

Cb1-5-HT_{2A} heteromers and neurological soft signs in schizophrenia patients: human studies in pro-neurons of the olfactory epithelium

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INTRODUCTION

Despite multiple clinical and pre-clinical studies investigating schizophrenia, the neurobiological basis of this disease is still unknown. The dysregulation of the serotonergic system, in particular the 5-HT_{2A} receptor and the endocannabinoid system have been postulated as possible causes of schizophrenia.

OBJECTIVES

The aim of this study is from a translational approach, is to compare and quantify the expression of CB₁-5-HT_{2A} receptor heteromers in primary cultures of pro-neurons from the olfactory neuro-epithelium in schizophrenia patients.

METHODS

We recruited a group of 10 patients diagnosed with schizophrenia, who were treated with atypical antipsychotics, who are and were clinically stable and had an illness duration range from 1 up to 15 years. The patients were diagnosed with schizophrenia from the medical record and confirmed by the Structured Clinical Interview for DSM Disorders. We also recruited a group of 11 healthy volunteers. We quantified the expression of CB₁-5-HT_{2A} receptor heteromers in primary cultures of pro-neurons from the olfactory neuro-epithelium of using PLA immunoassays and confocal microscopy.

RESULTS

Cells were viable and expressed the neuronal marker, III- β tubulin. We also established the presence and the functionality of CB₁-5-HT_{2A} receptor heteromers in these cells using the proximity ligation and cAMP activity assays, respectively. CB₁-5-HT_{2A} Heteromer expression was significantly increased in schizophrenia patients with respect to controls. Patients with schizophrenia show alterations in working memory, attention, verbal fluency and Neurological Soft Signs.

Figure 1. Immunofluorescent staining with β -III tubulin and CB₁-5-HT_{2A} heteromers by PLA healthy controls

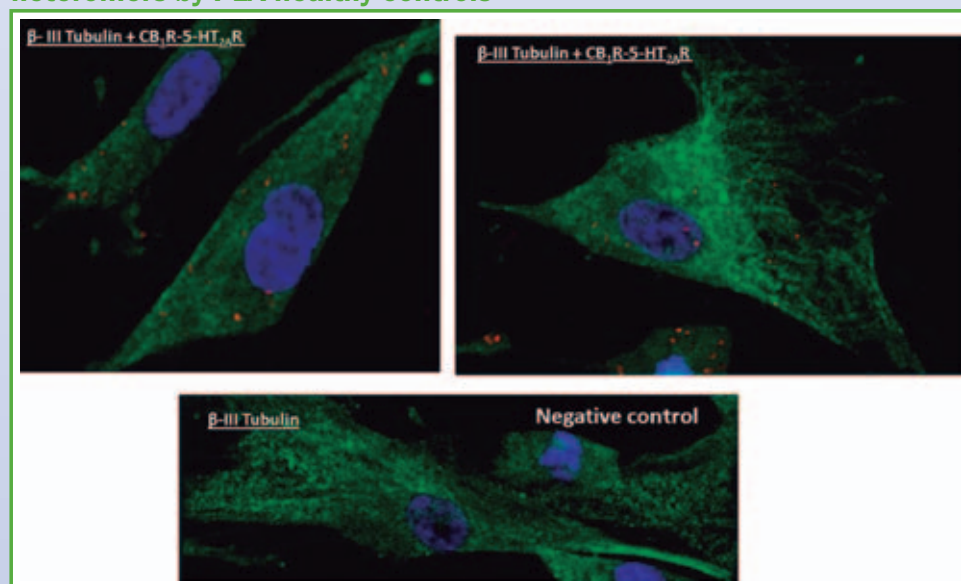


Figure 2. CB₁-5-HT_{2A} heteromers in control subjects (CS), and patients with schizophrenia (PS) detected by in situ PLAs

