Association between inflammation and neural plasticity biomarkers in olfactory neuroepithelium – derived cells and cognitive performance in patients with major depressive disorder

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Introduction

Major depressive disorder (MDD) is a disabling disorder that is amongst the most prevalent mental health disorders worldwide and is highly recurrent [1]. Growing evidence suggests a significant role of inflammation and neural plasticity processes in the pathogenesis of major depressive disorder and its cognitive dysfunction [2]. For example, some studies has found an association between altered BDNF regulation and neurocognitive functions [3]. The olfactory neuroepithelium (ON), closely related to the central nervous system (CNS), allows a non-invasive, low-cost study ofnew biomarkers and therapeutic targets for neuropsychiatric disorders [4]. However, s revision of the literature has shown only a few studies about novel biomarkers of MDD using cell cultures from the olfactory neuroepithelium (ON).

Objectives

The aim of this work was to determine the relationship between inflammatory and neural plasticity markers and cognitive functioning in MDD patients and healthy controls.

Methods

The sample of this study was composed by 9 MDD patients with MDD (DSM-IV criteria) and 7 healthy controls. The exclusion criteria were other Axis I mental disorders for patients or any mental disorder for controls (assessed with MINI) and any inflammatory, autoimmune or CNS diseases. All participants underwent a comprehensive assessment that included sociodemographic, clinical (as illness course), and cognitive variables (CANTAB). The local ethics committee approved this study, and all participants provided written informed consent. The method used to the exfoliation of ON cells and their culture was described in *Guinart et al.* [5]. The determination of the olfactory neuroepithelium cells biomarkers was assessed by mRNA isolation from ON cells and MAPK14, IL6, TNF-α, Mecp2, BDNF, GSK3, GRIA2 and FosB gene expression levels were quantified using quantitative polymerase chain reaction (q-PCR). For the statistical analysis, firstly, a Shapiro - Wilk test was used to assess the normality of the data. Then, qualitative variables were analyzed with Fisher exact test and differences in quantitative variables were analyzed with one-way ANOVA. The Pearson's correlatuon was performed for determining the relationship between mRNA biomarkers levels and cognitive variables. All statistical analyses were performed in SPSS Statistics for Windows, version 20 (IBM Corp.); p values ≤ 0.05 were considered statistically significant.

Results

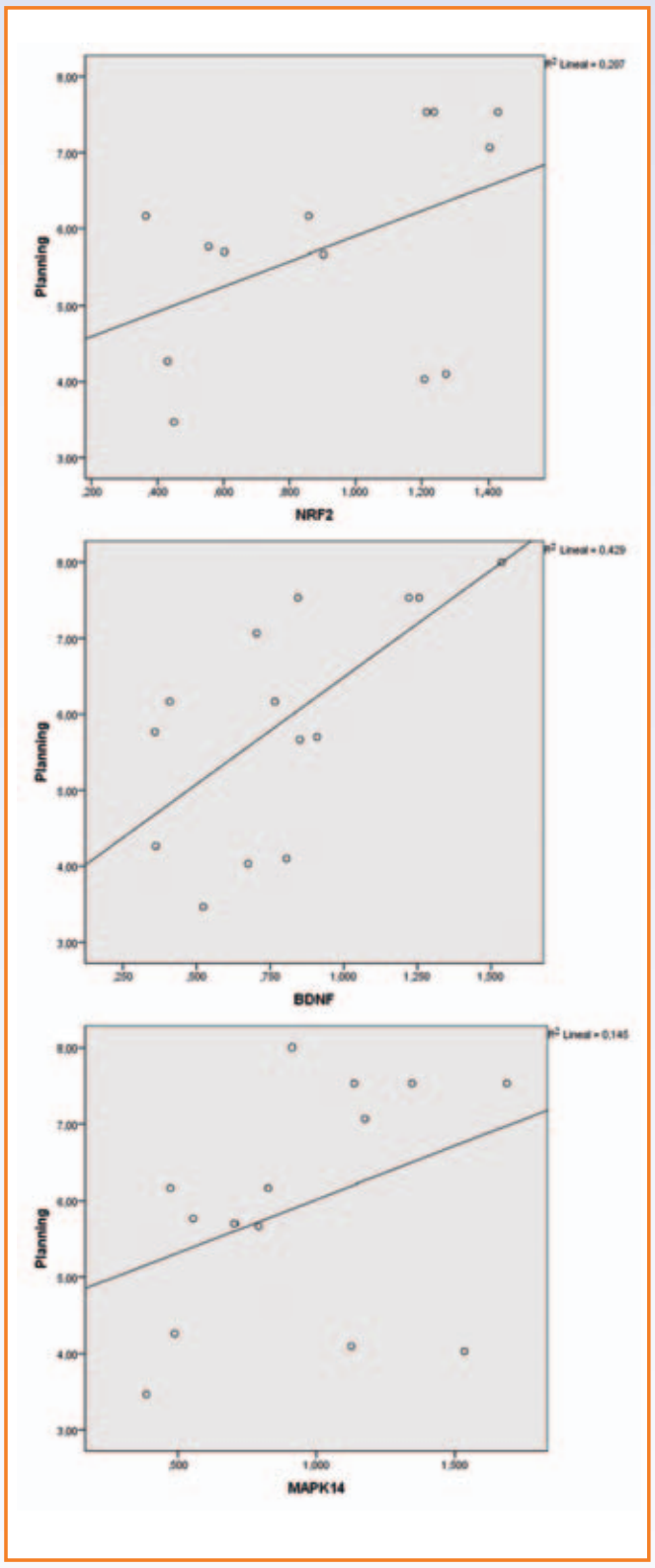
MDD patients showed decreased levels of BDNF (p=0.022), GSK3 (p=0.027) and working memory (p=0.024) compared with healthy controls. In healthy controls, planning was positively correlated with NRF2, BDNF and MAPK14 gene expression. In MDD patients no correlation between cognitive parameters and inflammation/neural plasticity biomarkers was found.

Table 1. Demographic, clinical and cognitive data

	Controls (N = 7)	MDD patients (N = 9)	p
Age in years (m, SD)*	45.29 (11.03)	51.67 (8.96)	0.222
Sex (%)**			
Male	3 (42.9)	5 (55.6)	
Female	4 (57.1)	4 (44.4)	
Age onset in years (m, SD)*		29.67 (13.71)	
Episode duration in months (m, SD)*		15 (18.6)	
Processing speed (m, SD)*	12807.94 (2315.43)	16887.83 (7539.71)	0.191
Working memory (m, SD)*	36.71 (3.71)	30.17 (5.98)	**0.024**
Impulsivity (m, SD)*	10772.93 (4219.08)	9499.39 (2241.68)	0.605
Planning (m, SD)*	6.42 (1.59)	5.43 (1.34)	0.231

Abbreviations: *Mann-Whitney test, **Fisher's test, N= sample size, MDD= major depressive disorder, m= mean, SD= standard deviation.

Figure 1. Positive correlation between NRF2, BDNF and MAPK14 levels and planning in healthy controls



Conclusions

These results reveal that: (1) Plasticity biomarkers such as BDNF and GSK3 could be useful diagnostic tools for MDD (2) MDD is associated with working memory deficits; (3) no association could be determined between planning and NRF2, BDNF and MAPK14 gene expression in MDD and (4) the ON is a promising model in the study of neuropsychiatric disorders.

** The authors have no conflicts of interest to declare that are relevant to the content of this study.*

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