

## Research paper

# Determinants of the remission heterogeneity in bipolar disorders: The importance of early maladaptive schemas (EMS)



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## ABSTRACT

**Background:** A crucial health issue is to understand the remission heterogeneity of Bipolar Disorders by considering symptomatology as well as functioning. A new perspective could be elements of the construction of individual identity. This exploratory study aimed to explore the remission heterogeneity of patients with BD in terms of Early Maladaptive Schemas (EMS) by preferring a person-oriented approach.

**Methods:** This study included euthymic patients recruited into the FACE-BD cohort. The remission was assessed by the Montgomery-Asberg Depression Rating Scale and the Young Mania Rating Scale for its symptomatic dimension and by the Functioning Assessment Short Test for its functional dimension. The activation of the eighteen EMS was assessed by the Young Schema Questionnaire 3 Short Form. Clustering was performed to identify profiles according to the patients' remission. Clusters identified were compared on the EMS activation by using analysis of variance and post-hoc tests.

**Results:** Among the 100 euthymic patients included, four profiles of remission were identified: cluster 1 "Global Remission" (34%), cluster 2 "Hypomanic residual" (20%), cluster 3 "Depressive residual and functional impairment" (36%) and cluster 4 "Global handicap" (10%). Two out of three EMS discriminated against these profiles. The activation of specific EMS clarifies the singularity of each remission profile.

**Limitations:** For the symptomatic dimension, cut-offs chosen could be discussed as well as the scale assessing residual depressive symptoms.

**Conclusions:** This study participates in a comprehensive model of remission by integrating the symptomatology, the functioning, and the EMS. Identifying and treating EMS may improve patients remission to reach recovery.

## 1. Introduction

Euthymic phase in Bipolar Disorders (BD) is a crucial health issue that remains difficult to obtain and stabilize. Euthymia is defined as a normal mood state, which implies the absence of (hypo)mania and depression (DSM-5, APA, 2013), namely symptomatic remission. However, there is a significant interindividual variability concerning symptomatic remission, which is not necessarily associated with a return to premorbid functioning (Tohen et al., 2009). Indeed, even without characterized mood episodes, one out of three patients have manic or depressive subthreshold symptoms (Henry et al., 2015). Furthermore, these symptoms contribute to functional impairment in

patients' daily life (MacQueen et al., 2001). Leaving aside symptomatic remission, other studies investigate functional recovery, which is characterized by a preserved psychosocial functioning (Bonnín et al., 2018). These studies indicate that almost half of the patients are impaired in their functioning (Judd et al., 2005; Samalin et al., 2016). Thus, considering symptomatic remission as well as functional recovery is essential during the euthymic phase, especially since patients spend more time in this phase than in acute manic or depressive phases (Joffe et al., 2004; Kupka et al., 2007).

Nevertheless, studies assess either symptomatology or functioning independently, but few assess both patients' symptomatology and functioning to describe the patients' remission. Thus, despite the close

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link between symptomatology and functioning, current data are not sufficient to understand the remission heterogeneity during the euthymic phase: we don't know why some patients are void of symptoms but have functional impairments (Tohen et al., 2000) whereas others are functionally remitted but have subthreshold symptoms (Morriss, 2002). It is currently essential to identify the brakes and levers of remission for patients with BD and to propose a new perspective of understanding. The schema-focused approach appears to be a relevant model of comprehension.

Theoretical arguments support the understanding of BD through the schema-focused approach. This approach stems from attachment theory (Bowlby, 1958) and Beck's cognitive schemas (Beck, 1967). It assumes the existence of Early Maladaptive Schemas (EMS), which are defined as “broad, pervasive themes regarding oneself and one's relationship with others, developed during childhood and elaborated throughout one's lifetime, and dysfunctional to a significant degree” (Young et al., 2003). EMS color the perception of individuals' world, and they are also elements of the construction of their identity: they are rooted in their personality. EMS are formed when basic emotional needs are not met (e.g., autonomy, safety, and security). This frustration is nurtured by the interaction between adverse childhood experiences (contextual factor) and the innate temperament (biological factor). These two factors are present in BD and justify the relevance of EMS in these disorders (Hawke et al., 2013). Indeed, studies show a higher prevalence of adverse childhood experiences (ACE) in people who suffer from BD than in healthy subjects (Etain et al., 2010; Janiri et al., 2015; Maguire et al., 2008). Studies also show a temperamental dysregulation in these patients (Mendlowicz et al., 2005; Savitz et al., 2008).

Moreover, Ball and colleagues' model (Ball et al., 2003) supports the interest of EMS in BD. This conceptual model considers EMS as a cognitive and schematic vulnerability in interaction with genetic vulnerability, that trigger bipolar symptoms with the intervention of stressful life events (stress-vulnerability model). This model also postulates that EMS would play a part in psychosocial adjustment and adaptation of people who suffer from BD. This model gives EMS a key role in symptomatology emergence on the one hand and individuals' functioning, on the other hand. Thus, Ball and colleagues' model constitutes theoretical support towards the comprehension of remission heterogeneity regarding EMS.

Furthermore, as highlighted by a recent systematic review (Munuera et al., 2020), empirical arguments also support the understanding of BD through the schema-focused approach. First, EMS could appear as a cognitive vulnerability to the onset of symptomatology. Indeed, studies show a greater EMS activation in individuals who suffer from BD than in healthy control (Ak et al., 2012; Hawke and Provencher, 2012; Khosravi et al., 2017; Nilsson et al., 2010; Özdin et al., 2018; Richa et Richa, 2013) but there is not a shared pattern of specific activated EMS, suggesting a global presence of these dysfunctional schemas. Furthermore, studies demonstrate the unfavorable influence of EMS on the course of BD. More precisely, suicidality is predicted by EMS such as social isolation, dependence/incompetence, entitlement/grandiosity, and defectiveness/shame (Khosravani et al., 2019; Nilsson, 2016), whilst functional impairment is predicted by the EMS social isolation, dependence/incompetence, failure to achieve, vulnerability to harm or illness, emotional inhibition, lack of self-control/self-discipline and negativity/pessimism (Nilsson, 2012).

In summary, it appears that EMS play a role either in the symptomatology or the functioning of patients who suffer from BD. Thus, these two points are in accordance with Ball and colleagues' model (Ball et al., 2003): EMS are a promising avenue towards understanding remission (Munuera et al., 2020). However, as we said before, the studies included focused on either symptomatology or functioning. Besides, they share a major limitation: the scientific approaches employed are based on statistical models using mean and standard deviation. This kind of statistical analysis focuses on an average trend which is not necessarily representative of the population because of the

great BD heterogeneity (e.g., bipolarity type, dominant polarity, comorbidities; Kupfer et al., 2015). For these reasons, current data do not yet allow us to understand the remission heterogeneity regarding EMS. New research must address these limitations of the literature.