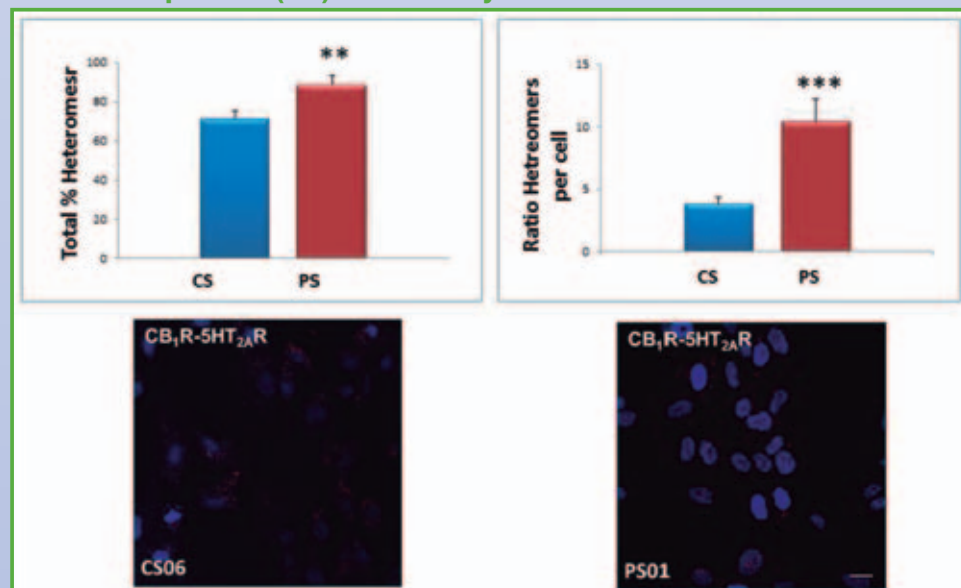
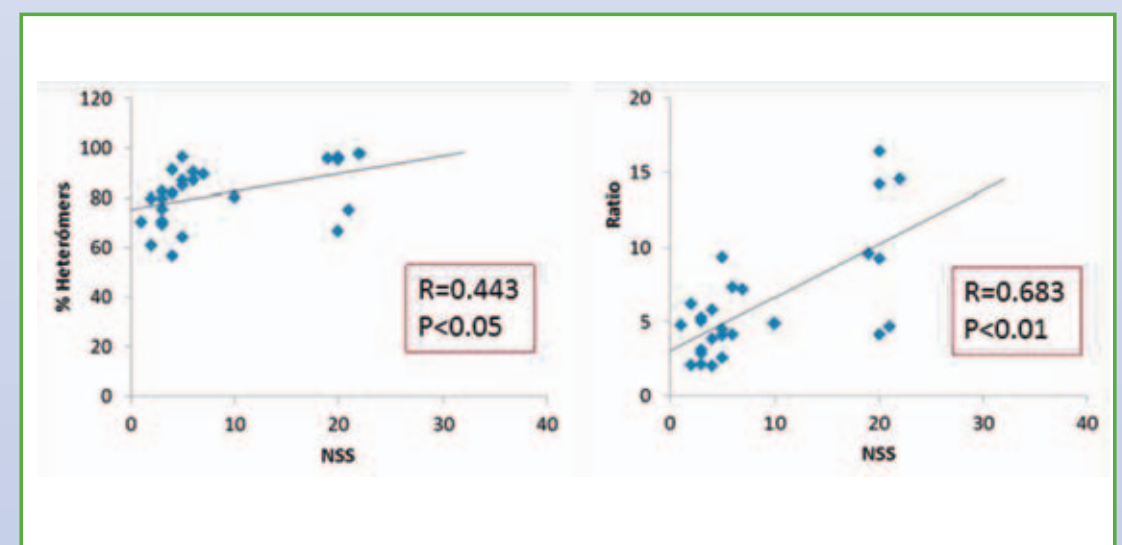


Figure 3: Correlations between CB₁-5-HT_{2A} Heteromers and NSS



CONCLUSIONS

This highly innovative methodology will allow the non invasive, low-cost study of new biomarkers for schizophrenia in a model closely related to the central nervous system.

Higher Neurological Soft Signs in schizophrenia patients is associated with and increase in heteromers CB₁-5-HT_{2A}.

Alterations in working memory, attention, verbal fluency and emotional recognition are associated with higher NSS

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***Acknowledgments:** Supported in part by grants of Instituto de Salud Carlos III-FEDER FIS (PI10/01708)