

What Can We Do About Cognitive Symptoms Caused by AED Use?

Q *What are the mechanisms of cognitive and behavioral change due to AED use in epilepsy patients? Which AEDs are known to cause this effect? Are some drugs more likely to than others?*

A The mechanisms by which cognitive and behavioral changes occur are not known with certainty and there are likely several effects that lead to these changes. First, alterations of cellular functioning may manifest as cognitive symptoms, according to Dr. Sperling. “For example, by modulating sodium channel firing, learning might be impaired if that inhibits long-term potentiation or facilitation of strengthening of synaptic firing.”

Also, alteration of neuronal firing may lead to changes in brain circuit function, he says. Changing input at one or more parts in a complex system may produce alteration in the net output of that system.

One instance of this is that “enhancing inhibition might change firing patterns so that output from a region of cortex is reduced,” Dr. Sperling says.

Symptoms can be drug-specific as well. Dr. Kanner says studies have revealed that carbamazepine, phenytoin (PHT) and valproic acid (VPA) have comparable cognitive adverse events of mild severity. “In contrast, phenobarbital yielded more severe cognitive impairment in a third of the tests in comparison to PHT and VPA,” adds.

“Some drugs depress cerebral metabolism, which might change patterns of neuronal firing and lead to system effects,” Dr. Sperling says. “If metabolism is preferentially altered more in some areas than others, that too might



lead to behavioral change.”

Dr. Sperling contends that since behavior is ultimately a network phenomenon, alteration of the interactions of large pools of neurons is the final common pathway.

Q *Do cognitive changes affect all epilepsy patients taking AEDs? Is there a way to predict which ones will be most severely affected? What are the implications in children regarding academic performance? Would you be more aggressive in attempting to minimize these symptoms in children for those reasons?*

A “Some people claim to have no adverse effects from some drugs [and] some patients occasionally claim that drugs may improve function,” Dr. Sperling says.

It’s possible that detailed neuropsychological testing would show minor alterations in select tests, but drugs don’t invariably cause problems. “There is no way to predict what will happen, so sometimes the drugs that on average are best tolerated are terrible for some people, and vice versa,” Dr. Sperling says.

Since children are constantly under testing conditions, they are most inclined to show adverse effects and must be

monitored most closely, Dr. Sperling adds. A balance must be struck between beneficial effect (seizure suppression) and side effects, and ideally one would find a drug that blocks seizures with no or minimal side effect.

Q *What are the long-term effects of AED use on cognition and behavior? Do these symptoms diminish over time as the patient adapts to AED use? What steps can the patient and/or neurologist take to minimize cognitive and behavioral changes?*

A “Long-term effects are not fully known, since we cannot separate out the effects of epilepsy from those of the drug,” Dr. Sperling says. “Mostly, cessation of drug leads to improvement.”

Both experts agree that patients, physicians and nurses must be aware of potential adverse effects and strive to eliminate them whenever possible.

Dr. Kanner urges all clinicians to consider that all AEDs can cause cognitive adverse effects (CAE) when used at high enough doses and that monotherapy regimens should be considered whenever possible. Also, “when add-on therapy is contemplated, it is important to be aware of the combination of AEDs used, as their pharmacokinetic interaction can result in a significant elevation of AED blood levels. In such cases, dose adjustments must be planned before the occurrence of CAE.”

He also recommends slow titration schedules, saying these should be considered above all in AEDs with sedative properties. “Finally, patients and family members should be instructed on the recognition of CAE,” he adds. **PN**

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