Thereby, the theoretical, methodological, and statistical approach of this study is based on a person-oriented approach (Bergman and Wångby, 2014) that allows us to highlight the remission heterogeneity in terms of symptomatic and functional dimensions. It constitutes a paradigm shift from what is usually done in the literature. This approach is part of a holistic and interactionist trend which considers the whole individuals' characteristics without breaking them down as it is done in a classical approach. Indeed, starting from individuals of a population, we take into account individuals' specificities, and we gather people who share specific features together. This approach makes it possible to expose within the same population several subgroups of homogeneous individuals (i.e., profiles). The person-oriented approach is particularly relevant in heterogeneous populations such as BD (Kupfer et al., 2015) and will allow us to account for the remission variability existing within BD.

Thus, this exploratory study aims to explore the remission heterogeneity of patients with Bipolar Disorders (BD) in terms of Early Maladaptive Schemas (EMS), by considering individuals symptomatology as well as functioning thanks to a person-oriented approach (Bergman and Wångby, 2014).

## 2. Methods

### 2.1. Study design and characteristics of the recruiting network

This monocenter, transversal study included patients recruited into the FACE-BD (FondaMental Advanced Centers of Expertise for Bipolar Disorders) cohort within the BD Expert Center of Versailles. The BD Expert Centers were set up by the Fondation FondaMental ([www.fondation-fondamental.org](http://www.fondation-fondamental.org)), which created an infrastructure and provided resources to follow clinical cohorts and comparative-effectiveness research in patients with BD.

### 2.2. Patients

All patients were enrolled in the Versailles FACE-BD cohort. The period of recruitment was between July 2012 and March 2017. Inclusion criteria were age between 18 and 65; to be outpatients with bipolar I disorder or bipolar II disorder or not otherwise specified BD. BD was diagnosed via the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I/P; First et al., 2002) by trained professional clinicians; and to be euthymic at the time of testing, according to the DSM-IV-TR criteria (APA, 2000), with a cut-off score of 14 (Chevrier, 2014) on the Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979) and the Young Mania Rating Scale (YMRS; Young et al., 1978). Non-inclusion criteria were to be in acute depressive or manic episode according to the DSM-IV-TR criteria (APA, 2000).

All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2013. All procedures involving human patients were approved by the local ethics committee (Comité de Protection des Personnes Ile-de France IX) on January 18, 2010, under French laws for non-interventional studies (observational studies without any risk, constraint, or supplementary or unusual procedure concerning diagnosis, treatment, or monitoring). The board required that all patients be given an informational letter but waived the requirement for written informed consent. However, verbal consent was witnessed and formally recorded.

### 2.3. Measurement

We selected the MADRS, the YMRS, and the FAST by following the International Society for Bipolar Disorders guidelines (ISBD; Tohen et al., 2009) to assess the two criteria of symptomatic remission (i.e., depressive remission and manic remission) and to assess functional recovery.

#### 2.3.1. Montgomery-Asberg depression rating scale (MADRS; Montgomery and Asberg, 1979)

Patients' depressive symptomatology was assessed during the week preceding the interview using the MADRS (Montgomery and Asberg, 1979), an interviewer-administered instrument, composed of ten items graded on a 0 to 6 scale (0 = not present; 6 = extreme). We defined the symptomatic depressive remission by cut-off: a score below 6 out of 12 reveals that patients were in depressive remission, whereas a score between 6 and 12 shows the presence of subsyndromal depressive symptoms (Chevrier, 2014). Cronbach's alpha was 0.41.

#### 2.3.2. Young mania rating scale (YMRS; Young et al., 1978)

The manic symptomatology of the week preceding the interview was assessed by the YMRS (Young et al., 1978), an interviewer-administered instrument with eleven items. Seven of them are rated from 0 (not present) to 4 (extreme), whereas the remaining four items are rated from 0 (not present) to 8 (extreme). We defined the symptomatic manic remission by a cut-off: a score below 5 out of 12 means that patients are in manic remission while a score between 5 and 12 shows the presence of subsyndromal manic symptoms (Chevrier, 2014). Cronbach's alpha was 0.97.

#### 2.3.3. Functioning assessment short test (FAST; Rosa et al., 2007)

The FAST (Rosa et al., 2007), an interviewer-administered instrument, was developed to assess the functional impairment of patients who suffer from BD. It assesses six functioning areas through twenty-four items: (1) autonomy, (2) occupational functioning, (3) cognitive functioning, (4) financial issues, (5) interpersonal relationships, and (6) leisure time. Each item is graded on a 0 to 3 scale (0 = no difficulty; 3 = severe difficulty). Functional recovery was defined by a global score below 11 out of 72 (Bonñín et al., 2018). The higher the score, the higher the impairment. Cronbach's alpha was 0.86.

#### 2.3.4. Young schema questionnaire 3 short form (YSQ-S3; Young et al., 2005)

We used the YSQ-S3 (Young et al., 2005), a self-administered questionnaire, to measure the Early Maladaptive Schemas activation of patients. Eighteen EMS have been identified and classified into five main domains (Young et al., 2003; see Table 1): (1) disconnection and rejection (e.g., abandonment, mistrust/abuse), (2) impaired autonomy and achievement (e.g., dependence/incompetence, failure to achieve), (3) impaired limits (e.g., grandiosity, insufficient self-control), (4) other-directedness (e.g., subjugation, approval-seeking) and (5) hypervigilance and inhibition (e.g., negativity/pessimism, punitiveness). All the eighteen EMS were assessed through 90 items, five items per schema. Each item is rated from 1 to 6 (1 = completely untrue of me; 6 = describes me perfectly). We calculated an activation percentage of EMS based on the total score (out of 30) for each EMS. Thus, we have a dimensional approach by considering the intensity of EMS activation. Cronbach's alpha for YSQ-S3 was 0.95. Cronbach's alpha for each of the EMS subscales are presented in Supplementary Information 1.

### 2.4. Statistical analyses

Statistical computing was made with the software environment R (version 3.5.3; R Development Core Team, 2005).

We investigated the heterogeneity of BD by identifying profiles (or clusters) in the population. These profiles were identified by

**Table 1**  
The eighteen Early Maladaptive Schemas (EMS) classified into five domains (Young et al., 2003).

(1) Disconnection and rejection	(2) Impaired autonomy and achievement	(3) Impaired limits	(4) Other-directedness	(5) Hypervigilance and inhibition
Abandonment/Instability Mistrust/Abuse Emotional deprivation Defectiveness/Shame Social isolation/alienation	Dependence/Incompetence Vulnerability to harm or illness Emmeshment/Undeveloped self Failure to achieve	Entitlement/Grandiosity Lack of self-control/self-discipline	Subjugation Self-sacrifice Approval-seeking/Recognition-seeking	Negativity/Pessimism Emotional inhibition Unrelenting standards/Hypercriticalness Punitiveness

considering patients' characteristics together.

