

PEER-REVIEW REPORT

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Title: Metabolic Disturbances Associated with Antipsychotic Drug Treatment in Patients with Schizophrenia: State-of-the-Art and Future Perspectives

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Scientific quality	[<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish
Language quality	[<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection
Conclusion	[<input checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Re-review	[<input checked="" type="radio"/>] Yes [<input type="radio"/>] No
Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No

SPECIFIC COMMENTS TO AUTHORS

Excellent paper, few comments. In Abstract, "Emerging evidence indicates the role of genetic polymorphisms associated with antipsychotic-induced AIWG and metabolic disturbances." You have already abbreviated AIWG, so shift antipsychotic-induced before metabolic disturbances. "Although antipsychotic medications are essential for schizophrenia treatment, clinicians should monitor and manage the resulting weight gain and metabolic disturbances" should be "Antipsychotic medications are essential for schizophrenia treatment, hence clinicians should monitor and manage the resulting weight gain and metabolic disturbances". In ANTIPSYCHOTIC DRUGS AND WEIGHT GAIN, "increased risk of overweightness and obesity" should be "increased risk of being overweight and with obesity". Further on, "Low-potency FGAs", specify you refer to their D2 blocking ability. In the next paragraph, "the incidence of weight gain is nonsignificant", change to "the incidence of weight gain is not significant". In MECHANISM UNDERLYING WEIGHT GAIN AND METABOLIC DISTURBANCES DUE TO ANTIPSYCHOTIC DRUGS, Hormones, "Acylated ghrelin (AG) and desacylated ghrelin (DAG)" contains two abbreviations that may be confusing; DAG is commonly associated with diacylglycerol. I suggest that you change to AGh and DAGh and their ratio to AGh/DAGh. In this section, there is no mention of cholecystokinin (CCK); there is evidence of its implication in metabolic syndrome (Zwirska-Korczala K, Konturek SJ, Sodowski M, Wylezol M, Kuka D, Sowa P, Adamczyk-Sowa M, Kukla M, Berdowska A, Rehfeld JF, Bielanski W, Brzozowski T. Basal and postprandial plasma levels of PYY, ghrelin, cholecystokinin, gastrin and insulin in women with moderate and morbid obesity and metabolic syndrome. J Physiol Pharmacol. 2007;58 Suppl 1:13-35; Mesgari-Abbasi M, Abbasalizad Farhangi M. Serum concentrations of cholecystokinin, peptide YY, ghrelin and high sensitive C-reactive protein in association with metabolic



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syndrome ingredients in obese individuals. *Acta Endocrinol* (Buchar). 2020;16(1):37-42. doi: 10.4183/aeb.2020.37). Sane section, Neurotransmitters, "The support for α 1- and α 2- adrenergic receptors' involvement in the AIWG etiology" change to "The support for α 1- and α 2- adrenergic receptor involvement in the etiology of AIWG". In Potential predictors, you conclude "Lan et al applied artificial intelligence to develop a neurofuzzy model with a 93% prediction rate for weight changes among patients with schizophrenia treated with antipsychotics; variables included physical factors (baseline weight, height, and waist and hip circumferences), lifestyle factors (smoking, dietary patterns, and exercise levels), genetic factors (ADRA1A, ADRB3, ADRA2A, HTR2A, and HTR2C), and psychopathology severity[84]." You should discuss what were their conclusions. At the end of INTERVENTIONS, add that all interventions should be adequately monitored, as individual patients may respond unpredictably to any of these pharmacological and natural agents. REFERENCES. Add 11 to Misiak et al.