Fluoxetine: Pharmacology, Mechanisms of Action and Potential Side Effects
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Since its introduction nearly 30 years ago, fluoxetine and related SSRIs have been taken by millions, possibly billions of patients worldwide to treat depression and anxiety-related disorders. Their naming as Selective Serotonin Reuptake Inhibitors, implying safety and specificity, was a clever marketing ploy to inspire confidence in this new class of antidepressants. However, evidence has been accumulating that now shows unequivocally that fluoxetine has a heterogeneous pharmacology, which is far from selective for serotonin reuptake.

In reviewing the pharmacology of fluoxetine this timely book, shows that In addition to its well-established actions on 5-HT reuptake, fluoxetine has powerful effects on brain neuroactive steroid metabolism; it increases BDNF signaling, modulates activity of the glutamate system and induces neuronal structural plasticity by stimulating neurogenesis, synaptogenesis and cellular survival. Fluoxetine has anti-inflammatory actions, anti-oxidant effects, enhances fibrinolysis and also exhibits potent sigma-1 receptor chaperone activity. There is evidence that it can modulate or even reverse the epigenetic mechanisms that contribute to the pathogenesis of major depression.

But fluoxetine is not a panacea and must be used with caution. There are contra-indications for prescribing during pregnancy and also to the young in whom it may affect development; there is a risk of hepatotoxicity with long-term use. In combination with certain other drugs fluoxetine may also enhance addiction liability, especially in the developing brain. In this category, evidence of alarming osteolytic effects, would have warranted inclusion.

There is no doubt that fluoxetine represents a significant addition to the pharmacopeia. It is likely however that its therapeutic potential has yet to be exploited to best advantage. Certainly there is scope for improving its efficacy in treatment of depression and anxiety-linked disorders and its developing use in stroke rehabilitation holds promise. Re-engineering the molecule to target its non-SSRI properties could also pay dividends.

Graziano Pinna has done a good job in assembling a caste of experts to review the current status of the pharmacology of fluoxetine. The content of this volume is relevant not only to those who use fluoxetine as an experimental tool but also to those who utilize it in clinical practice.

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