically related to the socio-emotional cues. Finally, two studies testing the efficacy in modulating psychophysiological activity of a specific intervention (i.e., mindfulness) will be presented. Starting from the data obtained in these studies and the evidence in literature, in the discussion chapter a theoretical model of BPD will be presented.

Borderline personality Disorder, a general introduction

Borderline Personality Disorder is one of the most studied Personality Disorders (PD, Chou, Goldstein, Huang, Stinson, Saha et al., 2008) and one of the most diagnosticated in the clinical population (Gunderson, 1984; Lieb, Zanarini, Schmahl, Linehan, Bohus, 2004; Zimmerman, Rothschild e Chelminski, 2005). The prevalence of people with BPD is around 3% in the general population, and it is diagnosticated between 30% and 60% in the population of people with a diagnosis of a PD (Lenzenweger, Lane, Loranger e Kessler, 2007; Trull, Jahng, Tomko, Wood, Sher, 2010; Widiger & Trull, 1993).

According to the fifth edition of the Diagnostic and statistical manual of mental disorders (DSM-5), BPD is characterized by a pervasive pattern of instability in interpersonal relationships, identity, impulsivity, and affect; it begins by early adulthood, and it is manifested in a variety of contexts (APA, 2013). One of the core characteristics of BPD is that clinical manifestations of the disorder include dangerous and self-destructive behaviours (e.g., Brown, Comtois, & Linehan, 2002; Oldham, 2006; Turner, Dixon-Gordon, Austin, Rodriguez, Rosenthal, & Chapman, 2015).

To diagnose BPD, according to the section II of DSM-5 (APA, 2013), the patient must present five criteria:

1. Desperate efforts to avoid abandonment whether is real or imagined (Note: Do not include suicidal or self-mutilating behaviour covered in Criterion 5).

People with BPD are characterized by a rejection sensitivity. When BPD patients perceive to have lost the other member of the relationship, they perceive a negative schema of aloneness and try in every possible way to avoid these feelings (e.g., Staebler, Helbing, Rosenbach, & Renneberg, 2011).

2. A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation.

This criterion is strongly related to the first one. The fear of losing a significant one will create a pattern of unstable relationships, where the other person is usually idealized or devaluated, creating intense and contradictory relationships.

3. Identity disturbance: markedly and persistently unstable self-image or sense of self.

Borderline patients tend to self-judge increasing or decreasing his/her self-esteem depending on the circumstances he/she is living. In fact, people with BPD are usually characterized by negative schemas of dependency, unlovability, lack of personal control, badness, interpersonal distrust, and vulnerability (Arntz, Dietzel, & Dreessen, 1999; Butler, Brown, Beck, & Grisham, 2002).

4. Impulsivity in at least two areas that are potentially self-damaging (e.g., promiscuous and unprotected sexual intercourses, substance abuse, reckless driving, binge eating). (Note: Do not include suicidal or self-mutilating behaviour covered in Criterion 5).

To reduce the sense of void and loneliness, BPD patients try to escape from feelings through the abuse of alcohol or drugs. However, once calmed the feelings of loneliness,

feelings of shame and guilt take over, driving the patients to find a way out of these negative feelings and creating a vicious loop (Kreisman & Straus, 2010).

5. Recurrent suicidal behaviour, gestures, or threats, or self-mutilating behaviour.

As stated above, self-harm, suicidal behaviours, and high-risk activities are usually acted by people with BPD to reduce emotional activity (Kleindienst, Bohus, Ludascher, 2008). Dulit (1994) and Lieb (2004) show how 50-90% of BPD population commit self-injuring behaviours. Moreover, these behaviours seem to be acted by BPD patients to elicit a response from their environment (Linehan, 2011).

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).

As other disorders (e.g., Major Depressive Disorder and Bipolar Disorder), BPD patients are characterized by continuous shifting in mood. However, usually, these fluctuations only last for hours/days (Kreisman & Straus, 2010).

7. Chronic feelings of emptiness.

Those feelings are usually perceived as a combination of physical and psychical sensations. Usually, these feelings are the ones that drive the patients to commit impulsive behaviours

8. Inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights).

Historically, the inability to cope with rage and anger is a common element of BPD throughout all the DSM editions (Linehan, 2011). This could be due both to a genetic factor or an environmental cause (Kreisman & Straus, 2010).

9. Transient, stress-related paranoid ideation, or severe dissociative symptoms.

This feature of BPD is shared with psychotic disorder. In both pathologies, patients could undergo experiences of detachment from reality. As for criterion 6, to have a differential diagnosis, the duration of these episodes should be considered: BPD patients tend to perceive these feelings in the temporal magnitude of hours/days (Kreisman & Straus, 2010).

It is important to underline that the requirement of 5 criteria over 9 to get a diagnosis of BPD makes this disorder extremely heterogenic. In fact, two people might share a diagnosis of BPD but only with one diagnostic criterion in common.

The categorical diagnosis is not the unique way to diagnose BPD presented in the DSM-5 (APA, 2013). The approach reported in Section III of DSM-5 presents an alternative model to help in PDs diagnosis. This model is represented by a hybrid dimensional and categorical approach in the diagnosis of PDs (Morey, Benson, Busch, & Skodol, 2015). The model evaluates personality on a continuum and is focused on personality impairment related to the functioning of the subject in relation to self and the interpersonal functioning. Moreover, DSM-5 section III describes the PDs not as a discrete categorical entity but as maladaptive and extreme alternatives of common personality dimensions (Suzuki, Samuel, Pahlen, & Krueger, 2015; Widiger, & Trull, 2007). This hypothesis is supported by the study of Suzuki and colleagues (2015), which shows that most DSM-5 dysfunctional traits could be seen as an extreme version of four of the traits presented in the Five Factor Model (i.e., Neuroticism, Extraversion, Openness, Conscientiousness, and Agreeableness) (Suzuki, Samuel, Pahlen Krueger, Robert, 2015).

This new conceptualization, presented in Section III of DSM-5 permits to diagnose six different PDs, namely: Borderline Personality Disorder, Obsessive-Compulsive Personality Disorder, Avoidant Personality Disorder, Schizotypal Personality Disorder, Antisocial Personality Disorder, Narcissistic Personality Disorder. In Section III BPD is

defined as characterized by instability of self-image, personal goals, interpersonal relationship, and affects. Moreover, other characteristics of BPD reported in this section are impulsivity, risk-taking, and hostility.

The criteria to diagnose BPD presented In Section III of DSM-5 are:

A) a Moderate or greater impairment in personality functioning, manifested by characteristic difficulties in two or more of the following four areas:

1) Identity: Markedly impoverished, poorly developed, or unstable self-image, often associated with excessive self-criticism; chronic feelings of emptiness; dissociative states under stress.

2) Self-direction: Instability in goals, aspirations, values, or career plans.

3) Empathy: Compromised ability to recognize the feelings and needs of others associated with interpersonal hypersensitivity (i.e., prone to feel slighted or insulted); perceptions 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 relationships often viewed in extremes of idealization and devaluation and alternating between overinvolvement and withdrawal.

And B) Four or more of the following seven pathological personality traits, at least one of which must be Impulsivity, Risk-taking, or 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 in 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 and suicidal behaviour.

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 self-harming behaviour 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 limitations 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.

Finally, BPD is a disorder characterized by high levels of comorbidity. The main co-diagnosis are mood disorders (e.g., Major Depressive Disorder and Bipolar Disorder), eating disorders (e.g., Bulimia Nervosa), substance use disorder, and post-traumatic stress disorder (APA, 2013; Leichsenring et al., 2011). In detail, around of BPD patients meet criteria for other psychiatric (84,5%) and personality (73,9%) disorders lifetime (Grant, Chou, Goldstein, Huang, Stinson, Saha et al., 2008, Lenzenweger, Lane, Loranger, & Kessler, 2007). The manifestation of BPD seems to be different between males and females (Sansone & Sansone 2011). Women seems to be characterized by depressive, anxious and obsessive-compulsive states. Moreover, BPD female population seems to be characterized by cognitive dysfunction and negative affective states. Women with BPD are more likely to evidence eating, mood, anxiety, and posttraumatic stress disorders, and Histrionic personality Disorder in comorbidity. On the other hand,

male subjects with BPD seem to be more characterized by impulsivity and comorbidity with Antisocial and Narcissistic Personality Disorder and Substance Use Disorder.

The Biosocial model

Many clinical models were developed to study BPD (e.g., Linehan, 1993; Fonagy, Target, & Gergely, 2000; Judd & McGlashan, 2003; Kernberg, 1967). The most used and studied is the Biosocial Model proposed by Marsha Linehan in 1993. According to this model, continuous interaction between a biological vulnerability and an invalidating environment is the main cause that generates emotional dysregulation, the main core of the disorder. According to this model, emotional dysregulation is caused by inadequate functional emotional regulation skills learning. Moreover, this model strongly supports the idea that emotional dysregulation is biologically and physiologically based.

The biological vulnerability identified in the Biosocial model is manifested in three main aspects that characterize BPD subjects according to the Biosocial model: hypersensitivity, hyperreactivity, and the slow return to baseline (Linehan, 1993) and, according to the model these three component are supported by physiological data, often measured through the study of the heart rate variability (HRV).

Mixed data are reported in the literature for hypersensitivity. *Hypersensitivity* is defined as the tendency to react to emotional cues, in particular negative ones, to react in a fast way and to consider low-intensity emotional stimuli as highly activating. Several studies were conducted to test whether empirical data support this construct. Many studies report higher basal activity for both emotional and physiological indexes in BPD patients compared to healthy controls (HC) and other psychopathological disorders. With BPD patients reporting higher negative emotional activity and higher self-reported arousal (e.g., Bland, Williams, Scharer, & Manning, 2004; Cheavens & Heiy, 2011; Bortolla, Cavicchioli, Galli, Verschure & Maffei, 2019, Bortolla, Galli, Ramella, Sirtori, Visintini & Maffei, 2020; Ebner-Priemer & Sawitzki, 2007; Elices, Soler, Fernandez, Martin-Blanco, Portella; Perez et al., 2012; Kuo & Linehan, 2009;) and lower vagal indexes at baseline levels (e.g., Bortolla et al., 2020, Koenig, Kemp, Feeling, Thayer, & Kaess, 2016; Kuo & Linehan, 2009; Weinberg, Klonsky, & Hajcak, 2009). On the other hand, other studies did not show support for a lower vagal activity

at basal level in BPD patients (e.g., Bortolla et al., 2019; Herpertz, Werth, Lukas, Qunaibi, Schuerkens et al., 2001; Lobbestael, Arntz, Cima, & Chakhssi, 2009; Schmahl, Elzinga, Ebner, Simms, Snisloiw, Vermetten et al., 2004; Taylor & James, 2009).

Hyperreactivity is defined as an enhanced response to emotional stimuli in terms of an extreme reactivity to emotional cues or higher changes in the intensity of the emotional responding after a presentation of an emotional trigger (Linehan, 1993). Several studies were conducted to test the hyperreactivity hypothesis in BPD patients. Mixed results were found regarding self-reported arousal and emotion intensity in response to emotional cues. While several studies reported higher intensity in emotion and arousal (e.g., Bortolla et al., 2019, Bortolla et al., 2020, Bichescu-Burian, Steyer, Steinert, Grieb, & Tschöke, 2016; Elices et al., 2012), other did not show these differences of reactivity in BPD patients (e.g., Baschnagel, Coffey, Hawk Jr, Schumacher, & Holloman, 2013; Herpertz, Kunert, Schwenger, & Sass, 1999; Herpertz et al., 2001; Kuo & Linehan, 2009). On the other hand, a recent metanalysis showed no pattern of physiological hyperreactivity in BPD patients (Bortolla, Cavicchioli, Fossati, Maffei, 2020).

Finally, the *Slow return to the baseline* could be described as a prolonged high-arousal state leading to impaired habituation (Linehan, 1993; Cavazzi & Becerra, 2014). Very few studies were conducted to study this topic. Still this last construct seems well-supported by the literature, which shows how BPD patients reported high physiological arousal over time (Austin, Riniolo, Porges, 2007), slower habituation to emotional cues (Dziobek, Preißler, Grozdanovic, Heuser, Heekeren, & Roepke, 2011) and social stressors (Weinberg, Klonsky, Hajack, 2009). Figure 1.1 represent the biological vulnerability of BPD subjects according to the Biosocial Model.

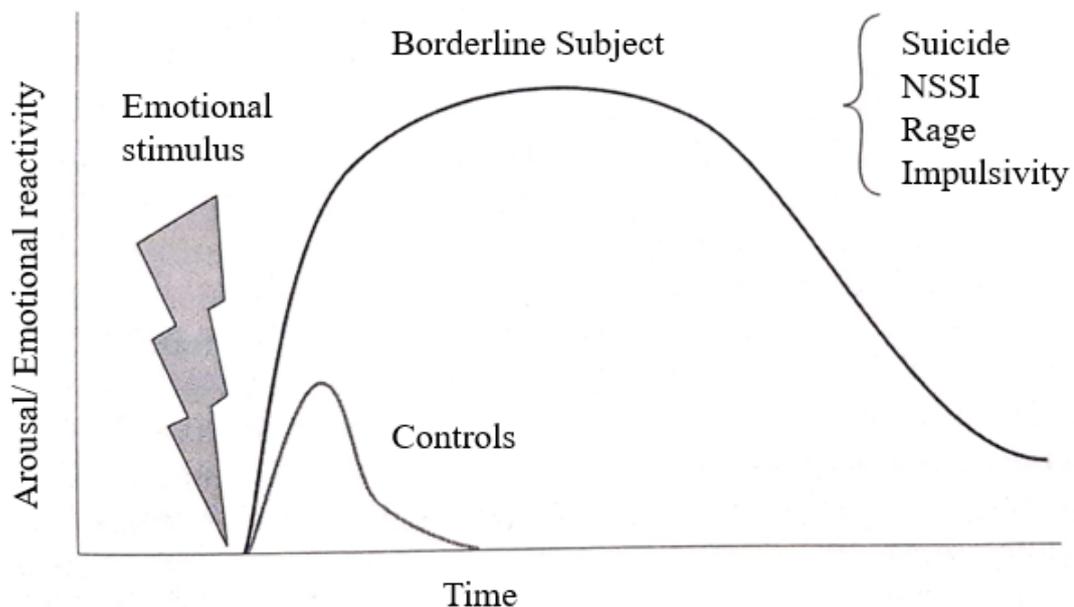


Figure 1. 1 Biological vulnerability in BPD patients (Adapted from “Oltre la Personalità” Maffei 2021)

The other fundamental core in the Biosocial model is an invalidating social environment. This refers to an environment characterized by intolerance, to the expression of the emotional responses, in particular to the emotions that are not supported by external and observable events (Crowell, Beauchaine & Linehan, 2009). This leads the child to express only extreme emotions, which are the only ones reinforced and that could produce a reaction in the significant other (Linehan, 1993). However, these emotions are unwarranted, which impedes the subjects from learning adequate emotion regulation strategies and understanding, labelling, and tolerating strong emotional activity (Crowell et al., 2009). Finally, these invalidating processes are self-adopted by the child during the development, leading to shame, self-criticism and self-punishment (Linehan, 1993).

The study and the validation/innovation of the Biosocial model are fundamental since this model was originally formulated to guide the treatment of BPD patients.

In detail, one of the most used approaches to treat BPD patients, based on the Biosocial model, is Dialectical Behavioural Therapy (DBT) (Linehan, 1993). This therapeutic approach tackles the difficulties in emotion regulation, and it is based on

giving BPD patients emotion regulation skills and helping these subjects accept their current emotional state. Accordingly, treatment strategies focus on helping patients develop a greater acceptance of self, others, and life in general through a dialectical stance between acceptance and change strategies (Robins & Rosenthal, 2011). The efficacy of DBT has been demonstrated by several experimental studies (for a review, see: Kliem, Kröger, & Kosfelder, 2010; Panos, Jackson, Hasan, & Panos, 2014). In detail, DBT showed efficacy in reducing maladaptive and self-destructive behaviours and improving patient compliance for both BPD outpatients and inpatients (Bloom, Woodward, Susmaras, & Pantalone; 2012), showing reductions in suicidal ideation, self-injurious behaviours, and symptoms of depression and anxiety. Finally, symptom reduction resulted stable between 1 and 21 months after the treatment (Bloom et al., 2012). The goal and the overall purpose of DBT are represented by the development, in borderlines, of behavioural patterns of a dialectical type. This means helping the patients to assume a dialectical way of thinking and helping them in changing their extreme responses in favour of more integrated and functional behaviours (Linehan, 1993). Given the centrality of emotional dysregulation in disorder, the therapy goes toward two goals: to ensure that the patient learns how to regulate, manage, and control their emotion, reduce maladaptive behaviours; and validate their thoughts, emotions, and actions. The treatment consists of four parts:

- weekly individual psychotherapy.
- weekly group training.
- the availability of a telephone consultation when needed.
- interviews between therapists who use DBT.

The primary goal is to reduce suicidal behaviours, behaviours that interfere with treatment and to moderate those that interfere with the quality of life, improving behavioural skills (Linehan, 1993).

Emotional Regulation

As stated above, emotional regulation difficulties are central in BPD. Emotion regulation is conceptualized as the usage of adaptive ways of responding to emotional distress, rather than referring to the control of emotion or the dampening of emotional arousal in general (Gratz & Roemer, 2004). This conceptualization not only emphasizes the functionality of all emotions but in addition defines emotion regulation as a multidimensional construct including the awareness, understanding and acceptance of emotions; the ability to engage in behaviours directed to a goal and the inhibition of impulsive behaviours when facing a negative emotion (Gratz & Tull, 2010).

On the other hand, emotion managing could present opposite and less functional strategies and behaviours, such as experiential avoidance, altered attentive state (such as rumination), and emotional suppression. As stated before, core characteristics of BPD are related to difficulties in managing emotional regulation in daily-life functioning. Emotion dysregulation was defined by Gratz and Roemer (2004) as a multidimensional construct concerning: A lack of comprehension and understanding of the perceived emotion,

the difficulty in accessing and selecting adaptive strategies for regulating the intensity and duration of the emotion, an unwillingness to experience emotional distress as a part of reaching the desired goal, and the incapacity of selecting goal-directed behaviours when experiencing distress.

Altogether, emotional dysregulation seems to be related to strategies of emotional experiences avoidance, difficulties in information processing and arousal regulation, inability to control impulsive behaviours and select and engage goal-directed behaviours when emotionally aroused (Linehan, Bohus, & Lynch, 2007). As stated before, these features are characteristics and play a central role in BPD. In fact, borderline patients are reported to present high levels of alexithymia (Loas, Speranza et al., 2012; New, Rot, Ripoll, Perez-Rodriguez, Lazarus, Zipursky et al., 2012), to use avoidance strategies when facing an emotional stimulus (Bortolla, Galli, Ramella, Sirtori, Visintini & Maffei et al., 2020; Bortolla, Cavicchioli, Galli, Verschure & Maffei, 2019), rumination (Baer & Sauer, 2009; Selby & Joiner, 2009), thought suppression (Cavicchioli, Rugi, & Maffei, 2015; Cheavens et al., 2005; Rosenthal,

Cheavens, Lejuez, & Lynch, 2005); and present difficulties elicited by emotional distress during goal-directed behaviour (Gratz, Rosenthal, Tull, Lejuez, & Gunderson, 2006) and in strategies selection.

A model that can describe the role of maladaptive strategies of BPD in emotion and behaviour regulation is the Emotional Cascade Model proposed by Selby and Joiner (2009). In this model, ruminative states are considered a central node in behavioural dysregulation. In detail, rumination plays a role in enhancing the intensity of negative affective states which in turn increase rumination creating a self-perpetuating loop. Maladaptive behaviours help BPD patients in shifting their attention from negative triggering situations and this close emotional loop, interfering with ruminative thoughts.

In detail, rumination is a process of uncontrolled, narrowly focused negative thinking that is often self-referential, with negative content that could be considered as a constrained part of mind-wandering (van Vugt & van de Velde, 2018). Although mind-wandering (i.e., stimulus-independent thoughts that state the independence of experiences from sensory perceptions and ongoing actions (Giambra, 1989)) could also be connected to positive thoughts (e.g., goal-oriented problem solving, theory of mind) (Schooler Mrazek, Baird & Winkielman, 2014), it is usually associated to negative thoughts (Smallwood & Schooler, 2015, Andrews-Hanna et al., 2014), negative mood (Smallwood & O'Connor, 2011) and sadness (Andrews-Hanna, Smallwood & Spreng, 2014). As stated by a study recently published (Bortolla & Galli, Spada, Maffei, 2021), mind-wandering is reported to be associated with reduced levels of happiness in both non-clinical (Hobbiss, Fairnie, Jafari & Lavie, 2019) and clinical samples (Handy & Kam, 2015). Mind-wandering states could become a risk factor for health whenever it becomes a rigid, inflexible, and perseverative pattern focused specifically on negative thoughts, such as ruminative states in BPD (Ottaviani, Shapiro, & Couyoumdjian 2013). So far, few studies have been conducted on psychophysiological aspects of mind-wandering in clinical and healthy populations. Literature suggests that mind-wandering states might be directly connected to increased physiological activity (Smallwood, Heim, Finnigan, Sudberry, O'Connor, & Obonsawin, 2004; Smallwood, O'Connor, Sudberry, Haskell, & Ballantyne, et al., 2004). This could be due to the presence of negative perseverative thoughts during mind-wandering which seems to relate to a higher Heart Rate and a lower level of HRV (Ottaviani et al., 2015). On the other hand,

emotional regulation overlaps largely with the mindfulness ability of the subject (Grazt & Roemer, 2010), given its focus on observing and describing the emotional state and focusing on present-moment activities even in distressing contexts. In fact, mindfulness might be defined as the ability to focus one's attention on the present moment in a non-judgmental way (Kabat-Zinn, 1994) and a tolerant observation of incoming and outgoing stimuli (Baer, 2003). According to recent theories, the construct of mindfulness embodies two aspects: a specific orientation to experience characterized by curiosity, openness and acceptance, and self-regulation of attention (Baer, 2003; Bishop, Lau, Shapiro, Carlson, Anderson, Carmody et al., 2006). Mindfulness practice can also be used in the context of individual therapy. Mindfulness abilities help the patient in managing their emotions through four intersecting ways: increasing attentional control, increasing awareness of internal experiences, decreasing impulsivity, and improving self-validation (Lynch, Rosenthal, Kosson, Cheavens, Lejuez & Blair 2006).

As stated before, an invalidating environment leads to self-invalidation, thought suppression or avoidance. However, thought suppression and avoidance could lead to a paradoxical increase in ruminative thoughts (Gross & John, 2003). The purpose of mindfulness is to convey a way of relating to the experience that is accepting and non-judgmental. The ability to stay focused on a task – the ability that characterizes mindfulness practice - seems to oppose the mind's tendency to wander. Mindfulness pursuit would reduce the dysfunctional aspects of mind-wandering, especially negative thoughts and anxious future planning. Mindfulness experience is expected to decrease mind-wandering, improving cognitive control processes and metacognitive awareness (Chiesa & Serretti, 2011; Dorjee, 2016; Jo, Malinowski & Schmidt, 2017; Tang, Hölzel & Posner, 2015). In addition, the mindfulness effect in reducing wandering thoughts might be reflected in the increased autonomic flexibility (i.e., high HRV) reported by previous studies (e.g., Christodoulou, Salami & Black, 2020; Ditto, Eclache & Goldman., 2006; Peressutti, Martín-González, García-Manso & Mesa, 2010), which is associated to the individual ability to adequately regulate emotional and cognitive states (Thayer, Hansen, Saus-Rose, & Johnsen, 2009). The practice that has shown promising results in avoiding wandering thoughts -even without previous specific training- is related to breathing observation (Mrazek, Smallwood & Scholer, 2012). Finally,

mindfulness and meditation practices have been shown to rewire brain circuitry to produce beneficial effects (Ricard, Luz & Davidson et al., 2014). In detail, the brain areas that seem more affected by meditation and mindfulness are the ACC, insula, OFC, the hippocampus, and amygdala (e.g., Taren, Creswell, & Gianaros, 2013; Taren, Gianaros, Greco, Lindsay, Fairgrieve, Brown et al., 2015).

In summary, the literature points out serious difficulties in the ability to manage and regulate emotion in BPD. Emotional dysregulation in BPD patients is reported to be related to a transactional interaction between a biological vulnerability (physiologically measurable), and an invalidating environment (Linehan, 1993). Emotional dysregulation in BPD patients is manifested through the usage of strategies of emotional avoidance, deficits in information processing and arousal regulation, inability to control impulsive behaviours and select and engage goal-directed behaviours (Linehan, Bohus, & Lynch, 2007). According to the model of emotional regulation proposed by Gratz e Trull (2010), a mindfulness approach to emotional difficulties could help patients in regulating emotion. However, so far, no studies were conducted on the analysis of the efficacy of a mindfulness exercise in modulate physiological and affective states in BPD patients. To better understand BPD pathology is necessaire expand our knowledge on emotional, behavioural functioning of these subject and on possible solution to emotional difficulties.

