The effect of stress and antipsychotic treatment on inflammatory and metabolic markers in first episode psychosis

Valeria Mondelli, Monica Aas, Alessandro D’Albenzio, Marta Di Forti, Marco Di Nicola, Helen Fisher, Rowena Handley, Nilay Hepgul, Tiago Reis Marques, Craig Morgan, Serena Navari, Heather Taylor, Kathy J Atchison, Paola Dazzan, Robin M Murray, Carmine M Pariante

Division of Psychological Medicine, King’s College London, Institute of Psychiatry, London, UK
Email: Valeria.Mondelli@iop.kcl.ac.uk

ABSTRACT

Background: The high incidence of physical illness in psychosis has been mainly attributed to antipsychotic treatment. However, recent studies have suggested that stress may induce a chronic inflammatory process which may also predispose to the development of metabolic and cardiovascular problems. The aim of this study was to investigate the association between stress, inflammatory and metabolic markers in first-episode psychosis patients and controls.

Methods: We collected information about childhood trauma, recent stressful events and perceived stress in 30 first-episode psychosis patients and 30 healthy controls. In the same subjects we measured metabolic and inflammatory variables. We investigated differences in these variables between patients and controls, and tested the possible association between stress and inflammatory and metabolic measures in patients.

Results: Patients had higher levels of stress and childhood trauma compared with controls (p<0.05). Patients showed higher leptin (p=0.008) and IL-6 (p=0.006) while they did not differ significantly in other inflammatory or metabolic parameters. Patients with less than 2 weeks of antipsychotic treatment also presented higher IL-6 levels when compared with controls (p=0.006). The number of stressful life events was significantly positively correlated with triglycerides (p=0.04) and negatively with HDL (p=0.04) and leptin levels (p=0.04) among patients. Patients reporting childhood trauma had greater weight (p=0.03) and waist circumference (p=0.07).

Conclusions: An activation of the inflammatory system is already present in early course of psychosis and precedes clinically relevant changes in metabolic status. Stressful events only partially influence metabolic parameters in first episode psychosis, and this effect does not seem to be mediated by the inflammatory markers explored in this study.

BACKGROUND

Patients with psychosis suffer from higher incidence of metabolic syndrome and physical illnesses compared with the general population (Spelman et al., 2007). Indeed, treatment with antipsychotics has been reported to be associated with weight gain and development of metabolic abnormalities (Allison et al., 1999).

Recently it has been suggested that repeated episode of acute or chronic psychological stress can induce a chronic inflammatory process which may predispose to development of metabolic abnormalities and cardiovascular problems (Black 2003).

High rate of childhood trauma, high levels of stress and number of stressful events have been described to precede onset and relapse of psychosis (Reid et al., 2005; Walker et al. 2009).

The aim of the present study was to investigate the association between stress, inflammatory and metabolic markers in first-episode psychosis patients and controls.

METHODS

We recruited 30 first-episode psychosis patients (mean±SEM age: 27.7±1.0 years; gender: 66.7% males) and 30 healthy controls (age: 26.3±0.7 years; gender: 70% males) as part of the “Genetics And Psychosis” study carried out in South-East London.

We collected information about childhood trauma, recent stressful events and perceived stress, using the Childhood Experience of Care and Abuse questionnaire, the Brief Life Events questionnaire and the Perceived Stress Scale. We measured weight, BMI, waist circumference, and collected blood samples to measure leptin, IL-6, TNF-α, hsCRP, HDL, LDL, triglycerides levels.

To investigate differences between patients and controls, taking into account the possible effect of antipsychotic treatment, a one-way ANOVA was conducted among controls, patients with less or more than 2 weeks of antipsychotic treatment, a one-way ANOVA was conducted among controls, patients with less or more than 2 weeks of antipsychotic treatment.

RESULTS

Patients did not differ from controls for metabolic parameters.

Patients showed higher leptin, IL-6 and trend for higher hsCRP levels than controls, while they did not differ significantly for TNF-α levels.

Patients had higher number of recent stressful events (2.3±0.3) and perceived stress (20.4±1.9) than controls (respectively 1.2±0.3, p=0.008 and 12.5±1.2, p=0.001). Patients also had a trend for higher rate of childhood trauma compared with controls (66.7% vs 35.7%, p=0.05).

In first-episode psychosis patients the number of stressful life events was significantly positively correlated with triglycerides and negatively with HDL. Patients reporting childhood trauma had greater weight and a trend for larger waist circumference. No further significant associations were found between stress and metabolic measures.

In first-episode psychosis patients the number of stressful life events was significantly negatively correlated with leptin levels; the perceived stress scale was negatively correlated with IL-6 levels. We did not find any other significant association between stress and inflammatory measures.

CORRELATION ANALYSES IN FIRST-EPIODOPSYCHOSIS PATIENTS:

<table>
<thead>
<tr>
<th>Correlation analyses in first-episode psychosis patients:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N. of stressful events</td>
<td>Perceived stress</td>
<td>Childhood Trauma</td>
</tr>
<tr>
<td>Weight</td>
<td>n=0.33, p=0.1</td>
<td>n=0.05, p=0.8</td>
</tr>
<tr>
<td>BMI</td>
<td>n=0.14, p=0.6</td>
<td>n=0.15, p=0.5</td>
</tr>
<tr>
<td>Waist</td>
<td>n=0.26, p=0.3</td>
<td>n=0.08, p=0.8</td>
</tr>
<tr>
<td>HbA1c</td>
<td>n=0.31, p=0.1</td>
<td>n=0.04, p=0.9</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>n=0.46, p=0.04</td>
<td>n=0.30, p=0.2</td>
</tr>
<tr>
<td>Tot. Cholesterol</td>
<td>n=0.01, p=1.0</td>
<td>n=0.16, p=0.5</td>
</tr>
<tr>
<td>HDL</td>
<td>n=0.46, p=0.04</td>
<td>n=0.40, p=0.1</td>
</tr>
<tr>
<td>LDL</td>
<td>n=0.15, p=0.5</td>
<td>n=0.04, p=0.9</td>
</tr>
<tr>
<td>hsCRP</td>
<td>n=0.08, p=0.7</td>
<td>n=0.03, p=0.9</td>
</tr>
<tr>
<td>Leptin</td>
<td>n=0.46, p=0.04</td>
<td>n=0.03, p=0.9</td>
</tr>
<tr>
<td>IL-6</td>
<td>n=0.10, p=0.7</td>
<td>n=0.46, p=0.04</td>
</tr>
<tr>
<td>TNF-α</td>
<td>n=0.29, p=0.2</td>
<td>n=0.20, p=0.4</td>
</tr>
</tbody>
</table>

CONCLUSIONS

In conclusion, we found that an activation of the inflammatory system is already present in early course of psychosis, as supported by higher levels of leptin, hsCRP and IL-6, and that this precedes clinically relevant changes in metabolic status.

Stressful events only partially influence metabolic parameters in first-episode psychosis, and this effect does not seem to be mediated by the inflammatory markers explored in this study.

Future prospective studies are needed to clarify the possible role of high levels of inflammatory markers in the development of metabolic abnormalities after the psychosis onset.

References


Acknowledgments and Disclosure

This research is funded by NARSAD, British Academy, and NIHR Biomedical Research Centre Institute of Psychiatry (Kings’ College London). We have no conflict of interest to declare.