

Evolutionary Treatments: New approaches to known mechanisms

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Since many of the difficulties with available AEDs relate to side effects and pharmacokinetic issues, it makes sense that alteration of the structure of existing compounds might produce new drugs with substantial benefits over old. Indeed, in some cases these new compounds may also offer efficacy advantages, such as increased potency. Of interest, some of the more successful new AEDs are in fact “evolutionary” (alteration of structures of available compounds) rather than revolutionary (new mechanisms). An advantage of this strategy is that evolutionary compounds have a high likelihood of demonstrating an effect in clinical trials, and the spectrum of activity is likely to be similar to the parent compound, which simplifies development. Some recent examples of “evolutionary” compounds already approved for use include oxcarbazepine, levetiracetam, and pregabalin (modeled on carbamazepine, piracetam and gabapentin, respectively). Compounds currently in trials include the levetiracetam analogues brivaracetam and seletracetam, and the “3rd generation” AED eslicarbazepine. In addition, there are a number of analogues of valproate either in preclinical or clinical development, that may provide substantial benefit over the parent drug.