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## ABSTRACT

**Background:** The high incidence of metabolic syndrome in patients with psychosis has been mainly attributed to treatment with antipsychotics. However, it has been recently suggested that repeated acute or chronic psychological stress may also play a role in physical illnesses, inducing a chronic inflammatory process which may predispose to the development of metabolic abnormalities. The aim of this study is to investigate the association between psychosocial stress and inflammatory and metabolic biomarkers in subjects with first-episode psychosis and healthy controls.

**Methods:** Body Mass Index (BMI), weight and waist circumference were assessed in 96 first-episode psychosis patients (mean±SEM age: 27.0±0.6 years; gender: 62.5% males) and 99 healthy controls (age: 26.3±0.6 years; gender 67.7% male). High sensitive C reactive protein (hsCRP), leptin and metabolic parameters were measured in a sub-sample of 37 of the patients (age: 28.5±1.1 years; gender: 65.8% males) and 49 controls (age: 26.3±0.6 years; gender: 73.5% males). In all the subjects we collected information about childhood trauma and recent stressors.

**Results:** First-episode psychosis patients showed significantly higher BMI (24.8±0.5 vs. 23.3±0.4), higher hsCRP levels (0.7±0.2 vs. 0.2±0.1), higher levels of triglycerides (1.5±0.2 vs. 1.1±0.1) and a higher number of childhood trauma (1.2±0.1 vs. 0.6±0.1) when compared with healthy controls. Patients with childhood trauma had both higher BMI (F=3.1, df=2,191, p=0.049) and higher levels of CRP (F=2.5, df=2,70, p=0.089) when compared to patients without any trauma as well as controls. This was specific to childhood sexual abuse. Patients who had experienced childhood sexual abuse had both higher BMI (F=4.4, df=2,189, p=0.013) and higher levels of hsCRP (F=8.3, df=2,69, p=0.001) when compared to patients who had not experienced sexual abuse and when compared to healthy controls. Furthermore, hsCRP levels were found to be associated with BMI (Spearman's rho=0.49, p=0.012). There was no effect of childhood trauma on triglyceride levels.

**Conclusion:** Childhood trauma plays a role in the increased inflammation found in first-episode psychosis. Increased inflammation is associated with worse metabolic profile. Further studies would need to confirm if the association between childhood trauma and higher BMI seen in patients could be partly mediated by increased inflammation.

## BACKGROUND

Patients with psychosis suffer from higher incidence of metabolic syndrome and physical illnesses compared with the general population. Indeed, treatment with antipsychotics has been reported to play a role in weight gain and development of metabolic abnormalities in patients with psychosis. However, recent findings of metabolic abnormalities in drug naïve first-episode psychosis patients suggest that antipsychotic treatment is not the only cause of these abnormalities (Spelman et al., 2007).

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

Indeed, high rates of childhood trauma and increased inflammatory markers have been separately described in patients with first-episode psychosis (Mondelli et al., 2010; Fernandez-Egea et al., 2009).

The aim of this study is to investigate the role of psychosocial stress (childhood trauma and recent stressors) in metabolic and inflammatory abnormalities in first-episode psychosis patients.

## METHODS

We recruited 96 first-episode psychosis patients (mean±SEM age: 27.0±0.6 years; gender: 62.5% males) and 99 healthy controls (age: 26.3±0.6 years; gender: 67.7% males) as part of the "Genetics And Psychosis" study carried out in South-East London.

Inflammatory markers were measured in a smaller sample of 37 first-episode psychosis patients (mean±SEM age: 28.5±1.1 years; gender: 64.9% males) and 49 healthy controls (mean±SEM age: 26.3±0.6 years; gender: 73.5% males).

We collected information about childhood trauma using the Childhood Experience of Care and Abuse questionnaire. This included loss of parents, separation from parents for more than 6 months, severe physical abuse and severe sexual abuse. This variable was dichotomised to divide for patients without any trauma and patients with at least one type of trauma.

We assessed; weight, BMI, waist circumference, and collected blood samples for measuring; HbA1c, total cholesterol, HDL, LDL and triglycerides, as metabolic parameters. We measured serum levels of leptin and high sensitive C reactive protein (hsCRP) as inflammatory markers.

