Cerebrospinal fluid biomarkers of brain injury in bipolar disorder

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Background

Bipolar disorder is a common psychiatric disorder characterized by recurrent episodes of mania/hypomania and depression. Structural imaging studies suggest that bipolar disorder is associated with morphological abnormalities of the brain (Kempton et al., 2008). We previously investigated a neuro-degenerative component of bipolar disorder by analyzing several cerebrospinal fluid (CSF) biomarkers for neurodegenerative processes in bipolar patients and healthy controls (Jakobsson et al., 2013). No major alterations were observed between patients and controls thus excluding neurodegenerative processes related to these biomarkers (T-tau, P-tau, and amyloid beta). There are, however, other established CSF biomarkers reflecting injuries in different cells/structures in brain. These biomarkers include: neurofilament light chain (NF-L), Heart-type fatty acid binding protein (hFABP), calcium binding protein S100B, and myelin basic protein (MBP) (Olsson et al., 2011).

Purpose

The aim in this study was to test the suggested neuroprogressive component in bipolar disorder and to investigate possible associations between CSF markers for brain injury and disease severity, ongoing medications, and/or cognitive functions.

Method

Patients (N=119) were recruited from the St. Göran bipolar project, enrolling patients from the bipolar unit at the Northern Stockholm Psychiatric Clinic, Stockholm, Sweden (Table 1). 86 age and gender matched healthy, population-based controls were randomly selected by Statistics Sweden (SCB). Cerebrospinal fluid sampling (lumbar puncture) was performed when the participants were in a stable euthymic mood. NF-L was analyzed using previously described ELISA methods (Rosengren et al., 1996). S-100B was determined by an electrochemoluminescence immunoassay using the Modular system and the S100 reagent kit (Roche Diagnostics). MBP was measured using a commercially available ELISA method. hFABP was measured using a commercially available ELISA method (Hycult Biotechnology, Uden, The Netherlands).

Table 1. Demographics and clinical characteristics of the study population.

Characteristic	Bipolar disorder	
	N	%
Males	46	38.7
Diagnosis		
Bipolar disorder type I	73	61.3
Bipolar disorder type II	46	38.7
Prior psychosis	62	52.1
Medications		
Lithium	70	58.8
Lamotrigine	26	21.8
Valproate	14	11.8
Antidepressants	54	45.4
Benzodiazepines	25	21.0
Atypical APs	27	22.7
	Median	**IQR**
Age (years)	34	28-50
BMI	24.4	22.0-27.7
Total number of episodes	10	6-20
GAF	70	60-75
Clinical global impression (CGI) [1]	4	4-5
YMRS	0	0-1
MADRS	1	0-4

[1] N = data from 117 patients,

APs = antipsychotics, IQR = interquartile range, BMI = body mass index, YMRS = young mania rating scale, MADRS = Montgomery–Åsberg Depression Rating Scale

Results

The concentrations of MBP, S100B, and NF-L were positively associated with age and gender in both controls and patients (data not shown). hFABP was positively associated with age but not gender (data not shown). The CSF concentrations of NF-L were higher in bipolar disorder type I patients and the MBP concentrations higher in bipolar disorder type II patients when compared with healthy controls (Figure 1). There were no significant differences in the concentration of S100B and hFABP between patients and controls (Figure 1). We also observed a weak association between lamotrigine treatment and higher MBP concentrations (p=0.010, ANCOVA with age and gender as covariates). There were however no associations between any of the CSF-markers and the clinical characteristics outlined in Table 1.

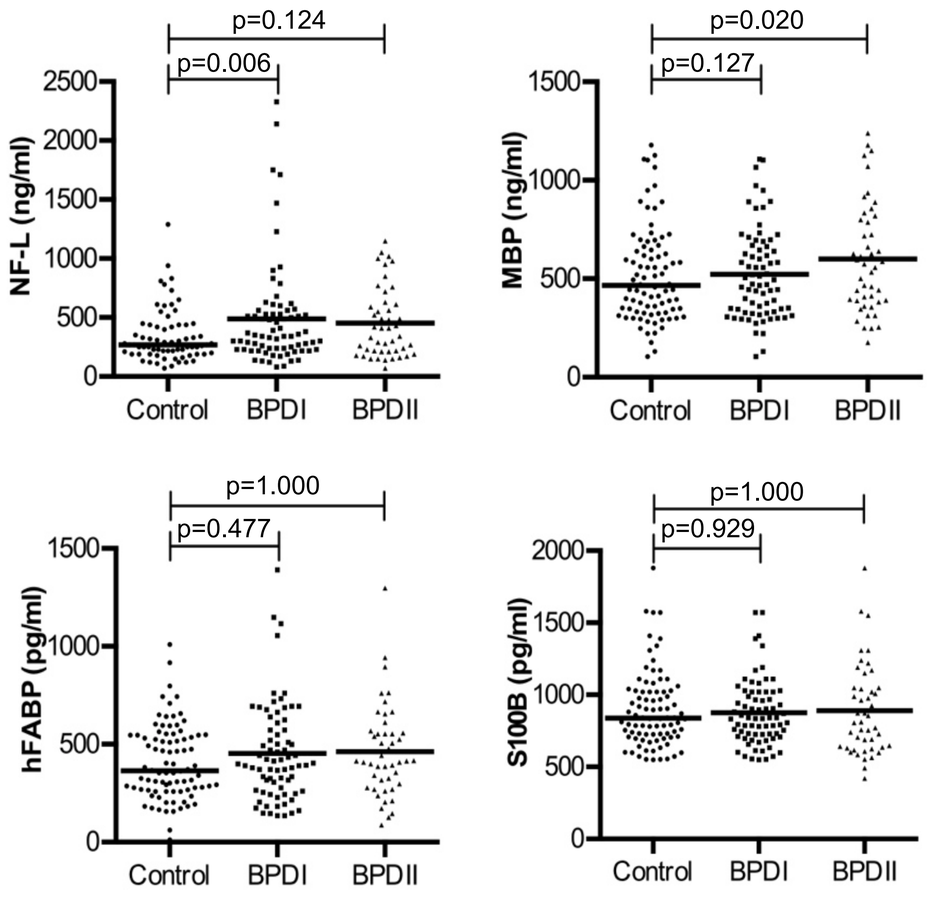

Figure 1. Brain injury biomarker concentrations in controls, bipolar disorder type I (BPDI), bipolar disorder type II (BPDII) patients. Statistics: ANCOVA with age and gender as covariates, adjusted for multiple comparisons (Bonferroni).

Discussion and conclusions

We found elevated concentrations of NF-L, a marker of subcortical axon damage, and MBP, a marker of oligodendro-cytes/myelin. These findings indicate that bipolar disorder is associated with white matter alterations, which is in line with previous brain imaging studies. Future studies will give empha-size to the identification of associations between these cerebro-spinal fluid markers and alterations in brain structures, genetic variations, and cognitive functions since these data is also available for this study population.

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Disclosures

There is no potential conflict of interest.

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