Behavioural dysregulation

As stated above, behavioural dysregulation is a central characteristic of BPD. Several studies support the hypothesis that emotional dysregulation could be the basis of BPD behavioural dysregulation. Non-suicidal self-injuring (NSSI) behaviours are acted to relieve an emotional situation perceived as hostile and overwhelming (Brown, Comtois & Linehan, 2002; Klonsky, 2007). Main self-destructive behaviours regard cutting (80%), burning (20%), biting (7%), banging head (15%), and other self-damaging acts (24%) (Andrews, Hulbert, Cotton, Betts, & Chanen et al., 2017). One of the major reasons reported by BPD in clinical trials on why committing NSSI is the willingness to reduce the experienced negative arousal and regulate the emotional state (Klonsky,

2007). Suicidal and parasuicidal behaviours are frequently reported in BPD (APA, 2013). According to literature, the percentage of BPD subjects which present a history of NSSI range from 50% to 90% (Dulit, Fyer, Leon, Brodsky, & Frances, 1994; Soloff, Lis, Kelly, Cornelius, & Ulrich, 1994; Wedig, Silverman, Frankenburg, Reich, Fitzmaurice, & Zanarini, 2012; Zanarini, Laudate, Frankenburg, Wedig, & Fitzmaurice, 2013; Zanarini Frankenburg, Reich, Fitzmaurice, Weinberg, & Gunderson, 2008). Self-injuring behaviours, together with the average level of impulsivity and depression, seems to be a good predictor for completed suicide (Chapman, Specht, & Cellucci, 2005; You, Lin, & Leung, 2015). Around 9% of BPD subjects end their life committing suicide (Pompili, Girardi, Ruberto, & Tatarelli, 2005). Even though there are some overlapping, suicidal and non-suicidal behaviours present differences. While suicide attempts seem to be related more to demonstrative behaviours toward others, NSSI are more often connected to expressing frustration and anger, distracting oneself, coping with negative emotional states, or punishing oneself (Brown, Comtois, & Linehan, 2002).

Behavioural dysregulation is not related to NSSI; other maladaptive and dysregulated behaviours acted to relieve emotional distress range from high-risk behaviours such as alcohol and substance use, risky sexual behaviour, eating disorders, and pathological gambling (e.g., Haaland & Landrø, 2007; Sansone & Levitt, 2004; Trull, Sher, Minks-Brown, Durbin, & Burr, 2000; Trull, Gratz, & Weiss, 2011). Coherently, BPD samples present high comorbidity with substance use disorder (Trull et al., 2000) and eating disorder (Cassin & von Ranson, 2005; Rosenvinge, Martinussen, & Østensen, 2000). Moreover, pathological gambling is highly manifested in the BPD cohort since is the most diagnosed personality disorder among pathological gamblers (Dowling, Cowlshaw, Jackson, Merkouris, Francis, & Christensen, 2015).

Finally, other aspects of behavioural dysregulation in BPD concern the sexuality of these patients. Sexual life in BPD is characterized by a double valence given to sexuality. On one side, sexual dysregulated behaviours are used to cope with emotion; on the other hand, these behaviours generate elevated sexual preoccupation, sexual

depression, and sexual dissatisfaction (Hurlbert, Apt, & White, 1992), as well as strong negative attitudes (Bouchard, Godbout & Sabourin, 2009).

As stated above, behavioural dysregulation is strictly connected to the marked impulsivity presented by BPD patients (APA 2013). Finally, significant inverse associations were found between the severity of BPD symptoms and the active time spent in performing a stressful task (Lejuez et al., 2005). Altogether, these data suggest the incapability of BPD patients in predicting the consequences of an action and the tendency to present intense reaction when negatively activated.

The difficulties presented in BPD patients regarding behavioural regulation (e.g., impulsive behaviours, difficulties in managing distress, difficulties in selecting adequate regulation strategies) suggest that executive functioning are compromised in the disorder.

In detail, BPD patients show a marked inability in withstanding present-moment experiences. This is supported by the well-documented usage of avoidance or escape strategies to modulate their emotional experiences (Cavicchioli, Rugi & Maffei, 2015). In particular, when intense emotions are perceived BPD patients tend to commit to specific maladaptive emotional regulation strategies. Coherently, the usage of mindful regulation strategies could help BPD subjects in better understand their emotion and regulate affective states.

Executive functioning

As stated before, behavioural dysregulation and the inability in adaptive strategies selection in BPD could be connected to cognitive functions deficits (Bazanis, Rogers, Dowson, Taylor, Meux, Staley et al., 2002; Nigg, 2017).

In the last decades, several studies focused on studying the cognitive function of BPD in order to understand how behavioural patterns and strategies are selected. Several studies report deficit in executive functioning in BPD (e.g., Bazanis et al., 2002; Dougherty, Bjork, Huckabee, Moeller, & Swann, 1999; LeGris, Toplak, & Links, 2014; Paret, Jennen-Steinmetz, & Schmahl, 2017; Sánchez-Navarro, Weller, López-Navarro, Martínez-Selva, & Bechara, 2014; Unoka & J. Richman, 2016; V.O., Haaland, &

Landro, 2007). Two meta-analytic reviews on neuropsychological functioning in BPD report deficits in global dimensions of attention, cognitive flexibility, learning and memory, planning, speed processing, and visuospatial abilities (Unoka and Richman, 2016; Ruocco, 2005). However, no differences were observed in the overall intellectual ability and language domains (Unoka & Richman, 2016). These deficits seem to be related to some core symptoms of BPD, such as impulsivity and affective instability (Haaland & Landrø, 2007). Heightened impulsiveness and affective instability could damage the ability to control competing motivational states (e.g., approach and avoidance), which is fundamental for making good choices (Kirkpatrick, Joyce, Milton, Duggan, Tyrer, & Rogers, 2007). Heightened impulsiveness presented by BPD patients is related to a well-established tendency to rapid and unplanned action, which could lead to impulsive and dysfunctional choices (Critchfield, Levy, & Clarkin, 2004); accordingly, BPD patients showed faster responses in a decision-making task (Bazanis et al., 2002).

On the other hand, affective instability is supported by the well-documented involvement of the orbitofrontal cortex and amygdala in decision-making (Bechara, Damasio, Damasio, & Lee, 1999; Damasio, Everitt & Bishop, 1996), whose functionality is clearly altered in BPD (e.g., Wolf, Thomann, Sambataro, Vasic, Schmid & Wolf, 2012). Moreover, emotions constitute potent and pervasive drivers for decision-making (Lerner, Li, Valdesolo, & Kassam, 2015), and difficulties in dealing with them could affect such function (Damasio, Everitt & Bishop, 1996).

A strict relation between the previous two components was demonstrated by several authors. For example, BPD disadvantageous decisions were mostly associated with intense negative emotions (Brown et al., 2002; Hallquist, Hall, Schreiber, & Dombrovski, 2017; Linehan, 1993; Trull et al., 2000).

Interestingly, it was well-demonstrated in healthy controls how current mood influences subjective choice (Lerner, Li, Valdesolo & Kassam, 2015). In detail, positive and negative emotional elicitation guided individual decisions and actions. However, given the affective difficulties presented by BPD subjects, no final evidence is present on emotional signals affects subjective choices. Moreover, it was demonstrated that the ability to identify and distinguish among current subjective feelings was associated with

higher decision-making performance since the subject can control the possible biases induced by those feelings (Seo & Barrett, 2007). However, the well-documented impairment of BPD patients in emotion recognition and regulation could affect such a process. It could be possible that BPD patients do not manifest a general impairment in decision-making. On the contrary, they could present difficulties only when they must deal with specific emotional states.

Generally, the executive refers to high-level processes such as selective and sustained attention, attention shifting, planning, problem-solving, cognitive flexibility, self-monitoring and error detection, inhibition of automatic responses, and self-regulation (Alvarez, 2006). All these elements coordinate the activities necessary to achieve an objective: formulate intentions, develop action-planning, adopt strategies to implement plans, monitor performance and evaluate results.

As stated before, a lack of cognitive flexibility might play a central role in BPD. Cognitive flexibility is defined as the ability to adapt cognitive strategies to cope with unexpected conditions and changes in the environment (Cañas, Fajardo, Salmeron et al., 2003). The behavioural dysregulation presented by BPD subjects could indeed depend on difficulties in selecting the correct strategies to adapt to the request of the environment. We can hypothesize that BPD patients tend to select non-optimum strategies to cope with emotional distress (e.g., NSSI, substance abuse) because the emotional state could interfere with the executive functioning (i.e., the cognitive flexibility ability) and impede the selection of alternative and more adaptive strategies.

Moreover, studies on attentional processes (sustained and selective attention) revealed a well-established impairment in BPD compared to HCs (e.g., LeGris & van Reekum, 2006; Monarch, Saykin, & Flashman, 2004). In detail, attentional bias in executive functioning refers to the tendency to preferentially focus or allocate attentional focus to certain types of emotional stimuli (Mathews & MacLeod, 2005). The studies conducted on BPD using the emotional Stroop paradigm showed evidence for an attentional bias to generally negative stimuli, assessing the ability to inhibit stimulus interference. In addition, a stronger attentional bias to BPD related stimuli was reported (Baer, Peters, Eisenlohr-Moul, Geiger, & Sauer, 2012; Kaiser, Jacob, Domes & Arntz, 2016). This attentional bias for negative stimuli is not also supported by visual dot probe task, which assesses the allocation of visual attention. However, an initial

support for attentional bias for positive cues was reported in such task (Kaiser, Jacob, Domes & Arntz, 2016).

The study of attentional processing of BPD patients relies on three major hypotheses: hypervigilance, attentional bias, and attentional avoidance hypotheses. Hypervigilance mechanisms in BPD are expressed with a faster orientation toward negative emotional stimuli (Frick, Lang, Kotchoubey, Sieswerda, Dinu-Biringer, Berger et al., 2012), as well as by rapid shifts of attention towards the eye of an angry and neutral face (Bertsch, Gamer, Schmidt, Schmidinger, Walther, Kästel et al., 2013; Bertsch, Krauch, Stopfer, Haeussler, Herpertz, & Gamer 2017). Attentional bias refers to difficulties in disentangling attention from emotional stimuli. Borderline patients seem to present difficulties disentangling attention from negative stimuli and threatening information (Kaiser, Jacob, Domes, Arntz, 2017; Kaiser, Jacob, van Zutphen, Siep, Sprenger, Tuschen-Caffier et al., 2018). Finally, the third group of research focused on avoidance mechanisms or escape strategies acted by BPD patients to modulate their emotional experiences, this hypothesis is supported by studies that reported a reduced visual exploration of prolonged emotional stimuli (e.g., Bortolla et al., 2019, 2020). While the attentional strategies of attentional bias and attentional avoidance seem to be the opposite, we can hypothesize that the emotional content of the stimulus presented could play a role in the attentional process. It is possible that after a fast allocation of the attention toward the emotional cue (i.e., hypervigilance), patients could have difficulties in disentangling their attention from a specific type of emotional stimuli (e.g., negative stimuli) while showing an attentional bias for other typologies of stimuli (e.g., neutral, or positive stimuli) in the later stages of visual processing.

The executive functioning of BPD patients could be affected by patients' difficulties in regulating the feedback system. Various studies support the idea of difficulties related to BPD patients' reward and punishment system (Berenson, Van De Weert, Nicolaou, Campoverde, Rafaeli & Downey, 2020). Individuals with this disorder are reported to be more sensitive to negative feedback, to present tendencies in selecting behaviours associated with immediate reward (APA, 2013) and to prefer immediate and smaller reward to a delayed although larger one (Berenson et al., 2016; Lawrence, Allen & Chanen, 2010). In addition, emotional activity seems to affect the reward system in

BPD patients, modulating the sensitivity to rewards when negative emotions are elicited (Dixon-Gordon, Tull, Hackel, & Gratz, 2017).

Social functioning

As stated before, emotional dysregulation, might affect executive functioning in BPD patients and this could lead to the behavioural dysregulation and the usage of self-destructive behaviours characteristic of the disorder. According to literature, most BPD maladaptive behaviours (e.g., NSSI) are generated by difficulties regarding interpersonal and social contexts (Frick et al., 2012; Lis & Bohus, 2013; Minzenberg, Poole, & Vinogradov, 2006). Is it possible to hypothesize, that the social environment could be the major trigger in the emotion-executive-behavioural dysregulation loop presented in Borderline patients. Specifically, BPD subjects present impairment in social cognition, theory of mind, reactivity to interpersonal stressors, interpersonal aggression, and lack of trust and cooperation (Lazarus, Cheavens, Festa, & Rosenthal, 2014). Moreover, BPD subjects present more dysfunctional emotion regulation in the form of rumination in response to social (Napolitano, Yaroslavsky & France, 2020).

Borderline patients are characterized by a disposition to expect anxiously, readily perceive, and intensely react to rejection (Downey, Mougios, Ayduk, London, & Shoda, 2004). This rejection sensitivity relates to BPD clinical features and dysfunctional behaviours (e.g., Tragesser, Lippman, Trull & Barrett, 2008; Selby, Ward, & Joiner, 2010). Rejection sensitivity appears to play a central role in BPD pathology. In fact, it seems to play a major role in triggering emotional regulation difficulties such as impulsive behaviours, anger, rumination, difficulties in selecting and maintaining goal-oriented behaviours, and difficulties in accepting and recognizing emotion (Peter, Smart & Baer 2015). Finally, rejection sensitivity seems to be strictly connected with the difficulties reported by BPD patients regarding social cognition (Miano, Fertuck, Arntz, & Stanley, 2013), trust appraisal (Miano, Fertuck, Arntz, & Stanley, 2013), and the ability to create social contacts (Zielinski & Veilleux, 2014). On the evolutionary side, rejection sensitivity could be generated through the experience of a continuous invalidating environment, characterized by repeated experiences of rejection, exclusion,

and neglect during the development of BPD subjects (Downey & Feldman, 1996). As stated before, BPD subjects could develop anxious beliefs of being rejected and become hypervigilant and hypersensitive to rejection cues (Downey & Feldman, 1996) through a transactional system of interactions with the environment.

Scientific literature suggests that one of the principal cores of the difficulties presented by BPD patients in social functioning is related to the presence of a perceptive bias (Arntz & Veen, 2001). According to this theory, BPD patients tend to present an extreme and negative view of other subjects. In addition, other studies support the idea that BPD subjects could not invest emotionally in social relationship due to this negative view of others (Segal et al., 1992; Whipple & Fowler, 2011). These difficulties could be related to the presented inability of BPD patients in recognizing emotion in other subjects (Bland et al., 2004; Levine et al., 1997; Unoka, Fogd, Füzy, & Csukly, 2011). However, other studies did not support this hypothesis, showing no differences in emotion recognition between BPD and healthy subjects (Domes et al., 2008; Gardner, Qualter, Stylianou, & Robinson, 2010). This last aspect puts the focus on the information processing mechanism that characterizes patients in social functioning. While most of the studies present in the literature evaluated how BPD patients react to emotional stimuli, the study of visual information processing through the usage of the eye-tracking methodology allows studying an earlier phase of emotional processing. This methodology permits us to study which stimuli attract patients' attention and how patients process visual stimuli through eye movements, promoting a reliable measure of attentional mechanisms (Pomplun, Ritter, & Velichkovsky, 1996; Rehder, & Hoffman, 2005; Wooding, Mugglestone, Purdy & Gale, 2002).

Romantic relationships are another central core in BPD social functioning. Several studies showed how BPD patients report difficulties in maintaining functional and healthy romantic relationships compared to non-clinical or other clinical groups (Krueger, Eaton, Derringer, Markon, & Skodol, 2013; Sharp, Kalpakci, Mellick, Venta, & Temple, 2015). Romantic relationships of BPD subjects are usually short-term and characterized by low levels of emotional satisfaction and high hostility for both partners (Navarro-Gómez, Frias & Palma, 2017). Subjects with BPD need high levels of intimacy in a romantic relationship; however, high levels of uncertainty about the

partner were reported in the clinical sample (Agrawal et al., 2004). Moreover, BPD symptoms are correlated with the usage of verbal and physical aggression, together with a lack of communication when emotional distress is perceived in a romantic relationship (Christensen & Shenk, 1991; Weinstein, Gleason & Oltmans, 2012). Finally, women with BPD seem to perceive the romantic relationship as more negative compared to healthy controls, and this could be connected to the fear of being rejected, and to a tendency to underestimate positive interaction with the partner and to remember more clearly negative situations (Miano, Fertuck, Roepke & Dziobek, 2017).

Literature supports that BPD interpersonal dysfunction is strictly related to insecure attachment styles (Bender & Skodol, 2007). Relevantly, BPD patients' childhood is often characterized by trauma, including physical, emotional, or sexual abuse (Bierer, Yehuda, Schmeidler, Mitropoulou, New, Silverman et al., 2003) that can severely impact the development of secure attachment relationships and on the creation of mistrust and problems in regulating closeness and distance to others (Agrawal, Gunderson, Holmes, & Lyons-Ruth, 2004). Moreover, insecure attachment style seems to mediate the relationship between BPD psychopathological manifestations and difficulties with intimate relationships (Bouchard & Sabourin, 2009; Bouchard, Sabourin, Lussier & Villeneuve 2009; Helgeland & Torgersen, 2004; Oliver, Perry & Cade, 2008; Zanarini, Yong & Frankenburg, 2002). Accordingly, typical BPD symptoms such as impulsivity, affective instability, and rejection sensitivity may directly contribute to the interpersonal conflict, increasing BPD difficulties in the interpersonal area (Lazarus, Cheavens, Festa, & Rosenthal, 2014).

Finally, sexuality is affected in BPD. As stated above, sexual relationships of BPD patients are characterized by dysregulated and promiscuous sexuality usually acted to reduce emotional activity (Kernberg, 1967). Borderline subjects report a higher number of sexual partners, unwanted pregnancies, and higher sexual fluidity (Thompson et al., 2019). Moreover, BPD patients are characterized by lower age at their first sexual intercourse and a higher number of forced sexual intercourses compared to healthy controls (Thompson et al., 2019). Traumatic experiences during the development seem to play a central role in BPD sexuality. A high percentage of BPD patients report associations between physical or emotional trauma and an altered sexuality (e.g., sexual

impulsivity or sexual avoidance) (Schulte-Herbrüggen, Ahlers, Kronsbein, Rüter, Bahri, Vater & Roepke, 2009).

As a whole, BPD emotional reactivity might be manifested, especially in interpersonal situations. Limited studies have been published in this field showing that female patients with BPD report higher levels of stress in response to conflictual quarrel (Miano, Grosselli, Roepke, & Dziobek, 2017), as well as higher anger and sadness scores when facing social situations compared to healthy controls (Tragesser, Lippman, Trull, Barrett, 2008). From a physiological point of view, the few data available support a higher physiological reactivity in interpersonal contexts. Borderline subjects report altered cortisol, electrodermal activity and HRV responses to socio-emotional cues (Bortolla, Cavicchioli, Galli, Verschure & Maffei, 2019; Walter, Bureau, Holmes, Bertha, Hollander, Wheelis et al., 2008; Simeon, Knutelska, Smith, Baker & Hollander 2007). These results suggest the idea of an altered autonomous regulation in patients when exposed to social contexts. Coherently, several authors referred to an enhanced social sensitivity in BPD patients. This hypersensitivity is manifested by an increased vigilance for social cues, together with a tendency to misinterpret ambiguous emotional stimuli as negative (e.g., Arntz, Appels, & Sieswerda, 2000; Frick et al., 2012; Arntz & Veen, 2001; Dyck, Habel, Slodczyk, Schlummer, Backes, Schneider, & Reske, 2009; Daros, Zakzanis, & Ruocco, 2013; Hidalgo, Oelkers-Ax, Nagy, Mancke, Bohus, Herpertz, & Bertsch, 2016).

However, given the multifaced manifestations of hyperreactivity (i.e., subjective, behavioural, and physiological), more studies are needed to deepen BPD psychophysiological responses to interpersonal situations.

Neurobiology

Structural differences

The improvement of diagnostic procedures and the technologies in the neuroscientific field have favoured the production of a large literature on BPD neurobiology, to study both structural and functional characteristics of BPD patients

(e.g., Nunes, Wenzel, Borges, Porto, Caminha & de Oliveira, 2009; Rodrigues, Wenzel, Ribeiro, Quarantini, Miranda-Scippa, De Sena et al., 2011; Hall, Olabi, Lawrie & McIntosh, 2010; Ruocco, Amirthavasagam & Zakzanis, 2012; de-Almeida, Wenzel, de-Carvalho, Powell, Araújo-Neto, Quarantini et al., 2012; Kimmel, Alhassoon, Wollman, Stern, Perez-Figueroa, Hall et al., 2016, Visintin, De Panfilis, Amore. Balestrieri, Sambataro, 2016).

However, results in literature are wide and not always coherent. Starting from the structural neural characteristic of BPD patients, the two main areas that seem implicated in the disorder are the hippocampus and the amygdala. In fact, most of the meta-analyses present in literature report how BPD patients report smaller grey matter volume (GMV) of these areas (Nunes, Wenzel, Borges, Porto, Caminha & de Oliveira, 2009; Rodrigues, Wenzel, Ribeiro, Quarantini, Miranda-Scippa, De Sena et al., 2011; Hall, Olabi, Lawrie & McIntosh, 2010; Ruocco, Amirthavasagam & Zakzanis, 2012; de-Almeida, Wenzel, de-Carvalho, Powell, Araújo-Neto, Quarantini et al., 2012; Kimmel, Alhassoon, Wollman, Stern, Perez-Figueroa, Hall et al., 2016). These two areas play a central role in emotional regulation and subsequent behavioural patterns. While the amygdala plays a central role in regulating the emotional response and forming memories related to emotional stimuli (Banks, Eddy, Angstad, Nathan, & Phan, 2007, Berboth & Morawetz , 2021) the hippocampus not only is involved in the formation of new memories but also play a central role in mediating the response to stress- due to its connection with the hypothalamic-pituitary–adrenal (HPA) axis – and the regulation of aggressive behaviour (Tottenham, Sheridan, 2010). Analyzing for possible confounding factors, these two structural patterns seem to be specific for BPD. When controlling for the presence of a co-diagnosis of Major Depression or Post-traumatic stress disorder, no significant differences were found for the two areas (de-Almeida et al., 2012; Ruocco Amirthavasagam, Zakzanis, 2012).

Interestingly, ageing seems to impact the reduction of GMV in these two areas: Kimmel and colleagues (2016) show how the volume of the hippocampus and amygdala reduces with ageing. Even though the results are not conclusive, these data suggest the specificity of this structural pattern as a possible endophenotype specific for BPD. It is possible to hypothesize that the transactional interaction with the environment could

lead to progressive deficits in those areas. This hypothesis will be explained more in detail in the next sections.

The hippocampus and the amygdala are not the only areas that present differences when comparing HC and BPD. Cortical areas show altered volume in BPD when compared to HC. In particular, the temporal pole, supplementary motor area, and middle frontal gyrus (Kimmel et al., 2016; Yang, Hu, Zeng et al., 2016). All those areas seem related to the characteristics presented by BPD patients, such as the processing of socio-emotional stimuli (Adolphs, 2002), impulsivity, and suicidal thoughts (Reisch, Seifritz, Esposito et al., 2010). Finally, significant differences were reported for the posterior cingulate cortex and the precuneus, with BPD patients presenting more GMV than HC in those areas (Rodrigues, Wenzel, Ribeiro et al., 2011; Yang, Hu, Zeng, Tan & Cheng, 2016). Those areas are related to autobiographical memory, self-consciousness, and the integration between external and internal emotional stimuli (Guterstam, Bjornstodder, Gentile, Ehrsson, 2015; Fransson, Marrelec, 2008; Vogt, 2005). The differences reported in those areas could be related to the difficulties of BPD patients in forming and maintaining a stable representation of themselves. Figures 1.2 and 1.3 report the principal areas involved in BPD pathology.

The structural differences in BPD brain are not related only to different levels of GMV. Numerous studies support the presence of an alteration of white matter integrity. Several studies report alteration in fronto-limbic connections in BPD patients (e.g., Carrasco, Tajima-Pozo, Díaz-Marsá, Casado, López-Ibor, Arrazola & Yus, 2012; Maier-Hein, Brunner, Lutz, Henze, Parzer, Feigl et al., 2014; Whalley, Nickson, Pope, Nicol., Romaniuk, Bastin et al., 2015). These results are in line with BPD symptomatology since fronto-limbic connections play a central role in emotion regulation processes (Banks, Eddy, Angstadt, Nathan, & Phan, 2007).

