

Antineuronal antibodies and epilepsy: treat the patient, not the lab

Stephan Rüegg^{1,2}

The study results implicate that starting immunosuppressive treatment in new-onset epilepsy should be guided by clinics, not simply antibody presence

Epilepsy affects about 70–80 million people worldwide; about one-third of patients cannot become seizure free. New diagnostic and therapeutic avenues to improve this situation are welcome. The impact of autoimmune phenomena on pathogenesis of some epilepsies increasingly gained attention as these mechanisms open the door for alternative medical treatments beyond antiseizure medications, that is, immunosuppressants. Thus, ‘autoimmune’ has become one of the six aetiologic categories of the new International League Against Epilepsy classification of seizures and epilepsies. Numerous neuronal surface autoantibodies (NSAbs) identified in the past years cause autoimmune encephalitis (AE),¹ often associated with severe seizures and status epilepticus. Additionally, the prevalence of NSAbs in patients with chronic epilepsies of unknown aetiology yielded a prevalence between 3% and 21%, but the question whether all epilepsy patients with NSAbs or only those with pharmacoresistant epilepsy (PRE) and/or additional signs of AE warrant immunosuppressants remained unresolved yet. A study looking at the presence of NSAbs in PRE found that 62% of patients responded to immunotherapy, and 34% even became seizure free, indicating that a trial may be justified.² But how does this result relate to patients with new-onset focal epilepsy (NFE)? The paper by Mc Ginty *et al*,³ tackles this issue by prospectively looking at those patients with NFE and a test positive for at least one NSAbs. The authors established an NSAbs prediction score based on clinical and paraclinical information and evaluated the value of immunotherapy in patients with NFE. About

10% of their cohort was NSAbs positive and 40% of them were diagnosed with AE. They identified six features which in combination were highly predictive for the presence of NSAbs, that is, age >54 years, ictal piloerection, self-reported lowered mood, MRI changes in the limbic system, the absence of ‘conventional’ epilepsy risk factors and intact attention. This ‘NSAbs-detecting’ Score compared better with the recently published ‘antibody prevalence in epilepsy and encephalopathy’ (APE2) Score⁴ in terms of forecasting AE, but worse in predicting presence of NSAbs.

According to the present study (with an admittedly small sample of patients), immunotherapy could be omitted in those patients with NSAbs-positive new-onset epilepsy without signs or symptoms of AE. Conversely, the study also indicates that immunosuppressants are warranted in patients with even subtle AE. This is in line with another study where patients with AE even without NSAbs benefitted from immunosuppressants.⁵ The authors conclude that the administration of immunotherapy in NSAbs-positive patients should be guided by clinical signs for (subtle or obvious) AE and not only by NSAbs positivity per se.

The study did not rely on cerebrospinal fluid data, probably leading to some missed cases of NSAbs positivity and AE. It is also interesting that 5/16 NSAbs positive, but AE-negative patients had mRS >0 and, thus, likely were pharmacoresistant, although this information was not exactly verifiable without follow-up phone interview. Statistically, this would exactly fit the one-third of patients basically becoming pharmacoresistant in chronic epilepsy of various aetiologies. Thus, future trials should test whether immunotherapy given to these patients would prevent pharmacoresistance despite the fact that outcome without such treatment was mostly promising in this study.

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¹Medical Faculty, University of Basel, Basel, Switzerland
²Neurology, University Hospital Basel, Basel, Switzerland

Correspondence to Dr Stephan Rüegg, Medical Faculty, University of Basel, Basel 4031, Switzerland; S. Rueegg@unibas.ch