

# Inflammatory cytokines and BDNF levels are correlated with different states of bipolar disorder, but not with anxiety comorbidities

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**Background:** Immune system dysregulation constitute an important component for the pathophysiology and neuroprogressive process in bipolar disorder (BP) and anxiety disorder. We therefore investigated the changes of cytokines and BDNF levels between different disease states, as well as between different comorbid anxiety disorder conditions in BP. We also compare the possible difference in cytokines and BDNF presentations between BP patients and controls.

**Methods:** BP patients were determined into remission ( $HDRS \leq 7$  and  $YMRS \leq 6$  for at least 8 weeks,  $n=61$ ) or non-remission group ( $HDRS > 7$  or  $YMRS > 6$  for more than half year,  $n=113$ ) and with ( $n=73$ ) or without anxiety comorbidities group ( $n=101$ ). Inflammatory cytokines (TNF- $\alpha$ , CRP, IL-8, IL-10 and TGF- $\beta 1$ ) and BDNF levels were measured. Multivariate analysis of covariance (MANCOVA) was used to analyze.

**Results:** MANCOVA adjusting for age and sex and a main effect of BP was found ( $p < 0.001$ ). Four of 6 measured biomarkers (TNF- $\alpha$ , IL-8, TGF- $\beta 1$  and BDNF) were significantly different in BP than in controls (Table 1). The changes in TNF- $\alpha$ , TGF- $\beta 1$  and BDNF levels were significantly different between remission and non-remission group (Table 2&Figure 1). The IL-8 levels were significantly decreased along with the treatment course (Table 2), but there was no significantly difference in IL-8 levels between remission and non-remission groups. The anxiety comorbidity did not show significantly impact on all of the measured cytokines and BDNF variations(anxiety comorbidities: Pillai  $V=0.01$ ,  $F [6,163] = 2.94$ ,  $P=0.94$ ).

**Conclusion:** Changes in cytokine and BDNF levels were correlated with BP treatment response, but not with anxiety comorbidities.

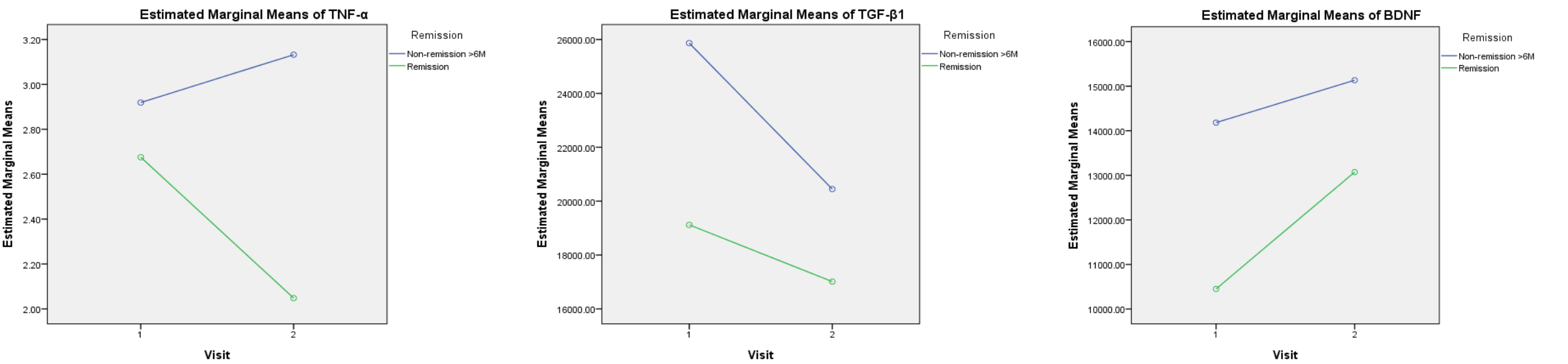
Table 1 Baseline demographic data, cytokine and BDNF levels in the BP (subgroup with remission state) and control group

	BP (n=174)		Control(n=140)		P	
	Remission(n=61)	Non-remission(n=113)				
Age	34.3±13.0	35.2±13.7	31.7±7.9		0.05	
Sex(M/F)	29/32	42/71	81/59		0.005*	
Anxiety comorbidity(-/+)	23/38	50/63			0.40	
TNF-α	2.72±2.31	2.90±2.55	1.68±1.59		<0.001*	
CRP	1578.15±1417.68	1810.41±1460.78	1545.75±1363.45		0.43	
IL-8	2.64±2.74	2.89±2.81	1.59±3.31		0.001*	
IL-10	0.85±0.58	0.77±0.68	0.71±0.60		0.26	
TGF-β1	19625.91±11711.24	25662.03±14342.89	27245.44±15728.57		0.004*	
BDNF	10792.18±4863.82	15304.94±9374.25	16744.73±9086.74		<0.001*	*P<0.05

Table 2 Changes of the cytokine and BDNF levels in different groups

	TNF-α		CRP		IL-8		IL-10		TGF-β1		BDNF	
	F	P	F	P	F	P	F	P	F	P	F	P
Remission state	5.73	0.02*	0.47	0.50	1.20	0.27	1.22	0.27	10.64	0.001*	15.96	<0.001*
Visit	0.002	0.97	0.08	0.78	5.89	0.02*	3.07	0.08	0.32	0.57	1.37	0.24

Figure 1 Estimated marginal means of TNF-α, TGF-β1 and BDNF in different remission state



Author disclosures:

All authors declare that they have no conflicts of interest.

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