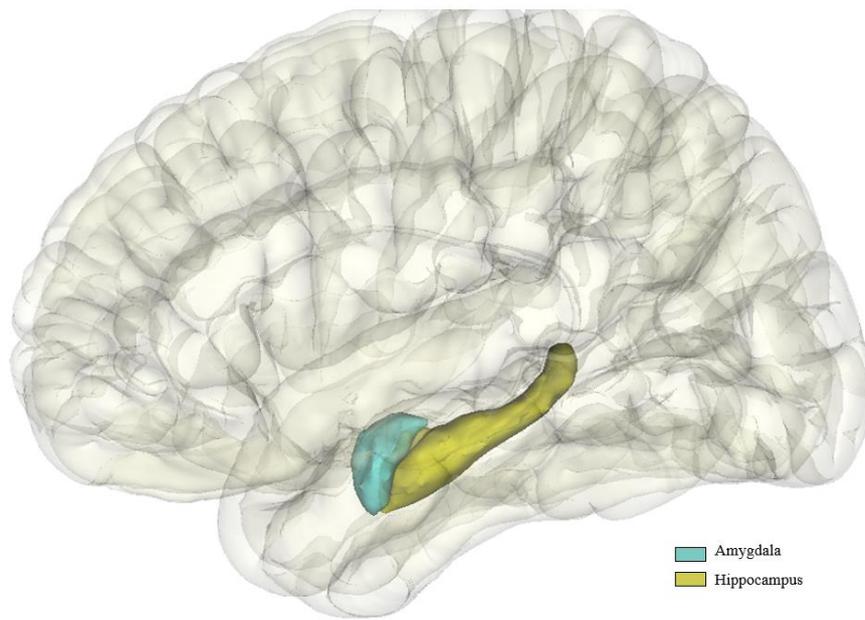


Figure 1. 2 Amygdala and Hippocampus

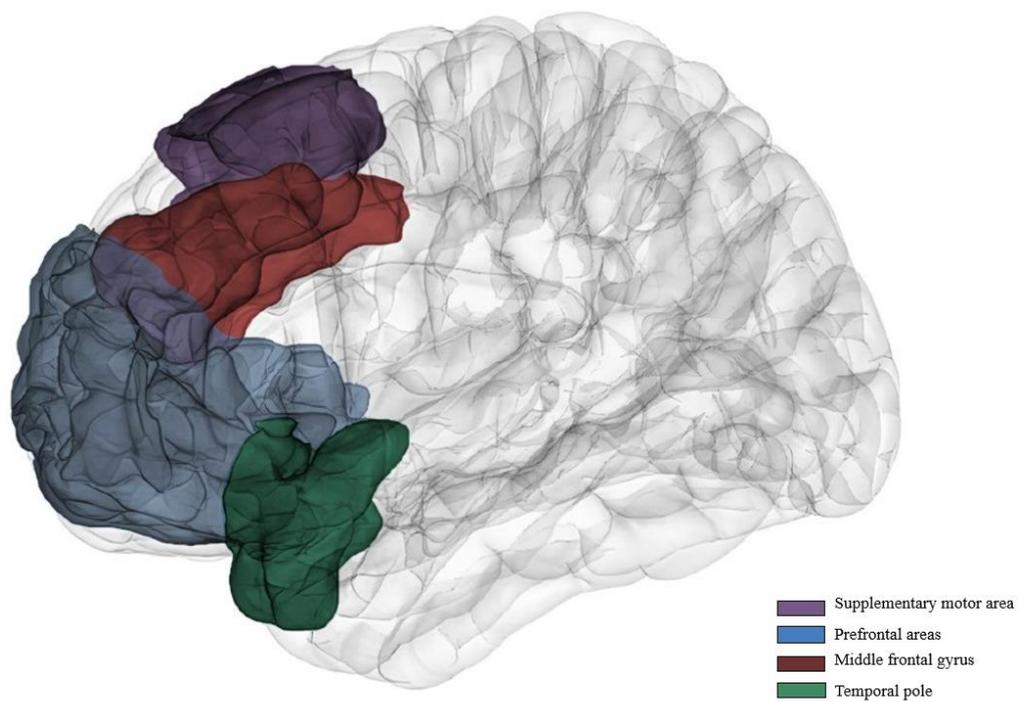


Figure 1. 3 Cortical Areas

Functional differences

Subjects with BPD and HC present functional differences during resting state and emotional processing. At resting state, BPD patients show higher activity in the medial prefrontal cortex, cingulate cortex, and precuneus compared to HC (Visintin, De Panfilis, Amore, Balestrieri, Sambataro, 2016). These areas are related in the processing of emotion-related to social, interpersonal, and self-centred cues (Etkin, Egner, Kalisch, 2011; Saxe, 2006; van Overvalle, 2009). Again, these results align with the pathology presented by BPD patients in the socio-emotional context. At the baseline level, BPD patients also present lower temporal and orbitofrontal cortexes (Visintin, De Panfilis, Amore, Balestrieri, Sambataro, 2016). A deficit in orbitofrontal areas could represent a biological substrate of the difficulties presented in BPD patients in emotional regulation, time perception and could underlie the dissociative state often presented in the pathology (Bechara, Damasio, Damasio, Anderson; Berlin, Rolls, Iversen, 2005; Berlin, Rolls, Kischka, 2004; Rolls, Hornak, Wade & McGrath, 1994; Mueller-Pfeiffer, Schick, Schulte-Vels, Schulte-Vels, O'Gorman, Michels, Martin-Soelch et al., 2013; Schenk, Bear, 1981; Sellitto, Ciaramelli, di Pellegrino, 2010; Tsuchida, Doll, Fellows, 2010).

Analyzing the literature on neural functioning during emotional tasks, several metanalysis report a reduction in the dorsolateral prefrontal cortex activity in response to emotional stimuli (Ruocco, Amirthavasagam, Choi-Kain & MC Main, 2013; Schulze, Schmahl & Niedtfeld, 2016) and in the anterior cingulate cortex (ACC) (Ruocco, Amirthavasagam, Choi-Kain & MC Main, 2013) two areas central in the emotional processes. Mixed results, on the contrary, have been shown regarding the amygdala. While in the metanalysis conducted by Ruocco and colleagues (2016) shows a reduction in the amygdala activity during the processing of emotional data, another metanalysis (Schulze, Schmahl & Niedtfeld, 2016) shows a pattern of hyperactivity related to a cluster composed of hippocampus and amygdala in BPD patients. At first sight these results could seem misleading; however, emotional dysregulation implies an oscillation

between avoidance of triggering stimuli (e.g., Bortolla, Cavicchioli, Galli, Versschure & Maffei, 2019) and strong emotional reactions. These considerations could support the different activity patterns in the amygdala; those could be related to the type of response elicited in BPD patients; however, more studies are needed to clarify this hypothesis.

An evolutionary perspective

The clinical characteristics of the disorder and the neurobiological differences found in BPD patients permit us to propose an etiopathogenetic hypothesis on the development of the disorder. From the study of BPD pathology, the presence of physical and emotional abuse during the development in the clinical sample is well-documented. Several studies stated that at least 91% of BPD subjects had experienced childhood abuse (Zanarini, Williams, Lewis & Reich 1997; Davidson, Devaney e Spratt, 2010; Spatz Widom, Czaja & Paris, 2009; Zanarini et al., 2002). Moreover, the intensity of the abuse experienced during the development is associated with the severity of BPD symptoms in early adult life in psychosocial functioning (Sansone, Songer e Miller, 2005; Silk, Lee, Hill e Lohr, 1995; Zanarini, Yong, Frankenburg, Hennen, Reich, Marino et al., 2002). Moreover, dissociation and derealization characteristics of BPD patients are reported to be related to the experience of emotional and sexual abuse during childhood (Chu e Dill, 1990; De Zulueta, 1999; Korzekwa, Dell, Links, Thabane e Fougere, 2009; Meehl, 1995; Ross, Joshi & Currie, 1991; Sar, Kundakci, Kiziltan, Yargic, Tutkun, Bakim et al, 2003; Shearer, 1994; Van Ijzendoorn & Schuengel, 1996). Finally, the familiar context seems to impact the development of BPD pathology (Linehan, 1993). Longitudinal studies report high levels of conflictual and contradictory relationships with family members and lack of empathy in the BPD cohort (Allen, Abramson, Whitson, Al-Taher, Morgan, Veneracion-Yumul et al., 2005; Gunderson e Lyoo, 1997; Guttman e Laporte, 2000). Thus, the presence of continuous aversive events during the development impacts the neurogenesis of different neural areas, affecting both cortical and subcortical structures (for a review, see Pecthel, Pizzagalli, 2011). Adverse environmental events activate the HPA axis, circuitry that regulates the individual response to stress through the interaction with the hippocampus, amygdala, locus coeruleus (LC) and brain stem. When a stressor triggers the

hypothalamus, corticotropin-releasing hormone (CRH) and arginine vasopressine are secreted. This, in turn stimulate the secretion of the adrenocorticotropine hormone and the activation of the sympathetic system, generatic the classic fight or flight response, through the activation of the LC (Guilliams & Edwards, 2010). A continuous activation of the HPA axis in a chronic stress condition, together with a continuous release of CRH might lead to differences in GMV in cortical and subcortical regions (e.g., hippocampus and amygdala), causing aberrant responses to emotional triggers, and deficits in HPA axis regulation and, consequently in autonomous regulation (Pechtel and Pizzagalli, 2010). Coherently, BPD patients showed coherent deficits in amygdala, hippocampus, and HPA axis regulation (e.g., Lieb, Rexhausen, Kahl, Schweiger, Philipsen & Hellhammer, 2004; Simeon, Bartz, Hamilton, Crystal, Braun, Ketay, & Hollander, 2011; Charmandari, Kino, Souvatzoglou & Chrousos, 2003). As stated before, an invalidating environment seems central in the development of BPD symptomatology (Linehan, 1993). Given the slow and non-linear development of the human brain (Gogtay and Thompson 2010), the relevance of the environment in the process, and the timing in which BPD patients experience the aversive events, we can then hypothesize that continuous interaction with an aversive environment could be a major cause of the neural differences presented in BPD subjects. Thus, the transactional interaction between biological vulnerability and an invalidating environment could lead to difficulties in neuroception in these patients. The term neuroception represents the unconscious perception of dangers and threats present in the subject's surroundings (Porges, 2004). An altered neuroception leads to difficulties in social engagement and emotional regulation in response socio-emotional contexts (Porges, 2007), eliciting defensive behaviours and altered physiological states usually related to anxiety disorders (Leckman, Gricce, Boardman, Zhang, Vitale, Bondi et al., 1997).

This process is mostly mediated by the vagus nerve, which is fundamental in regulating the autonomous response and connected to the regulation of facial expression, social engagement and the coordination between breathing, suctioning, and swallowing behaviours (Porges, 2007). A major hypothesis could be that an altered neuroception in BPD could be the principal core of the disorder and this alteration in processing the security of the socio-emotional environment could lead to the emotional and consequently behavioural dysregulation typical of the disorder.

Aim of the dissertation

Toward a new conceptualization of BPD emotional reactivity

In the end, given all the evidence presented in this introductory chapter, we can underline how data presented on BPD emotional, executive and social functioning are not conclusive. A major problem is represented by the fact that the most used and studied theoretical model of BPD (Linehan, 1993) is not totally supported by the empirical studies (for a metaanalysis see Bortolla, Cavicchioli, Fossati & Maffei, 2020). Moreover, this model hypothesizes alteration regarding autonomous functioning without giving an idea of what cerebral area could be relevant for the disorder. One of the main aims of this thesis is to present a possible theoretical neural model that can describe in detail the emotional difficulties presented by BPD subjects.

In the developing of this model a central role will be given to the study of the emotional reactivity of BPD patients. Given the lack of support for a general hyperreactivity in BPD patients (Bortolla et al., 2020), and the well-documented hypersensitivity of these patients, regarding socio-emotional situations (e.g., Bortolla, Cavicchioli, Galli, Verschure & Maffei, 2019; Bortolla, Galli, Ramella, Sirtori, Visintini & Maffei 2020; Frick et al., 2012; Lis & Bohus, 2013; Minzenberg, Poole, & Vinogradov, 2006), together with the importance of socio-emotional distress in the developing of the pathology (e.g., Linehan, 1993), as stated in the previous paragraph, we can hypothesize that the intense patterns of reactivity of these patients could be specific to socio-emotional contexts and due to a dysregulated neuroception. However, no studies were conducted so far on the analysis of the psychophysiological reactivity of BPD patients in response to different typologies of socio-emotional stimuli. Moreover, as stated before, executive functioning plays a central role in managing behavioural responses to emotional stimuli. However, no studies have been conducted on the effect of negative emotion on executive functioning and attentional responses in BPD patients. Finally, given the strict connection between emotional regulation and mindfulness ability (Gratz & Trull, 2010) and the relation between mind-wandering and ruminative states that characterize BPD patients and drive to difficulties in emotional and behavioural regulation, more studies on the efficacy of mindfulness in regulating

psychophysiological responses are needed to better understand how this practice affects HC and BPD subjects in real-time.

Five studies will be presented in this dissertation.

The first study (*Executive functioning study*) focus on how negative affective states could impact executive functioning and attentional processes in BPD subjects. In detail, self-reported, physiological and behavioural data were analyzed during an emotional induction (negative or neutral) and a cognitive flexibility task.

After that, two studies on socio-emotional reactivity will be presented. These two studies were conducted to prove that the emotional reactivity of BPD patients is specifically related to socio-emotional stimuli, due to difficulties in neuroception. In the first study (*Dot.probe study*), through a dot-probe task and the usage of eye-tracking methodology, attentional and visual processes were analyzed to confirm the presence of specific attentional bias in BPD related to social cues. Moreover, the impact of a negative emotional state on the behavioural responses of the patients during the task was analyzed. The second social study (*Clip study*), focus on emotional and physiological reactivity to a pool of socio-emotional clips. Self-reported and physiological data were analyzed to prove the specificity of the hyperreactivity of BPD patients in response to social cues.

Finally, two studies on the efficacy of mindfulness in modulating physiological and emotional states will be reported. These studies analyzed how a breathing observation exercise could affect autonomous regulation, affective states and mind wandering in a sample of HC (first study) and BPD (second study). Finally, the results of all the studies will be discussed and together with the neurobiological evidence presented in the literature a new theoretical model of emotional regulation in BPD patients will be presented.

Results

Before the testing, in all the studies, all the participants were screened with the Personality Inventory for DSM-5 (PID-5; Krueger, Eaton, Clark, Watson, Markon, Derringer et al., 2011), the Difficulties in Emotion Regulation Scale (DERS; Giromini, Velotti, De Campora, Bonalume, & Zavattini, 2012) and the Beck Depression Inventory -II (BDI-II) (Beck, Steer & Brown, 1996) to exclude the presence of maladaptive traits, difficulties in regulating emotion and depression in the HC sample. In all the studies, BPD reported significant higher score for most of PID-5 domains and BPD related facets. DERS scales and PID-5 domains and BPD subscales as postulated by DSM-5, Section III (APA, 2013). Results are presented in table 2.1.

Table 2. 1 Descriptive statistics for clinical indexes in all the studies

	<i>Executive functioning study</i>		<i>Social studies</i>		<i>Mindfulness study</i>	
	<i>HCs</i> M(SD)	<i>BPD</i> M(SD)	<i>HCs</i> M(SD)	<i>BPD</i> M(SD)	<i>HCs</i> M(SD)	<i>BPD</i> M(SD)
<i>DEERS</i>						
Non acceptance	9.82(3.07)	22.09(7.49)	12.58(5.85)	22.32(7.49)	12(3.82)	20.57(8.11)
No Goals	11.47(3.67)	18.33(3.96)	12.23(5.02)	20.16(5.17)	12(3.59)	19.78(5.34)
Impulse	9.64(1.41)	19.53(7.01)	10.81(4.56)	21.92(6.47)	11.10(2.67)	19.47(7.61)
No awareness	22.94(4.47)	19.53(6.39)	13.45(4.86)	18.20(6.13)	20.89(5.10)	18(6.66)
No strategy	13.41(3.02)	28.09(7.09)	16.26(6.85)	30.00(9.16)	15.24(3.69)	27.57(8.86)
No Clarity	12.65(1.16)	14.85(3.10)	10.84(4.61)	17.84(4.77)	12.34(2.25)	16.31(4.80)
Ders Tot	2.22(.31)	3.39(.69)	2.11(0.68)	3.62(0.77)	2.32(.37)	3.38(.93)
<i>PID-5 facets</i>						
Anxiousness	.65(.39)	1.96(.72)	1.17(.073)	2.07(0.73)	1.02(.65)	1.99(.70)
Emotion Lability	.89(.59)	2.54(.50)	1.06(.62)	2.45(.54)	1.10(.55)	2.47(.47)
Hostility	.66(.40)	1.40(.74)	0.65(.44)	1.61(.73)	.64(.45)	1.43(.62)
Sep. insecurity	.64(.50)	1.53(.72)	0.72(.56)	1.68(.78)	.78(.49)	1.56(.99)
Depressivity	.16(.15)	1.94(.74)	0.43(.49)	2.01(.77)	.32(.31)	1.83(.79)
Risk taking	.95(.18)	1.39(.33)	1.01(.42)	1.64(.67)	.84(.27)	1.46(.55)
Impulsivity	.86(.39)	1.68(.71)	0.56(.60)	1.87(.77)	.74(.58)	1.55(.73)
<i>PID-5 domains</i>						
Neg. affectivity	.90(.29)	1.72(.39)	1.07(.37)	1.80(.38)	1.10(.28)	1.72(.42)
Detachment	.57(.16)	1.51(.48)	0.53(.35)	1.58(.47)	.56(.23)	1.40(.49)
Antagonism	.63(.30)	.83(.53)	0.41(.32)	0.92(.68)	.44(.28)	.78(.58)
Disinhibition	.94(.16)	1.52(.36)	0.91(.30)	1.60(.48)	.92(.26)	1.48(.39)
Psychoticism	.26(.33)	1.30(.79)	0.31(.36)	1.45(.68)	.15(.17)	1.01(.52)

Executive functioning study

To study the effect of negative emotions on executive functioning, after baseline emotional and physiological measurements, HC and BPD participants were randomly divided in two groups. One group of BPD group underwent the neutral paradigm (BPDO) and the remaining BPD participants underwent the negative paradigm (BPDN), no significant differences for the clinical questionnaires were reported in the two subgroups at baseline level. Similarly, HC were divided in two subgroups and the two different paradigms were assessed. No differences were found between the HC group that underwent the neutral paradigm (HCO) and the HC group that underwent the negative paradigm (HCN) for all the screening questionnaires given at baseline level. After the induction all participants completed a cognitive flexibility task (Berg's Card Sorting Test (BCST) (Mueller & Piper, 2014)). Finally, through a machine learning model reward, punishment sensitivity and decision consistency of participants were calculated. Figure 2.1 represent the methodology of the *Executive functioning task*.

With this study I would like to test the hypothesis that a negative emotional state affects executive functioning in BPD patients, with a particular focus on cognitive flexibility, reward sensitivity and attentional processes. Additionally, this task wanted to disconfirm the hypothesis of an unspecific emotional and physiological hyperreactivity to emotional triggers in BPD. Full detail on the methodology and indexes analysed could be found in the Methodology section.

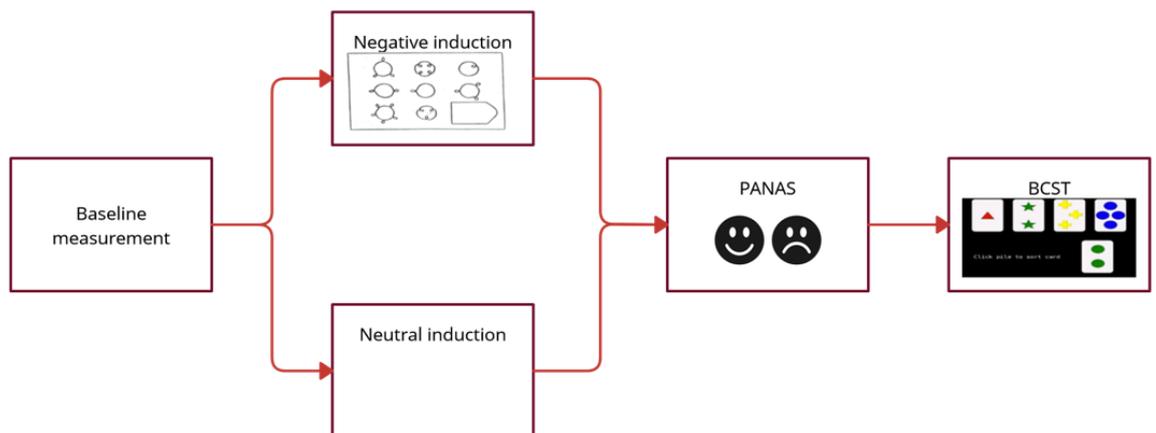


Figure 2. 1 Executive functioning study methodology

Baseline

Affective state

Significant differences were found between the two groups regarding the affective state at baseline. In detail, BPD participants showed lower levels of PA ($U=142.5$, $z= -4.04$, $p<.001$; Monte Carlo 99% CI [.000;.000]) and higher levels of NA ($U=227$, $z= -2.66$, $p=.004$; Monte Carlo 99% CI [.002; .006]) compared to HC. Moreover, post-hoc analysis did not show differences for affective states between BPDN and BPDO. Finally, no differences were found between the HCN and HCO regarding affective states. Data are reported in Table 2.2.

Physiological activity

Physiological indexes at baseline varied between 4.01 and 4.65 (mean=4.35, SD=.17) for HR -between 54.98 and 104.41 (mean= 78.98, SD =13.53) when considering bpm for HR-; 2.92 and 4.88 (mean=3.08, SD=.48) for RMSSD; and between 5.21 and 2.84 (mean = 4.001, SD = .45) .Significant differences were found between HC and BPD patients at baseline level for HR ($U=82$, $z=-3.62$, $p<.001$; Monte Carlo 99% CI [.000; .000]) and SDNN indexes ($U=90$, $z=-2.81$, $p=.002$; Monte Carlo 99% CI [.001; .004]) with BPD reporting higher HR and lower SDNN compared to HC. Moreover, post-hoc analysis did not show significant differences between the BPDN and BPDO and between HCN and HCO for physiological indexes. No significant correlations were found between affective and physiological states at baseline. Data are reported in table 2.

Table 2. 2 Descriptive statistics and group comparison at baseline for PANAS and physiological indexes

	<i>HCs</i>	<i>BPD</i>
	M(SD)	M(SD)
<i>Panas</i>		
PA	36.96(5.83)***	27.06(8.3)
NA	13.16(4.09)**	19.73(9.5)
<i>Physiological indexes</i>		
HR(ln)	4.26(.14)***	4.43(.14)
HR(bpm)	71.59(10.83)***	86.73(11.75)
RMSSD(ln)	4.08(.48)	3.55(.43)
SDNN(ln)	4.23(.44)**	3.78(.41)

*p<.05, **p<.005, ***p<.001

Induction paradigm

Affective state

Considering neutral condition, significant differences were found between HCO and BPDO regarding PA ($U=28$, $z=-3.06$, $p=.001$; Monte Carlo 99% CI [.000; .002]) with BPD patients reporting lower levels of positive affectivity compared to HCO after the neutral induction. Moreover, HCO showed a significant reduction of NA index ($Z=-2$, $p=0.028$; Monte Carlo 99% CI [.023; .031]) when confronting affective state pre and post induction. On the contrary, BPDO did not show significant changes for PA and NA after the neutral induction.

Considering negative condition, significant differences were found between HCN and BDPN after the negative induction for both PA ($U=33.5$, $z=-3.15$, $p<.001$; Monte

Carlo 99% CI [.000; .001]) and NA ($U=29.5$, $z=-3.33$, $p<.001$; Monte Carlo 99% CI [.000; .001]), with patients reporting lower levels of PA and higher levels of NA compared to the non-clinical sample.

Moreover, BPDN showed a significant decrease of PA ($Z=-1.7$, $p=.05$; Monte Carlo 99% CI [.039; .049]) and increase of NA -only as a trend- ($Z=-1.5$, $p=.07$; Monte Carlo 99% CI [.067; .081]) after the negative induction.

Finally, HCN showed a significant reduction of PA after the negative induction ($Z=-2.01$, $p=.020$; Monte Carlo 99% CI [.017; .024]). Data on affective states are reported in Table 3.

Physiological activity

No significant differences were found between HCO and BPDO during neutral induction for HR and SDNN indexes. Values ranged between 4.19 and 4.66 (mean=4.43, SD=.14) for HR -between 65.88 and 105.4 (mean= 84.24, SD =11.99) when considering bpm for HR-; between 3.02 and 4.71 (mean=3.92, SD=.49) for RMSSD; and between 3.52 and 4.50 (mean=3.99, SD=.26) for SDNN.

Similarly, no differences were found for physiological indexes between HCN and BPDN during the negative induction. No significant correlations were found between the activation before and after the inductions and the physiological activity during the inductions. ECG values ranged between 3.60 and 4.88m (mean=4.36, SD=.32) for HR -between 46.71 and 131.16 (mean= 74.54, SD =23.58) when considering bpm for HR-; between 3.54 and 5.25 (mean=4.40, SD=.42) for RMSSD; and between 3.73 and 5.05 (mean=4.37, SD=.38) for SDNN. Data on physiological activation are reported in Table 2.3.

Table 2. 3 Descriptive statistics and within induction paradigm comparison (baseline vs induction) in the emotional inductions for PANAS and physiological indexes

	<i>HCO</i>	<i>HCN</i>	<i>BPDO</i>	<i>BPDN</i>
	M(SD)	M(SD)	M(SD)	M(SD)
<i>Panas</i>				
PA	38.15(6.7)	27.92(7.9) [^]	27.92(7.9) ^{**}	22.13(6.4) ^{***, ^}
NA	32.92(8.6) [^]	16.14(7.53)	16.14(7.56)	24.86(9.76) ^{***, #}
<i>Physiological indexes</i>				
HR(ln)	4.24(.16)	4.39(.15)	4.28(.43)	3.35(.12)
HR(bpm)	70.36(11.95)	82.19(13.11)	78.30(20.70)	86.30(10.96)
RMSSD(ln)	4.55(.39)	3.98(.47)	4.28(.43)	3.86(.53)
SDNN(ln)	4.53(.29)	3.99(.28)	4.23(.42)	3.99(.26)

Between group (BPD vs HC) comparison *p<.05, **p<.005, ***p<.001; Within condition comparison with baseline ^p<.05, ^^p<.005, ^^p<.001, #p=.007

BCST cognitive flexibility task

Behavioural responses

In the negative condition no significant differences were found between HCN and BPDN for correct answers, errors, and perseverative errors.

However, BPDN showed significant lower decision consistency ($U=72.0$, $z=-.26$, $p=.008$; Monte Carlo 99% CI [.005; .010]) compared to HCN.

In the neutral condition, significant differences were found between HCO and BPDO regarding total correct answers ($U=56.0$, $z=-1.93$, $p=0.029$; Monte Carlo 99% CI [.025; .033]) and total errors ($U=53.0$, $z=-1.18$, $p=.020$; Monte Carlo 99% CI [.016; .024])

with BPD patients reporting higher number of errors and lower number of correct answers.

No significant differences were found for perseverative errors between BPDO and HCNO. Finally, a significant difference between BPDO and HCO was found for reward sensitivity in the neutral paradigm ($U=57$, $z=-1.88$, $p=.033$; Monte Carlo 99% CI [.027; .036]) with BPD patients reporting higher sensitivity to reward compared to the control group.

Supplementary analyses were conducted to analyze the effect of emotional state on cognitive flexibility.

