

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Psychiatry*

**Manuscript NO:** 66580

**Title:** Resilience to the effects of social stress on vulnerability to developing drug addiction

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05946096

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Lecturer

**Reviewer's Country/Territory:** Turkey

**Author's Country/Territory:** Spain

**Manuscript submission date:** 2021-03-31

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-04-01 00:31

**Reviewer performed review:** 2021-04-05 17:11

**Review time:** 4 Days and 16 Hours

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 Grade E: Do not publish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



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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## **SPECIFIC COMMENTS TO AUTHORS**

All of them seen in tih article.

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**Title:** Resilience to the effects of social stress on vulnerability to developing drug addiction

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05520883

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Brazil

**Author's Country/Territory:** Spain

**Manuscript submission date:** 2021-03-31

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-04-02 01:56

**Reviewer performed review:** 2021-04-09 22:23

**Review time:** 7 Days and 20 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No
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## SPECIFIC COMMENTS TO AUTHORS

Dear, The review presented by authors is very interesting. The authors made the revision about the difference between resilient and susceptible mice exposed to stress animal models. Another point involved is addiction disorder, but it seems to be in the second plan, and not in the first plan as in the title of review. Because of this, some phrases and specific points are confused. I suggest revising the references too, because the authors cite many reviews instead of the original article. I did not find attached the figures cited in the text. I suggest putting some figures to explain the main text parts. The aim should be revised, because the authors describe much more about other points and less about addiction disorder. Abstract . I suggest that authors do not use the words: first, second... 2. The authors speak: "... models of stress-related psychiatric disorders (depression- and anxiety-like behavior, cognitive impairment and addiction-like symptoms)...", but these are behaviors of animals and not models. 3. The authors need to define: 1. chronic social defeat or 2. Repeated social defeat. Look in the keywords. Text 1. The concept of resilience in the field of drug addiction - The authors explain other things in this topic, they could use: 1 and 1.1. - I think that it is important to define PTSD and it is the first time of initials (second paragraph). Remove the words in the third paragraph. - There are lack of references, for example, the author's write "Most research about resilience has....", but they cited only one reference. Please revise similar cases. - The authors must revise the references, for example, Bruce S. McEwen, 2016, did not speak about substance use disorders. Morgan, 2002, speaks about scholar stress and not AUD. - I did not understand the question, resilience and resiliency. Are there the same or different words to authors? Please, the authors need to

explain better. 2. Behavioral traits and protective factors associated with resilience - "Different protective (resilience) factors..." Why is resilience between ( )? - The authors explain many times what resilience is, I think that is unnecessary. 3. Physiological response to stress and resilience - "... and acute stress increases serotonin turnover in the amygdala, hypothalamus, PFC and NAcc [36]". In these cases there are many studies demonstrating the opposite effect, I believe that the authors can cite at least one reference. Furthermore, the reference is wrong. - Duman, 2009, is the review, other authors demonstrated the effects cited. - "Communication between neural, hormonal and immune systems is mediated by cytokines, small molecules that mediate inflammatory processes". This phrase is lacking to speak about other molecules involved or cite the reference that only cytokines mediate the tree systems. - I suggest the authors explain more about gut microbiota or remove "These bidirectional relationships between resilience and immunity are modulated by the gut microbiota [45]." 4. Animal models to study resilience to social stress - The authors need to explain the difference of depression/anxiety in the humans x rodents. I disagree with this following sentence: "As with humans, some animals exposed to chronic stress develop depression-, anxiety-like symptoms"; - The introduction of his part of the review is confusing. What the authors really want shown in the section? This point needs references. - The authors explain the FST in this point, but the FST and other behavioral tests are behavioral tests and not animal models. These behavioral tests are used to evaluate the animal models. "The forced swim test (FST) is a classic model of depression". - The authors say in the introduction of this part "This is not an exhaustive review of these models...", but they use 8 pages to speak about behavioral tests. I suggest revising this part, if it is very necessary. The authors can make the table. - The following sentence is confused: "... and a varied combination of physical stressors (chronic unpredictable stress). Another widely used animal model is the chronic "mild" stress (CMS) paradigm [58], in which

animals are exposed to varying physical and psychosocial stressors". Chronic unpredictable stress and CMS are the same animal model. - Vidal, 2011 in your study comparing Wild-type Groningen rats x Wistar rats; Sprague Sprague Dawley rats are Wild-type Groningen rats? - In the middle of text have: " [143, 144, 14, 145] (Ferrer-Pérez et al., 2018; Burke et al, 2011; Aguilar et al., 2013; Montagud-Romero et al., 2016)." Please, the authors must revise the text. - Please, revise the citation 148. - The point 4 must be better organized. 5. Advances concerning the neurobiological substrates of resilience - I did not understand why the authors cited the references 5 and 29 to "The study of the neurobiology of resilience is a relatively young area of scientific investigation". - Please, the authors could explain exNMDA receptors in the text. - I tried understanding the aim with this point, but I did not find a connection with addiction disorders. I think that the authors need more focus or change the aim. The revision in turn of resilience is very good, but the text lacks its connection with addiction disorders. - BDNF has antidepressant-like effects and enhances hippocampal neurogenesis [215, 216]. Why was this phrase used in the context? - In rodents exposed to SD, activation of hippocampal BDNF/TRKB signaling (by means of branched-chain amino acids, exercise and high protein diets) induces resilience to social avoidance [221]. The authors cited one reference, there are other references. - Sometimes the authors use the HPA axis and other times HPA system. Please standardize it. - "but not in resilient, mice" .... Revise the commas in all text. - What is LC? Revise the initials in all text. You can have fewer initials. 6. Resilience to the effects of social defeat on the rewarding properties of drugs of abuse - When I put the three words (social defeat; addiction; resilience) in the Pubmed I found 862 papers. Revise it, I can be mistaken.