**Responses to the reviewer’s questions**

Thank you Reviewer E for your constructive criticism. We hope that the following replies satisfy your recommendations.

**Reviewer E question 1:**

At 27 years of age a white male was diagnosed with schizophrenia. Could the authors explain the clinical picture at that time? Were there red flags for a diagnosis of schizophrenia?

**Reply:**Thank you for the question. The following will be added to the initial sentence: “At 27 years of age a white male was diagnosed with schizophrenia after a clinical presentation of loosely structured persecutory delusions and auditory hallucinations”.

**Reviewer E question 2:**

The urine toxicology test was positive for cannabis. What was the result  
of other relevant lab tests?

**Reply:**Thank you for the question. As you know there is a limit for the number of words we can use in this manuscript so we opted for using only the positive or relevant negative findings so we could meet the word criteria. To clarify that there were no other relevant laboratory findings the following will be added to manuscript: “His urine toxicology was positive for cannabinoids, without other relevant laboratory findings”.

**Reviewer E question 3:**

Neurologic examination at admission / in the Psychiatry ward should be  
detailed and a description of seizure semiology would enrich the paper as  
well.

**Reply:**Thank you for the question. We will address more formally the neurological examination in our case description with the following amendment: “Neurologic examination revealed hypophonia and slowness of speech, generalized rigidity with dorsal and cervical dystonia (in sustained flexion) and limb waxy flexibility”.

A characterization of the seizure and observation after the seizure will be included in the text: “generalized tonic-clonic seizure” instead of “seizures” and “post-ictal observation revealed eye and limb myoclonus”.

**Reviewer E question 4:**

An EEG epoch is shown. However, a complete montage is necessary,  
addressing the state of awareness of the patient. Additionally, if a seizure  
was documented it should be shown as well. On another hand, what is the  
meaning of “diffuse slow waves” in this case? Are there other EEG  
characteristics suggestive of anti-NMDAR encephalitis?

**Reply:**The EEG revealed theta-delta slowing recorded in awakeness with progressive improvement until normalization after treatment was started. The electrographic seizure will be displayed in an additional figure (Figure 3 in the new manuscript). In both we will refer the state of awareness.

**Reviewer E question 5:**

Authors state that CSF showed a lympfocytic pleocytosis but later on the  
text they say that cytochemestry was normal. This contradiction should be  
corrected in the text.

**Reply:**Thank you for the question. It wasn’t a mistake. The CSF in different stages of the disease showed different results. In an initial CSF examination (21/4/2015) it showed 22.5 leucocytes/uL with a majority of lymphocytes and a few days later, 24/4/2015, it showed a normal cytochemistry with 3.0 leucocytes/uL. Flutuations of the cytochemistry have been described in anti-NMDAR encephalitis.

**Reviewer E question 6:**

Authors state that brain MRI showed a fronto-parietal lesion compatible  
with head trauma. Did the patient have history of trauma? Could it be seen  
in the CT scan at the emergency department? Or can it be in the context of  
encephalitis? I think authors should clarify this aspect.

**Reply:**Thank you for the question. We hypothesize that the lesions are from head trauma in probable relation with an epileptic seizure that happened during hospitalization in our psychiatric ward, as it wasn’t present in the CT scans done at the Emergency Department. In discussion with the neuroradiologist we agreed that given the location of the lesions this was the more plausible hypothesis, but we cannot exclude completely the encephalitis as the cause. We added the following to the manuscript to clarify this aspect: “The brain magnetic resonance imaging (Figure 3) scan showed a right fronto-opercular and anterior temporal lesion compatible with head trauma in probable relation with unattended epileptic seizures during hospitalization in the psychiatric ward”

**Reviewer E question 7:**

A neoplasia occurs in a significant percentage of cases. Was this study  
repeated during follow-up?

**Reply:**This study was not repeated given the excellent treatment response and the negativity of the anti-NMDAR antibodies. He is still under clinical surveillance with complete physical examination every 6 months.

**Reviewer E question 8:**

Again, about follow-up, authors should elaborate more about the  
neuropsychiatric evaluation and neurologic examination.

**Reply:**Thank you for the question. Data regarding neurological, behavior and neuropsychological evolution will be addressed. The following text will be included: “Seven months after discharge, neurological examination revealed bilateral postural tremor with myoclonic jerks and axial and limb rigidity more prominent on the left side; neuropsychological evaluation revealed severe executive and memory deficits an puerile behaviour disturbance; a new brain MRI was performed that showed a partial resolution of the previously described lesions and a new search for anti-NMDAR antibodies in serum and CSF was negative. Three years after discharge, the patient has a normal neurological examination and showed a clear improvement in repeated neuropsychological assessment, revealing only a mild deficit in working memory and learning ability”.

**Reviewer E question 9:**

In the discussion, authors should elaborate more about neuropsychiatric  
symptoms presentation and discuss which are the red flags for a diagnosis of  
schizophrenia, as a “take home message”.

**Reply:**Thank you for the recommendation. We hope that the following change to the manuscript elaborates on the presentation of neuropsychiatric symptoms.

“A pattern that may start with a flu-like prodrome, followed by psychiatric symptoms, seizures and later on movement disorders and autonomic instability, along with resistance or intolerance to antipsychotics, should always raise the suspicion of an autoimmune encephalitis. We hope that this case underscores the importance of close surveillance for neuropsychiatric symptoms.”

Instead of “*We hope this case underscores the importance of close surveillance for neuropsychiatric symptoms and to recognize in the differential diagnosis of psychotic disorders with neurological symptoms and resistance or intolerance to antipsychotics.”*

As for the red flags for a diagnosis of schizophrenia, the authors don’t think that this should be the take-home message for the article. Schizophrenia is a well studied clinical entity for which a brief summary of all its complexities would be difficult and would move the focus away from the main purpose of the article. We want to alert clinicians about the diagnostic possibility of an autoimmune encephalitis in psychotic episodes with prominent neuropsychiatric symptoms.