When comparing HC in the two paradigms, no significant differences were found for total number of errors, perseverative answers, correct answers, reward sensitivity, punishment sensitivity, nor decision consistency between HCO and HCN. On the contrary a significant difference was found between BPDO and BPDN for decision consistency ($U=64$, $z=-2.38$, $p=.007$; Monte Carlo 99% CI [.005; .009]) with BPDN reporting lower decision consistency compared to BPDO. Data on behavioural responses are reported in Table 2.4.

Physiological activity

In the negative condition ECG indexes ranged between 4.00 and 4.59 (mean=4.38, SD=.14) for HR - between 54.73 and 98.48 (mean= 81.21, SD =11.49) when considering bpm for HR-; between 3.06 and 4.94 (mean=4.38, SD=.14) for RMSSD; and between 3.24 and 4.81 (mean=3.72, SD=.33) for SDNN.

significant differences were found comparing BPDN with HCN for SDNN index ($U=14$, $z=-2.83$, $p=.002$; Monte Carlo 99% CI [.001; .003]) and HR ($U=35$, $z=-1.68$, $p=.050$; Monte Carlo 99% CI [.047; .058]) with BPD patients reporting higher HR and lower SDNN compared to HC.

In the neutral condition similar significant differences were found, with BPDO reporting higher HR ($U=20$, $z=-2.04$, $p=.021$; Monte Carlo 99% CI [.017; .024]) and

lower SDNN ($U=9$, $z=-2.53$, $p=.004$; Monte Carlo 99% CI [.002; .005]) compared to HCO. No significant correlations were found between physiological activity and responses to BCST task in both paradigms.

Supplementary analysis did not show significant differences between BPDN and BPDO and between HCN and HCO. Data on physiological activation during BCST are reported in Table 2.4.

In summary, BPD patients showed higher negative activation at baseline, compared to HC. Coherently, BPD patients showed higher sympathetic activity at baseline. During the emotional induction paradigm, no differences were found between BPD and HC. Finally, during the BCST task, differences in decision consistency were found in the negative condition between HC and BPD, with patients reporting lower levels of the index. On the other hand, in the neutral paradigm BPD showed less correct answers, more errors and higher reward sensitivity compared to HC. A paper regarding this experiment is *in preparation* and will be submitted in the next months.

Table 2. 4 Descriptive statistics and group comparison in the BCST for behavioural and physiological indexes

	<i>HCO</i>	<i>BPDO</i>	<i>HCN</i>	<i>BPDN</i>
	M(SD)	M(SD)	M(SD)	M(SD)
<i>Behavioral data</i>				
Corrects	99.46(8.35)	91.14(15.44)*	95.20(15.30)	94.33(.14)
Errors	25.42(9.50)	35(17.24)*	29(17.75)	30.4(15.86)
Perseverative errors	14.35(3.56)	16.85(8.13)	19.06(11.42)	15.73(6.94)
Reward sensitivity	.43(.36)	.64(.28)*	.64(.36)	.58(.33)
Punishment sensitivity	.46(.33)	.47(.30)	.39(.37)	.57(.32)
Decision consistency	.23(.24)	.49(.61)	.45(.61)	.10(.004)**
<i>Physiological indexes</i>				
HR(ln)	4.29(.18)	4.45(.10)*	4.34(.12)	4.44(.11)*
HR(bpm)	74.47(13.46)	86.19(8.49)*	78(10.36)	85.79(9.75)*
RMSSD(ln)	3.99(.51)	3.41(.19)**	3.62(.25)	3.41(.19)**
SDNN(ln)	4.04(.42)	3.55(.15)	3.78(.13)	3.55(.15)

*p<.05, **p<.005, ***p<.001

Social studies

To study BPD reactivity to socio-emotional stimuli, two studies were conducted on two different days, in random order.

In the *dot-probe study*, after a block of practice to understand the task, a socio-emotional dot-probe task was administered to both HC and BPD participants.

The task consisted in two blocks with two different exposition times (i.e., 500ms and 1500ms) and four stimuli categories (i.e., neutral, negative, positive and erotic socio-relational images).

Reaction times (RT), behavioural responses and eye-tracking indexes were collected.

On the other hand, in the *clip study*, after a block of practice to understand the task, participants underwent the Clip task. Twenty-four socio emotional clip belonging to four different emotional categories (i.e., positive, negative, erotic and neutral) were administered. Participants had to indicate the intensity of the emotion perceived after the view of each clip. Physiological data were collected during the view of each clip.

Figure 2.2 and Figure 2.3 represent *Dot-probe* and *Clip task* methodology. The aim of these studies was to test the presence of difficulties in early phase of neuroception in BPD patients. In particular, with the usage of a social dot-probe this experiment wanted to test whether BPD patients reported differences in attentional mechanisms (i.e., Hypervigilance, Attentional Biases and avoidance strategies) with stimuli related to social contexts. Moreover, this study wanted to test whether a specific condition of negative arousal could affect behavioural responses to the task. Similarly, the *Clip study* wanted to test a different moment of neuroception, focusing in detail on physiological and self-report emotional responses to the view of prolonged social situations. In this studies differences in both typologies of responses are expected: BPD patients are expected to report a higher physiological reactivity to socio-emotional stimuli and higher levels of negative emotion, confirming the hypothesis of a specific hyperreactivity to social situations, related to difficulties in neuroception. Finally, correlation between indexes of childhood trauma and responses to the task were analyzed, in order to confirm the evolutionary perspective presented in the introduction: significant correlations are expected between indexes of traumatic events in the childhood (e.g., emotional abuse, emotional neglect) and responses to the tasks. Full

detail on the methodologies and indexes analysed could be found in the Methodology section.

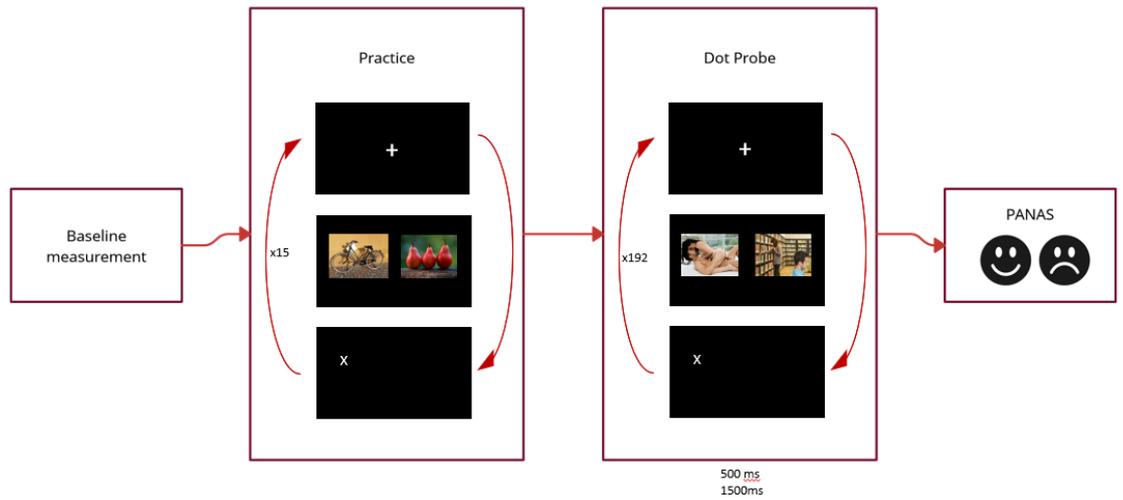


Figure 2. 2 Dot-probe task methodology

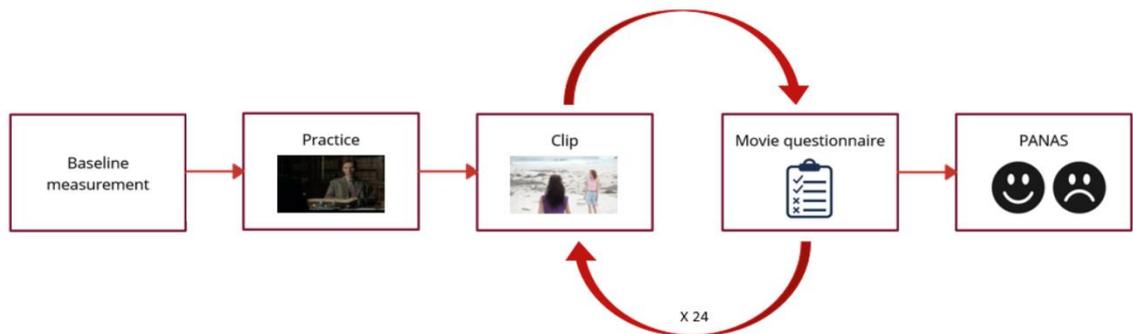


Figure 2. 3 Clip task methodology

Dot probe study

Positive and Negative affect: group and pre-post comparisons.

BPD group reported higher NA ($U=289.00$; $Z= -2.27$; $p = .011$; Monte Carlo 99% CI [.008-.013]) and lower PA ($U=296.00$; $Z= -2.10$; $p = .017$; Monte Carlo 99% CI [.015-.022]) at the beginning of the experiment, as well as significantly higher NA

($U=202.00$; $Z= -3.46$; $p < .001$; Monte Carlo 99% CI [.000-.001]) and lower PA ($U=259.50$; $Z= -2.50$; $p = .001$; Monte Carlo 99% CI [.001-.004]) at the end on the dot-probe study.

Descriptive statistics and group comparisons for PANAS scale scores were presented on table 2.5.

Supplementary analysis conducted considering only female participants ($n=27$) confirmed the results, with BPD reporting lower PA at baseline ($U=275.00$; $Z= -1.4691$; $p = .03$; Monte Carlo 99% CI [.026-.024]) and post-task ($U=224.00$; $Z= -2.50$; $p = .006$; Monte Carlo 99% CI [.004-.008]) and higher NA at baseline ($U=243.50$; $Z= -2.53$; $p = .006$; Monte Carlo 99% CI [.004-.008]) and post-task ($U=172.50$; $Z= -3.53$; $p < .001$; Monte Carlo 99% CI [.000-.001]).

Table 2. 5 Descriptive statistics and non-parametric group comparisons related to PANAS scales in the Dot-probe study

		<i>BPD</i>	<i>HC</i>
		M(SD)	M(SD)
<i>Pre-task</i>	PA	27.53(8.84)*	32.54(7.50)
	NA	18.64(8.80)*	14.48(7.32)
<i>Post-Task</i>	PA	23.92(7.89)**	29.63(8.39)
	NA	19.75(9.01)**	12.90(5.657)

* $p < .05$, ** $p < .005$, *** $p < .001$

Correct responses and bias score

Patients reported slightly lower correct responses in the negative condition of 1500ms presentation time ($U=341.50$; $Z= -1.95$; $p = .012$; Monte Carlo 99% CI [.001-.011]) compared to HCs.

Moreover, patients reported higher bias score in the erotic condition ($U=362.00$; $Z= -1.67$; $p = .015$; Monte Carlo 99% CI [.026-.034]) as well as lower bias score in the negative condition ($U=317.00$; $Z= -3.30$; $p = .005$; Monte Carlo 99% CI [.004-.007]) compared to HCs.

For both conditions the group difference is particularly manifested for 1500 presentation time (erotic: $U=308.00$; $Z= -2.27$; $p = .005$; Monte Carlo 99% CI [.003-.007] negative: $U=289.00$; $Z= -2.54$; $p = .003$; Monte Carlo 99% CI [.002-.006]) (Bonferroni correction $\alpha = .0167$). No significant differences were found for positive stimuli.

Descriptive statistics for correct responses and bias score are reported in Table 2.6.

Supplementary analysis conducted considering only female participants ($n=27$) confirmed the results, with BPD participants showing a trend of less correct responses in the negative condition condition ($U=317.00$; $Z= -1.54$; $p = .065$; Monte Carlo 99% CI

[.058-.071]) as well as a lower bias score in the negative condition condition (U=285.00; Z= -2.10; $p = .018$; Monte Carlo 99% CI [.009-.015]) and in the erotic condition (U=312.00; Z= -1.61; $p = .045$; Monte Carlo 99% CI [.040-.050]). Again, for both conditions the group difference is particularly manifested for 1500 presentation time (erotic: U=265.00; Z= -2.51; $p = .012$; Monte Carlo 99% CI [.009-.015] negative: U=249.00; Z= -2.10; $p = .018$; Monte Carlo 99% CI [.014-.021]) (Bonferroni correction $\alpha = .0167$). No significant differences were found for positive stimuli.

Table 2. 6 Descriptive statistics and non-parametric group comparisons related to behavioral data

	BPD			HC		
	M(SD)			M(SD)		
	Negative	Positive	Erotic	Negative	Positive	Erotic
<i>500ms</i>						
Correct	47.42(.81)	45.50(7.75)	44.48(9.12)	47.42(.807)	47.00(1.39)	47.03(1.32)
Bias	-.016(.05)	-.010(.04)	-.016(.05)	-0.01(0.02)	-0.01(0.04)	-.013(0.36)
Score						
<i>1500ms</i>						
Correct	45.27(7.94)*	45.73(8.33)	44.77(9.63)	4.52(.625)	47.45(.859)	47.26(1.18)
Bias	-.02(.04)**	-.017(.04)	.013(.04)*	-.004(0.03)	-.013(0.3)	-.009(.032)
Score						

* $p < .05$, ** $p < .005$, *** $p < .001$

Eye tracking indexes

Small but significant reduced latency was reported by BPD patients for erotic and negative conditions both at 500 (erotic: U=326.00; Z= -1.65; $p = .05$; Monte Carlo 99% CI [.043-.054] negative: U=325.00; Z= -1.54; $p = .05$; Monte Carlo 99% CI [.045-.050]) and 1500ms presentation (erotic: U=324.00; Z= -1.67; $p = .04$; Monte Carlo 99% CI [.0037-.049] negative: U=308.00; Z= -1.72; $p = .04$ Monte Carlo 99% CI [.039-.049]). However, those results did not result significant after Bonferroni's correction ($\alpha = 0.0167$).

Moreover, a specific group difference was found for time spent in negative pictures in negative conditions at 1500ms (U=295.00; Z= -1.93; $p = .034$ Monte Carlo 99% CI

[.029-.039]) with patient spending less time comparing to HCs. Finally, no significant differences were found for positive stimuli regarding eye-tracking indexes. Descriptive statistics for eye data are reported in table 2.7

Supplementary analysis conducted considering only female participants (n=27) confirmed the results, with BPD participants showing reduced latency for er erotic and negative conditions both at 500 (erotic: U=259.00; Z= -2.71; $p = .014$; Monte Carlo 99% CI [.011-.017] negative: U=269.00; Z= -1.83; $p = .34$; Monte Carlo 99% CI [.030-.039]) and 1500ms presentation with a trend for both erotic and negative cues (erotic: U=298.00; Z= -1.54; $p = .061$; Monte Carlo 99% CI [.055-.064] and negative: U=283.00; Z= -1.59; $p = .68$ Monte Carlo 99% CI [.039-.049]). Moreover, a specific group difference was found for time spent in negative pictures in negative conditions at 1500ms (U=272.00; Z= -.64; $p = .036$ Monte Carlo 99% CI [.032-.041]) with patient spending less time comparing to HCs.

Table 2. 7 Descriptive statistics and non-parametric group comparisons related to eyes data

	<i>BPD</i>			<i>HC</i>		
		M(SD)		M(SD)		
	<i>Negative</i>	<i>Positive</i>	<i>Erotic</i>	<i>Negative</i>	<i>Positive</i>	<i>Erotic</i>
<i>500ms</i>						
Allocation	.45(11)	.39(.15)	.42(.18)	.41(.13)	.38(.14)	.35(.14)
Latency	.17(.08)*	.13(.08)	.17(.07)*	.19(.07)	.18(.09)	.17(.08)
Time in	.20(.08)	.18(.09)	.17(.09)	.19(.06)	.18(.06)	.18(.06)
<i>1500ms</i>						
Allocation	.34(.17)	.39(.11)	.41(.09)	.40(.11)	.32(.13)	.41(.09)
Latency	.40(16)*	.43(.15)	.46(.19)	.47(.18)	.55(.21)	.46(.19)
Time in	.27(.21)*	.28(.19)	.30(.11)	.30(.12)	.27(.11)	.30(.11)

* $p < .05$, ** $p < .005$, *** $p < .001$

Association between pre task positive and negative affect and task scores

Small but significant associations were found in the clinical group between scores of pre task NA and task scores.

In detail high levels of NA resulted associated with lower correct responses in the erotic condition ($\rho=-.51$, $p=.01$ bootstrap 95% CI: [-.771; -.086]).

The same variable was significantly correlated with latency manifested to negative ($\rho=-.57$, $p=.004$ bootstrap 95% CI: [.206; .803]) and positive ($\rho=-.52$, $p=.01$ bootstrap 95% CI: [0.52; .809]) conditions (Bonferroni's correction $\alpha=.167$).

Moreover, small but significant association were found between NA and initial allocation in the erotic ($\rho=.42$, $p=.04$ bootstrap 95% CI: [-.734; 0.14]), negative (negative: $\rho=.42$, $p=.04$ bootstrap 95% CI: [-.685; -0.25]) and positive ($\rho=.46$, $p=.02$ bootstrap 95% CI: [-.762; .023]) conditions.

However, those results did not result significant after Bonferroni's correction ($\alpha = 0.167$). No significant association were found with CTQ scales or total score.

Clip study

Positive and Negative Affect: group and pre-post comparisons

BPD group reported slightly higher NA ($U=258.00$; $Z= -1.69$; $p = .04$; Monte Carlo 99% CI [.039-.050]) and lower PA ($U=252.00$; $Z= -1.76$; $p = .04$; Monte Carlo 99% CI [.034-.044]) at the beginning of the experiment, as well as significantly higher NA ($U=212.00$; $Z= -2.40$; $p = .009$; Monte Carlo 99% CI [.006-.011]) and lower PA ($U=198.00$; $Z= -2.56$; $p = .004$; Monte Carlo 99% CI [.002-.006]) at the end on the Clip study. Descriptive statistics and group comparisons for PANAS scale scores were presented on table 2.8.

Supplementary analysis conducted considering only female participants ($n=27$) partially confirmed the results with BPD reporting higher NA at baseline ($U=191.00$; $Z= -1.81$; $p = .04$; Monte Carlo 99% CI [.032-.042]) and after the task ($U=190.00$; $Z= -$

1.61; $p = .05$; Monte Carlo 99% CI [.040-.062]) and lower PA after the task ($U=154.50$; $Z= -2.34$; $p = .006$; Monte Carlo 99% CI [.004-.008]).

Table 2. 8 Descriptive statistics and non-parametric group comparisons related to PANAS scales in the Clip study

		<i>BPD</i>	<i>HC</i>
		M(SD)	M(SD)
<i>Pre-task</i>	PA	28.80(6.81)*	32.92(7.99)
	NA	16.50(7.91)*	13.37(5.64)
<i>Post-Task</i>	PA	26.20(9.87)**	32.11(7.29)
	NA	16.08(8.26)**	12.07(3.60)

* $p < .05$, ** $p < .005$, *** $p < .001$

Subjective responses to clip administration

No *group* effect was found for arousal, valence and dominance scores reported after each clip. However, a significant *group x category* interaction was found for arousal ($F(3,52) = 3.39$; $p = .025$; $p\eta^2 = .17$). Descriptive statistics and group comparisons for arousal, valence and dominance scores are reported in table 2.9.

Table 2. 9 Descriptive statistics and non-parametric group comparisons related to self-reported data

	<i>BPD</i>				<i>HC</i>			
	M(SD)				M(SD)			
	<i>Negative</i>	<i>Positive</i>	<i>Neutral</i>	<i>Erotic</i>	<i>Negative</i>	<i>Positive</i>	<i>Neutral</i>	<i>Erotic</i>
Arousal	5.04(2.21)	4.55(2.31)	3.59(2.03)	5.37(2.08)	5.12(1.86)	5.12(1.86)	3.16(1.38)	5.50(1.85)
Valence	3.77(1.55)	7.02(1.31)	6.24(1.04)	6.24(1.33)	3.31(1.15)	7.30(1.55)	5.95(1.15)	6.59(1.48)
Dominance	3.14(2.18)	2.45(2.08)	2.12(1.86)	3.20(2.13)	2.59(1.62)	2.32(2.03)	1.86(1.87)	2.73(1.99)
Positive emotions	1.17(1.13)	3.39(1.95)	2.91(1.29)	2.22(1.64)	.98(.76)	4.27(1.51)	3.46(1.36)	2.92(1.55)
Negative emotions	1.76(1.59)	.46(.67)***	.48(.60)**	.76(.99)***	1.35(.75)	.14(.21)	.11(.15)	.21(.25)

*p<.05, **p<.005, ***p<.001

When the intensity of discrete emotions was taken into account a significant *group* effect was found for the intensity of negative emotions ($F(1,55) = 5.61$; $p = .022$; $p\eta^2 = .10$). Higher level of negative emotions was reported by patients in response to erotic ($U=219.50$; $Z= -2.68$; $p = .003$; Monte Carlo 99% CI [.002; .005]), positive ($U=203.50$; $Z= -2.97$; $p = .001$; Monte Carlo 99% CI [.001; .003]) and neutral ($U=198.00$; $Z= -3.06$; $p = .002$; Monte Carlo 99% CI [.000; .002]) clips (Bonferroni correction: $\alpha=.0125$).

Supplementary analysis conducted considering only female participants ($n=27$) again showed no *group* or *group x category* effect for arousal, valence and dominance scores reported after each clip. When the intensity of discrete emotions was taken into account a significant *group* effect was found for the intensity of negative emotions ($F(1,53) = 5.79$; $p = .020$; $p\eta^2 = .11$). Again, higher level of negative emotions was reported by patients in response to erotic ($U=167.00$; $Z= -2.67$; $p = .003$; Monte Carlo 99% CI [.002; .005]), positive ($U=145.50$; $Z= -3.18$; $p < .001$; Monte Carlo 99% CI [.000; .001]) and neutral ($U=158.00$; $Z= -2.87$; $p = .002$; Monte Carlo 99% CI [.001; .003]) clips (Bonferroni correction: $\alpha=.0125$).

No *group* effect nor *group x category* interaction was found for the intensity of positive emotions.

Considering difference in the intensity of specific emotions reported after each clips category, in the erotic condition BPD patients reported higher scores of sadness ($U=237.50$; $Z= -2.59$; $p = .004$ Monte Carlo 99% CI [.003; .007]), fear ($U=285.00$; $Z= -2.33$; $p = .004$ Monte Carlo 99% CI [.003; .007]), anger ($U=246.00$; $Z= -2.58$; $p = .004$ Monte Carlo 99% CI [.004; .008]) and indignation ($U=247.00$; $Z= -2.64$; $p = .003$ Monte Carlo 99% CI [.003; .006]) compared to HCs (Bonferroni correction: $\alpha=.005$).

In the positive condition, clinical subjects reported higher scores of sadness ($U=279.00$; $Z= -3.59$; $p < .001$ Monte Carlo 99% CI [.000; .001], Bonferroni correction: $\alpha=.005$). For negative clips, no significant difference was found.

Eventually, higher scores of sadness ($U=242.00$; $Z= -2.39$; $p = .005$ Monte Carlo 99% CI [.006; .011]), anger ($U=223.00$; $Z= -3.33$; $p < .001$ Monte Carlo 99% CI [.000; .002]) and tension ($U=242.00$; $Z= -2.41$; $p = .005$ Monte Carlo 99% CI [.006; .010]) was found in the clinical group compares to HCs for neutral clips (Bonferroni correction: $\alpha=.005$).

Supplementary analysis conducted considering only female participants (n=27) confirmed these results. In the erotic condition BPD patients reported higher scores of sadness (U=190.0 Z= -2.45; $p = .009$ Monte Carlo 99% CI [.007; .012]), fear (U=229.00; Z= -2.09; $p = .013$ Monte Carlo 99% CI [.010; .0116]), anger (U=200.00; Z= -2.34; $p = .011$ Monte Carlo 99% CI [.010; .016]) and indignation (U=197.50; Z= -2.138; $p = .006$ Monte Carlo 99% CI [.003; .006]) compared to HCs, however these results do not remain significant after Bonferroni correction (Bonferroni correction: $\alpha=.005$). In the positive condition, clinical subjects reported higher scores of sadness (U=122.00; Z= -3.87; $p < .001$ Monte Carlo 99% CI [.000; .001]), and higher levels of anger (U=205.0; Z= -2.60; $p = .004$ Monte Carlo 99% CI [.002; .006], Bonferroni correction: $\alpha=.005$). Higher scores of anger (U=161.50; Z= -3.39; $p < .001$ Monte Carlo 99% CI [.000; .002]) and tension (U=183.00; Z= -2.40; $p = .005$ Monte Carlo 99% CI [.004; .008]) was found in the clinical group compares to HCs for neutral clips (Bonferroni correction: $\alpha=.005$). Finally, no significant difference was found for negative clips.

Physiological responses

Considering physiological data, no significant differences between groups were found comparing baseline measurement.

Delta scores (clips – baseline) were computed for each physiological index (HR, RMSSD, SDNN) for each condition. Descriptive statistics for physiological variables are reported in Table 10.

