Metabolic disturbances in mental illness

SUMMARY

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People with SMI die earlier than the general population, mostly related to the premature cardiovascular disease (CVD). Contributors of the increased CVD rate in SMI is usually related to antipsychotic medication side effects, innate metabolic factors and lifestyle factors. The general aim of this thesis is to examine the factors that lead to the increased obesity rates and cardio-metabolic risk in people with SMI.

Chapter 2 sought to explore the differences of glucose metabolism outcomes between first episode psychosis and mood disorders through a systematic review and meta-analysis. In total 31 eligible studies were identified in this meta-analysis. Compared to the healthy control outcomes, insulin and insulin resistance levels were found higher in patients with first episode psychosis. Additionally, glucose tolerance test levels were found to be higher in patients with first episode psychosis and mood disorders. No significant difference was found in glucose metabolism outcomes between SMI groups. Findings presented in **Chapter 2** suggest both patients with first episode psychosis and mood disorders are high risk groups for diabetes development and a subsequent increase in the risk of diabetes-related complications such as cardiovascular diseases and cognitive deterioration later in life.

In **Chapter 3**, individual effects of antipsychotic medications on body weight was examined in patients with first episode psychosis through a meta-analysis. This meta-analysis revealed that almost all antipsychotic medications were associated with body weight gain. Average body weight gain with antipsychotic medications was 3.2 kg in the short-term (<12 weeks) and 5.3 kg in the long-term (>12 weeks). Specifically, olanzapine and clozapine caused the greatest weight gain compared to placebo. Clinically significant weight gain risk was increased about two-fold with antipsychotic use. Weight gain was also associated with the duration of antipsychotic mediation use. These findings demonstrate the early and continuing effects of various antipsychotic medications on body weight gain.

Chapter 4 provided outcomes from alpha-lipoic acid meta-analysis. Results of this meta-analysis revealed a significant reduction of body weight (-1.2 kg) and body mass index (-0.4) with alpha-lipoic acid compared to placebo treatment. Meta-regression analyses showed that shorter duration of alpha-lipoic acid treatment achieved greater body mass reduction than longer duration treatments. Incidences of side effects and all-cause discontinuation were similar between alpha-lipoic acid and placebo.

Chapter 5 examined the risk of gestational diabetes associated with antipsychotic exposure during pregnancy. Compared to healthy controls, both unadjusted (risk ratio=1.63) and adjusted cumulative risk ratio (1.30) for GDM were found to be significantly higher in antipsychotic-exposed pregnant women. The adjusted RR for GDM was similar between the antipsychotic-exposed group and the antipsychotic-ceased group. No significant association was found between study quality, smoking, alcohol use, gestational age and cumulative GDM risk. Findings in **Chapter 5** suggest that antipsychotic exposure may lead to the development of gestational diabetes in pregnancy.

Chapter 6 focused on a disordered eating pattern, the Night Eating Syndrome, in patients with major depression. In this cross-sectional study, the prevalence of Night Eating Syndrome in depressed patients was 21.3%. Additionally, findings in this chapter showed that patients with Night Eating Syndrome had higher body mass index levels, depression, anxiety levels and poorer sleep qualities compared to those without Night Eating Syndrome. These findings indicate a complex relation between Night Eating Syndrome and depression.

Chapter 7 tested the effectiveness of add-on curcumin treatment on cognitive functioning and inflammatory markers in patients with schizophrenia. In this randomized, double-blind, placebo-controlled study, we found that add-on curcumin improved working memory in patients

with schizophrenia. Add-on curcumin also reduced IL-6 levels after 8-weeks of treatment. These findings suggest that anti-oxidant and anti-inflammatory properties of curcumin may have beneficial effects on cognitive functioning and decrease inflammatory response in patients with schizophrenia.

In general, findings represented in this thesis underline the importance of early identification of major risk factors for CVDs, and also initiating early strategies to prevent cardiovascular related morbidity and mortality, in people with SMI.

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