When using combination antiepileptic drug therapy, should be preferentially prescribe drugs with different mechanisms of action? Position: Con

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From a mechanistic point of view, it seems possible that antiepileptic drugs with the same mechanism of action, e.g. the sodium-channel-blockers (SCB) lamotrigine and oxcarbazepine, do not have an additive effect in regard to efficacy but synergistically produce more typical adverse effects compared to the combination of a SCB with a non-SCB. One study analyzed the pooled data of some randomized controlled trials on the SCB lacosamide and exactly produced the results mentioned above (Sake et al. 2010 CNS Drugs). However in that study, patients with SCB seemed to have more severe epilepsy with higher current and lifetime numbers of antiepileptic drugs. Thus, a more unfavorable response to additionally administered lacosamide in this patient group is not surprising. Other studies failed to demonstrate any outcome differences when comparing combinations of two SCB to combinations of a SCB with antiepileptic drug acting via a different mechanism of action. Personal experiences have shown that in most patients e.g. lamotrigine can be combined with another SCB without clinically relevant adverse events as long as the doses and serum concentrations are within moderate ranges.