Borderline Personality Disorder and Inflammation: clinical and biological effects of Metacognitive Interpersonal Therapy

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Introduction

Borderline personality disorder (BPD) is a serious and debilitating psychiatric disorder affecting about 2% of the general population [1]. It is mainly characterized by emotion dysregulation (ED) and difficulties in impulse control [2]. The etiology of BPD is complex and includes genetic vulnerability as well as dysfunctional stress regulation. Several studies have indeed reported that many BPD patients have been exposed to sexual, physical or emotional abuse and/or neglect during childhood [3]. Interestingly, exposure to stress and traumatic events early in life has been demonstrated as a trigger for activating immune-inflammatory mechanisms, both in the brain and in peripheral cells [4].

Although only a few studies have investigated peripheral markers of inflammation in BPD, changes in the regulation of the inflammatory response, including elevated concentrations of pro-inflammatory cytokines have been also reported in BPD patients [5].

Aim

- To further characterize the alterations in the inflammatory response in BPD patients and their relationship with clinical features, including ED and childhood trauma.
- To evaluate if the inflammatory response could be involved in the effects of psychotherapy.

Methods

82 patients diagnosed with BPD (according to the DSM-IV-TR) and 27 healthy controls were enrolled and assessed for multiple clinical features. BPD patients were randomly assigned to 2 psychotherapeutic treatments: Metacognitive Interpersonal Therapy (MIT) and Structured Clinical Management (SCM). Both treatments consisted in individual and group sessions covering one year.

Serum samples were collected from patients at the baseline (T0) and after 6 (T6) and 12 (T12) months of treatment and from control subjects only at T0. A panel of 21 cytokines (ITAC, GM-CSF, Fractalkine, IFNγ, IL-10, MIP-3α, IL-12 (p70), IL-13, IL-17A, IL-1β, IL-2, IL-21, IL-4, IL-23, IL-5, IL-6, IL-7, IL-8, MIP-1α, MIP-1β, TNFα) was assessed at each time point by using the Milliplex HSTCMAG28SPMX21 Human High Sensitivity T Cell MAG Premix 21plex Kit (Merck Millipore) on a BioPlex 200 Instrument (Bio Rad) .

Comparisons between BPD patients and controls at the baseline and between the subgroup of BPD patients allocated to the two intervention groups (MIT and SCM) were performed by using chi-square test, t test, or Mann–Whitney tests, according to distribution of the variables.

A composite Z-score was calculated considering the concentration of all cytokines: the individual Z-score of each cytokine per subject was obtained using the percentage of variation of BPD patients compared to controls: Z score = (X – control group mean) / control group standard deviation (SD). Anti-inflammatory cytokines were calculated by using their inverse percentage of variation. Then, the Z-scores of all cytokines were averaged for each experimental group.