Thereby, Hierarchical Ascendant Classification (HAC) was performed by preferring Ward's method. HCA was preferred against other clustering methods because it is the most replicated method used in a bunch of prior studies on BD (Green et al., 2019). This clustering is based on a factor analysis using nine variables: the two symptomatic remission criteria that is manic remission and depressive remission, and the functional recovery (dichotomous variables: remission/recovery or not), and the six functioning areas (quantitative variables: standardized scores). Indeed, to assess the patients' functioning in all its dimensions, we considered standardized scores of each area of functioning. These standardized scores were calculated from the mean and the standard deviation obtained by the total sample for each area. Thus, our clusters are constituted according to the symptomatology as well as the functioning of patients. Data were complete on the nine variables used for clustering. However, there were very few missing data at the item level for EMS, which were handled by computing an average score from the scores obtained by the same participant in the other items within the same EMS (replacement by the intra-subject and intra-EMS mean score). Finally, the number of clusters was defined by visual inspection of the dendrogram plot and by considering the gain within inertia. A linear discriminant analysis was also performed to assess the quality of the classification.

Then, we compared the different clusters using the nine variables to clarify their remission heterogeneity. Moreover, in order to know if the heterogeneity of profiles highlighted could be understood regarding EMS, the activation percentages of each EMS were compared between clusters. To do these inter-clusters comparisons, a chi-square test of independence with Monte-Carlo simulation and a Fisher's exact test with Bonferroni-Holm correction were performed for qualitative variables. In case of quantitative variables, analysis of variance (one-way ANOVAs) and post-hoc Tukey's test (or non-parametric tests if necessary) for non-equivalent samples were performed. Non-parametric tests were applied when data were not normally distributed. Lastly, analysis of covariance (ANCOVA) were also performed to test if contrasts regarding EMS remained significant by integrating the variable age as a covariate.

### 3. Results

#### 3.1. Participants

This study included 100 participants. Overall, 61% of the sample were female. The mean age was 40.42 (SD = 11.33). We found that 54% suffered from bipolar II disorder, 33% suffered from bipolar I disorder, 10% from BD not otherwise specified, and 3% were cyclothymic. Other socio-demographic and clinical data are presented in Table 2.

#### 3.2. Cluster analysis: identification of subgroups according to the symptomatology and the functioning

Four clusters of patients were identified by HAC: Cluster 1 "Global remission" (R) included 34% patients ( $n = 34$ ), Cluster 2 "Hypomanic residual" (Hyp) comprised 20% patients ( $n = 20$ ), Cluster 3 "Depressive residual and functional impairment" (DepF) collected 36% patients ( $n = 36$ ) and Cluster 4 "Global handicap" (H) included 10% ( $n = 10$ ). Scores obtained in each cluster for each variable are presented in Fig. 1. The cluster characterization is presented in Table 3. This characterization was made compared to the total sample.

Overall, the "Global remission" cluster was characterized by a more frequent remission in all criteria: 88.24% of patients were in depressive remission; 100% of patients were in manic remission, and 91.18% of patients were in functional recovery. The "Hypomanic residual" cluster was characterized by a less frequent manic remission: none of the patients (0%) was in manic remission. In other words, 100% of patients in

this cluster suffered from subsyndromal manic symptoms. The "Depressive residual and functional impairment" cluster was characterized by a less frequent depressive remission: 36.11% of patients were in depressive remission. It was also characterized by a less frequent functional recovery: none of the patients was in functional recovery (0%). On the contrary, this cluster is characterized by a more frequent manic remission, concerning 97.22% patients. Lastly, the "Global handicap" cluster was characterized by a less frequent depressive remission and a less frequent functional recovery, concerning respectively 20% of patients and 0% of patients.

The linear discriminant analysis revealed that 91.18% of patients were correctly classified in "Global remission" cluster, 100% of patients were correctly classified in "Hypomanic residual" cluster, 97.22% of patients were correctly classified in "Depressive residual and functional impairment" cluster, and 70% of patients were correctly classified in "Global handicap" cluster. A total of 93% of patients were correctly classified.

#### 3.3. Intercluster comparisons: differences on the symptomatology and the functioning between the four clusters identified

Depressive remission, manic remission, and functional recovery were significantly associated with clusters membership: depressive remission ( $X^2 = 25.60, p < .001$ ), manic remission ( $X^2 = 82.02, p < .001$ ) and functional recovery ( $X^2 = 68.02, p < .001$ ). The six functioning areas were significantly associated with clusters membership: autonomy ( $F(3,28) = 11.34, p < .001$ ), occupational ( $F(3,28) = 13.96, p < .001$ ), cognitive ( $F(3,96) = 20.44, p < .001$ ), financial issues ( $F(3,31) = 9.35, p < .001$ ), interpersonal ( $F(3,96) = 17.02$ ) and leisure time ( $F(3,32) = 28.60, p < .001$ ). Results of the post-hoc analyses are summarized in Table 3.

The main differences were between the "Global remission" and "Global handicap" clusters as if they were the two extreme levels of a remission continuum. Indeed, these clusters differed on all variables. The percentage of patients in depressive remission is lower in the "Global handicap" cluster (20%) than in the "Global remission" cluster (88.24%,  $p < .001$ ). The percentage of patients in manic remission in the "Global handicap" cluster (60%) is also lower compared to the "Global remission" cluster (100%,  $p < .01$ ). Similarly, the percentage of patients in functional recovery is lower in the "Global handicap" cluster (0%) than in the "Global remission" cluster (91.18%,  $p < .001$ ). Furthermore, all functioning areas were more impaired in the "Global handicap" cluster than in the "Global remission", as evidenced by significant higher standardized scores on autonomy ( $M = 1.62$  vs.  $-0.49, p < .01, d = 2.87$ ), on occupational functioning ( $M = 0.67$  vs.  $-0.58, p < .05, d = 2.16$ ), on cognitive functioning ( $M = 1.73$  vs.  $-0.49, p < .001, d = 2.93$ ), on financial issues ( $M = 1.78$  vs.  $-0.29, p < .01, d = 2.36$ ), on interpersonal relationships ( $M = 0.99$  vs.  $-0.58, p < .001, d = 2.47$ ) and on leisure time ( $M = 1.77$  vs.  $-0.61, p < .001, d = 3.82$ ).

