

## LOCALIZATION OF GENERALIZED SPIKE AND WAVE DISCHARGE AND VALPROATE RESPONSE

Investigators at Universities of Cincinnati, OH, and Birmingham, Alabama; and Montreal Neurological Institute, Canada, studied the EEG and functional magnetic resonance imaging (fMRI) in 89 patients with idiopathic generalized epilepsy (IGE), (25 with generalized spike and wave discharges (GSWD) identified in EEG), and compared patients with valproate (VPA)-refractory and VPA-responsive IGE. The fMRI blood oxygen-level dependent (BOLD) correlates of GSWD in the entire group of patients involved midline thalamus, frontal regions and temporal lobes. A comparison of VPA-responsive and VPA-resistant patients showed BOLD signal increases in the VPA-resistant patients in medial frontal cortex, along the paracingulate gyrus and anterior insula bilaterally. VPA-resistant and VPA-responsive patients have different GSWD generators that may explain the reason for different responses and resistance to VPA in some cases. (Szaflarski JP, Kay B, Gotman J, Privitera MD, Holland SK. The relationship between the localization of the generalized spike and wave discharge generators and the response to valproate. **Epilepsia** 2013 Mar;54(3):471-80). (Response: Jerry P Szaflarski, Department of Neurology, UAB Epilepsy Center University of Alabama at Birmingham, AL 35294. E-mail: [szaflaj@uab.edu](mailto:szaflaj@uab.edu)).

COMMENT. The combining of EEG and fMRI is a noninvasive method of investigation of brain regions involved at the time of epileptic discharges (Gotman J, Pittau F. **Epilepsia** 2011 Jul;52 Suppl 4:38-42). Neuronal discharges during an interictal spike or spike-wave burst result in increased metabolism and blood flow, reflected in the blood oxygen-level dependent (BOLD) signal measured by fMRI. EEG-fMRI helps localize epileptic foci in nonlesional frontal lobe epilepsy; it also demonstrates thalamic involvement in generalized epileptic discharges.

## UPDATED ILAE REVIEW OF ANTIEPILEPTIC DRUG EFFICACY

The International League Against Epilepsy (ILAE) Subcommission on AED Guidelines reviewed the literature from July 2005 to March 2012 and combined results with previous analysis (2006) to provide a comprehensive update of level of AED efficacy as initial monotherapy with newly diagnosed or untreated epilepsy. Class of study (I, II, and III) and level of efficacy (A, B, C, and D) are recorded. The combined analysis (1940-2012) includes a total of 64 randomized controlled trials (RCTs) [7 with class I evidence, 2 with class II], and 11 meta-analyses.

*In children with partial-onset seizures*, 2 RCTs were class III because of an open-label design, too short treatment duration, and a forced exit criteria, and 4 new meta-analyses included OXC versus PHT, LTG versus CBZ, and CBZ versus OXC. CBZ is most frequently studied (n=12) followed by VPA (n=7) and PHT (n=6). OXC is the only adequate comparator for childhood partial-onset seizures and is established (level A); CBZ, PB, PHT, TPM, VPA, and VGB are possibly (level C); and clobazam (CLB), CZP, LTG, and ZNS are potentially (level D) efficacious/effective as initial monotherapy.

*In children with generalized-onset tonic-clonic seizures*, CBZ, PB, PHT, TPM, and VPA are possibly (level C) and OXC is potentially (level D) efficacious/effective,

but there are no adequate comparators. CBZ and PHT may precipitate or aggravate generalized-onset tonic-clonic seizures (class IV suggestive evidence).

*In children with absence seizures*, 3 AEDs (VPA, ESM, and LTG) had new class I or class II evidence of efficacy; LEV had additional class III evidence of efficacy. ESM and VPA are adequate comparators and are established (level A); LTG is possibly (level C) effective. GBP is established as ineffective (level F); AEDs that may precipitate or aggravate absence seizures (class IV scattered reports) include CBZ, OXC, PB, PHT, TGB, and VGB. LEV failed class III placebo-controlled trial and efficacy is undetermined.

*In children with BECTS*, CBZ and VPA are possibly (level C) and GBP, LEV, OXC, and STM are potentially (level D) effective. For *juvenile myoclonic epilepsy*, TPM and VPA are potentially (level D) effective; CBZ, GBP, OXC, PHT, TGB, and VGB may precipitate or aggravate absence, myoclonic, and sometimes, generalized tonic-clonic seizures. LTG exacerbated seizures in JME (level F) in one report. (Glauser T, Ben-Menachem E, Bourgeois B, et al. Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. **Epilepsia** 2013 Mar;54(3):551-63). (Response: Tracy A Glauser, Comprehensive Epilepsy Center, Division of Neurology, Cincinnati Children's Hospital, OH 45229. E-mail: tracy.glauser@cchmc.org).

COMMENT. The authors stress that their report is a working framework and not a mandatory rulebook. Multicenter studies and trial designs are needed to determine the efficacy of new AEDs compared to the old, but the most appropriate AED for a specific patient is decided by the judgment and expertise of the individual physician. Management of epilepsy remains partly an art as much as a science, especially when polytherapy is involved and overused.

## ENCEPHALOPATHIES

### **POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME**

Investigators at University of Milan, Italy, report a 6-year-old boy who presented with left-sided weakness followed by status epilepticus, left-sided tonic-clonic seizures with secondary generalization, without fever. The seizure was preceded by an acute gastroenteritis in the week prior to admission. His blood pressure was 139/112 mm/Hg (>95<sup>th</sup> percentile). Control of status by iv phenobarbital was accompanied by resolution of hypertension. Neurological examination revealed hypotonia and hyporeflexia of the left side. Blood and CSF examinations were normal, including PCR for Enterovirus. MRI showed bilateral asymmetric low intensities in the white and gray matter of posterior parietal and occipital lobes, affecting the right hemisphere predominantly. EEG showed an encephalopathic pattern in posterior regions with no epileptiform discharges. The patient recovered completely within the following 6 days, and follow-up exams in 3 and 12 months were normal, including neurological, EEG, MRI, and blood pressure, and with no recurrence of seizures. (Mameli C, Dilillo D, Spiri D, Cerini C, Fasan S, Zuccotti GV. Status epilepticus as manifestation of posterior reversible encephalopathy syndrome in a healthy child. **Pediatr Neurol** 2013 May;48(5):418-20). (Response: Dr Mameli,