Table 2. 10 Descriptive statistics and non-parametric comparison baseline vs emotional category related to physiological data

	<i>BPD</i>					<i>HC</i>				
	<i>Baseline</i>	<i>Negative</i>	<i>Positive</i>	<i>Neutral</i>	<i>Erotic</i>	<i>Baseline</i>	<i>Negative</i>	<i>Positive</i>	<i>Neutral</i>	<i>Erotic</i>
	<i>M(SD)</i>					<i>M(SD)</i>				
<i>HR(ln)</i>	4.35(.14)	4.34(.12)	4.33(.13)	4.33(.13)	4.33(.11)	4.31(.16)	4.29(.11)	4.29(.10)	4.29(.14)	4.28(.12)
<i>RMSSD(ln)</i>	3.85(.54)	4.10(.40)**	4.09(.33)***	4.08(.34)**	4.22(.40)***	3.89(.37)	4.03(.28)*	4.04(.29)*	3.98(.26)*	4.06(.30)**
<i>SDNN(ln)</i>	4.06(.47)	4.06(.38)	4.09(.31)	4.09(.34)	4.20(.42)	4.20(.25)	4.02(.23)	4.05(.26)	4.01(.22)	4.02(.25)

*p<.05, **p<.005, ***p<.001

No significant *group* effect, nor *group x category* interaction were found for Δ HR. Δ RMSSD showed a significant *group* effect ($F(1,55) = 3.77; p = .05; p\eta^2 = .08$). Finally, Δ SDNN reported a significant *group* effect ($F(1,55) = 6.98; p = .01; p\eta^2 = .08$) as well as a *group x category* interaction ($F(3,52) = 3.56; p < .022; p\eta^2 = .20$). Descriptive statistics for delta scores are reported in Table 11. Supplementary analysis conducted considering only female participants ($n=27$) confirmed the absence of *group* and *group x category* interaction for Δ HR. *Group* effects were found for both RMSSD and SDNN (RMSSD: $F(1,53) = 4.98; p = .03; p\eta^2 = .11$; SDNN: $F(1,53) = 7.32; p = .01; p\eta^2 = .15$), moreover a *group x category* effect was found for SDNN ($F(1,53) = 4.48; p = .06; p\eta^2 = .10$).

Table 2. 11 Descriptive statistics and non-parametric group comparison related to delta scores

	<i>BPD</i>				<i>HC</i>			
	M(SD)		M(SD)		M(SD)		M(SD)	
	<i>Negative</i>	<i>Positive</i>	<i>Neutral</i>	<i>Erotic</i>	<i>Negative</i>	<i>Positive</i>	<i>Neutral</i>	<i>Erotic</i>
Δ HR	-.01(.79)	-.01(.71)	-.02(.91)	-.24(.74)	-.02(.07)	-.01(.08)	-.02(.09)	-.02(.07)
Δ RMSSD	-1.94(.45)	.25(.39)	.28(.39)*	.42(.46)*	-1.94(.45)	.25(.39)	.28(.39)	.42(.46)
Δ SDNN	2.16(.43)	.03(.47)	.06(.46)*	.18(.56)*	-2.35(.23)	-.17(.21)	-2.07(.20)	-2.03(.25)

*p<.05, **p<.005, ***p<.001

More in detail, patients reported higher changes in RMSSD and SDNN for erotic (Δ RMSSD: $U=196.00$; $Z= -1.86$; $p = .030$; Monte Carlo 99% CI [.026; .035]; Δ SDNN: $U=180.00$; $Z= -2.19$; $p = .015$; Monte Carlo 99% CI [.011; .017]) and neutral (Δ RMSSD: $U=205.00$; $Z= -1.68$; $p = .04$; Monte Carlo 99% CI [.042; .053]; Δ SDNN: $U=203.00$; $Z= -1.71$; $p = .044$; Monte Carlo 99% CI [.038; .048]) stimuli compared to HCs (Bonferroni correction: $\alpha=.025$).

Supplementary analysis conducted considering only female participants ($n=27$) confirmed the previous results showing higher changes in RMSSD and SDNN for erotic (Δ RMSSD: $U=149.00$; $Z= -1.97$; $p = .024$; Monte Carlo 99% CI [.020; .028]; Δ SDNN: $U=137.00$; $Z= -2.26$; $p = .012$; Monte Carlo 99% CI [.009; .015]) and neutral (Δ RMSSD: $U=157.00$; $Z= -1.77$; $p = .039$; Monte Carlo 99% CI [.034; .044]; Δ SDNN: $U=143.00$; $Z= -2.18$; $p = .017$; Monte Carlo 99% CI [.014; .020]) stimuli in BPD compared to HCs (Bonferroni correction: $\alpha=.025$).

RMSSD scores significantly increased in all the relational stimuli conditions compared to the baseline measurement both in the BPD group (erotic: $Z=-3.43$, $p < .001$; Monte Carlo 99% CI [.000; .00]; positive: $Z=-3.00$, $p = .001$; Monte Carlo 99% CI [.000; .002]; negative: $Z=-2.65$, $p = .004$; Monte Carlo 99% CI [.002; .005]; neutral: $Z=-3.71$, $p = .003$; Monte Carlo 99% CI [.002; .005]) and in the HC group (erotic: $Z=-2.63$, $p = .005$; Monte Carlo 99% CI [.003; .007]; positive: $Z=-2.38$, $p = .001$; Monte Carlo 99% CI [.008; .013]; negative: $Z=-2.25$, $p = .013$; Monte Carlo 99% CI [.010; .016]; neutral: $Z=-1.84$, $p = .003$; Monte Carlo 99% CI [.002; .005]).

No significant difference between clips and baseline assessment was found for SDNN.

Associations between childhood abuse and task scores

To analyse possible association between traumatic experience during childhood and the scores in the task, Spearman's correlations were conducted analysing the Childhood trauma questionnaire (CTQ; Bernstein & Fink, 1998) subscales.

Significant correlations between CTQ scales and task scores were exclusively manifested in the clinical group.

In detail, in the erotic condition a significant association was reported between CTQ emotional abuse and valence score ($\rho = -.59$, $p = .004$ bootstrap 95% CI: [-.832; -.194], Bonferroni correction: $\alpha = .01$).

In the positive condition, significant correlations were found for CTQ emotional abuse ($\rho = -.56$, $p = .007$ bootstrap 95% CI: [-.830; -.160]), emotional neglect ($\rho = -.65$, $p = .001$ bootstrap 95% CI: [-.802; -.427]) (Bonferroni correction: $\alpha = .01$), CTQ tot ($\rho = -.64$, $p = .001$; bootstrap 95% CI: [-.872; -.243]) and valence score.

Considering the intensity of positive and negative emotions reported after each clip, in the erotic condition significant relations were found between CTQ emotional abuse ($\rho = -.69$, $p < .001$ bootstrap 95% CI: [-.851; -.370]) and CTQ tot ($\rho = -.50$, $p = .01$ bootstrap 95% CI: [-.812; -.051]) and positive emotions (Bonferroni correction: $\alpha = .01$). In the positive condition, CTQ emotional neglect significantly correlated with levels of positive emotions ($\rho = -.53$, $p = .01$ bootstrap 95% CI: [-.769; -.085]) (Bonferroni correction: $\alpha = .01$).

Eventually, in the neutral condition significant associations were found between CTQ emotional abuse and positive emotions ($\rho = -.3$, $p = .01$ bootstrap 95% CI: [.026; .149]) (Bonferroni correction: $\alpha = .01$).

Considering physiological indexes, no association with CTQ scores remained significant after Bonferroni correction.

In summary, in the *Dot-probe* study BPD reported higher attentional bias regarding erotic stimuli and lower attentional bias for negative stimuli compared to HC. Moreover, BPD reported pattern of hypervigilance for erotic and negative stimuli. In addition, negative affectivity and negative stimuli had an impact on the performance of BPD patients.

In the *Clip study* patients reported a complex physiological response together with high levels of self-reported negative emotion. Moreover, significant associations were found between self-reported emotional state and traumatic events during the childhood. Two papers were written starting from these experiments and are currently *under submission*.

Mindfulness studies

To study the efficacy of a mindfulness exercise in modulating in real time psychophysiological functioning of the subjects, two studies were conducted. While the participants of the first studies were all HC, in the second studies BPD and HC subjects were analyzed and compared.

In both studies, participants underwent 3 different phases. In the first and last phase (i.e., baseline and recovery) participants were asked to relax and do nothing. On the other hand, in the second phase participants were asked to complete a mindfulness exercise (i.e., mindfulness phase).

After each phase mind wandering and affective states were assessed with the PANAS and the Amsterdam Resting State Questionnaire (ARSQ; Diaz et al., 2014).

Moreover, after the mindfulness phase a questionnaire on mindfulness ability was assessed (i.e., MODQ). Full detail on the methodology and indexes analysed could be found in the Methodology section. Figure 2.4 represent mindfulness studies methodology. These studies were conducted to confirm the efficacy of a mindfulness in real time. In detail mind-wandering states are expected to decrease during the mindfulness exercise, together with an increase in HRV indexes and in positive emotional states. Moreover, direct correlation between the quality of the performance of the mindfulness exercise and changes in mind-wandering, emotional and physiological indexes are expected. The same patterns of responses are expected in both BPD and HC.



Figure 2. 4 Mindfulness studies methodology

Study 1

Changes in mind-wandering scores

Significantly lower Theory of mind (TOM) scores were reported during the mindfulness phase compared to the initial baseline phase ($Z=-3.18$, $p=.001$; Monte Carlo 99% CI: [.000-.001]). Planning scale score was significantly lower during the mindfulness exercise compared to the initial baseline condition ($Z=-3.00$, $p=.002$; Monte Carlo 99% CI [.001-.003]).

Likely, Visual Thoughts scale results were significantly lower during the mindfulness phase ($Z=-3.04$, $p=.003$; Monte Carlo 99% CI [.001-.004]).

Finally, significantly higher Somatic Awareness scores were reported during the mindfulness phase ($Z=-3.73$, $p<.001$; Monte Carlo 99% CI [.001-.004]) (Bonferroni correction: $p=.005$). Somatic Awareness was the only ARSQ scale that reported a significant difference between the mindfulness and the recovery phase ($Z=-4.9$, $p<.001$; Monte Carlo 99% CI [.000-.001]) (Bonferroni correction: $p=.005$).

In detail, both the baseline and the recovery phase were characterized by lower levels of Somatic Awareness compared to the mindfulness phase.

No significant differences between phases were found for the ARSQ Discontinuity, Self, Sleepiness, Comfort, Health Concern and Verbal Thoughts scales. Results are reported in Table 2.12.

Changes in physiological activation

HR indexes ranged between 4.01 and 5.18 for HR - between 55.22 and 120.48 when considering bpm for HR- at baseline. During mindfulness, HR ranged between 4.08 and 4.57 - between 59.00 and 96.48 when considering bpm for HR-. Finally, during recovery phase, HR ranged between 4.05 and 4.51 - between 57.28 and 91.83 when

considering bpm for HR-. Considering RMSSD, at baseline values ranged between 3.08 and 4.80; during mindfulness values ranged between 3.30 and 5.14; finally, during the recovery, values ranged between 3.24 and 5.19. Regarding SDNN, at baseline values ranged between 3.33 and 4.64; during mindfulness values ranged between 3.34 and 5.26; finally, during the recovery, values ranged between 3.37 and 5.13.

Significant differences between baseline and mindfulness phases were found for all the physiological indexes investigated (Bonferroni correction: $p=.0125$).

In detail, HR ($Z=-2.65$, $p=.006$; Monte Carlo 99% CI [.004-.008]), RSA ($Z=-2.57$, $p=.008$; Monte Carlo 99% CI [.006-.011]) RMSSD ($Z=-3.24$, $p=.001$; Monte Carlo 99% CI [.000-.001]) and SDNN ($Z=-4$, $p<.001$; Monte Carlo 99% CI [.000-.001]) significantly increased during mindfulness phase compared to the previous condition.

While investigating for significant differences between the mindfulness and the recovery phase significant differences were found for HR ($Z=-3.49$, $p<.001$; Monte Carlo 99% CI [.000-.001]) and SDNN ($Z=-3.75$, $p<.001$; Monte Carlo 99% CI [.000-.001]) (Bonferroni correction: $p=.0125$). In detail, these indexes were lower both in the baseline and in the recovery phase compared to the mindfulness phase. Results are reported in Table 12.

Changes in affective states score

A significant change was found for PANAS positive and negative affectivity only between the beginning of the experiment and the end of the baseline phase (Bonferroni correction: $p=.012$). In detail, participants showed a reduction in both PA ($Z=-2.44$, $p=.012$; Monte Carlo 99% CI [.10.16]) and NA ($Z=-3.84$, $p<.001$; Monte Carlo 99% CI [.000-.001]) indexes. No other significative differences were found regarding affectivity indexes. Results are reported in Table 12.

Associations between MODQ, ARSQ, affective states, and physiology during mindfulness phase

Significant associations were found between levels of ARSQ Somatic Awareness and MODQ Distractions scale ($\rho=.62$, $p<.001$ bootstrap 95% CI: [.330-803]) and between ARSQ Visual Thoughts and MODQ Distractions scale ($\rho=-.64$, $p=.001$ bootstrap 95% CI: [-.833- -.237]). Moreover, a significant association was found between ARSQ Discontinuity scale and MODQ distraction scale ($\rho=.64$, $p<.001$ (bootstrap 95% CI: [.351; .675] Bonferroni's correction $p=.001$). .

Moreover, significant associations were found between PA levels after mindfulness phase and MODQ Distraction Scales ($\rho=.63$, $p<.001$ bootstrap 95% CI: [.458-.851]) (Bonferroni correction: $p=.006$).

No significant associations were found between physiological indexes and self-reported outcomes in the mindfulness exercise.

Table 2. 12 Descriptive Statistics of ARSQ and PANAS scores measured after each phase and physiological indexes measures during the three conditions.

	<i>Baseline phase M(SD)</i>	<i>Mindfulness phase M(SD)</i>	<i>Rest phase M(SD)</i>	<i>Baseline- Mindfulness comparison Z</i>	<i>Mindfulness- Rest comparison Z</i>
<i>ARSQ</i>					
Discontinuity	2.66(.76)	2.63(.68)	2.49(.75)	<i>ns</i>	<i>ns</i>
TOM	3.21(.88)	2.49(.95)	2.82(.98)	-2.52 **	<i>ns</i>
Self	3.11(.70)	3.27(.95)	3.01(.75)	<i>ns</i>	<i>ns</i>
Planning	3.37(.94)	2.57(.98)	3.01(1.01)	-3.47**	<i>ns</i>
Sleepiness	3.14(1.25)	2.71(1.16)	3.01(1.19)	<i>ns</i>	<i>ns</i>
Comfort	3.46(.63)	3,30(.96)	3.67(.71)	<i>ns</i>	<i>ns</i>
Somatic	3.00(1.03)	3.64(.85)	2.45(1.03)	-3.01**	-4.57***
<i>Awareness</i>					
Health	1.46(.44)	1.79(.79)	1.45(.63)	<i>ns</i>	<i>ns</i>
<i>Concern</i>					
Visual	3.85(.86)	3.13(1.02)	3.58(1.01)	-2.50**	<i>ns</i>
<i>Thoughts</i>					
Verbal	2.32(.91)	1.98(.82)	2.44(.88)	<i>ns</i>	-2.46**
<i>Physiological indexes</i>					
HR(ln)	4.29(.15)	4.32(.13)	4.28(.13)	-2.98**	-3.49***
RMSSD(ln)	3.91(.55)	4.16(.58)	4.03(.53)	-3.21***	<i>ns</i>
SDNN(ln)	3.94(.41)	4.29(.46)	4.03(.41)	-4.03***	-3.75***
<i>PANAS</i>					
PA	27.04(8.62)	27.43(9.01)	25.78(10.13)	<i>ns</i>	<i>ns</i>
NA	12.36(4.85)	11.96(3.78)	11.32(2.40)	<i>ns</i>	<i>ns</i>

*p<.05, **p<.005, ***p<.001

Study 2

Changes in mind-wandering scores

Significant phase effect was found for TOM index ($F(1,58) = 11.73$; $p < .001$, $p\eta^2 = .17$). In detail, both groups showed significant reduction of TOM during the mindfulness exercise (HC: $Z = -3.37$, $p < .001$; Monte Carlo 99% CI [.000;.0001]; BPD: $Z = -2.52$, $p = .006$; Monte Carlo 99% CI [.004;.008]). Similarly, significant phase effect was found for Planning index ($F(1,58) = 13.33$; $p < .001$, $p\eta^2 = .18$).

Again, both groups showed significant reduction of Planning during the mindfulness exercise (HC: $Z = -3.47$, $p < .001$; Monte Carlo 99% CI [.000;.000]; BPD: $Z = -2.52$, $p = .006$ Monte Carlo 99% CI [.002;.005]). For Somatic awareness scale, a phase effect was found ($F(1,58) = 45.85$; $p < .001$, $p\eta^2 = .61$). In detail, Somatic awareness were lower in the baseline compared to mindfulness in both HC ($Z = -3.01$, $p = .001$; Monte Carlo 99% CI [.000;.002]) and BPD ($Z = -2.29$, $p = .011$; Monte Carlo 99% CI [.007;.012]).

Finally, Somatic awareness level was higher in mindfulness compared to recovery phase in HC ($Z = -4.57$, $p < .001$; Monte Carlo 99% CI [.000;.000]) and BPD ($Z = -4.25$, $p < .001$ Monte Carlo 99% CI [.000;.000]). Regarding Visual thoughts scale, a phase effect was found ($F(1,58) = 45.85$; $p < .001$, $p\eta^2 = .26$).

In detail, HC participants reported lower levels of Visual thoughts in mindfulness phase compared to baseline ($Z = -2.50$, $p = .009$ Monte Carlo 99% CI [.005;.009]), but no differences were found between mindfulness and rest phases.

On the other hand, BPD subjects report lower values of Visual thought index in mindfulness compared to baseline phase ($Z = -3.45$, $p < .001$; Monte Carlo 99% CI [.000;.001]) and rest phases ($Z = -2.33$, $p = .008$ Monte Carlo 99% CI [.005;.010]).

Finally, a phase effect was found for Verbal thoughts scale ($F(1,58) = 10.01$; $p < .001$, $p\eta^2 = .13$).

In detail, both groups showed significant reduction of Verbal thoughts during the mindfulness exercise (HC: $Z=-2.36$, $p=.008$ Monte Carlo 99% CI [.007;.012]; BPD: $Z=-1.82$, $p=.039$; Monte Carlo 99% CI [.030;.040]); a significant increase of Verbal thoughts during the recovery was found only for HC ($Z=-2.46$, $p=.006$; Monte Carlo 99% CI [.003;.007]).

No significant differences nor effects were found for Discontinuity, Self, Sleepiness, Comfort, and Health Concern scales. No differences were found for MODQ questionnaire between groups. Results are reported in Table 13.

Changes in Physiological activation

In HC HR values ranged between 4.01 and 4.68 -between 55.22 and 107.86 for bpm- at baseline, between 4.08 and 4.76 -between 59.00 and 116.45, when bpm were considered- during the mindfulness exercise, and between 4.05 and 4.68 – between 57.28 and 107.67 when considering bpm- during the recovery. On the other hand, in BPD HR values ranged between 4.10 and 4.69 -between 60.30 and 108.38 for bpm- at baseline, between 4.14 and 4.65 -between 62.73 and 104.05, when bpm were considered- during the mindfulness exercise, and between 4.07 and 4.66 – between 58.68 and 106.08 when considering bpm- during the recovery.

Regarding HRV indexes, in HC RMSSD ranged between 3.08 and 5.90 at baseline, between 3.19 and 6.19 during the mindfulness exercise; and between 3.25 and 5.96 during the recovery phase. In BPD RMSSD ranged between 2.57 and 5.87 at baseline, between 2.61 and 4.45 during the mindfulness exercise; and between 2.61 and 4.73 during the recovery phase.

Finally, in HC SDNN ranged between ranged between 3.33 and 5.33 at baseline, between 3.49 and 5.67 during the mindfulness exercise; and between 3.37 and 5.48 during the recovery phase. In BPD SDNN ranged between 2.52 and 5.39 at baseline, between 2.74 and 4.59 during the mindfulness exercise; and between 2.81 and 4.54 during the recovery phase.

No differences at baseline for physiological indexes were found between the two groups.

Significant phase effect was found for HR index ($F(1,58) = 14.14$; $p < .001$, $\eta^2 = .45$). Only HC showed significant increase of HR during the mindfulness exercise ($Z = -2.98$, $p = .001$ Monte Carlo 99% CI [.000;.002]); while a significant decrease of HR during the rest was found only for both groups (HC: $Z = -4.07$, $p < .001$; Monte Carlo 99% CI [.000;.000]; BPD: $Z = -2.88$, $p = .002$; Monte Carlo 99% CI [.001;.006]).

Significant phase ($F(1,58) = 4.63$; $p = .015$, $\eta^2 = .17$) and group ($F(1,58) = 6.12$; $p = .02$, $\eta^2 = .12$) effects were found for RMSSD index. In detail, HC showed an increase in RMSSD during mindfulness ($Z = -3.21$; $p < .001$; Monte Carlo 99% CI [.000;.001]) while BPD showed an increase in RMSSD during the rest phase ($Z = -2.22$, $p = .011$; Monte Carlo 99% CI [.011;.017]).

Similarly, significant phase ($F(1,58) = 8.10$; $p = .001$, $\eta^2 = .26$), and group ($F(1,58) = 7.63$; $p = .008$, $\eta^2 = .14$) effects were found for SDNN index, with BPD patients reporting lower levels of SDNN during the whole task.

Moreover, while BPD presented only an increase of SDNN in mindfulness phase compared to baseline ($Z = -1.65$; $p = .049$; Monte Carlo 99% CI [.044;.055]), HC showed a significant higher SDNN during mindfulness phase compared to baseline ($Z = -4.03$; $p < .001$ Monte Carlo 99% CI [.000;.000]) and recovery ($Z = -2.89$; $p = .005$; Monte Carlo 99% CI [.000;.000]) phases. Results are reported in Table 13.

Changes in affectivity scores

Significant phase effects were found for PA ($F(1,58) = 6.13$; $p = .001$, $\eta^2 = .19$) and NA ($F(1,58) = 9.72$; $p < .001$, $\eta^2 = .25$).

In detail, HC showed significant reductions in PA ($Z = -2.16$, $p = .016$) and NA ($Z = -4.04$, $p < .001$) after the baseline measurement.

Similarly, BPD showed significant reductions of PA ($Z = -2.88$, $p = .002$ Monte Carlo 99% CI [.011;.017]) and NA ($Z = -2.54$, $p = .011$; Monte Carlo 99% CI [.000;.000]) after the baseline.

No differences were found for the two indexes after the mindfulness in both groups.

Finally, significant differences were found only in HC after the rest, with HC showing a decrease in PA ($Z=-3.17$, $p=.001$; Monte Carlo 99% CI [.000;.001]) and NA ($Z=-1.99$, $p=.025$; Monte Carlo 99% CI [.023;.031]) after the last measurement.

Moreover, significant group effects were found for both PA ($F(1,58) = 7.82$; $p = .007$, $\eta^2 = .12$) and NA ($F(1,58) = 8.06$; $p = .006$, $\eta^2 = .14$) with BPD patients reporting higher levels of PA and lower levels of NA. Results are reported in Table 13.

Associations between MODQ, ARSQ, affective states, and physiology during mindfulness phase

In HC a significant association was found between ARSQ Discontinuity scale and MODQ distraction scale ($\rho=.65$, $p<.001$ (bootstrap 95% CI: [.356; .853]).

Moreover, a significant association was found between ARSQ Planning scale and MODQ distraction scale and ($\rho=.59$, $p=.001$ (bootstrap 95% CI: [.294; .800] (Bonferroni's correction $\alpha=.001$).

In BPD group, significant associations were found between MODQ distraction scale and ARSQ Discontinuity scale ($\rho=.65$, $p<.001$ bootstrap 95% CI: [.364; .803]) and between MODQ judgment scale and ARSQ Self scale ($\rho=.55$, $p=.001$ bootstrap 95% CI: [.135; .805]) Bonferroni's correction $\alpha=.001$.

Moreover, significant associations were found between PA levels after mindfulness phase and MODQ Distraction Scales ($\rho=.52$, $p=.004$ bootstrap 95% CI: [-.737;-.228]).

In BPD sample significant associations were found between NA and MODQ distraction scale ($\rho =.46$, $p=.011$ bootstrap 95% CI: [-.118;-.724]) and MODQ judgment scale and NA pre ($\rho =.49$, $p=.008$ bootstrap 95% CI: [.167;.727]) and post task ($\rho =.48$, $p=.009$ bootstrap 95% CI: [.124; .733]).

However, these last results did not remain significant after Bonferroni's correction (Bonferroni correction: $p=.005$). Results are reported in Table 2.13 and 2.14.

No significant associations were found between physiological indexes and self-reported outcomes in the mindfulness exercise.

