

When using combination antiepileptic drug therapy, we should preferentially prescribe drugs with different mechanisms of action-pro

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Despite the availability of a range of novel antiepileptic drugs (AEDs) with different mechanisms of action, outcomes for adolescents and adults with the common epilepsies have been unchanged over the past 20 years. Nevertheless, it is possible to make some patients seizure free with suitable combinations of 2 or 3 AEDs. Since we do not understand the pathophysiology of pharmacoresistant epilepsy, it makes sense to target a range of pharmacological mechanisms in the hope of finding the right schedule for each individual patient. The only combination that has proven synergism is sodium valproate with lamotrigine, which are mechanistically dissimilar. We are aware now that fast and slow sodium channel blockers can be regarded as working differently on the sodium channel i.e. is not mechanistically identical. In our outcome audit exploring seizure freedom with combination therap, the top 10 successful duotherapies all contained AEDs with different mechanisms of action, including phenobarbital (a GABAergic drug) and phenytoin (a sodium channel blocker), which was third on the list. The positive conclusion to this debate is particularly self-evident, since the majority of available AEDs possess different mechanisms of action!