An independent t-test was used to analyze differences in metabolic and inflammatory parameters between patients and controls. To investigate the possible effect of childhood trauma, a one-way ANOVA, followed by post-hoc analyses, was conducted among three groups: controls, patients with trauma and patients without trauma. Correlation analyses were conducted to investigate the association between inflammatory and metabolic measures. All results are expressed as mean±SEM.

## References

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## RESULTS

First-episode psychosis patients showed higher BMI compared with healthy controls (24.8±0.5 vs 23.3±0.4, p=0.014).

Consistent with previous data on similar samples (Mondelli et al., 2010) patients also show a higher number of childhood traumatic events, a higher number of recent stressful life events and a higher perceived stress scale score.

When testing the effects of childhood traumatic events, there was a significant difference between the three groups (F=3.1, df=2,191, p=0.049). Post hoc tests revealed that BMI was higher for patients who had experienced childhood abuse when compared to controls (Figure 1).

The association between childhood trauma and BMI was specific for severe sexual abuse where again there was a significant difference between the three groups (F=4.4, df=2,189, p=0.013).

Post hoc tests revealed that patients who had experienced severe sexual abuse had higher BMI when compared both to healthy controls and when compared to patients who had not experienced any severe sexual abuse (Figure 2)

Figure 1. Childhood Trauma and Body Mass Index

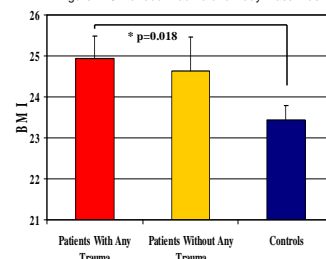
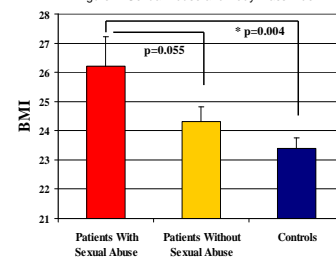


Figure 2. Sexual Abuse and Body Mass Index



Levels of hsCRP were significantly higher in patients when compared to controls. Furthermore, correlation analysis revealed that levels of hsCRP were associated with BMI (Spearman's rho=0.49, p=0.012) and also with weight (Spearman's rho=0.47, p=0.012) in the patient group, but not in healthy controls.

When testing the effects of childhood traumatic events on hsCRP, there was a trend for a difference between patients with trauma, patients without trauma and controls (F=2.5, df=2,70, p=0.089). Post hoc tests revealed that hsCRP was higher for patients who had experienced childhood trauma when compared to controls (Figure 3).

Similarly to the results seen for BMI, the association between childhood trauma and hsCRP was specific for severe sexual abuse. There was a significant difference in hsCRP between the three groups (F=8.3, df=2,69, p=0.001).

Post hoc tests revealed that patients who had experienced severe sexual abuse had higher levels of hsCRP when compared to patients who had not experienced any severe sexual abuse (Figure 4).

Figure 3. Childhood Trauma and C Reactive Protein

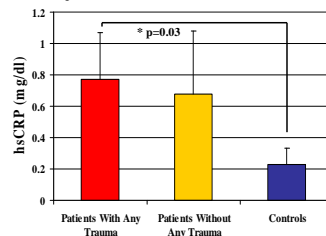
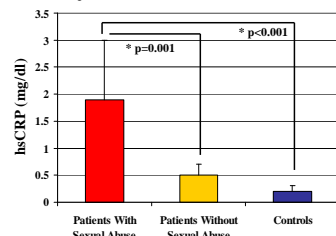


Figure 4. Sexual Abuse and C Reactive Protein



Levels of triglycerides were also significantly higher in patients compared to controls, however, there was no effect of childhood trauma on triglyceride levels.

## CONCLUSIONS

In conclusion, our study shows a role of childhood trauma in the increased prevalence of metabolic and inflammatory abnormalities observed at the onset of psychosis.

This suggests we might be able to identify and target more vulnerable individuals among patients with psychosis to prevent and treat poor physical health.

Future longitudinal studies would need to clarify if the increase in inflammatory markers may, at least in part, mediate the link between early life stress and subsequent metabolic abnormalities in patients with psychosis.

## Acknowledgments and Disclosure

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