Table 2. 13 Descriptive Statistics of ARSQ and PANAS scores measured after each phase and physiological indexes measures during the three conditions in BPD

	<i>Baseline phase M(SD)</i>	<i>Mindfulness phase M(SD)</i>	<i>Recovery phase M(SD)</i>	<i>Baseline- Mindfulness comparison Z</i>	<i>Mindfulness- Rest comparison Z</i>
<i>ARSQ</i>					
Discontinuity	3.00(1.0)	2.74(1.07)	2.83(1.12)	<i>ns</i>	<i>ns</i>
TOM	2.92(.96)	2.31(1.11)	2.64(.94)	-3.18**	<i>ns</i>
Self	3.0(1.02)	3.16(1.11)	3.08(1.18)	<i>ns</i>	<i>ns</i>
Planning	3.07(1.11)	2.41(1.19)	2.85(1.43)	-3.00**	<i>ns</i>
Sleepiness	2.95(1.27)	3.21(1.13)	2.85(1.37)	<i>ns</i>	<i>ns</i>
Comfort	3.24(1.04)	3.03(1.04)	3.21(.96)	<i>ns</i>	<i>ns</i>
Somatic	2.92(1.13)	3.54(.83)	2.41(1.03)	-3.74**	-4.25***
<i>Awareness</i>					
Health	1.81(.69)	1.73(.75)	1.74(.62)	<i>ns</i>	<i>ns</i>
<i>Concern</i>					
Visual	3.38(1.10)	2.52(1.28)	3.05(1.36)	-3.04**	-2.33**
<i>Thoughts</i>					
Verbal	2.66(1.00)	2.42(.96)	2.30(1.08)	<i>ns</i>	<i>ns</i>
<i>Thoughts</i>					
<i>Physiological indexes</i>					
HR(ln)	4.36(.15)	4.36(.15)	4.34(.15)	<i>ns</i>	-2.88***
RMSSD(ln)	3.68(.70)	3.57(.51)	3.74(.56)	<i>ns</i>	-2.22*
SDNN(ln)	3.70(.58)	3.74(.50)	3.83(.47)	1.65*	<i>ns</i>
<i>PANAS</i>					
PA	23.10(9.67)	22.60(9.67)	22.68(9.74)	<i>ns</i>	<i>ns</i>
NA	15.90(6.43)	15.10(6.46)	13.75(5.00)	<i>ns</i>	<i>ns</i>

*p<.05, **p<.005, ***p<.001

Table 2. 14 Descriptive Statistics of ARSQ and PANAS scores measured after each phase and physiological indexes measures during the three conditions in HC

	Baseline phase M(SD)	Mindfulness phase M(SD)	Recovery phase M(SD)	Baseline- Mindfulness comparison Z	Mindfulness- Rest comparison Z
<i>ARSQ</i>					
Discontinuity	2.67(.74)	2.58(.74)	2.41(.71)	<i>ns</i>	<i>ns</i>
TOM	3.17(.82)	2.37(.99)	2.90(.91)	-3.18**	<i>ns</i>
Self	3.31(.74)	3.37(.87)	3.20(.74)	<i>ns</i>	<i>ns</i>
Planning	3.46(.84)	2.48(1.11)	3.11(.94)	-3.00**	<i>ns</i>
Sleepiness	2.90(1.16)	2.46(1.16)	2.94(1.15)	<i>ns</i>	<i>ns</i>
Comfort	3.65(.52)	3.43(.89)	3.88(.58)	<i>ns</i>	<i>ns</i>
Somatic Awareness	3.31(.91)	3.83(.68)	2.60(.88)	-3.74**	-4.57***
Health Concern	1.43(.43)	1.70(.70)	1.50(.62)	<i>ns</i>	<i>ns</i>
Visual Thoughts	2.33(.90)	3.02(.95)	3.32(.94)	-3.04**	<i>ns</i>
Verbal Thoughts	4.01(.61)	1.92(.76)	2.35(.86)	-2.36**	-2.46**
<i>Physiological indexes</i>					
HR(ln)	4.31(.16)	4.35(.14)	4.29(.14)	-2.98**	-4.07***
RMSSD(ln)	3.80(.57)	4.07(.68)	4.03(.55)	-3.21***	<i>ns</i>
SDNN(ln)	3.89(.42)	4.25(.48)	4.04(.42)	-4.03***	-2.89**
<i>PANAS</i>					
PA	30.04(11.52)	29.86(8.16)	27.23(9.54)	<i>ns</i>	<i>ns</i>
NA	11.76(3.57)	11.30(2.94)	10.73(1.28)	<i>ns</i>	<i>ns</i>

*p<.05, **p<.005, ***p<.001

In summary, Mindfulness breathing observation exercise modulated the mind-wandering state of the participants (both BPD and HC) in a similar way. However, physiological responses suggest us an alternative functioning in BPD autonomic regulation. Finally, significant associations were found between the mindfulness exercise performance and the affective states. The first study is already published in *Applied Psychophysiology and Biofeedback*, while the second study is *under preparation* and will be submitted in the next month.

Discussion

Borderline Personality Disorder is the most diagnosed personality disorder and one of the most studied disorders (APA; 2013; Zimmerman & Mattia, 1999) both for the impact of its symptoms (e.g., NSSI, affective instability, addiction, anxiety) on subjects and health care services (Bateman & Fonagy, 2003; Van Asselt, Dirksen, Arntz, & Severens, 2007). In the last decades, several studies have been conducted to analyze BPD, providing a huge number of relevant information essential for understanding and treating such disorder. However, the results present in literature are mixed and non-coherent. Consequently, models of BPD functioning presented in the literature are not completely supported by empirical data. This dissertation aimed to shed light on a possible alternative model that considers the efficacy of specific emotional states in relation to the executive disfunction presented by BPD patients (Ruocco, 2005).

Given the lack of support for a general hyperreactivity hypothesis postulated in the Biosocial model (Linehan, 1993), and the well-documented impairments presented by BPD subjects in the interpersonal functioning (APA, 2013), the aim of this thesis was to give primary support to the hypothesis that the hyperreactivity construct could be specifically related to specific triggers (i.e., socio-emotional cues). Moreover, given the relation between the mindfulness abilities and the emotional regulation processes (Gratz & Roemer, 2010) and the strict connection between ruminative states, and dysfunctional emotional regulation strategies in BPD patients (Quirk, Wier, Martin, & Christian, 2015), during this dissertation two studies were conducted to analyze the efficacy of a mindfulness exercise in modulating mind wandering states together with emotional and physiological reactivity. Finally, coherently with the data presented in literature and the data presented in this dissertation, at the end of this chapter a possible neural model of BPD emotional functioning is proposed.

In all the studies presented in this dissertation, data on baseline emotional activity confirmed the hypothesis of hypersensitivity in the BPD sample. Self-reported data on current affective states showed that BPD patients present higher negative activation at the basal level in all the studies. On the other hand, mixed results are again reported regarding physiological indexes. In detail, BPD showed higher basal activity than HC in

the *Executive functioning task*, regarding HR and HRV indexes. However, in the other studies presented (*Clip study* and *Mindfulness study 2*), no significant differences for basal physiological activity were found, even though patients reported higher HR and lower levels of HRV. These results suggest the presence of high sympathetic activity in BPD patients and a proneness to be predisposed to a "fight or flight" response even when asked to relax and to do nothing, modulated by to a low parasympathetic activity. These results are partially in line with the literature and give further support to the hypersensitivity hypothesis in BPD patients, which is more negatively activated without a specific emotional triggering stimulus. Given the well-documented sensitivity of BPD patients to judgment and rejection (Staebler, Helbing, Rosenbach, & Renneberg, 2011), these different basal activities could be dependent on a different appraisal and neuroception of the patients regarding the experimental setting, that could be perceived as more or less threatening and judging.

While analyzing emotional reactivity in the Executive functioning task, significant effects on affective states were found after the negative induction. While a dampening of general affective state was found for HC, no differences were found regarding affective states in the neutral induction paradigm in BPD patients.

Moreover, given the decreases presented by HC and BPD in positive affectivity and the increases of negative affectivity after the negative induction, we can assume that the inductions effectively influenced the participant's affective state.

However, while analyzing physiological indexes, no differences were found according to the study hypothesis. These last results suggest that both BPD and HC react similarly, at least regarding HRV indexes, to emotional induction, whether negative or neutral, giving further evidence, and in disconfirming of a general hyperreactivity hypothesis in BPD patients (Linehan 1993).

Interestingly, and in line with the hypotheses of this dissertation, differences of self-reported emotional and physiological reactivity were found when socio-emotional cues were presented to the two samples in the *Clip study*.

While socio-emotional clips were administered, BPD and HC showed significant increases of SDNN and RMSSD between the baseline and the view of the clip,

independently from the stimulus category. In detail, when looking at the intensity of this change, BPD patients manifested a higher increase for both indexes compared to HC. Even though these results do not fully support the socio-emotional physiological specific hyperreactivity hypothesis in BPD patients, these data could be informative of BPD emotional and neuroception functioning during interpersonal interactions.

In detail, HRV increases during the exposition to socio-emotional cues could signify an attempt of emotional regulation while facing and interpreting a social situation, in line with the theory of emotional regulation proposed by Thayer (2000) and the role of the cardiac variability in the regulation of social interaction proposed by Porges in the Polyvagal theory (2007). Heart rate variability is an index of parasympathetic activity and is representative of a functional sympathetic brake. However, in addition to an increase in HRV, BPD subjects reported higher HR than HC (albeit group comparison did not reach statistical significance after Bonferroni's correction). Taken together, these results could represent a complex physiological response in BPD that could involve the co-activation of the sympathetic and parasympathetic nervous systems. This physiological activation pattern could be related to a condition of physiological breakdown generated by the emotional contents of the stimuli, mediated by the vagus nerve (Porges, 2007). It is possible that BPD patients could manifest an initial sympathetic activation, due to a dysfunctional neuroception, followed by a parasympathetic activation to cope with the emotional state. Coherently with this hypothesis, the fight/flight response would not happen, and it would be substituted by a physiological immobilization response associated with stimulus processing (Sarlo, Palomba, Buodo, Minghetti & Stegagno, 2005).

Differences in emotional and physiological responses could also depend to differences in stimuli exploration.

The *Dot-probe study* presented in this dissertation directly tackles the presence of altered attentional mechanisms in BPD regarding socio-emotional stimuli. Obtained results support the hypothesis of hypervigilance in BPD (e.g., Bertsch et al., 2013; Bertsch et al., 2017; Frick et al., 2012), bringing patients to move the attention rapidly toward stimuli that are potential triggers for the disorder. In detail, in line with the hypotheses, BPD patients showed lower latency in response to erotic and negative stimuli. These mechanisms could be particularly manifested since typical BPD

interpersonal difficulties -such as marked rejection sensitivity (Berenson et al., 2009; Staebler, Gebhard, Barnett & Renneberg, 2009), fear of abandonment, unstable and unsatisfactory relationships (APA, 2013)- might impact on patients' alertness. Additionally, these results were exclusively manifested in response to negative and erotic stimuli. Whether research on the processing of negative stimuli is well-documented in BPD patients (e.g., Bortolla, Cavicchioli, Galli, Verschure & Maffei, 2019; Bortolla, Galli, Ramella, Sirtori, Visintini & Maffei, 2020; Frick et al., 2012), showing increased responsivity to such emotional situations (Reichenberger, Eibl, Pfaltz, Wilhelm, Voderholzer, Hillert et al., 2017; Stepp, Scott, & Jones, 2016), there are only a few studies on the processing of erotic contents. Data on the elaboration of erotic contents in the general population showed that sexual stimuli are particularly engaging for the subject (Bradley et al., 2001; Sarlo, Palomba, Buodo, Minghetti & Stegagno, 2005), requiring appetitive motivational systems. On the other hand, as stated before, the sexual life of patients is often characterized by high levels of sexual dissatisfaction and preoccupation (Hulbert et al., 1992; Schulte-Herbrüggen et al., 2009) and high scores of sexual abuses (Sansone & Sansone 2011; Hurlbert et al., 1992; Spokas, Wenzel, Stirman, Brown & Beck, 2009; Schulte-Herbrüggen et al., 2009; Wong Leung, Chow, Kam & Tang, 2010; Afifi, Mather, Boman, Fleisher, Enns, MacMillan et al., 2011; Westphal, Olfson, Bravova, Gameroff, Gross, Wickramaratne, et al., 2013). These aspects could determine the condition of alertness to these stimuli found in our study that are evaluated as a potential threat and impact subsequent phases of visual exploration, in line with the evolutionary perspective described in the introduction.

Interestingly, although negative and erotic stimuli triggered a similar pattern of hypervigilance, different subsequent phases of visual exploration were reported in BPD patients. Compared to HC, BPD reported a higher bias score for erotic stimuli and a lower bias score for negative stimuli. Moreover, BPD patients reported less time in the negative picture than HC.

Indeed, patients seemed to be rapidly attracted by erotic stimuli, and subsequently, they showed difficulties in disentangling the attention to these cues. This condition is in line with the attentional bias hypothesis (e.g., Kaiser et al., 2017). Erotic stimuli are appealing for nature (Bradley, Codispoti, Cuthbert & Lang, 2001; Sarlo, Palomba,

Buodo, Minghetti & Stegagno, 2005), but given the difficulties presented relative to sexuality (e.g., sexual preoccupation, dissatisfaction, and abuse), patients might manifest difficulties in disengaging attention due to their typical symptoms in this area. Borderline subjects could have difficulties in processing the erotic stimulus given its ambiguous nature: from one hand, they recognize its appetitive nature that attracts attention and interest, at the same time, the contents of the stimulus could activate distress and intrusive negative thoughts in line with previous subjective experiences, resulting in problems in disengaging attention from the sexual contents.

On the other hand, BPD patients' fast shift of attention was immediately followed by a rapid shift of attention away from the same contents when exposed to negative cues. These results confirm previous data on the marked use of attentional avoidance mechanisms in BPD, especially when interpersonal contents are considered (Bortolla, Cavicchioli, Galli, Verschure & Maffei, 2019; Bortolla, Galli, Ramella, Sirtori, Visintini & Maffei, 2020).

Patients might show hyper-vigilance associated with heightened sensitivity for negative information (Reichenberger, Eibl, Pfaltz, Wilhelm, Voderholzer, Hillert, et al., 2017; Stepp, Scott, Jones, Whalen, & Hipwell, 2016) that could result in intense emotional states, bringing the subject to engage in abnormal behavioural strategies to avoid threats. Relevantly, the negative cues reported contents related to abandonment, quarrels, breakups that are strictly related to typical BPD interpersonal difficulties. Interestingly and coherently with the hypothesis that socio-emotional difficulties could be a specific trigger for the executive dysfunction of BPD patients, pre-task negative affectivity resulted associated with dot-probe indexes exclusively in the BPD group. In detail, patients reported lower latency to negative and positive stimuli and higher initial allocation to negative, positive, and erotic stimuli in association to high levels of negative affectivity.

It could be hypothesized that negative affective states could bring patients to be particularly alerted to a potential threat. Indeed, they bring the attention rapidly to relational cues compared to a neutral one, probably to detect signals of danger independently from the content of the stimulus, confirming the role of affective context in the modulation of attentional biases (Smith et al., 2006).

Coherently, even though no significant association was found between childhood trauma and eye-tracking indexes, significant associations were found between the CTQ subscales and the self-reported emotional states during the view of the socio-emotional stimuli in the *Clip study*. Less positive emotional state correlated with high levels of emotional neglect, while neutral clips were considered as less positive given high levels of emotional abuse. In detail, only BPD patients reported higher levels of negative emotion during the view of the erotic stimuli in relation to high levels of abuse received during infancy.

Finally, it is interesting to notice that high negative affectivity measured before the administration of the dot-probe, related to a higher number of behavioural errors during the task. In detail, the negative condition is the only one in which patients reported lower numbers of correct responses. Previous studies on BPD patients using dot-probe methodology did not show alteration in attentional processes in this pathology (Kaiser et al., 2016). High negative affectivity levels affected patients' ability to correctly complete the task, disrupting the attentive ability of BPD patients, confirming the emotional interference on cognitive processes presented before. Taken together, these results are coherent with what has been found in the *Executive functioning study*.

Together with the specificity of the results presented on the number of errors in the Dot-probe study confirms the importance of social situations as the potential core of the executive and behavioural dysregulation presented by BPD patients. As a whole, these results obtained from the two social studies support the hypothesis that conceptualizes BPD as a neuroception-based disorder: difficulties in understanding the social cues seem to lead to altered visual exploration and physiological and emotional reactivity.

As stated in the introduction, BPD patients present structural and functional differences at cortical and limbic levels. In particular, given the presented results OFC seems to play a central role in BPD. Orbitofrontal cortex is fundamental in executive functioning, cognitive flexibility, dissociation, and time perception (Bechara, Damasio, Damasio et al., 1994; Berlin, Rolls, Iversen, 2005; Berlin, Rolls, Kischka, 2004; Rolls, Hornak, Wade et al., 1994; Mueller-Pfeiffer, Schick, Schulte-Vels et al., 2013; Schenk, Bear, 1981; Sellitto, Ciaramelli, di Pellegrino, 2010; Tsuchida, Doll, Fellows, 2010). Moreover, the orbitofrontal cortex receives information about the sight of objects from

the temporal lobe cortical visual areas, and its functioning is related to regulating emotion-attention interaction (Hartikainen, Ogawa & Knight, 2012). Dysfunctionalities in OFC are related to increasing attentional bias to emotional stimuli, as reported in the Dot-probe study presented in this dissertation. Prefrontal and orbitofrontal cortexes play a central role in modulating and inhibiting amygdala activity due to their connections with the central nucleus of the amygdala (Barbas, Zikopoulos, 2007; Shekhar, Sajdyk, Gehlert et al., 2003) and a complex system of internal feedback. An efficient cortical inhibition produces a regulated amygdala response and an adaptive autonomic functioning. On the contrary, reduced cortical inhibition or high amygdala activity leads to difficulties in emotion regulation and behavioural dysregulation.

Coherently, in line with the experimental hypotheses, when analyzing results obtained in the *Executive functioning study*,

after a negative induction patients reported a lower level of decision consistency compared to HC. Interestingly, the negative affective state disrupted decision consistency only in the clinical sample. When in a negative emotional state, BPD patients tended to select their answer independently from the attention levels given to each rule, following a random pattern of haphazard selection. This result could explain why BPD patients perform self-destructive maladaptive behaviours when negatively activated. BPD patients could find it problematic to direct their attention to adaptive coping alternatives and retrieve adaptive behavioural strategies when negatively activated. This will cause patients to select the automatized maladaptive coping behaviours that give faster and easier rewards than a more adaptive alternative behaviour (Berenson et al., 2016; Lawrence, Allen & Chanen, 2010).

On the other hand, BPD patients committed more errors and gave fewer correct answers than HC after a neutral emotional induction.

Even though patients in the neutral condition committed more errors than HC, no differences in perseverative responses were found. These results could be due to the differences in the affective states presented by the two groups after the neutral induction. In fact, after the neutral induction, differences between groups in the affective states were still present, even though emotional state of the patients is not

altered compared to baseline. Interestingly, BPD patients in the neutral condition showed higher reward sensitivity levels than HCs.

Working on positive reward and feedback systems during clinical intervention could help BPD patients in learning alternative and adaptive ways of coping with emotional distress. In the neutral condition, when a correct choice was selected, and a positive reward was given, the patients' attention shifted more toward the correct rule than HC. This result might be relevant in developing clinical trials for BPD patients.

Considering physiological activity, patients report higher sympathetic activity than healthy control, but these results are independent of the emotional condition.

These results suggest that executive tasks such as BCST could impact physiological responses of BPD, eliciting a strong sympathetic response, independently from their emotional state.

Finally, the studies presented in this dissertation focused on a possible functional intervention that could help BPD patients regulate problematic affective states. As stated in the introduction, BPD patients present several dysfunctional strategies when dealing with emotional regulation. In particular, socio-emotional difficulties trigger ruminative states (Quirk, Wier, Martin, & Christian, 2015). Rumination is defined as a process of uncontrolled, narrowly focused negative thinking that is often self-referential, with negative content and could be considered as a constrained part of mind-wandering (van Vugt & van de Velde, 2018) and is strictly connected to maladaptive and self-destructive behaviours in BPD such as NSSI (Quirk, Wier, Martin, & Christian, 2015). The last two studies presented in this thesis assessed the efficacy of a mindfulness exercise in helping HC and BPD to regulate affective states and reduce mind-wandering. The two studies follow the same methodology. While the first was conducted only on HC participants, the second compared BPD patients and HC reactivity to a mindfulness task. While several studies were conducted to study the efficacy of mindfulness training overtime at both physiological, affective, and neural levels (e.g., Taren, Creswell, & Gianaros, 2013; Taren, Gianaros, Greco, Lindsay, Fairgrieve, Brown et al., 2015; Christodoulou, Salami & Black, 2020; Ditto, Eclache & Goldman., 2006; Peressutti, Martín-González, García-Manso & Mesa, 2010) these are the first studies that analyze in detail changes at emotional and physiological states in a mindfulness breathing exercise during its assessment.

These studies showed differences among phases in mind wandering scales and physiological activity in both HC and BPD. In detail, a mindfulness breathing exercise seems to reduce the level of thoughts made about other people (i.e., ARSQ TOM scale), future-oriented thoughts (i.e., ARSQ Planning scale), verbal and visual thoughts (i.e., ARSQ Visual Thoughts and Verbal Thoughts scales) in both HC and BPD participants. Moreover, during the mindfulness exercise, somatic awareness (i.e., ARSQ Somatic Awareness scale) significantly increased compared to the baseline phase in both groups. Finally, borderline patients significantly reduced thoughts regarding their health, feelings of pain, and bad feelings (i.e., ARSQ health concern scale) during the mindfulness exercise. These findings are coherent with the principles of mindfulness practice which requires a process of self-observation through staying on a specific point of focus (e.g., the breath), around with other experiences (thoughts, emotions, sensations). Moreover, according to mindfulness principles the body could be used as an object of focus (Kabat-Zinn, 1990; Holland, 2004), and this leads to an increase in the awareness of the somatic states (Dahl, Lutz & Davidson, 2015; Dorjee, 2016). These results are confirmed by the correlations found in both groups between the quality of the mindfulness exercise completed and the changes in self-reported indexes of mind wandering.

Interestingly, no differences were found in both groups for mind-wandering indexes that decrease during mindfulness (i.e., TOM, Planning, Visual Thoughts, and Verbal Thoughts), between the mindfulness phase and the subsequent recovery phase. We could then hypothesize that mindfulness effect on mind-wandering is maintained beyond mindfulness exercise practice. These results confirm preliminary data present in literature that shows the effect of a mindfulness exercise on reducing mind wandering overtime, supporting the hypothesis that mindfulness breathing exercise efficiently reduces mind wandering and that this effect is continuous over time (Mrazek, Smallwood & Schooler, 2012).

The presence of this response pattern in BPD patients supports the utility of mindfulness techniques in clinical trials to help patients regulate emotion and reduce ruminative states.

In detail, reducing the thoughts about the other and the social context (i.e., ARSQ TOM subscales) and reducing the feeling of physical and emotional pain (i.e., ARSQ Health

Concern subscale) could play a major role in regulating ruminative states and help patients in decrease an intense emotional negative intensity.

However, contrary to initial hypotheses, results did not show a significant efficacy of the mindfulness exercise in changing affective states. The only changes reported for affective states were found after the baseline measurement, with all the participants showing numbing emotional states (i.e., lower positive and negative affective states). On the other hand, the increase of awareness typical of mindfulness exercise could have risen emotional awareness in the two samples, preventing the change of the emotional states during the mindfulness and recovery phase.

Moreover, reported results showed a significant correlation between mindfulness outcomes and affective states in both HC and BPD. In detail, higher levels of mindfulness ability to manage distractions (i.e., MODQ Distraction scale) were associated with higher levels of positive affectivity after the mindfulness exercise in the HC group. On the other hand, difficulties in managing distraction were associated to a higher level of negative affectivity after the mindfulness exercise in BPD patients. This result is in line with the well-documented association between mindfulness and positive affectivity and components of well-being (Brown & Ryan, 2003). Moreover, significant associations were found between the negative affectivity pre and post mindfulness exercise and self-judgmental attitude during the task in BPD participants. In detail, high levels of self-judgment were associated with high intensity of negative state. Again, these results confirm the centrality of the ruminative state in the emotional regulation processes in BPD patients and confirm the necessity of an intervention to specifically tackle this component of emotional dysregulation.

Finally, HC changes in physiological activity followed the changes presented in mind-wandering. During the mindfulness phase, significant increases in HRV (RMSSD, and SDNN) indexes were found. These results are coherent with previous studies showing mindfulness effect in increasing HRV (e.g., Ditto, Eclache, Goldman, 2006; Peressutti, Martín-González, García-Manso & Mesa, 2010; Christodoglou 2020). Heart rate variability mirrors susceptibility to stressor and potential threatening events (Lehrer, Woolfolk & Sime, 2007). And it is associated with both psychological and physiological adaptability (Malik, 1996), Moreover, HRV has been associated with cognitive, emotional, and behavioural regulation (Friedman & Thayer, 1998; Porges,

1992). Considering specific HRV indexes, increased SDNN during the mindfulness phase could represent the general cardiac variability mostly determined by the influence of the parasympathetic nervous system on heart rate.

On the other hand, RMSSD results could represent a vagal induced increase in the parasympathetic influences in the autonomic regulation. Specifically, the parasympathetic nervous system is related to relaxing and responding to environmental demands (Thayer & Lane, 2000). The adaptive function of the vagal efferences is to function as a brake on sympathetic influences and heart rate (Porges, 2007), for this reason, HRV is commonly increased in response to cognitive and affective demands (Park & Thayer, 2014). Difficulties in cognitive and emotional regulation can also be manifested in resting-state conditions (Deng, Li & Tang, 2014). This may be related to an altered balance of the autonomic system, as supported by presented data on decreased parasympathetic activity during baseline and recovery phases. On the contrary, the cognitive and emotional control, required by a mindfulness exercise could be manifested with the increases in HRV. In line with the difficulties in emotion regulation presented by BPD patients, BPD reported lower HRV than HC during the whole task.

Interestingly, while HC reported an increase in SDNN during the mindfulness exercise and during the recovery phase, BPD patients reported increases in this index only during the mindfulness exercise. On the other hand, while HC showed an increase in RMSSD during the mindfulness phase, BPD patients reported an increase in RMSSD during the recovery phase. These results suggest us a difference in autonomic functioning in BPD. It could be possible that BPD patients present a slower parasympathetic activity. These differences in latency, together with the altered perception of time presented by BPD patients (Berlin, 2014), could be the major cause of the impulsivity presented by BPD subjects. Perceiving the time as slower, the slower response in reducing physiological activity, together with an emotional hypersensitivity characterized by high levels of negative emotional state, could act as a behavioural drive to react fast and select the response with the faster reward, independently from the possible maladaptive-long term consequences.

