Alterations of COX-2 pathway: risk for the development of schizophrenia

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Background

Inflammatory processes have been discussed in the biology of schizophrenia. The binding of cytokines to membrane receptors initiates inflammatory response pathways, inducing cyclooxygenase2 (COX-2) activity in the cytoplasm (fig.1). This enzyme is associated with arachidonic acid (AA) metabolism and prostaglandin synthesis ⁽¹⁾.

Figure 1 – Inflammatory response pathways

Objective

To determine the levels of cytokines and inflammatory markers from COX-2 pathway, namely, thromboxane B₂ (TXB₂), prostaglandin E₂ (PGE₂) and prostaglandin F_{2α} (PGF_{2α}) in individuals at Ultra High Risk (UHR) for psychosis.

Material and Methods

Subjects

UHR was determined using the Prodromal Questionnaire ⁽²⁾: the lowest values were considered UHR and the highest values defined the controls.

Subjects	UHR (n=40)	Control (n=40)	p value*
Age (years)	23.2 ± 2.9	26.5 ± 4.5	0.004*
Scholarship (years)	11.1 ± 2.2	10.8 ± 2.2	0.668
Gender (M/F)	12/24	12/24	0.213

Metabolites quantification

Cytokines (IL-1β, IL-10, IL-6, GM-CSF, IL-5, IFN-γ, TNF-α, IL-2, IL-4 and IL-8) were quantified by Luminex® technology. TXB₂, PGE₂ and PGF_{2α} levels were measured using the ELISA assays.

Results

PGE₂ was significantly increased in UHR individuals.

Figure 2- PGF_{2α} – Prostaglandin F_{2α}, PGE₂ – Prostaglandin E₂, TXB₂ – Thromboxane B₂, UHR – Ultra High Risk

Cytokines levels at UHR individuals were lower than controls.

Cytokines	UHR (n=40)	Control (n=40)	p value
IL-1β	0.21 ± 0.28	1.25 ± 1.50	0.506
IL-10	0.54 ± 0.31	0.65 ± 0.89	0.594
IL-6	0.31 ± 0.26	0.36 ± 0.49	0.641
GM-CSF	0.39 ± 0.23	1.29 ± 2.34	0.391
IL-5	-	-	-
IFN-γ	0.05 ± 0.02	0.06 ± 0.05	0.442
TNF-α	0.52 ± 0.56	1.53 ± 3.63	0.423
IL-2	3.08 ± 1.55	4.22 ± 3.59	0.493
IL-4	4.20 ± 0.97	5.21 ± 3.64	0.199
IL-8	0.79 ± 0.36	1.17 ± 0.88	0.261

Figure 3- UHR – Ultra High Risk, IL – Interleukin, GM-CSF Granulocyte-macrophage colony-stimulating factor, IFN – Interferon, TNF- Tumor necrosis factor. Variables presented in mean±SD; Cytokines levels in pg/ml.

Conclusion

This finding while preliminary, suggests that inflammatory levels of PGE₂ are increased in UHR individuals.

The remaining inflammatory markers are not significantly different between UHR and controls, although they point into the contrary direction of the literature that suggests increased inflammatory markers in schizophrenia ⁽³⁾. We are presently investigating in this sample whether the inflammatory markers at baseline may predict the conversion to psychosis at follow up.

References

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