Letter to the editor: Lipid profile disturbances in antipsychotic-naive patients with first-episode non-affective psychosis

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Abstract

The study by Błażej Misiak and colleagues (Misiak et al., 2017) provides evidence that antipsychotic-naïve patients with first-episode non-affective psychosis may present with subclinical dyslipidaemia. These findings are replicated in the literature. However, there may be some significant limitations related to the included studies that warrant caution in interpreting the findings. This letter aims to discuss the potential limiting factors and present ideas for future research in field of increasing interest, that is the metabolic abnormalities present in first-episode psychosis.

Keywords

First-episode psychosis; schizophrenia; dyslipidaemia; metabolic syndrome

Letter to the Editor

The study by Błażej Misiak and colleagues (Misiak et al., 2017) provides evidence that antipsychotic-naïve patients with first-episode non-affective psychosis may present with subclinical dyslipidaemia, namely a significantly lower total cholesterol, LDL cholesterol, HDL cholesterol, and higher triglycerides, compared with healthy controls. The authors completed sensitivity analyses to view the effect of confounders they named as age, sex, BMI and smoking status.

The findings however are interesting and partly mirror our own meta-analysis (Perry et al., 2016), when we found significantly decreased HDL and total cholesterol in patients with first-episode psychosis compared with healthy matched controls. The sensitivity analysis in the study by Misiak and colleagues (Misiak et al., 2017) rendered LDL cholesterol non-significant, which also mirrors our findings.

Our work primarily aimed to view the association between first-episode psychosis and subclinical dysglycaemia, as we hypothesized that intrinsic disease links, possibly with an inflammatory basis, may

link the two clinical phenotypes. Interestingly, there is evidence in the literature that abnormal inflammatory markers are also associated with dyslipidaemia in studies of patients with first-episode psychosis (Russell et al., 2015, Miller et al., 2013), suggesting our hypothesis may be significant not only for dysglycaemia in first-episode psychosis, but dyslipidaemia also.

However, a significant limitation of the analysis has not been considered in the Misiak study. Whilst it is possible for dyslipidaemia to exist in subjects without obesity, it is not the norm. Dyslipidaemia far more commonly co-exists with its visible effects on the body, such as with increased BMI, waist: hip ratio, and waist circumference. A significant majority of included studies in the meta-analysis selected cases and controls matched for factors such as BMI (13/19 included studies), waist circumference (6/19 studies), and waist: hip ratio (3/19 included studies). None of the included studies provided evidence on how many potential participants were screened from inclusion, though considering the general trend toward a more Western life-style and its associated ballooning effects on the body, one might expect this number to be considerable. The authors in the Misiak study refer to these factors as potential confounders; however it is more likely that they are effect mediators, and therefore should not be subject to restriction, due to the risk of overadjustment bias (Schisterman et al., 2009).

There is therefore the distinct possibility that the true effect for dyslipidaemia may not have been adequately calculated in a significant number of the included studies due to over-restriction and/or overadjustment bias, meaning the results put forward in the Misiak study should be accepted with caution.

That is not to discount the findings in the Misiak study completely. Their comprehensive analysis, featuring 1803 participants across 19 included studies, finds several significant results in spite of the risk of overadjustment bias or over-restriction, which are replicated elsewhere in the literature (Perry et al., 2016). Evidence is now building of significant metabolic abnormalities at early stages of psychotic illness, and an increased understanding of these may lead to improved screening techniques, monitoring, and even management. Future research into dyslipidaemia in first-episode psychosis should seek to consider the difference between confounders and effect mediators, as this may help to unearth the true extent of the abnormality.

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