PEER-REVIEW REPORT

Name of journal: *World Journal of Psychiatry*

Manuscript NO: 74162

Title: Disrupted leptin-fatty acid biosynthesis is an early manifestation of metabolic abnormalities in schizophrenia

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03262105

Position: Peer Reviewer

Academic degree: FRACP, MD

Professional title: Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: United States

Manuscript submission date: 2021-12-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-03 10:28

Reviewer performed review: 2022-01-03 10:35

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Might be accepted for publication

PEER-REVIEW REPORT

Name of journal: *World Journal of Psychiatry*

Manuscript NO: 74162

Title: Disrupted leptin-fatty acid biosynthesis is an early manifestation of metabolic abnormalities in schizophrenia

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02445242

Position: Editorial Board

Academic degree: MAMS, MBBS, MD

Professional title: Professor

Reviewer's Country/Territory: India

Author's Country/Territory: United States

Manuscript submission date: 2021-12-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-09 15:48

Reviewer performed review: 2022-01-12 07:37

Review time: 2 Days and 15 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I think that the word "correlation" should be replaced by the word "association" in certain parts of the manuscript such as the Abstract-Background,   Introduction & Discussion.   The conclusions of the Abstract   do not seem to be based on the results of the study. This has to be modified.   Person first language should be used throughout the manuscript. Thus, for example, phrases such as " drug-naive first-episode psychosis (FEP) patients, medicated chronic schizophrenia (CSZ) patients, and healthy control (CNT) subjects." (Introduction)   - should be changed to patients/persons with   drug-naive first-episode psychosis and   patients/persons with medicated chronic schizophrenia   Certain aspects of the patient sample are relevant to the results of the study. Patients with FEP were recruited from an inpatient sample. They are thus probably not truly representative of community-based patients with FEP who attend early intervention services. This would explain the rather late onset (22 years) in this sample. Moreover, it has not been clarified whether   all patients with FEP were diagnosed with schizophrenia, because a proportion of them can turn out to have bipolar disorder later. The choice of only patients being treated with clozapine for the chronic group was not clear. Was there any particular reason for this?   More details of the literature search are required in the Methods and particularly in the Results section. Was this a systematic review? Where guidelines followed? How many articles were selected? Was a quality analysis or risk of bias estimation done?   The limitations of the study and of the extant literature (derived from the review) must be mentioned.

PEER-REVIEW REPORT

Name of journal: *World Journal of Psychiatry*

Manuscript NO: 74162

Title: Disrupted leptin-fatty acid biosynthesis is an early manifestation of metabolic abnormalities in schizophrenia

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05794765

Position: Peer Reviewer

Academic degree: DNB, MBBS, MRCP

Professional title: Doctor

Reviewer's Country/Territory: New Zealand

Author's Country/Territory: United States

Manuscript submission date: 2021-12-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-09 19:11

Reviewer performed review: 2022-01-21 00:00

Review time: 11 Days and 4 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Strengths of the study Chosen subjects are appropriate to the study within a case control design. Researchers used validated and most appropriate tools in evaluating psychiatric symptoms (BPRS and PANSS) Internal validity of the study is reasonably good with good methods, assessments and analysis.   Figures are appropriate and clear in its foot notes. References are adequate and up to date. Abstract is good and suggest no changes Literature review is adequate and up to date The researchers followed a guideline in reporting (ARRIVE) which improves quality of the reporting. Researchers have reported ethical approval.   Statistics is sufficiently detailed   Weaknesses and critique of the study 1. It is not clear how the researchers arrived at these numbers for the study. It would have been ideal for the researchers to do a power calculation or it would be ideal to explain in discussion why they did not do a power calculation in this study.   2. I would suggest making inclusion ad exclusion criteria more explicit in the study. 3. Paragraph beginning with "3. Literature search and inclusion criteria" did not show any inclusion criteria. Inclusion and exclusion criteria may be clearly mentioned in the study. Referral to their older study also did not give clear inclusion exclusion criteria (Ref 19 in the paper) 4. It was not clear when this study was done; period referring to original study dates back to early 2000's. It is of interest to know that medicated CSZ patients group were new and the control group were new. If they have done a historical comparison, that may be made clear in methods and in discussion.   It is also interesting to know over what period participants were recruited. 5. It may be appropriate to mention who evaluated patients for schizophrenia and what criteria were used.   6. Readers would like to know the socio demographic features of aptients in two groups

and the controls and this may be included as a table in results.   7. Result section 4 paragraph 2   Conclusion made on CSZ patients that they have a higher plasma leptin levels and no correlation to PANSS. This may require to be evaluated carefully as BMI in these patients were significantly higher compared to control group. This may be a treatment effect and researchers have pointed out this. But it is possible that there number of other confounders for higher BMI and plasma leptin levels which includes food habits, type of food they consume, even though previous studies has shown that clozapine increases weight gain. Unless researchers clarify their BMI prior to initiation of Clozapine in CSZ group this may be prone to errors concluding that they have a higher BMI and plasma leptin levels due to Clozapine.   6. Relevance of section 3 is not clear in this manuscript. Conventionally literature search and 8inclusion criteria for literature search are done in systematic reviews. This study being a case control design, need of such an approach may be reviewed   9. ARRIVE guideline is for reporting animal guideline. It would have been more acceptable if they would have gone through STROBE. I would suggest including a paragraph on strengths and limitations of the study External validity remains limited to low numbers and type of population they chose.   10. In the methods and material section 2.1   N=14 for CNT group was mentioned initially(Line 2).   But in line 22 controls were mentioned as 12 showing a disparity in numbers. 11. Typing error noted in its heading and in manuscript 2.1   a) last line "form" ; 5 Discussion, b)paragraph 2 line 4 "playa"

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Please   see the attached file