Contrary to the initial hypothesis, participants showed higher HR during the mindfulness phase compared to the baseline and recovery recordings. This result is in

line with previous studies conducted analyzing different type of meditations. It has been demonstrated that when a form of breath control was required during a meditation exercise, HR was higher compared to other form of meditation (Lutz, Greischar, Perlman & Davidson, 2009). Moreover, several types of meditation were reported to increase HR in association with an activation of the sympathetic nervous system (Ditto, Eclache, Goldman, 2006; Lutz, Greischar, Perlman & Davidson, 2009).

Moreover, this result could be related to the low level of expertise presented by participants. Even though in the instruction of the task no breathing-control effort were requested, results could suggest that participants put in place some forms of breathing control during the mindfulness phase, which in turn resulted in increased sympathetic activity. On the other hand, BPD participants only showed a decrease in HR during the recovery phase. This reduction could be due to the activation of the parasympathetic system, related to the increase of RMSSD during the recovery phase.

Taken together results obtained in the mindfulness studies support the efficacy of this methodology in reducing mind-wandering state and modulating physiological activity in both HC and BPD. Moreover, new insight on the emotional and autonomic functioning of BPD patients was found, giving us the opportunity to better understand this disorder's emotional functioning.

Toward a new conceptual model of BPD

All the data presented so far support a neural basis for the disturbances in the emotional area presented by BPD patients. Starting from these considerations and other models of emotional regulation, we can try to modulate a new neuroconnectivity model of BPD emotional functioning.

According to a metanalysis conducted by Koenig and colleagues (2016), BPD patients present lower heart rate variability at the baseline level. Moreover, BPD subjects present a pattern of altered HRV in response to emotional and neutral stimuli, in particular in response to socio-emotional cues.

This could be due to a difficulty in neuroception: unconscious perception of dangers and threats present in the subject's surroundings (Porges, 2004). As stated before, neuroception processes (i.e., how neural circuits distinguish whether situations or

people are safe, dangerous, or life-threatening), are mediated by the vagal nerve (Porges, 2007). One of the main functions of this nerve is to regulate the sympathetic and parasympathetic responses, starting from the internal state of the subject and the environmental perception. This perception depends mostly on the cortical and limbic activity and its interaction with the vagal system. When the subject faces potential threatening situations, with the mediation of the vagus nerve, the sympathetic branch (SNS) of the autonomous nervous system (SNA) is elicited. This mobilizes a high number of metabolic and energetic resources and prepares the individual to interact with a potentially dangerous environment, eliciting a fight or flight response. On the contrary, when the environment is perceived as safe, the interaction between the vagal and the corticolimbic systems elicited a state where social interaction is promoted. The vagal nerve presents two principal branches: the dorsal motor nucleus (DMNX) and the nucleus ambiguous (NA). The DMNX is evolutionally the most antique part of the vagal nerve and controls the responses of heart rate reduction and freezing. Moreover, it seems to be related to the generation of dissociative states (Scaer, 2001; Berdhal et al., 2010). The NA is the most evolved and myelinated part of the vagal nerve, and it functions as a "vagal brake". The activation of this branch inhibits SNS activity on the heart, modulating visceral states and impeding increases in heart rate. This "break" permits the individual to stay calm and interact with the environment without eliciting a fight or flight response. The vagal system is so forth central in emotion regulation: when the vagal tone (NA) increases, the SNS activity is reduced to avoid an unnecessary metabolic response. Moreover, through vagal functioning, autonomic states are modulated to protect the cortex from the conservative metabolic reaction of DMNX, which could potentially create serious damages related to bradycardia and a low level of oxygenation on neural tissues (Porges, 1997), figure 3.1 shows neurception mechanisms.

Literature supports the importance of vagal functioning in mental wellness, cognitive and emotional state regulation (Butler, Wilhelm, Gross, 2006; Ruiz-Padial, Sollers III, Vila & Thayer, 2003; Thayer, Brosschot, 2005; Hansen, Johnsen, Thayer, 2003; Thayer, Hansen, Saus-Rose & Johnsen, 2009; Porges, 2007). Cortical and subcortical components modulate vagal functioning through complex circuitries and feedback (Thayer, Lane, 2000, 2009). Amygdala activity modulates SNA leading to an

enhancing heart rate and a decrease of HRV through the vagal inhibition and the direct stimulation of the ventral rostromedial medulla (RVMP) (Saha, 2005). On the other hand, through its connections with the LC (Van Bockstaele, Peoples & Telegan, 1999), the vagus nerve -through the nucleus of solitary tract (NTS)- interacts with the prefrontal cortex and the basolateral nucleus of the amygdala (BLA). Prefrontal and orbitofrontal cortexes play a central role in modulating and inhibiting amygdala activity due to their connections with the central nucleus of the amygdala (Barbas, Zikopoulos, 2007; Shekhar, Sajdyk, Gehlert & Rainnie, 2003) and a complex system of internal feedbacks. An efficient cortical inhibition produces a regulated amygdala response and an adaptive autonomic functioning; on the contrary, reduced cortical inhibition or high amygdala activity leads to a reduced vagal tone and difficulties in emotion regulation. Several studies support this hypothesis, showing how cortical activity -both at baseline level and during stressful tasks- affect vagally modulated HRV (Ahern, Schwartz, 1985; Lane, Reiman, Ahern & Thayer, 2001; Thayer, Lane, 2007).

Given the connection between these patients' emotional and behavioural dysregulation characteristics (Linehan, 1993), the altered functioning of this circuitry could be central in selecting adaptive and maladaptive strategies. Several studies supported the efficacy of the maladaptive behaviours selected by BPD patients (e.g., non-suicidal self-injury behaviours, alcohol, and drugs abuse) in regulating and inhibiting amygdala activity (Corrigan, Davidson, Heard, 2000; Kraus, Esposito, Seifritz et al., 2009; Niedtfeld, Schulze, Kirsch et al., 2010). It could be hypothesized that BPD patients tend to select these behaviours to regulate emotional activity due to their efficacy in dampening amygdala activity faster than adaptive coping strategies. On the other hand, the preference for such strategies automatizes the selection of risky behaviours and elicits negative affective states (e.g., shame, guilt, anger), creating a loop of emotional distress.

Another brain areas central in behaviour selection and regulation, that seems to present deficit in BPD are basal ganglia, even though the literature is scarce on the topic. In the study of Soloff and colleagues (2017) a group of BPD subjects with a history of suicidality showed hyperactivation of basal ganglia during a go-no go task in a negative affectivity condition. Moreover, studying the effect of self-injuring as emotional regulation strategy, Niedfeld and colleagues (2012) showed that applying

noxious stimuli during the presentation of neutral cues produces an increase in connectivity between basal ganglia, paralimbic areas and posterior cingulate and precuneus. Finally, BPD patients present a trend in increased resting state functional connectivity between the amygdala, the insula, the orbitofrontal cortex and the putamen together with a hypometabolism of the basal ganglia (Krause-Utz, Veer, Rombouts Bohus & Elzinga, 2014; De La Fuente, Goldman, Stanus, Vizuete, Morlan, Bobes & Mendlewicz, 1997).

As stated before, cortical areas play a fundamental role in emotion regulation. According to the model proposed by Berdhal (2010), prefrontal, orbitofrontal, and ventromedial prefrontal cortexes (VmPFC) modulate the activity of the BLA through a complex feedback circuitry. Animal studies on monkeys and rats support this hypothesis, showing several patterns of inhibitory connection between BLA and VmPFC (Amaral and Price, 1984, Carmichael and Price, 1995, Porrino, Crane, Goldman-Rakic, 1981; Stefanacci and Amaral, 2002). According to Berdahl model (2010), the amygdala plays a central role in regulating emotional responses due to its connection with the ventrolateral and dorsolateral periaqueductal gray matter (vlPAG; dlPAG). According to several lesion studies and animal studies, dlPAG is central in controlling defensive aggression responses (Devinsky, Morrell, & Vogt, 1995; Keay & Bandler, 2001; Gregg & Siegel, 2001). As stated before, BPD functioning is related to intense anger or difficulties in controlling anger (APA 2013). These behaviours could be considered defensive aggression behaviours, related to the high incidence of childhood abuse associated with BPD subjects' development (Skodol et al., 2002). On the other hand, dissociation (i.e., an alteration of the perception of physical sensation, time, memory, sense of self, and reality (Scaer, 2001)) is related to vlPAG functioning. Several studies showed how the stimulation of this area in animals leads to dissociative-like states in animals (Keay & Bandler, 2001; Nijenhuis, Vanderlinden, & Spinhoven, 1998). Finally, various studies support the hypothesis that these two pathways course through the dlPAG and vlPAG and engage in an inhibitory interaction (Canteras & Goto, 1999; Comoli, Ribeiro-Barbosa, & Canteras, 2003; Lovick, 1992). According to several animal studies on fear and aggression, BLA and the central nucleus of the amygdala (CeA) plays a central role in regulating dlPAG and vlPAG and consequently

fight/flight and dissociative responses (Adamec, Blundell, & Collins, 2001; Royer, Martina, & Paré, 1999).

In the end, starting from all the data reported and merging all these models, we can hypothesize a new neuroconnectivity model of BPD emotional functioning (Figure 3.2).

While data in our possess seem to point out that this model could be central in BPD, from what is known so far, we cannot exclude the application of the same model in other personality disorder or pathologies that present difficulties in emotional regulation.

The physiological output that we observe in BPD patients depends on the interaction between the vagus nerve, the nucleus of the amygdala, the prefrontal cortex, and the periaqueductal gray. Interestingly, As reported in the introduction, all these neural elements present both structural and/or functional alteration in BPD patients. Moreover, the specificity of BPD hypersensitivity and reactivity to socio emotional stimuli, together with the effect of social environment in the development of emotional and neurobiological deficit is in line with the hypothesis that altered pattern in neuroception could be the main core of the disorder. Coherently, the vagus nerve plays a central role in this model of emotion regulation. Several studies, indeed, report how vagus nerve activity is central in emotion regulation (e.g., Butler, Wilhelm, Gross, 2006; Ruiz-Padial, Sollers III, Vila & Thayer, 2003; Thayer, Brosschot, 2005 Hansen, Johnsen, Thayer, 2003; Thayer, Hansen, Saus-Rose & Johnsen, 2009; Porges, 2007). Moreover, given the centrality of the vagal system in regulating neuroception and social engagement (Porges, 2007), it is possible to hypothesize that a direct intervention on the vagal functioning could help BPD patients in regulate their emotional states.

Vagal stimulation is a procedure already known treatment used in epilepsy and pharmaco-resistant depression (e.g., Marangell, Rush, George, Sackeim, Johnson, Husain et al., 2002; Schalepfer, Frick, Zobel, Maier, Heuser, Bajbouj et al., 2008). Moreover, very recent studies support the efficacy of transcutaneous vagal stimulation in helping in emotional regulation and cognitive processes (Broncel, Bocian, Kłos-Wojtczak, Kulbat-Warycha & Konopacki, 2020; Wittbrodt, Gurel, Nye, Ladd, Shandhi, Huang et al., 2020). In detail, vagal nerve stimulation has been proved to improve autonomic dysfunction, in reducing sympathetic and increasing parasympathetic tone,

modulating fear circuitry and neural plasticity, and central neurotransmitter function including norepinephrine, given its connections with locus coeruleus (Hays, Rennaker & Kilgard, 2013; Polak, Markulin, Ehlis, Langer, Ringel, & Fallgatter, 2009; Player, Taylor, Weickert, Alonzo, Sachdev, Martin et al., 2014; Peña, Engineer & McIntyre, 2013; Souza, Robertson, Pruitt, Gonzales, Hays, Rennaker et al., 2019). Given this evidence, it makes sense to hypothesize a possible therapeutic effect of vagal nerve stimulation for BPD patients.

The results presented in this dissertation confirm the centrality of the neuroception in BPD. This is further supported by the evolutionary theory described in the introduction. Difficulties generated by a transactional interaction between a biological vulnerability and an invalidating environment over time affect brain development and emotional regulation strategies. This is evident in response to social cues, which are perceived as more threatening due to a failure in the neuroception system. Even if the presented data are preliminary and more confirmatory studies are needed, is it possible to hypothesize, then, that this pattern of emotional functioning could be the principal core of BPD. Starting from this in clinical trial should focus on the appraisal of the social environment in order to facilitate patients with the neuroceptive difficulties. Moreover, results obtained from the mindfulness studies support the efficacy of this techniques in reducing mind-wandering states (in particular thoughts related to other people) and in modulating the physiological response. However, the physiological pattern presented by BPD patients seem to be slower when compared to HCs. Starting from this evidence, teaching mindfulness as an on-line emotional regulation strategy to BPD patients is recommended. Moreover, given the high sensitivity to judgment and the urge to act of these patients, is important to underly during the clinical intervention that their physiological response could be slow, as reported by the results of the Mindfulness study 2 and therefore focus on developing awareness of this biological sensitivity.

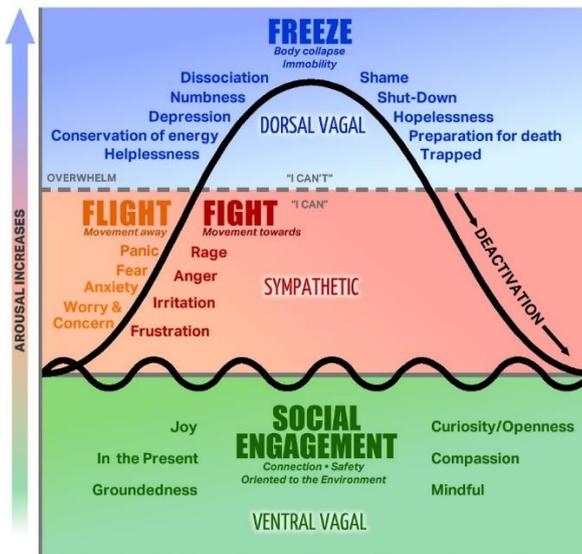


Figure 3. 1 Neuroception. Adapted form: Polyvagal Theory & “Interoception:” A Neuroscience Understanding Of Attachment Trauma (Rankin, 2009)

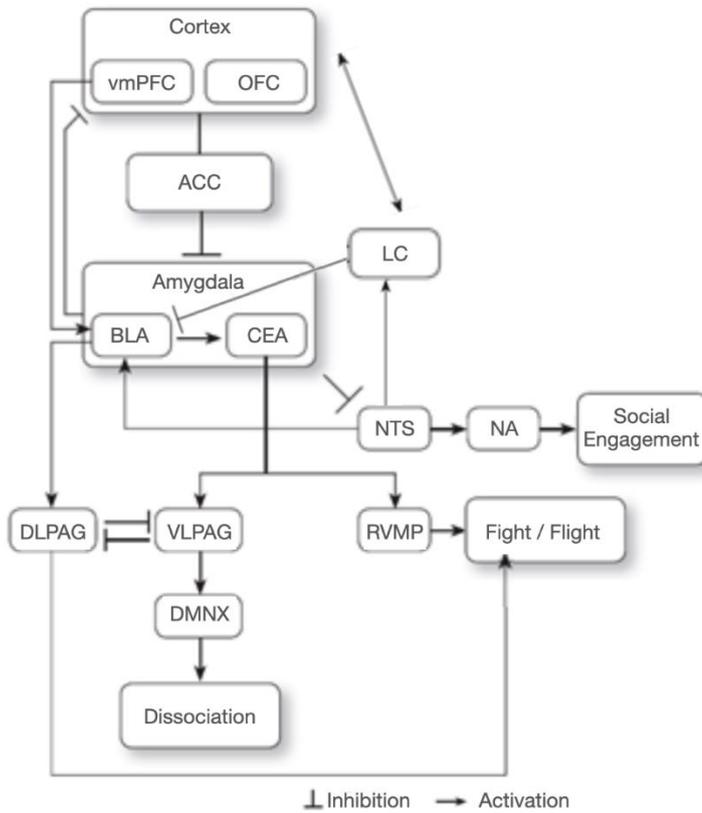


Figure 3. 2 A new neuroconnectivity model composed by Ventromedial prefrontal cortex (vmPFC), orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), Basolateral (BLA) and central (CEA) nucleus of the amygdala, locus coeruleus (LC), nucleus of solitary tract (NTS), nucleus ambiguus (NA), Dorsolateral (DLPAG) and ventrolateral (PAG) periaqueductal gray matter and rostral ventromedial medulla (RVMP).

Limits and future perspectives

Even though all the results presented in this dissertation are pretty coherent and show how negative emotional states (especially if related to socio-emotional context) affect executive functioning, several limitations need to be considered.

First of all, the majority of participants in our study were female. This is in line with the literature supporting that most BPD subjects that come to psychological attention are female (Maffei, 2021). However, the sample's lack of males prevents us from expanding our findings to the whole BPD population. The introduction states that BPD female and male subjects tend to present different pathological characteristics (Sansone & Sansone 2011). These differences in clinical features, together with the social construct of the female characteristics, could lead to an increase in pathologizing female subjects with BPD, as they go against the standards and expectations of social functionality (Maffei, 2021) and this could explain why the majority of BPD in clinical treatment are females. Future studies are needed on BPD male subjects to confirm our knowledge of the disorder or, on the contrary, highlight possible differences related to gender. Secondly, the number of subjects analyzed in all the studies should be increased to get more power in the statistical analysis. Moreover, as stated in the introduction, BPD patients report more fluidity related to gender identity (Thompson et al., 2019). Gender identity was asked prior to the tasks and results confirm these data. However, given the small sample size of the participants it was not possible to analyze specific differences in responses related to gender identity and related to the type of the content of the stimulus (e.g., homosexual or heterosexual cues). We can speculate that with a specific cue the physiological and emotional responses would be more accentuated and specific. Future studies should focus their attention on this topic to further analyze the role of gender and sexuality in BPD emotional functioning.

Another limitation is related to the current COVID-19 situation, which had reduced the possibility to sample more subjects for the studies conducted.

During the first year of my Ph.D., the drop-out rate of BPD participants was around 70%. Again, the low number of participants recruited in three years of studies is in line with the characteristic of BPD pathology. BPD difficulties in social relationships affect

clinical and therapeutical trials, leading to a high drop-off percentage. Future studies should focus more in detail on the personological characteristics that could lead BPD patients to drop-off to help clinicians during the treatment. Regarding the social studies presented in this dissertation, a possible limitation could be related to the stimuli used. As the two studies focused on BPD socio-emotional reactivity were preliminary studies, only socio-emotional cues (i.e., clips and images representing social interaction) were used to test BPD functioning in a different emotional context. Future studies should include other types of stimuli as a neutral comparison (e.g., objects, landscape) to test and confirm the specificity of the data presented in this dissertation. Moreover, given the emotional difficulties in emotion regulation presented by BPD patients, the methodology used in the social studies consisted in an exposition to socio-emotional cues rather than a specific social interaction. While this permit us to try to elicit specific emotion in participants, it is clear that studying and analyzing the emotional reactivity of the participants during a real social intercourse would have given more clear and specific results. On the other hand, the tasks used were addressed as highly stressful by BPD participants in the post-task psychological assessment. This could be due to the high level of engagement and identification that patients had with the stimulus. Future studies should focus on the study of specific social interaction in BPD patients. Actually, new technologies could help us in this. Through the use of virtual reality or the creation of avatars it could be possible to immerse participants in a controlled realty where the environment and the social interaction are safe and standardized. With our research group we are already working in that direction. However, given the centrality of the social environment on the emotional functioning of BPD patients, more studies are needed on the topic. Finally, the data collected and reported in this dissertation focused mostly on behavioural, physiological, and emotional reactivity of BPD patients in different situations, with a specific focus on the neuroception of these subjects. Given the quality of the instrument at disposition for the studies, data regarding physiological activation are related to changes in HRV (i.e., SDNN and RMMSD indexes), which is a common methodology used to study this disorder (e.g. Bortola, Cavicchioli, Galli et al., 2019; Austin, Riniolo & Porges, 2007) and could be used to represent vagal functioning, even though other indexes (e.g. respiratory sinus arrhythmia) could be used

to tackle directly vagal activity. Future study should focus on analyzing directly vagal activity to confirm these preliminary results.

Conclusion

In conclusion, this dissertation points out several aspects relevant in the study of BPD. Firstly, the BPD hypersensitivity hypothesis at the basal state seems to be confirmed by the studies presented. On the other hand, preliminary data supported the idea that BPD patients could report a specific hyperreactivity response in relation to socio-emotional cues. Additionally, emotional and physical abuse perceived during infancy were associated with emotional responses during the view of emotional stimuli confirming the evolutionary perspective described in the introductory chapter. Moreover, attentive responses and executive functioning were connected to emotional activity, with high levels of negative affective states impairing attentive and cognitive functioning. Finally, a theoretical neural model of emotion regulation in BPD was described, suggesting the hypothetical relevance for a new clinical intervention.

Materials and Methods

Commonality between studies

Participants' recruitment

BPD patients. BPD outpatients were included from the Clinical Psychology and psychotherapy Unit of San-Raffaele Hospital (Milan) from January 2018 to December 2021. Clinical participants met a BPD diagnosis following DSM-IV criteria assessed by the Structured Clinical Interview for DSM-IV axis II Personality Disorders, Version 2.0 (SCID-II). SCID-II was conducted during the routine diagnostic assessment by trained raters, who were blinded to the hypotheses of this study. Expert psychiatrists conducted clinical interviews for evaluating the presence of exclusion criteria. Exclusion criteria were represented by IQ lower than 70, psychotic disorders, and other active psychiatric symptomatology for at least one month before task administration (e.g., major depressive episode, current substance use, panic attacks). Lifetime co-diagnoses of other psychiatric disorders did not represent exclusion criteria from the study.

Healthy controls. Community-dwelling volunteers were included in the nonclinical sample (HC). HCs were aged-matched and presented a negative medical history for neurological or psychiatric disorders. Additional exclusion criteria were IQ lower than 70, current substance use, psychopharmacological treatments, and current psychological treatments. The affective state and additional clinical information were collected using paper and pen questionnaires before the tasks. Moreover, participants completed BDI-II to exclude the presence of depressive states in the last two weeks. Finally, before the testing, all the participants were screened with the Personality Inventory for DSM-5 (PID-5; Krueger, Eaton, Clark, Watson, Markon, Derringer et al., 2011) and the Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004) to exclude the presence of maladaptive traits or difficulties in regulating emotion in the HC sample.

The sample size was selected starting from similar studies present in literature on BPD population. Moreover, given the high drop rate percentage (70%) of the clinical population, and the COVID-19 pandemic, selecting higher sample size was not possible. To increase statistical power of the analysis, data simulation procedure (i.e., Monte Carlo and Bootstrap) were conducted during the analysis. The few missing data were managed using mean imputation. Limitations regarding sample size are reported in the discussion section.

Instruments

Difficulties in emotion regulation scale (DERS)

The DERS is a 36-items, on a 5-points Likert scale, multidimensional questionnaire for evaluating six emotion dysregulation scales (Nonacceptance 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). Additionally, good construct validity and a high internal consistency were found in clinical and nonclinical populations. The Italian version of the instrument was administered in the studies (Giromini, Velotti, De Campora, Bonalume, & Zavattini, 2012)

Personality inventory for DSM-5 (PID-5)

The PID-5 is a 220-item questionnaire evaluating DSM-5 maladaptive personality traits and domains. The 220 items were rated on a 4-point Likert scale. The PID-5 has 25 primary scales that load onto 5 higher order dimensions (Negative affectivity, Detachment, Disinhibition, Antagonism and Psychoticism). Adequate internal consistency was found for PID-5 traits and domains (Derringer, Markon, Watson, Skodol, 2012). Since robust psychometric properties were confirmed also for clinical and nonclinical Italian samples, both with regard to internal consistency and factorial

structure the Italian version of the questionnaire was administered (Fossati, Krueger, Markon, Borroni, Maffei, 2013) for all the studies.

Positive and Negative Affect Schedule (PANAS)

The PANAS is a 20 items 5-points Likert questionnaire developed to assess the current affective state. It is composed by two scales, composed by 10 items each, which assess positive affectivity (PA) and negative affectivity (NA) states. The original validation showed that these two scales are internally consistent, uncorrelated, and stable over a 2-month time period. We administered the Italian version of the scale (Terracciano, McCrae, & Jr, 2003). The PANAS factor structure and solid psychometric properties were also confirmed for the Italian version.

Physiological Data

Cardiac activity was recorded by electrocardiography (ECG) in all participants during the *Executive functioning study*, *Clip study*, and *Mindfulness study*. For each participant, an ECG was collected using BITalino (Da Silva, Guerreiro, Lourenço, Fred & Martins, 2014; Guerreiro, Martins, Silva, Lourenço & Fred, 2013), a biomedical data acquisition device, using a sampling rate of 1000 Hz. The ECG signal was then amplified and sampled at 500 Hz. Three disposable Ag/AgCl electrodes were positioned on the left side of participant's chest to obtain the ECG signal. After obtaining inter-beat intervals (IBIs), data were then analyzed in Kubios-Premium software (University of Kuopio, Kuopio, Finland). Using an automatic interpolation method that generates missing or corrupted values into the IBIs series data was further correct. ECG recordings were divided into samples lasting 30 seconds each with a 15-second grid interval.

HRV indexes were extracted from the ECG recordings. In detail, the following indexes were calculated: Heart rate (HR) The square root of the mean squared

differences of successive NN intervals (RMSSD) The standard deviation of normal-to-normal intervals (SDNN)

While RMSSD was analyzed to investigate vagal-mediated HRV (Malik, 1996), SDNN displays the cyclic components accountable for the variability of HR and is an index of the total heart rate variability. In all the studies, the natural logarithms of all physiological data were calculated to normalize the distributions. In the clip study, delta scores (clips – baseline) for each condition were calculated for physiological variables to measure subjective reactivity to relational stimuli. Given the nature of the device, no other HRV data were collected.