Clusters were also compared on socio-demographic and clinical variables (e.g., age, sex, dominant polarity, substance use). None of the variables tested discriminated against the four clusters identified (Table 2).

#### 3.4. Comparisons of clusters on EMS: differences in the EMS activation between the four clusters identified

Two out of three EMS discriminated against the four clusters identified. Indeed, these profiles differed from each other according to the percentage of EMS activation (Table 4 and Fig. 2). The activation percentage of EMS did not significantly differ between the clusters for failure to achieve ( $F(3,96) = 1.82, p = 0.149$ ), enmeshment ( $F(3,96) = 2.38, p = 0.075$ ), self-sacrifice ( $F(3,96) = 1.28, p = .287$ ), emotional inhibition ( $F(3,96) = 1.42, p = 0.243$ ), unrelenting standards ( $F(3,96) = 1.12, p = 0.345$ ) and punitiveness ( $F(3,96) = 1.28,$

**Table 2**  
 Socio-demographic and clinical characteristics of the total sample and the four clusters identified, and results of the interclusters comparisons.

Variables	Total sample (N = 100)	(R) Global remission (n = 34)	(Hyp) Hypomanic residual (n = 20)	(DepF) Depressive residual and functional impairment (n = 36)	(H) Global handicap (n = 10)	Test
Sex						
Females (%)	61	58.82	50	69.44	60	$\chi^2 = 2.17, p = .535$
Males (%)	39	41.18	50	30.56	40	
Age (years)						
M(SD)	40.42(11.33)	39.79(11.78)	41(11.33)	41.94(11.27)	35.90(10.21)	$F(3,96) = 0.80, p = .500$
Marital status						
Single, divorced or widowed (%)	41	44.12	35	44.44	30	$\chi^2 = 2.17, p = .551$
Occupational status						
Cohabiting or married (%)	58	55.88	65	55.56	60	
Unemployed (%)	29	17.65	35	36.11	30	$\chi^2 = 6.74, p = .347$
Employed (%)	67	82.35	60	58.33	60	
Type of bipolar disorder						
Bipolar I (%)	33	38.24	20	33.33	40	$\chi^2 = 11.41, p = .236$
Bipolar II (%)	54	44.12	70	58.33	40	
Cyclothymia (%)	3	17.65	10	2.78	10	
Not specified (%)	10	0	0	5.56	10	
Dominant polarity						
Depressive (%)	24	29.41	30	19.44	10	$\chi^2 = 16.13, p = .065$
Manic (%)	6	2.94	10	0	30	
Indeterminate (%)	33	35.29	25	36.11	30	
Number of episodes						
M(SD)	6.71(5.44)	6.61(2.59)	7.31(8.19)	7.10(6.56)	5(2.73)	$F(3,61) = 0.34, p = .795$
Distance to the last episode (weeks)						
M(SD)	42.55(80.41)	44.70(86.73)	34.78(41.76)	46.59(97.81)	33.88(37.72)	$F(3,72) = 0.10, p = .962$
Age of first episode (years)						
M(SD)	23.24(8.04)	24.18(8.02)	20.17(5.94)	24.24(7.95)	22.22(11.32)	$F(3,90) = 1.26, p = .293$

M = mean; SD = standard deviation.

Missing data percentage for qualitative variables are not mentioned (remaining percentage).

Missing data are deleted to calculate mean of quantitative variables.

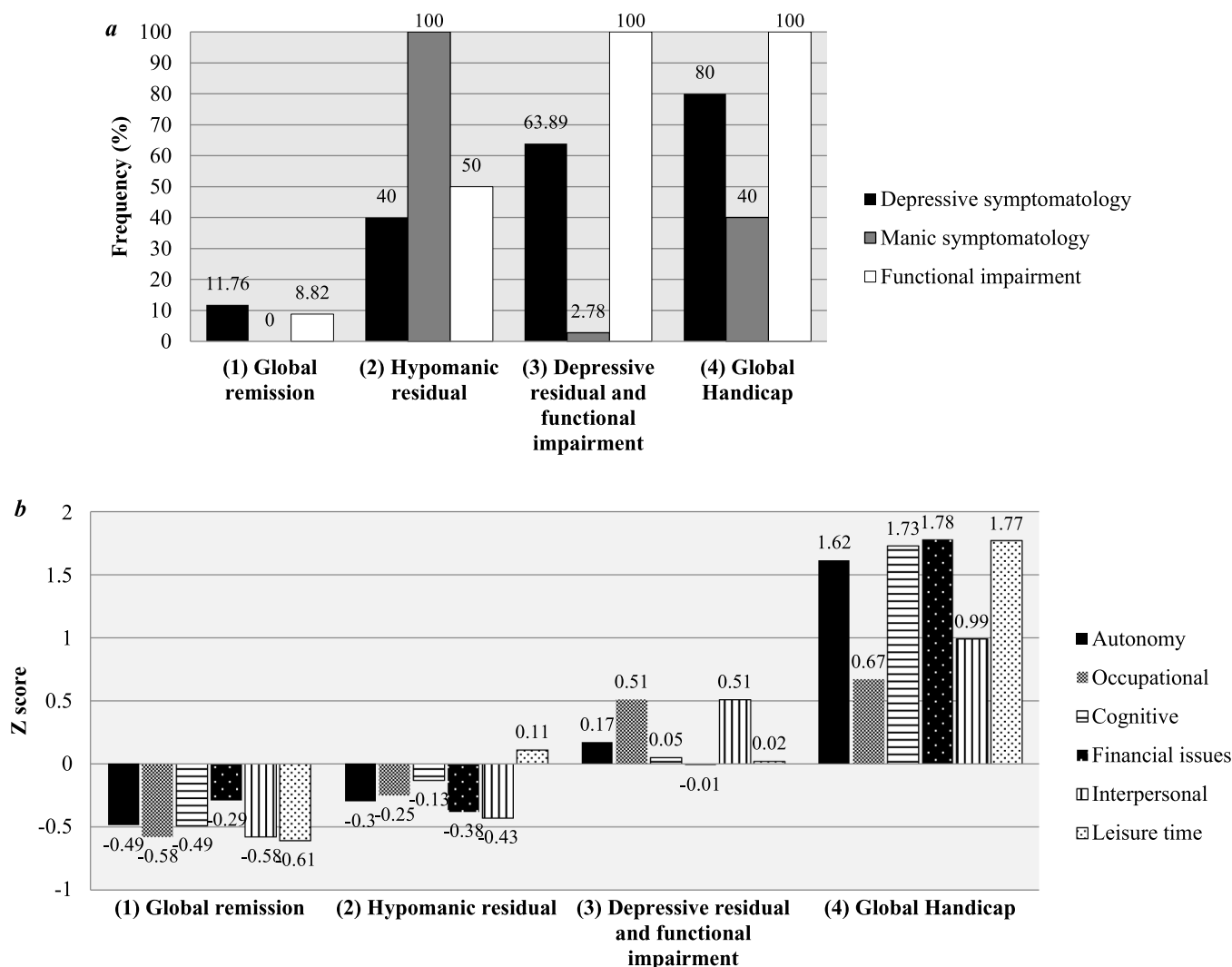


Fig. 1. (a) Percentage of individuals who are not in depressive remission, manic remission and functional recovery per the four clusters identified, (b) Standardized scores of the functional impairment obtained by the four clusters identified for each functioning area.

