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Letter to Editor

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Letter to Editor

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Dear Editors,
we are writing you regarding an interesting topic that is gaining resonance in the scientific community but is just beginning to be studied in Italy. Autoimmune encephalitis (AE) are inflammatory conditions of the brain often associated with neuronal synaptic antibodies (NSAbs) in the cerebrospinal fluid (CSF). Psychotic spectrum disorders (PSD) manifestations are common in AE, and in some cases represent the main or sole clinical feature, making this a relevant topic for psychiatrists. Indeed, up to 60% of patients with anti-NMDAR (the main ionotropic glutamate channel) encephalitis, the most common form of AE, present with PSD, and about one third are firstly evaluated in the psychiatric setting [1]. Red flags to help psychiatrists to identify AE in patients with PSD have been proposed [2], but never validated in clinical practice. In addition, some PSD patients without AE have NSAbs in serum, but not in CSF, with unclear clinical significance [3]. Since these NSAbs are pathogenic in-vitro, a blood brain barrier (BBB) impairment might allow them to cause chronic brain dysfunction without overt AE [4], but this has never been thoroughly assessed. To the best of our knowledge, the frequency of AE occurrence in PSD patients and the best strategy for their identification has never been investigated in Italy. Notwithstanding the expected low incidence of AE in the psychiatric setting, the identification of these patients is of the utmost importance, as the correct diagnosis might drastically change their management and prognosis.
Our research group has received a grant from the Ministry of Health (GR-2019-12369479) to specifically study this topic in our psychiatric services. Within the PHLAMES study, we aim to study the impact of a systematic diagnostic approach, that includes the evaluation of clinical red flags (Fig. 1) and the measurement of serum NSAbs to improve the diagnosis of AE in patients with acute and chronic PSD assessed in the psychiatric setting. Furthermore, we aim at investigating the meaning of serum NSAbs in patients with PSD

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Conflict of interest
The authors declare that they have no conflict of interest nor that they have received compensation from third parties for the creation of this article.

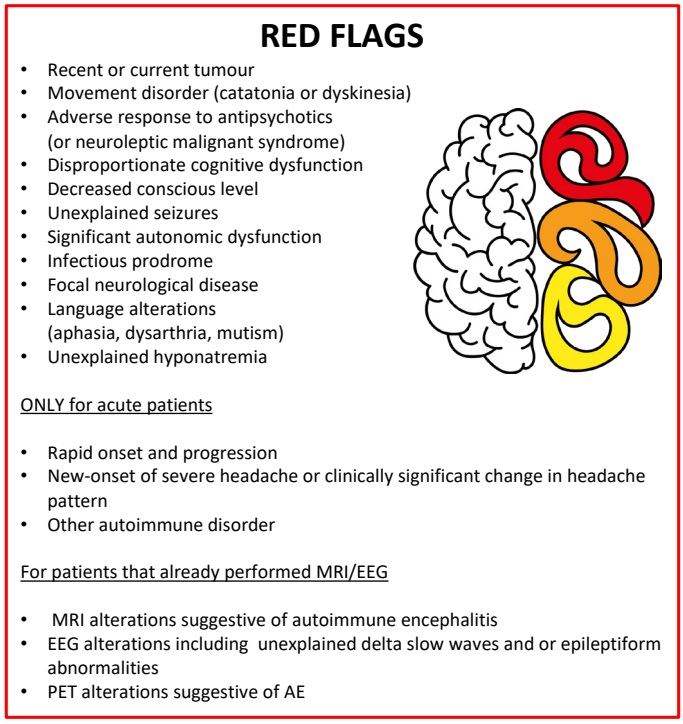

Figure 1.
Clinical red flags investigated in the PHLAMES study, adapted from Pollak, et al. [1].

without overt encephalitis, and to establish whether a BBB alteration might be one of the pathogenic mechanisms involved in PSD development in this subgroup. The first aim will have immediate and relevant clinical implications, providing a strategy to maximize the diagnostic accuracy for AE in the psychiatric setting, improve the outcome of the patients and rationalize costs. The second aim, although experimental, will provide insight into the role of NSAbs in chronic PSD patients that might have "mild forms" of encephalitis, and could pave the road for potentially efficacious immune treatments.

In conclusion, our study, that interweaves neurology and psychiatry, offers a unique opportunity to study the link between synaptic dysfunction and PSD from both a neuroimmunological and psychiatric perspective. We hope that this project will raise awareness of AE in the psychiatric community, as well as favor the collaboration between neurologists and psychiatrists.

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