

## Rasmussen's encephalitis: Autoantibodies and cytotoxic T cells

Takahashi et al. found autoantibodies against the NMDA-type GluR epsilon2 in patients with chronic epilepsy partialis continua, including patients with proven or clinically suspected Rasmussen's encephalitis, with an acute encephalitis or encephalopathy, and with nonprogressive epilepsy partialis continua. Antibodies were predominantly against cytoplasmic (C-terminal) epitopes but antibody profiles did not show consistent changes during the course of disease. The data suggest that cytotoxic T-cell-mediated neuronal damage occurs in these conditions.

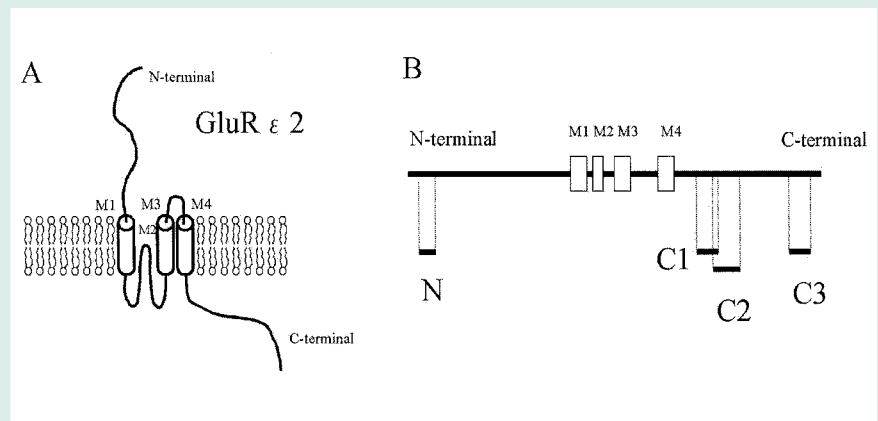
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## Intractable seizures: T cells vs antibodies

Commentary by Robert A. Gross, MD, PhD

Researchers seeking the basis for Rasmussen's encephalitis (RE) were galvanized by a report<sup>1</sup> of excitatory antibodies to the glutamate receptor GluR3, and the successful treatment of a patient with plasma exchange. Was excessive excitation the cause of the debilitating seizures and would immunotherapy therefore be effective?<sup>2</sup> The evidence for an autoimmune basis of RE is sound—involving both B- and T-cell-mediated processes—but was tempered by reports that some patients were seronegative for GluR3 antibodies.<sup>3,4</sup> The root cause, the identity of the antigens against which antibodies reacted, and whether they were causative of pharmaco-resistant seizures thus remained in some doubt.

In this issue, Takahashi et al. tested the hypothesis that T-cell-mediated immunity plays a role in the pathogenesis of RE and its seizures. To do this, they compared GluR epsilon2 subunit antibodies in serum and CSF in patients with epilepsy partialis continua (EPC) (some with RE), patients with other causes of intractable seizures (West and Lennox-Gastaut syndromes), and



controls. They found that GluR epsilon2 antibodies were present only in patients with EPC, antibodies were directed primarily against cytoplasmic epitopes (suggesting T-cell-mediated immunity), and the number of targeted epitopes increased during progression in some patients. They therefore concur with other investigators that in RE antibodies may exist against numerous antigens, but suggest further that although these antibodies could be the cause of debilitating seizures in RE (but not for other typically pharmaco-resistant seizure syndromes), the antibodies are made after T-cell-mediated damage. As we await the definitive

elucidation of cause and effect, the evidence in this carefully done study both expands and refines our view of the pathogenesis of seizures in RE.

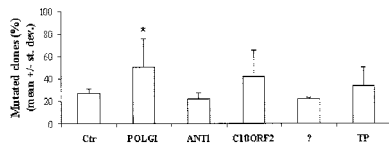
### References

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## mtDNA replicative infidelity due to *POLG1* mutations



Percentage of mutated D-loop region clones as detected in healthy controls, PEO, and MNGIE patients classified according to their nuclear gene mutations.

Del Bo et al. analyzed mitochondrial DNA (mtDNA) from muscle tissue of patients with mtDNA multiple deletions syndromes. The accumulation of a high level of mtDNA point mutations in subjects carrying specific *POLG1* gene mutations points to a relevant pathogenetic mechanism in this PEO subgroup.

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In the accompanying editorial, Patrick Chinnery reviews recent developments in the understanding of nuclear genetic disorders that cause secondary mtDNA damage. There is emerging evidence that subtle differences at the molecular level have important pathophysiologic consequences, possibly explaining the clinical variation between different disorders of mtDNA maintenance and opening new avenues for treatment.

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## DBS improves essential tremor

Vaillancourt et al. demonstrate that deep brain stimulation (DBS) of the ventral intermediate nucleus of the thalamus increased tremor frequency while reducing the amplitude, regularity, and tremor-EMG coherence.

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## Analgesic effects of botulinum toxin A

Voller et al. found no direct analgesic effect of botulinum toxin A on the skin of 16 subjects using three different pain models. Their work implies that botulinum toxin A reduces pain mainly by its effects on muscle tone.

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## Adjusting anticoagulation for endoscopy: The stroke risk

Anticoagulated patients undergoing invasive procedures often pose a management dilemma. Blacker et al. studied 987 patients with atrial fibrillation (with and

without valvular lesions) undergoing 1,137 procedures to determine the stroke risk when anticoagulation was adjusted for endoscopies. They identified factors associated with a high risk, including age >80 years, hypertension, and hyperlipidemia.

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## Rehabilitation therapy and corticospinal excitability

In a group of patients with chronic poststroke agraphia, aphasia, and right hemiparesis, Papathanasiou et al. found increased recruitment of corticospinal pathways following a session of prosthesis-aided rehabilitation therapy of writing. Their results suggest that, even in chronic, poorly recovered poststroke patients, rehabilitation therapy aimed at increased use of the paretic hand may induce reorganization of corticospinal pathways.

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## Induction of plastic change in motor cortex after stroke

Uy et al. employed paired TMS and nerve stimulation to induce motor cortical plasticity in patients with stroke with chronic hemiplegia. Some improvement in neurophysiologic and function measures were seen, but the results were inconsistent.

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The editorial by Felix M. Mottaghy accompanying these two articles reviews the possible mechanism for these intriguing effects of rehabilitation but concludes that this promising technique and its sophisticated rehabilitation concepts need to be tested in a larger number of patients with suitable controls, stratifying patients based on lesion site and degree of disability.

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## Orthostatic headaches caused by postural tachycardia syndrome

Mokri and Low report four patients with postural tachycardia syndrome who presented with orthostatic headaches. Not all cases of orthostatic headaches result from intracranial hypotension or CSF leaks. Occasionally orthostatic headaches may be the dominant clinical manifestations of postural tachycardia syndrome.

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## ■ HD-like 2 and chorea-acanthocytosis

Walker et al. report that affected members of a family originally reported as autosomal dominant chorea-acanthocytosis were found to carry the trinucleotide repeat expansion associated with Huntington disease-like 2.

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## ■ L-Dopa can induce daytime sleepiness in PD

Garcia-Borreguero et al. describe a double-blind, placebo-controlled study of a 74-year-old patient complaining of drug-induced daytime sleepiness. Administration of L-dopa increased daytime sleepiness documented by multiple sleep latency tests. Thus daytime sleepiness is not restricted to dopamine agonists.

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