$p = 0.287$ ). These EMS are part to three main domains: “impaired autonomy and achievement”, “other-directedness” and “hypervigilance and inhibition”. Clusters were different for approval-seeking ( $F(3,33) = 3.49, p < .05$ ), however, post-hoc analysis demonstrated that differences were not significant. Results of the inter-clusters comparisons by adjusting for age are presented in Supplementary Information 3 and are reported below if relevant.

The percentage of activation did not differ significantly for any EMS between “Hypomanic residual” and “Depressive residual and functional impairment” clusters and between “Depressive residual and functional impairment” and “Global handicap” clusters. “Global remission” and “Hypomanic residual” clusters differed only on the EMS entitlement: the activation percentage was significantly lower for the “Global remission” cluster ( $M = 42.35$ ) compared to the “Hypomanic residual” cluster ( $M = 53.58, p < .05, d = 0.77$ ). Also, “Hypomanic residual” and “Global handicap” clusters differed only concerning vulnerability to harm or illness: the percentage of activation was significantly higher for the “Global handicap” cluster ( $M = 57$  vs.  $40.33, p < .05, d = 0.92$ ), but this contrast became marginally significant by adjusting for age ( $p = 0.086$ ). The differences were mainly identified between “Global remission” and “Depressive residual and functional impairment” clusters, and between “Global remission” and “Global handicap” clusters. Indeed, compared to the “Global remission” cluster, EMS of “Depressive residual and functional impairment” and “Global handicap” clusters

were globally more activated.

Compared to the “Global remission” cluster, the activation percentage of EMS in the “Depressive residual and functional impairment” cluster was higher for abandonment ( $M = 59.07$  vs.  $44.90, p < .05, d = 0.76$ ), mistrust/abuse ( $M = 43.98$  vs.  $33.04, p < .01, d = 0.79$ ), social isolation ( $M = 54.93$  vs.  $38.33, p < .01, d = 0.95$ ), defectiveness/shame ( $M = 44.44$  vs.  $31.57, p < .05, d = 0.62$ ), dependence/incompetence ( $M = 44.91$  vs.  $32.06, p < .01, d = 0.86$ ), subjugation ( $M = 48.61$  vs.  $34.02, p < .001, d = 0.99$ ), lack of self-control ( $M = 51.20$  vs.  $37.38, p < .01, d = 0.92$ ) and negativity/pessimism ( $M = 57.89$  vs.  $44.68, p < .01, d = 0.85$ ).

In comparison with the “Global remission” cluster, the EMS activation percentage in the “Global handicap” cluster was higher for abandonment ( $M = 64.67$  vs.  $44.90, p < .05, d = 1.10$ ), social isolation ( $M = 62.33$  vs.  $38.33, p < .01, d = 1.52$ ), vulnerability to harm or illness ( $M = 57$  vs.  $36.86, p < .01, d = 1.10$ ), subjugation ( $M = 50.33$  vs.  $34.02, p < .05, d = 1.27$ ), entitlement ( $M = 59.67$  vs.  $42.35, p < .01, d = 1.32$ ) and negativity/pessimism ( $M = 66.67$  vs.  $44.68, p < .05, d = 1.35$ ). The EMS activation percentage were also higher in the “Global handicap cluster” for emotional deprivation ( $M = 54$  vs.  $36.47, p < .05, d = 1.13$ ), defectiveness/shame ( $M = 46.67$  vs.  $31.57, p < .05, d = 0.99$ ), however these contrasts became respectively marginally significant ( $p = 0.056$ ) and non-significant ( $p = 0.211$ ) by adjusting for age. Furthermore, by integrating the age as a covariate, the activation



**Table 3**  
Clusters characterization and comparisons on manic and depressive remissions, functional recovery and functioning areas.

Variable	Total sample (N = 100)	(R) Global remission (n = 34)	(Hyp) Hypomanic residual (n = 20)	(DepF) Depressive residual and functional impairment (n = 36)	(H) Global handicap (n = 10)	Test
Depressive remission (%)	57	<b>88.24***</b>	60	<b>36.11***</b>	<b>20*</b>	Main effect: $X^2 = 25.60, p < .001$ R vs. DepF: $p < .001$ R vs. H: $p < .001$
Manic remission (%)	75	<b>100***</b>	<b>0***</b>	<b>97.22***</b>	60	Main effect: $X^2 = 82.02, p < .001$ R vs. Hyp: $p < .001$ R vs. H: $p < .01$ Hyp vs. DepF: $p < .001$ Hyp vs. H: $p < .01$ DepF vs. H: $p < .05$
Functional recovery (%)	41	<b>91.18***</b>	50	<b>0***</b>	<b>0**</b>	Main effect: $X^2 = 68.02, p < .001$ R vs. Hyp: $p < .01$ R vs. DepF: $p < .001$ R vs. H: $p < .001$ Hyp vs. DepF: $p < .001$ Hyp vs. H: $p < .05$
Autonomy M(SD)	1.36(2.37)	<b>-0.49(0.27)***</b>	-0.30(0.65)	0.18(0.94)	<b>1.62(1.50)***</b>	Main effect: $F(3,28) = 11.34, p < .001^\dagger$ R vs. DepF: $p < .01$ R vs. H: $p < .01$ Hyp vs. H: $p < .05$ DepF vs. H: $p < .05$
Occupational M(SD)	4.81(5.37)	<b>-0.58(0.32)***</b>	-0.25(0.88)	<b>0.51(1.11)***</b>	<b>0.67(1.09)***</b>	Main effect: $F(3,28) = 13.96, p < .001^\dagger$ R vs. DepF: $p < .001$ R vs. H: $p < .05$ Hyp vs. DepF: $p < .05$
Cognitive M(SD)	2.66(2.79)	<b>-0.49(0.59)***</b>	-0.13(0.74)	0.05(0.86)	<b>1.73(1.18)***</b>	Main effect: $F(3,96) = 20.44, p < .001$ R vs. DepF: $p < .05$ R vs. H: $p < .001$ Hyp vs. H: $p < .001$ DepF vs. H: $p < .001$
Financial issues M(SD)	1.04(1.66)	<b>-0.29(0.73)***</b>	-0.38(0.53)	-0.01(0.83)	<b>1.78(1.27)***</b>	Main effect: $F(3,31) = 9.35, p < .001^\dagger$ R vs. H: $p < .01$ Hyp vs. H: $p < .01$ DepF vs. H: $p < .01$
Interpersonal M(SD)	4.11(3.03)	<b>-0.58(0.49)***</b>	<b>-0.43(0.78)*</b>	<b>0.51(1.01)***</b>	<b>0.99(1.00)***</b>	Main effect: $F(3,96) = 17.02, p < .001$ R vs. DepF: $p < .001$ R vs. H: $p < .001$ Hyp vs. DepF: $p < .001$ Hyp vs. H: $p < .001$
Leisure time M(SD)	1.71(1.74)	<b>-0.61(0.58)***</b>	0.11(0.98)	0.02(0.76)	<b>1.77(0.76)***</b>	Main effect: $F(3,32) = 28.60, p < .001^\dagger$ R vs. Hyp: $p < .05$ R vs. DepF: $p < .001$ R vs. H: $p < .001$ Hyp vs. H: $p < .001$ DepF vs. H: $p < .001$