Statistical analysis

In line with the violations of normal distribution for several measures included in all the studies, analyzed using the Saphiro-Wilk test, non-parametric procedures were used to analyze data. Between-group comparisons were based on Mann-Whitney U tests. Wilcoxon test was used to compute within-group comparisons (e.g., pre-post comparison). Monte Carlo simulation based on 10,000 independent samples and its 2-tailed 99% confidence interval (CI) was employed to evaluate the robustness of between-group and within-group comparisons. The Aligned Rank Transform (Wobbrock, Findlater, Gergle, & Higgins, 2011) was applied to evaluate the non-parametric main effect of group and interaction effects. The aligned transformation refers to a preprocessing procedure that aligns the data for each effect (main or interaction) before assigning ranks, averaged in the case of ties. After the aligned rank transformation of data for each effect, factorial ANOVA was conducted to evaluate the significance of main and interaction effects, estimated using the F-test (Wobbrock, Findlater, Gergle, & Higgins, 2011). Partial η^2 ($p\eta^2$) was utilized to measure non-parametric main and interaction effects. Spearman's correlation was used to evaluate associations between variables (bootstrap 2-tailed 95% confidence interval).

Executive functioning task

Participants

The clinical sample was composed of 30 female subjects (mean age = 24.3, $ds = 6.7$). 20% of participants had a middle school diploma, 50% had superior school diploma, 10% attended a professional school, 13.3% of the sample has a bachelor's degree, a 3.3% of the sample has a master's degree, while 3.3% conducted post university studies. Several comorbidities were reported in the sample (i.e., eating disorder, mood disorder, substance use disorder). Most of the participants in the clinical sample reported assuming pharmacological therapy (e.g., benzodiazepine, SSRI, antidepressant, antipsychotic, neuroleptic, and antiepileptic drugs). The non-clinical sample was composed by 30 female subjects (mean age = 23.2, $ds = 2.6$). 6.7% of participants had a middle school diploma, 16.6% had superior school diploma, 10% attended a professional school, 26.7% of the sample has a bachelor's degree, 33.3% of the sample has a master's degree, while 6.7% conducted post university studies.

Instruments

Negative induction task

Based on the study conducted by Schuch and colleagues (2017), we administered a bogus intelligence test based to induce negative affective states. The test was based on the progressive matrices test (Raven, 1965). After a short practical trial, where the subjects learned how to perform the task, we administered 12 difficult matrices to participants. In the introduction of the task, we indicated that 75% of the general population could solve all these puzzles without any difficulties to reduce the expected difficulty of the task. Moreover, we indicated that the performance in this test was predictive of future success in work and academic outcomes. Thirty seconds were given to each participant to complete each matrix, and eight possible solutions were provided. Among the eight alternatives, only one was correctly completing the puzzle. After the

30 seconds, automatic feedback was given for each matrix, showing if the participant solved the puzzle correctly or not. The whole setup was automatized. The task lasted 7 minutes and HRV was measured during the whole setup

Neutral induction task

For the neutral induction, we administered 12 easy matrices to participants indicating that subjects did not have to complete the puzzles but just to look at them and evaluate if this could be a good test to evaluate cognitive functions. The matrices were presented for 8 seconds each and only the correct answers were shown. No feedback was given. The task lasted 2 minutes and the HRV was measured during the whole task

Berg card Sorting Test (Grant & Berg, 1948)

After completing the PANAS each participant -whether in negative or neutral induction group- underwent the Berg Card Sorting Test (BCST) administered using Peble software (Mueller & Piper, 2014).

The BCST is a test that assesses cognitive flexibility in an individual. It measures the ability of a subject to form, maintain and switch from different rules based on the feedback given during the procedure. Four different decks of cards are presented to the participant during the task. Each deck is represented by a card that never changes during the procedure. One hundred twenty-eight cards are presented singularly to the participant. Participants are asked to sort the card into the right deck following three different rules (i.e., matching the deck and the card for shape, color or number of the symbols present on each card) that may change during the assessment. After each match, feedback is provided, showing if the sorting was correct or incorrect. Indexes analyzed were the number of correct responses, the number of errors, the number of perseverative errors (a perseverative error occurs when the participant continues following the previous rule after it has changed), reward sensitivity (i.e. how the attention of the participant changes after positive feedbacks), punishment sensitivity

(i.e. how the attention of the participant changes after negative feedbacks) and decision consistency (i.e. how decision made by participant depend on their attention to the active rule). The task lasted 5 minutes and the HRV was measured during the whole task.

BCST Model

To compute parameters assessing reward sensitivity, punishment sensitivity, and decision consistency the computational machine learning model proposed by Bishara and colleagues (2010) was recreated. The model was based on the prediction of the participant's choice in the next trial based on the attentional weights a given to each rule (i.e., color, form, number) in the previous trial and was trained with the data obtained during the BCST task from the participants. The parameters in a always sum to 1, so as attention to one dimension increases, attention to other dimensions tends to decrease. The values in the attentional vector change depending on the feedback received during the task, starting from a matching vector m whose values depend on the match between the card that must be sorted on trial t and the pile k in which it is eventually placed. If the feedback received is ambiguous (i.e., starting from the choice made and the feedback is not possible to choose the correct rule) or unambiguous (i.e., starting from the choice made and the feedback the correct rule is clear) two different types of feedback are given. Equations for unambiguous feedback are reported in Figure 4.1

$$\mathbf{s}_t \left| \begin{array}{l} \text{unambiguously} \\ \text{rewarded} \end{array} \right. = \mathbf{m}_{t,k}. \quad \mathbf{s}_t \left| \begin{array}{l} \text{unambiguously} \\ \text{punished} \end{array} \right. = \begin{bmatrix} 1 \\ 1 \\ 1 \end{bmatrix} - \mathbf{m}_{t,k}.$$

Figure 4. 1 Feedback equations (adapted from Bishara et al., 2010)

When the feedback given is ambiguous, another factor related to the decision consistency (d) is necessary to run the model. D represent how much the decisions of

the subjects are consistent with his/her attention weights. Figure y represents the probability to choose a pile, depending on the decision consistency factor d . As d becomes higher, choices become more deterministic and attention-based.

$$P_{t,k} = \frac{m'_{t,k} a_t^d}{\sum_{j=1}^4 (m'_{t,j} a_t^d)}$$

Figure 4. 2 d equation (adapted form Bishara et al., 2010)

In Figure 4.2 the calculation of the d factor is explained. M is the matching vector, and a_t^d is a column vector with the element for each rule raised to the d power. In the denominator, j ranges from 1 to 4 for the summation across all four possible piles.

Finally, depending on the typology of the feedback (i.e., correct or wrong) it is possible to calculate how the attention changes depending on the sensitivity to punishment (p) or reward (r). Figure 4.3 shows how the implementation of the two sensitivity measures to the model

$$\mathbf{a}_{t+1} | \text{punished}_t = (1 - p) \mathbf{a}_t + ps. \quad \mathbf{a}_{t+1} | \text{rewarded}_t = (1 - r) \mathbf{a}_t + rs.$$

Figure 4. 3 Punished and rewarded equation (adapted form Bishara et al., 2010)

Parameters were calculated using the best fitting model procedure. Starting from behavioural data collected during the experiment from the two groups (i.e., HC and BPD) maximum likelihood estimates of parameters for each individual participant were analyzed. Parameters were estimated by minimizing the goodness of fit independently for each participant. The model and the parameters estimations were implemented with Python, using the integration of a simplex method (Nelder & Mead, 1965) and multiple quasi-random starting points.

Procedure

The complete process was carried out in a laboratory setting at San-Raffaele Hospital, Milan, from 2.00 p.m. to 5.00 p.m. Participants were asked to avoid drinking coffee two h before the experiment or smoking cigarettes one h before the experiment.

Additionally, alcohol or illicit drugs used 24 h before the experiment represented an exclusion criterion. Informed consent was signed before the experiment. Before starting with the experiment, basal activation was measured using PANAS questionnaire to evaluate emotional states and a two-minute HRV baseline recording to assess physiological state.

After that, participants were divided randomly in two groups: one group underwent a negative emotional induction task, while the other underwent a neutral induction task. After the emotional induction, the emotional state was collected, and a cognitive flexibility task was then assessed to all participants. Physiological data were collected during the whole procedure to evaluate ECG activity. After the task a brief talk with a clinical psychologist were assessed to BPD patients in order to manage eventual emotional crisis.

Relational studies – *Clip study and Dot-probe Study*

Participants

The clinical sample was composed of 31 subjects (4 males and 27 females, mean age=23.19, $SD=3.74$). 22.6% of participants had a middle school diploma, 48.4% attended a professional school, 12.9% had a Bachelor, 3.2% of the sample had a master's degree while a 3.2% of the sample conducted post university studies. Several comorbidities were reported in the sample (i.e., eating disorder, mood disorder, substance use disorder). Given the nature of the study, we asked using a questionnaire we asked participant the sexual orientation. In the BPD group the 21.4% of participants reported top be more attracted to same-sex individuals, the 25.6% reported to be bisexual while the 54% reported to be more attracted form opposite-sex individuals. In the HC group, the 13.6% reported to be more attracted to same-sex individuals, the

6.8% reported to be more bisexual while the 79.6% reported to be attracted by opposite-sex individuals. Many of the participants in the clinical sample reported assuming pharmacological therapy (e.g., benzodiazepine, SSRI, antidepressant, antipsychotic, neuroleptic, and antiepileptic drugs). The non-clinical sample was composed of 31 subjects (4 males and 27 females, mean age = age=22.87, $SD=1.87$). 29% had a superior school diploma, 58.1% had a bachelor's degree and, 12.9% had a master's degree.

Instruments

Clips task

Twenty-four clips were administered during the experiment. Clips were extracted from commercial films and were selected by a previous validation study. The authors selected a pool of 48 stimuli presented with the audio in the original Italian dubbing, including contents that represented human social interactions within daily life contexts (e.g., friendly interactions between friend, quarrels, and romantic interactions). The length of the clips ranged between 2.30 to 3.30 minutes. The set was administered to 60 community-dwelling volunteers who rated each clip on four continuous bipolar sliding scales (arousal, valence, intimate relationship, sexual arousal; range 1-9). Six clips for each category (positive, negative, and erotic relationships and neutral stimuli) were selected considering the most representative stimuli for that category. Moreover, three different types of interaction were represented in the clips (i.e., heterosexual, homosexual and lesbian couples). Positive interpersonal stimuli were characterized by high valence (mean=7.83, $SD=.57$), high intimate relationship (mean=7.63, $SD=.67$), and low sexual arousal scores (mean=1.13, $SD=.16$); negative stimuli were characterized by low valence (mean=3.03, $SD=.86$), high intimate relationship (mean=7.77, $SD=.40$), and low sexual arousal scores (mean=1.94, $SD=.43$); erotic stimuli were characterized by high intimate relationship (mean=7.73, $SD=.75$) and high sexual arousal scores (mean=7.72, $SD=.43$). Finally, neutral stimuli were selected by clips with medium valence (mean=5.54, $SD=.59$), low intimate relationships (mean=2.61, $SD=1.20$), and low sexual arousal scores (mean=1.13, $SD=.16$). Categories

were matched for arousal values. Clips presentation order was randomized for each participant. After the presentation of each clip, the participants were asked to complete the Movie Questionnaire. Each clip lasted from 2 to 3 minutes, during the view of each clip, ECG was recorded.

Dot probe task

A selective attention task based on the dot-probe task was used with emotional photographs with interpersonal contents (positive, negative, and erotic relationships) as stimulus material (MacLeod, Mathews, & Tata, 1986). A fixation cross was presented for 1s in the center of a computer screen in the dot-probe task. Further, two pictures (either a neutral picture paired with an affective picture or two neutral pictures) were presented concurrently, left and right to the central fixation point. Two different presentation times were included (b1: 500 ms; b2:1500 ms) as it has been demonstrated that they capture different stages of attentional processing (Baum, Schneider, Keogh, & Lautenbacher, 2013). The 500 ms presentation period was used because it represents the most common presentation period and represents both preconscious and conscious attentional processing. The 1500 ms presentation was used in line with eye-tracking methodologies during a dot-probe task (Schofield, Johnson, Inhoff, & Coles, 2012). The orders of presentation times, affective picture categories, and sides of appearance of the affective picture at the screen were randomized. Immediately after the concurrent presentation of the two pictures, a probe (X) appeared in the same position as 1 of the two stimuli. The participants were instructed to indicate the side the X had appeared as quickly as possible, pressing “q” if the X was on the left and “p” if the X was on the right. Once the participant responded, the next trial started. Before the beginning of the experiment, a 26 trials practice block was administered. During the whole procedure, eye-tracking data were recorded. Numbers of correct responses, reaction time, Bias score (i.e., reaction time in the congruent trial- reaction time in the incongruent trial) as well as main eye-tracking indexed according to Price et (Price, Kuckertz, Siegle, Ladouceur, Silk, Ryan et al., 2015) were calculated. Pictures were selected by a previous validation study. A pool of 206 stimuli was selected by the authors including pictures that clearly represented human social interactions within daily life contexts

(e.g., quarreling, social interaction). The set was administered to 211 community-dwelling volunteers who rated each picture on four continuous bipolar sliding scales (valence, intimate relationship, sexual arousal; range 1-9). Twenty-four pictures for each category (positive, negative, and erotic relationships, and neutral stimuli) were selected considering the most representative stimuli for that category. Moreover, three different types of interaction were represented in the clips (i.e., heterosexual, homosexual and lesbian couples). Positive interpersonal stimuli were characterized by high valence (mean=7.63, SD=.35), high intimate relationship (mean=8.04, SD=.36), and low sexual arousal scores (mean=2.41, SD=.43); negative stimuli were characterized by low valence (mean=2.34, SD=.98), high intimate relationship (mean=7.09, SD=.95), and low sexual arousal scores (mean=1.19, SD=.28); erotic stimuli were characterized by high intimate relationship (mean=7.71, SD=.13) and high sexual arousal scores (mean=8.03, SD=.36). Finally, neutral stimuli were selected by pictures with medium valence (mean=5.09, SD=.34), low intimate relationship (mean=2.23, SD=.94) and low sexual arousal scores (mean=1.32, SD=.82). All the category with the exception for the erotic cues were matched for arousal. Figure 4.4 reports an example for each emotional category. The dot-probe task was composed of two blocks of 192 trials each. The interpersonal pictures were paired with pictures displaying neutral stimuli in each block. Additionally, neutral-neutral picture pairs served as control items. Overall, b1 and b2 included four conditions of 48 trials each: 1) positive vs neutral (P0), 2) negative vs neutral (N0), 3) erotic vs neutral (E0), and neutral vs neutral (NN).

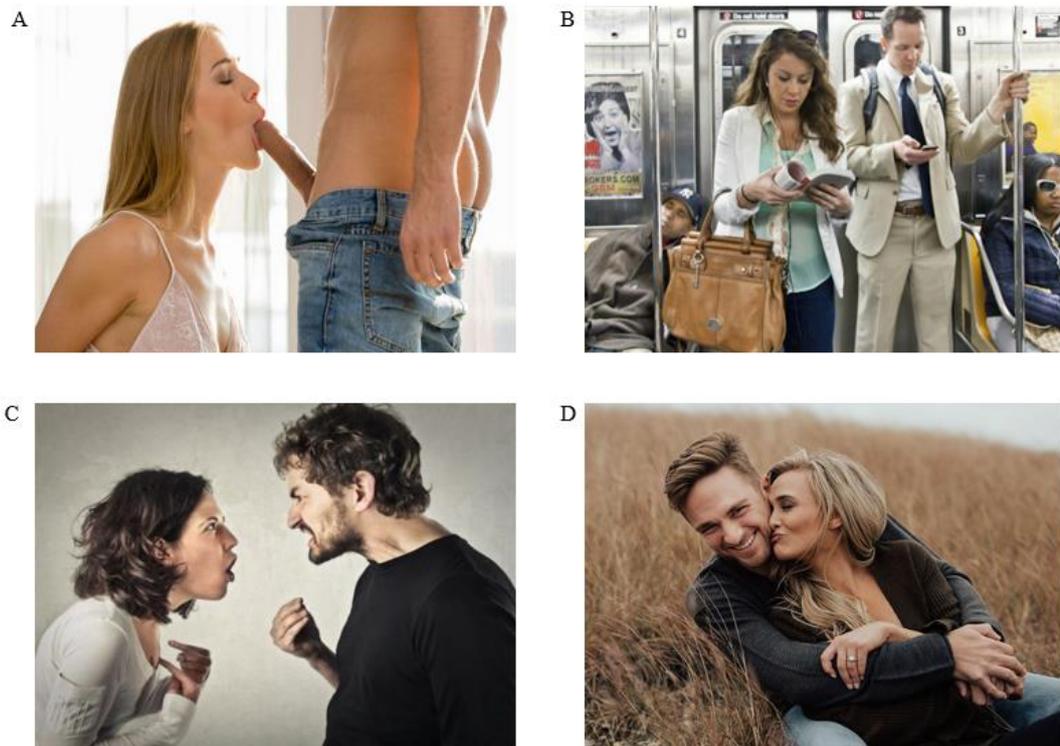


Figure 4. 4 Images categories in the social Dot-probe. A) erotic cue; B) neutral cue; C) negative cue; D) positive cue

Childhood trauma Questionnaire (CTQ; Bernstein & Fink, 1998) The CTQ is a 28-item self-report inventory based on a 5-points Likert scale that retrospectively assesses five categories of childhood trauma: emotional abuse, physical abuse, sexual abuse, emotional neglect, minimization, and physical neglect (Bernstein & Fink, 1998). The psychometric properties of the CTQ have been extensively validated in several samples (Bernstein & Fink, 1998). The Italian validation was proposed by Innamorati, Erbuto, Venturini, Fagioli, Ricci, Lester, et al., 2016.

Movie questionnaire

At the end of each video clip, subjects completed a self-administered questionnaire, earlier used in Maffei, Roder, Cortesan, Passera, Rossi, Segrini et al., 2014 to evaluate the quality and the intensity of emotional activation induced by each clip. Ten

emotional states were assessed on an eight-point Likert scale: serene, amused, happy, surprised, sad, scared, angry, disgusted, indignant, and tense. A general index of positive and negative emotions was computed averaging the intensity reported for each positive and negative discrete emotions for each clip. Moreover, the valence of the global mood generated by each video clip, its intensity, dominance, and levels of sexual arousal were measured with a Likert scale ranging from 1 to 9 (Betella, Verschure, 2016). Eventually, participants were asked to rate the level of intimate relationship perceived for the couple showed in the clip.

Eye-tracking

Eye-tracking data were collected during the dot-probe task by using The Eye-Tribe. Eye position was calculated based on the x- and y-coordinates of the recorded eye-gaze minus a corneal-reflection signal, which accounts for small head movements, and individually scaled and offset based on each individual's calibration parameters collected at the beginning of the session. Eye fixations were defined as eye positions stable within 1° of visual angle for at least 100ms. They were used to calculate the following gaze pattern indices: percentage of trials with initial fixations falling within regions of interest - defined by the pictures' boundaries - (an index of initial attentional capture; allocation); latency to interpersonal stimuli (an index of vigilance; latency); percentage of time spent fixating on positive, negative and erotic interpersonal pictures (positive, negative and erotic) compared to neutral one (an index of overall attentional preference; time in); mean duration of the first fixations on positive, negative, and erotic interpersonal vs neutral contents (an index of initial attraction vs avoidance; duration).

Procedure

The complete process was carried out in a laboratory setting at San-Raffaele Hospital. Informed consent was signed before the experiment. Participants completed two experiments of interpersonal functioning on two different days: the Clip study and the Dot-probe task. Participants were asked to avoid drinking coffee two h before the

experiment or smoking cigarettes one h before the experiment. Additionally, alcohol or illicit drugs used 24 h before the experiment represented an exclusion criterion. Informed consent was signed before the experiment. Before each experiment participants completed the PANAS and other pre-task questionnaires (e.g., additional clinical, personal, and medical information). Subsequently, the dot-probe task or the clips task were administered. The order of the two tasks was randomized for the participants in the two meetings. After each task, participants completed the PANAS. To avoid biases in physiological measurement, all the subjects were tested in the same room from 2 p.m. to 5 p.m. Before starting with the experiment, basal activation was measured using PANAS questionnaire to evaluate emotional states and a two-minute HRV baseline recording to assess physiological state. Eventually, participants were asked to complete a short part of 2 clips before the experiment to become acquainted with the tasks.

On the other hand, for the Dot-probe task, after the completion of the pre-task questionnaires, a practice block of the dot-probe task was administered to the participants to introduce them to the methodology used in the experiment. Before each dot-probe block, a 12-points calibration was conducted to calibrate the eye-tracker to the participant's eyes. After each task a brief talk with a clinical psychologist were assessed to BPD patients in order to manage eventual emotional crisis.

Mindfulness studies

Study 1 and Study 2

Participants

In the first study, the sample was composed of 28 female students (mean age = 24.44, ds = 1.40). 10.7% of the participants had a bachelor's degree while 89.3% of the

participants had a master's degree. In the second study, the HC sample was expanded. In the second study, the HC group was composed by 30 female subjects (mean age = 24.3, ds = 1.2). 16.7% of the participants had a bachelor's degree while the 83.3% had a master's degree. In the second study, the clinical sample was composed of 30 BPD subjects (BPD mean age = 26.47, ds = 9.7). 16.7% had a middle school degree, 43.3% had a superior school degree, 23.3% had a bachelor's degree, 10% had a master's degree while 6.7% conducted post-university studies. Several comorbidities were reported in the sample (i.e., eating disorder, mood disorder, substance use disorder). Most of the participants in the clinical sample reported assuming pharmacological therapy (e.g., benzodiazepine, SSRI, antidepressant, antipsychotic, neuroleptic, and antiepileptic drugs).

Instrument

Mindfulness task

Participants were asked to perform a mindfulness task following these instructions:

“This is a breath-observation exercise: you have to observe your breath. I ask you to observe the sensations that the air produces entering and exiting from your body. This is not a breath control exercise. Breath naturally. You might be distracted by noises, images, and body sensations during the exercise. This is normal. When this happens, be aware of what is happening and report your attention gently on your breath. You might worry about your performance during the exercise. If this happens, be aware of what is happening and report your attention gently on your breath. There are no correct or wrong ways in executing this exercise. You can interrupt the exercise whenever you want without any problem”. Then some indications on the posture to assume during the exercise were given: “You have to remain seated, with the foot on the ground. Put your hands on your knees and keep your back and shoulders straight (but not rigid or contracted). The neck and your head should form a continuous line with your back. Try to keep your eyes closed to better concentrate.”

Amsterdam Resting State Questionnaire (ARSQ)

ARSQ (Diaz, Van Der Sluis, Benjamins, Stoffers, Hardstone, Mansvelder et al., 2014) is a self-report questionnaire composed of 30 items on a 5-points Likert scale. The questionnaire covers 10 dimensions assessing subjective beliefs during a mind-wandering condition. Among the 10 scales, Discontinuity of Mind is linked to a subjective sense of control over one's flow of thoughts. Theory of Mind (TOM) and Self represent two categories regarding the mental activity focused on others and the self respectively. Planning regards future-oriented thoughts, mainly regarding their practical aspects. Sleepiness may be associated to the loss of coherence as one enters a state of drowsiness. Comfort clearly focuses on physical and mental well-being whereas Somatic Awareness focuses on proprioception. Health concern includes items related to worries and feelings about ones' health. Finally, Visual and Verbal Thoughts refer to the preferred modality used during the mind-wandering state. We administered the Italian version of the questionnaire (Marchetti et al., 2015). Good psychometric proprieties were demonstrated for the original and the Italian version of the scale.

Mindfulness Observing and Describing Questionnaire (MODQ)

The MODQ is a self-reported adaptation of the Mindfulness Observing and Describing Interview used to analyze mindfulness practice. The interview has been frequently used in clinical practice to evaluate a subject's outcomes during a mindfulness exercise based on breathing observation. For this study, the trained experts in mindfulness who contributed to the implementation of the original interview developed a self-assessment version. The MODQ is composed of 20 items on a 5-points Likert scale asking the subjects' information about their own ability to apply mindfulness principles during the mindfulness breathing exercise. Four subscales are evaluated: Breath (i.e., subject ability to keep his/her focus on the sensorial aspects of breathing); Distractions (i.e., subject efficacy in mindfully managing the distractions

during the task); Return (i.e., the capability to gently return to breathing observation after a distraction) and Judgment (i.e., the ability to maintain a non-judgmental attitude to the performance and the emotions that emerge during the exercise).

Procedure

The procedure is the same described in the study conducted by Galli, Bortolla and colleagues (2021). Two similar studies were conducted to test the efficacy of mindfulness: the first with HC and the second with BPD patients. To avoid biases in physiological measurement, all the subjects were tested in the same room from 2 p.m. to 5 p.m. Informed consent was signed before the experiment. Participants completed the PANAS as soon as they arrived at the laboratory, and the ECG sensors were attached. After 10 minutes of habituation, the first phase started (baseline): participants were asked to stay on a comfortable armchair in a quiet and isolated environment, and cardiac activity recording was carried out for 10 minutes under resting conditions. All participants were instructed to stay still during recordings to avoid movement artifacts. After this phase participants completed the ARSQ and the PANAS to evaluate mind wandering and affective states. Then, a second phase was recorded, and cardiac activity recording was carried out for 10 minutes under the mindfulness condition. Participants were asked to perform a breathing observation exercise (mindfulness phase). At the end of the mindfulness phase, participants completed the ARSQ, the MODQ, and the PANAS. Finally, the third phase consisted of a recovery resting-state condition (recovery), and cardiac activity recording lasted for the last 10 minutes. Then the ARSQ and the PANAS were administered again. After the task a brief talk with a clinical psychologist were assessed to BPD patients in order to manage eventual emotional crisis.

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