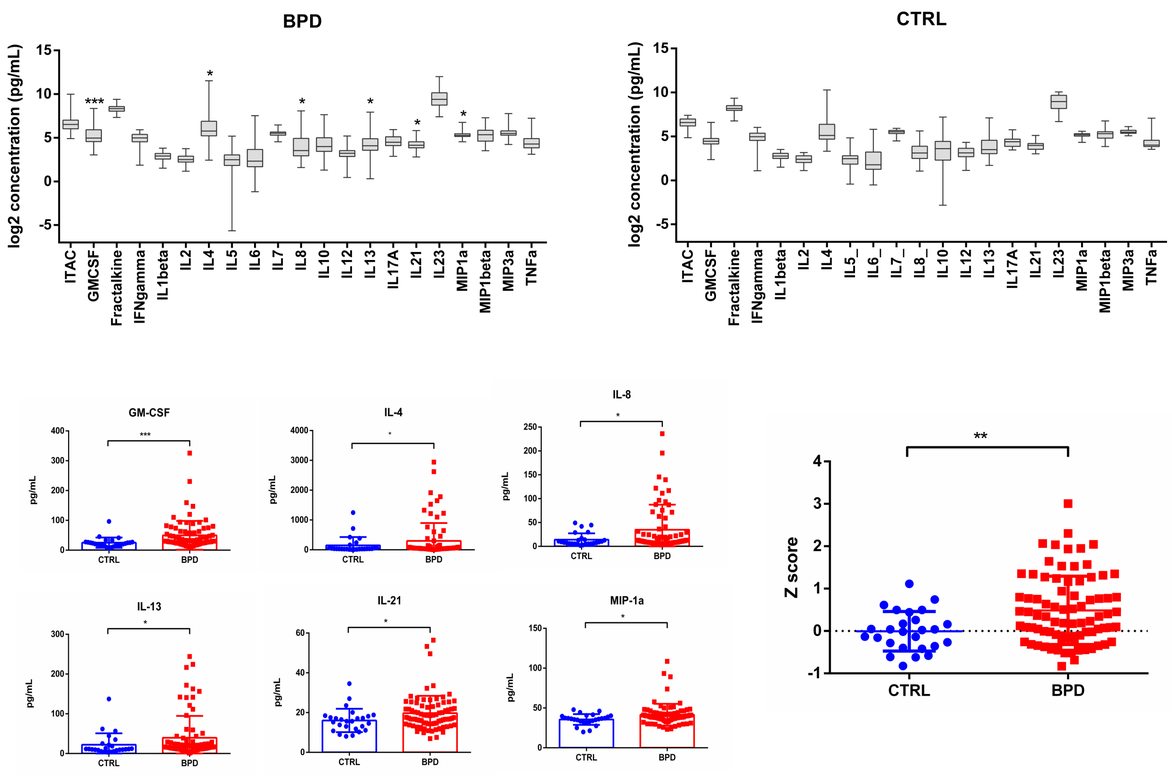
Results

	BPD patients (N=82)	Controls (N=27)	p-value
Sex female (N %)	67 (82.7%)	23 (85.2%)	1.000
Age years (mean, SD)	28.60 (8.12)	28.70 (6.85)	0.588
Age at onset years (mean, SD)	17.67 (5.64)	-	-
Length of illness years (mean, SD)	10.81 (7.40)	-	-
Inventory of Interpersonal Problems (IIP)	2.2 (0.7)	0.8 (0.5)	<0.001
Attachment Style Questionnaire (ASQ) subscales:			
Confidence	26.3 (6.4)	32.6 (4.0)	<0.001
Discomfort with Closeness	40.1 (6.0)	33.2 (5.3)	<0.001
Relationships as Secondary	17.7 (6.4)	14.2 (5.8)	0.024
Need for approval	29.4 (6.6)	18.6 (5.0)	<0.001
Preoccupation with Relationships	36.2 (6.9)	25.8 (5.5)	<0.001
Difficulties in Emotion Regulation Scale—DERS	121.7 (25.6)	62.5 (11.7)	<0.001
Zanarini Rating Scale for BPD (ZAN-BPD)	15.6 (4.6)	1.9 (1.3)	<0.001
Childhood Trauma Questionnaire score (CTQ)	57.2 (16.7)	32.2 (5.3)	<0.001

Table 1: Clinical and demographic characteristics of the study subjects

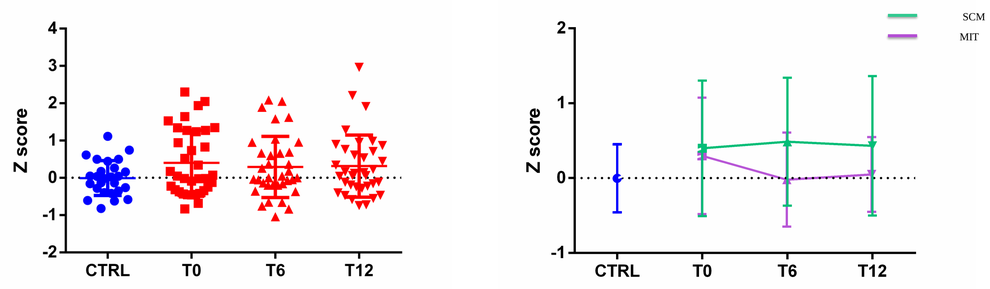
Baseline evaluations

Significantly higher baseline levels of 5 pro-inflammatory cytokines and 1 anti-inflammatory cytokine were found in BPD patients compared with controls: GM-CSF (p-value < 0.0001), IL8 (p-value = 0.033), IL13 (p-value = 0.023), IL21 (p-value = 0.034), IL4 (p-value = 0.047) and MIP1alpha (p-value = 0.017). The composite Z-score confirmed an overall inflammatory status in BPD patients (p-value = 0.007).



Longitudinal evaluations

Psychotherapies did not restore the baseline levels of the 6 cytokines, nor did they lower the Z-score. Interestingly, the subgroup of BPD patients randomly allocated to MIT showed a slightly decrease in the composite Z-score after treatment (both after 6 and 12 months follow-up) compared to the SCM group.



Conclusions

These preliminary results contribute to the hypothesis that BPD patients show an increased activation of the overall inflammatory profile, suggesting that inflammatory processes could be a part of the pathophysiology of the disorder. Non-pharmacological interventions targeting inflammation may be helpful in preventing the onset and improve symptoms of BPD. Future analysis will take into account the relationship between higher inflammatory markers and other clinical variables such as emotional dysregulation and childhood trauma.

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Conflict of interest: All the authors have no conflict of interest to disclose.