Mean(Standard deviation).

For the six functioning areas, the higher the score, the higher the impairment.

Significant results of the clusters characterization are in bold: significant p-value means that the cluster differs from the total sample on the considered variable; \*  $p < .05$ ; \*\*  $p < .01$ ; \*\*\*  $p < .001$ .

<sup>†</sup> = One-way non-parametric ANOVA with degree of freedom correction.

percentage of the EMS lack of self control became significantly higher in the “Global handicap” cluster than in the “Global remission” cluster ( $M = 57.40$  vs.  $37.20, p < .01$ ).

Lastly, a post-hoc power analysis was performed. The power of all comparisons was above 0.80 (see Supplementary Information 2), so it was satisfactory for every EMS.

#### 4. Discussion

This exploratory study aimed to explore the remission heterogeneity

of patients with BD in terms of EMS by preferring a person-oriented approach. Based on a model that considered the symptomatic remission as well as the functional recovery, there were different remission patterns in patients with BD. These remission profiles showed different activation patterns of EMS. In fact, two out of three EMS discriminated against these profiles. Indeed, according to their level of remission, patients had different dysfunctional perceptions of themselves, others, and the world.

First, there is not one euthymic period but several characterized by different remission profiles. Indeed, the identification of four profiles

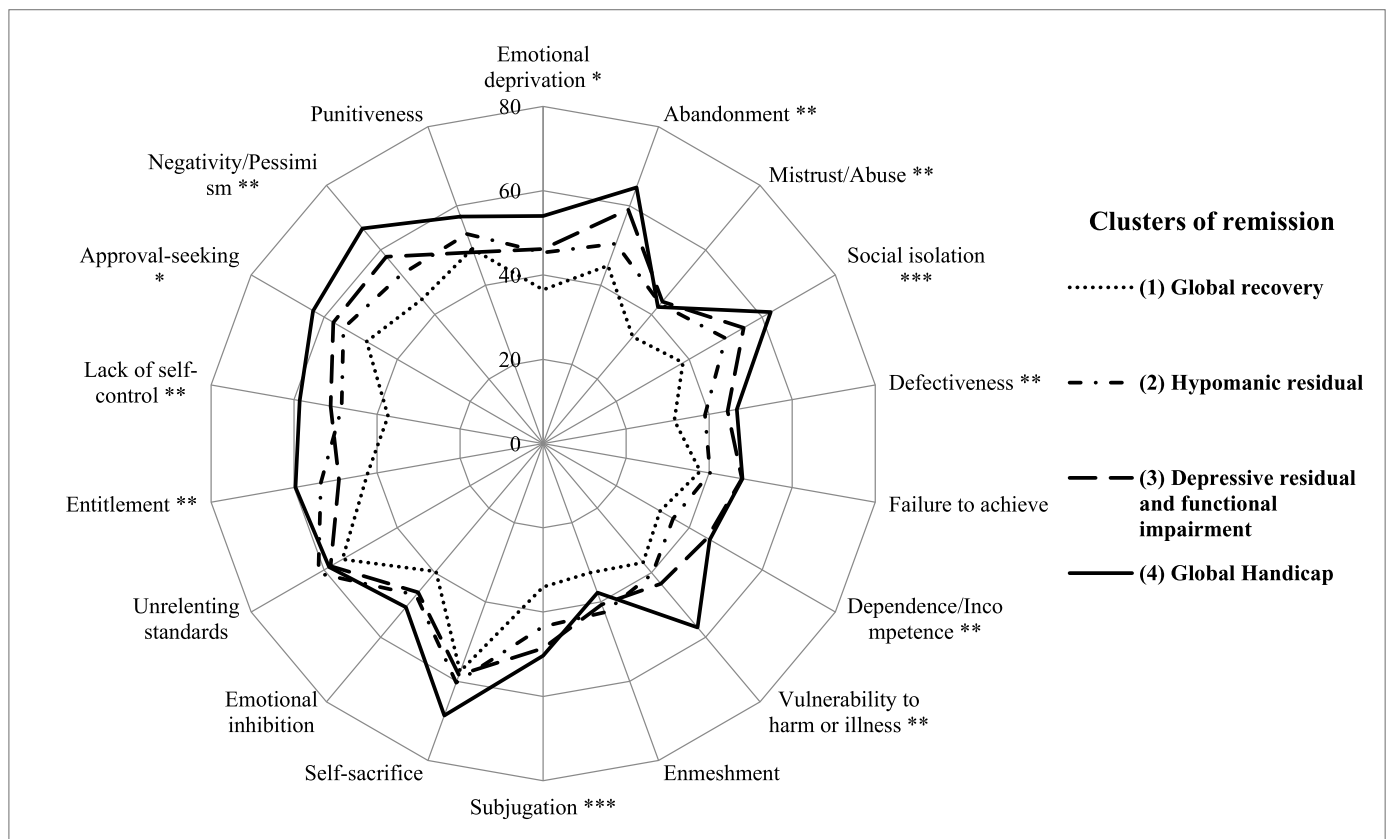
**Table 4**  
Comparisons between clusters on EMS.

