

Absence of GluD2 Antibodies in Patients With Opsoclonus-Myoclonus Syndrome

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Study Question

Are antibodies against glutamate $\delta 2$ (GluD2) receptors biomarkers for opsoclonus-myoclonus syndrome (OMS)?

What Is Known and What This Paper Adds

A recently published study showed that 14 (87%) of 16 children with OMS and 2 of 4 patients with neuroblastoma without OMS had GluD2 antibodies. Based on these findings the authors suggested that GluD2 antibodies were useful as diagnostic biomarkers of OMS. Here, using comprehensive antibody studies in a larger number of patients, we show that GluD2 antibodies cannot be used as biomarkers of OMS.

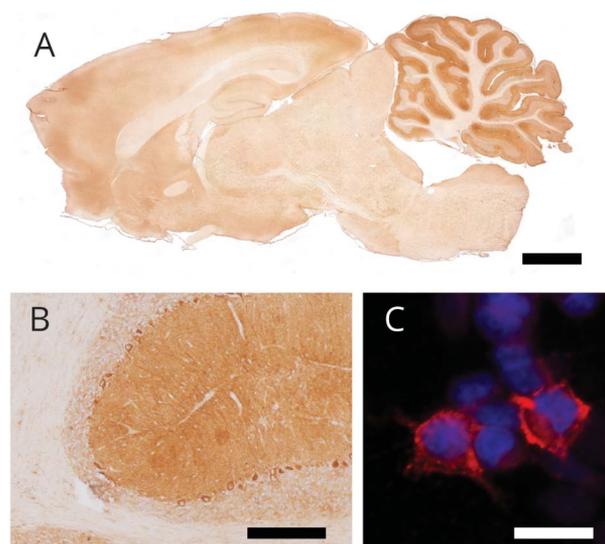
Methods

For this cross-sectional study, the investigators analyzed sera from 45 children with OMS, including 10 with neuroblastoma; 158 adults with OMS, including 53 with tumors; 172 OMS-free controls, including 134 patients with various types of encephalitis; 18 patients with neuroblastoma without OMS, and 20 healthy controls. The sera from the patients with OMS came from among those sent to research laboratories in Barcelona and Philadelphia between 1992 and 2018. To detect antibodies, the investigators used rat brain immunohistochemistry, a live cell-based assay (CBA) involving a standard secondary antibody, and a similar CBA involving secondary and tertiary antibodies. The investigators used 2 plasmids for the CBA studies, 3 commercially available GluD2 antibodies, and 2 human sera with GluD2 antibodies as positive controls. The primary outcome was the number of sera exhibiting immunoreactivity patterns consistent with the presence of GluD2 antibodies.

Results and Study Limitations

The commercially available GluD2 antibodies and 2 positive control sera exhibited reactivity with rat brain samples and produced positive results in CBA tests. None of the 203 sera from patients with OMS or the 172 OMS-free control

Figure Tissue Immunostaining and CBA Binding Patterns of a Commercially Available GluD2 Antibody



(A) Reactivity with a sagittal rat brain section. (B) Reactivity with the cerebellar molecular layer and Purkinje cells. (C) Reactivity (in red) in a 3-step CBA test.

sera exhibited immunoreactivity consistent with the presence of GluD2 antibodies.

Study Funding and Competing Interests

This study was funded by various foundations and the EU, Spanish, and Catalan governments. Some authors report holding patents for antibody tests, receiving royalties for the use of those tests, and serving on the editorial boards of *MedLink*, *Neurology*, and *Neurology*® *Neuroimmunology & Neuroinflammation*. Go to [Neurology.org/N](https://www.neurology.org/N) for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

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