The Catatonia Foundation

Why is lorazepam less effective when treating catatonia in autism?

Dr. Fricchione:
There is another problem with lorazepam that occasionally happens, and that's paradoxical agitation. There, I think, is another interesting thing, and this is an area that needs more research.

As we know, for example, that patients with autism have a delay. It's at least a delay in maturation of the GABA system because when any of us are born, GABA is excitatory when we're infants. And then as the system matures, it winds up being eventually inhibitory. If you are born with autism, however, there are certain systems in your brain that remain excitatory for a long time. And there are theorists who believe that that is a prominent reason why patients have autistic symptomatology is because their GABA system is different. It also is a big reason why, and I think most people accept this, it's a big reason why seizures are so prominent in autistic children. It's because the seizure threshold is dependent on the balance oftentimes in the hippocampus between glutamate and GABA.

When somebody has a healthy system, there's a balance, and this is that excitatory-inhibitory balance I was talking about. In certain patients, their hippocampus, unfortunately, has an imbalance at different times where glutamate goes way up and GABA can't keep up and is down here.

When you give an anticonvulsant, you're actually getting the balance back together. So this would make sense, that lorazepam is a good drug for that because sure it's a GABA-A agonist, and you're giving back the hippocampus the protection it needs against the over excitement. But think about if you've got a hippocampus and you're an autistic patient, and you have GABA excitation, so you have a double hit, you've got an excitatory glutamate and excitatory GABA at least in part of your hippocampus. And I think that that's something that we need to think more of in catatonia, that they may not only be autistic.

Catatonia is so prominent or prevalent in patients with autism, right? You can make a case that seizures — because we know that catatonia can be an ictal phenomenon as well as a postictal phenomenon. So catatonia is often connected up with epilepsy. But it doesn't have to be. It can be part of what I was saying before about the infrastructure for catatonia, the terms of excitatory-inhibitory balance, and these different switch areas in this very complicated cortico-striato-thalamo-cortical loop system that we have.

So, if in certain areas of the brain, GABA is excitatory, we don't even know because we're unsophisticated. We don't know who's at risk. If there are certain areas of their brain where GABA is not inhibitory, but is excitatory or has a lower threshold for switching from inhibitory to excitatory — you see what I mean? So there are a lot of mysteries, there are a lot of frontiers we haven't crossed into.