Variable	Total sample (N = 100)	(R) Global remission (n = 34)	(Hyp) Hypomanic residual (n = 20)	(DepF) Depressive residual and functional impairment (n = 36)	(H) Global handicap (n = 10)	Test
<i>Emotional deprivation</i>	43.50(19.17)	36.47(16.39)	45.33(18.24)	46.20(21.94)	54.00(11.63)	Main effect: $F(3,96) = 2.99, p < .05$ R vs. H: $p < .05$
<i>Abandonment</i>	53.10(20.63)	44.90(18.30)	50.50(23.77)	59.07(19.13)	64.67(16.57)	Main effect: $F(3,96) = 4.35, p < .01$ R vs. DepF: $p < .05$ R vs. H: $p < .05$
<i>Mistrust/Abuse</i>	39.94(16.40)	33.04(10.93)	43.21(22.63)	43.98(16.21)	42.33(11.87)	Main effect: $F(3,33) = 4.58, p < .01$ R vs. DepF: $p < .01$
<i>Social isolation</i>	49.03(19.76)	38.33(15.31)	49.96(20.97)	54.93(19.18)	62.33(17.57)	Main effect: $F(3,96) = 6.99, p < .001$ R vs. DepF: $p < .01$
<i>Defectiveness/Shame</i>	39.20(19.62)	31.57(16.27)	39.00(19.97)	44.44(22.23)	46.67(10.23)	R vs. H: $p < .01$ Main effect: $F(3,39) = 4.71, p < .01$ R vs. DepF: $p < .05$
<i>Failure to achieve</i>	42.93(20.17)	37.84(18.29)	40.17(18.05)	47.87(20.84)	48(25.10)	Main effect: $F(3,96) = 1.82, p = .149$
<i>Dependence/Incompetence</i>	38.75(16.69)	32.06(9.74)	35.58(19.29)	44.91(18.58)	45.67(13.88)	Main effect: $F(3,32) = 5.98, p < .01$ R vs. DepF: $p < .01$
<i>Vulnerability to harm</i>	41.93(17.23)	36.86(18.40)	40.33(18.09)	43.43(12.84)	57.00(18.15)	Main effect: $F(3,96) = 4.01, p < .01$ R vs. H: $p < .01$
<i>Enmeshment</i>	38.02(15.51)	32.65(13.48)	42.58(16.76)	40.65(16.40)	37.67(12.58)	Hyp vs. H: $p < .05$ Main effect: $F(3,96) = 2.38, p = .075$
<i>Subjugation</i>	42.78(16.67)	34.02(12.05)	43.42(18.10)	48.61(16.83)	50.33(15.51)	Main effect: $F(3,96) = 6.11, p < .001$ R vs. DepF: $p < .001$
<i>Self-sacrifice</i>	59.54(16.44)	57.55(14.71)	60.38(15.75)	58.43(18.18)	68.67(16.04)	R vs. H: $p < .05$ Main effect: $F(3,96) = 1.28, p = .287$
<i>Emotional inhibition</i>	44.52(18.33)	39.61(15.31)	46.96(21.19)	46.11(18.27)	50.67(21.30)	Main effect: $F(3,96) = 1.42, p = .243$
<i>Unrelenting standards</i>	57.85(13.02)	55.00(11.55)	61.58(13.95)	58.24(13.42)	58.67(14.16)	Main effect: $F(3,96) = 1.12, p = .345$
<i>Entitlement</i>	48.78(14.80)	42.35(13.35)	53.58(16.39)	49.17(13.41)	59.67(12.32)	Main effect: $F(3,96) = 5.25, p < .01$ R vs. Hyp: $p < .05$
<i>Lack of self-control</i>	46.73(17.89)	37.38(14.06)	48.58(19.47)	51.20(15.86)	58.67(20.98)	R vs. H: $p < .01$ Main effect: $F(3,31) = 6.52, p < .01$ R vs. DepF: $p < .01$
<i>Approval-seeking</i>	54.38(16.90)	48.36(15.30)	54.71(22.27)	57.50(14.24)	63.00(13.74)	Main effect: $F(3,33) = 3.49, p < .05$
<i>Negativity/Pessimism</i>	53.17(19.57)	44.68(15.42)	52.38(26.33)	57.89(15.57)	66.67(19.18)	Main effect: $F(3,32) = 5.92, p < .01$ R vs. DepF: $p < .01$
<i>Punitiveness</i>	50.43(14.64)	49.17(14.82)	52.92(17.15)	48.33(12.96)	57.33(13.68)	R vs. H: $p < .05$ Main effect: $F(3,96) = 1.28, p = .287$

Mean(Standard Deviation).

† = One-way non-parametric ANOVA with degree of freedom correction.





**Fig. 2.** Activation patterns of the 18 Early Maladaptive Schemas (EMS) per the 4 clusters identified, NB: significant main effect of comparison between the 4 clusters on each EMS: \*  $p < .05$ ; \*\*  $p < .01$ ; \*\*\*  $p < .001$ .

with their own characteristics highlights the remission heterogeneity of euthymic patients: cluster 1 “Global remission” (34%), cluster 2 “Hypomanic residual” (20%), cluster 3 “Subsyndromal depressive symptoms and functional impairment” (36%), and cluster 4 “Global handicap” (10%). This disparity is emphasized by significant differences between these different profiles concerning both the symptomatology and the functioning. Taking into account symptomatology and functioning together is essential because that allows us to bring out the different levels of remission. This relevant result shows that the categorical approach (presence or absence of symptoms) is insufficient to grasp the remission: to consider the level of functioning is primordial too. Thus, while the first studies on the euthymic period focused on either residual symptoms (Henry et al., 2015; Judd et al., 2008; Perlis et al., 2006) or functioning (MacQueen et al., 2001; Judd et al., 2005; Samalin et al., 2016) independently, the results of this study encourage concomitantly considering the two dimensions. Allowing patients to access global remission could subsequently allow them to access recovery, which can be considered as the next step after remission (Tohen et al., 2009). Indeed, according Liberman et al. (2002), patients achieve recovery by being in both symptomatic remission and functional recovery. However, current research shows how recovery goes further than a global remission (Leamy et al., 2011; Onken et al., 2007). Indeed, “recovery no longer means ‘being cured’ or ‘being normal again’. Instead, it is about gaining new meaning and purpose in life, being empowered to live a self-directed/determined and autonomous life” (WHO, 2017, p. 15). Recovery includes a holistic consideration of several components, such as the regain control of identity and life or hope (WHO). This view of recovery shows how it is crucial to take into account the identity elements of individuals such as EMS.

This study provides a new perspective for understanding the different profiles of remission by integrating EMS, which are elements of an individual's development. Actually, EMS would appear to be

prominent in explaining the singularity of each profile of remission, especially since socio-demographic and clinical characteristics do not explain it. Indeed, compared to the “Global remission” profile, a specific over-activation of the EMS entitlement in the “Residual manic symptoms” profile may explain the maintenance of manic symptoms: this EMS is in accordance with the grandiosity, a characteristic symptom of the manic period (Gilbert et al., 2007; Smith et al., 2017). This idea is reinforced by the activation of the same EMS in the “Global handicap” profile with patients who also suffer from subthreshold manic symptoms. Furthermore, the “Global handicap” profile and the “Depressive residual and functional impairment” profile shared the presence of subsyndromal depressive symptoms which may be explained by a greater activation than the profile “Global remission” concerning the EMS abandonment, social isolation, defectiveness/shame, subjugation and negativity/pessimism. Indeed, these EMS might be related to the depressive semiology (Dardennes, 2017). For example, the EMS defectiveness/shame can refer to feelings of worthlessness, and the EMS negativity/pessimism can relate to feelings of helplessness and hopelessness. This hypothesis is consistent with the literature: the EMS abandonment, defectiveness/shame, and negativity/pessimism were more activated in patients who suffer from unipolar depression than in the healthy control group (Özdin et al., 2018). Moreover, the functional impairment in these profiles may be related to their activated EMS because social isolation, dependence/incompetence, vulnerability to harm or illness, lack of self-control, and negativity/pessimism play a significant role in the functioning (Nilsson, 2012). More specifically, compared to the “Global remission” profile, the “Depressive residual and functional impairment” profile was more activated for EMS mistrust/abuse, dependence/incompetence, and lack of self-control. These EMS can impact professional functioning (e.g., passivity, avoidance of situations requiring self-discipline) and interpersonal relationships (e.g., afraid of being manipulated by the others, affective dependency),

two areas particularly impaired in this profile. Finally, the global lower activation of EMS in the “Global remission” profile compared to the patients who are neither in symptomatic remission nor functional recovery (i.e., “Depressive residual and functional impairment” and “Global handicap” profiles) may explain the absence of symptoms and functional impairment. All these findings support the Ball and colleagues’ model (Ball et al., 2003), suggesting EMS are determinants of the remission heterogeneity in BD.

Finally, this study participates in a comprehensive model of remission to reach the recovery issue in BD. It is the consideration of the symptomatology, the functioning and the EMS in an integrative and holistic way that allows us to better understand individuals in euthymia. Thus, improve the remission is possible by helping patients to modify their EMS. Psychotherapists could accompany them on the journey of recovery and facilitate it. Indeed, recovery is the consideration of the individuals in their objective and subjective dimensions (e.g., social functioning, identity, hope, connectedness; for a review see Onken et al., 2007). These dimensions are in interplay with each other and interact with the environment (Onken et al., 2007). Recovery is a process in which the patient plays a fundamental active part; the term “recovery journey” is used (Leamy et al., 2011). Recovery is also thought in a relational context where individuals’ interactions with their environment are highlighted (Price-Robertson et al., 2017). Thereby, EMS are relevant in the recovery issue because they are distortions in the way people conceive their identity, their social relationships, and the way they interact with others (Young et al., 2003). Thus, EMS may impede recovery by affecting the recovery dimensions such as identity, social connectedness, and perception of social support. Therefore, taking into account the EMS allows us to reach recovery and adapt therapeutic care in consequence, according to the remission profiles’ specificities. Indeed, improving therapeutic orientation is the main clinical perspective of this study. In addition to the schemas therapy, which would be relevant for all unremitted profiles, clinicians could identify a specific profile by assessing both patient’s symptomatology and functioning, and propose an adapted therapeutic orientation to support the patient towards recovery in a best way. All these findings could be highlighted thanks to the person-oriented approach (Bergman and Wångby, 2014): we were able to investigate the remission in a global way, starting from patients’ characteristics in interaction.

This is the first French exploratory study that considers the remission heterogeneity of BD in terms of symptomatology as well as functioning by investigating the EMS, but some limitations must be taken into account. First, even if our choice follows the recommendations (Tohen et al., 2009), the MADRS and the YMRS were not validated in a French population which suffers from BD specifically. Furthermore, there is no consensus among researchers on the cuts-off which define symptomatic (manic and depressive) remissions (e.g., Hawley et al., 2002; Tohen et al., 2009; Zimmerman et al., 2004). Moreover, the internal consistency of the MADRS was low in this study. This raises the question of whether this scale is appropriate for measuring residual depressive symptoms in euthymic patients. Despite its limitations, this study provides clinical and scientific perspectives. First, the post-hoc power analysis showed a satisfactory power for each pair-wise comparisons regarding EMS despite the small sample size. It encourages further studies to replicate this study by performing an a priori power analysis. Future research should integrate elements of personality construction, such as EMS. This study emphasizes that EMS are determinants in the remission. Regarding the previous study of Harding et al. (2012) concerning the identification of child sexual abuse survivor subgroups based on EMS, it would be relevant to test the opposite hypothesis that remission might be a determinant to modify the EMS activation by making clusters based on EMS. Furthermore, this first exploratory study encourages future research with more participants to integrate other variables than the age in analyses such as socio-demographic and clinical characteristics (e.g., sex, type of BD, age of

the first episode, dominant polarity). Moreover, in this study, the impact of comorbidities is unknown. Thus, further study could address this limitation by considering the impact that comorbidities (ADHD, personality disorder, anxiety disorders, trauma-related disorders ...) may have on the link between EMS and the remission in BD. Lastly, euthymia might sometimes be associated with residual cognitive symptoms impairing a full remission (Martínez-Arán et al., 2004). Improving cognitive abilities has indeed been associated with functional recovery in patients with depression (Motter et al., 2016), and cognitive impairment hampers functioning in bipolar disorder (Bonnín et al., 2019). Thus, future research should investigate cognitive performance as a moderator of the link between EMS and the remission.

In conclusion, it appears important to identify and treat EMS in clinical practice to improve the patient’s remission, and then, to reach recovery. Schemas therapy (Young et al., 2003), the therapy focused on EMS, may be an effective therapeutic avenue given that its efficacy in disorders which shared similar clinical characteristics with BD (unipolar disorder, Carter et al., 2013; borderline personality disorder, Jacob and Arntz, 2013). These results about remission constitute the first step and encourage future research to model the recovery in BD, as Jones et al. (2013) did by developing a questionnaire that assesses recovery in BD specifically. It would change the illness relationship by going further than the absence of characterized mood episode and by focusing on the patient’s experience.

#### Authors statement contributors

C. Munuera wrote the manuscript and undertook statistical analyses. P. Roux collected data and revised the article. F. Weil collected data and revised the article. C. Passerieux collected data and revised the article. K. MBailara wrote the manuscript. All authors contributed to and have approved the final manuscript.

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#### Declaration of Competing Interest

None.

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#### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2020.08.079.

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