

Antidepressant Drugs

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Editorial

Depression is a common mental disorder characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-esteem, sleep or appetite disturbances, fatigue and lack of concentration. The disorder can be either chronic or recurrent, substantially reducing the individual's capacity to work or study, or perform the activities of daily living [1]. Depression is more common in women than in men, and affects about 6% of the adult population in the world every year [2]. In the 1950s, the accidental discovery of iproniazid and imipramine caused a significant change in the pharmacological treatment for depression [3,4]. The subsequent discovery of the Monoamine Oxidase Inhibitors (MAOIs) and the Tricyclic Antidepressants (TCAs) was a landmark in antidepressant treatment, which was based on the catecholaminergic hypothesis, suggesting that depression was associated to a deficit of catecholamines, mainly serotonin and norepinephrine [5]. In the 1980s, fluoxetine emerged as a new hope for the treatment of depression [6]. A new class of antidepressants had then been created, the Serotonin Reuptake Inhibitors (SRIs), which had fewer side effects and were considered safer than the previous ones. In the following years, several SRIs were developed and, later, another class of antidepressants, the Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs). Although new antidepressant drugs have been developed, none of them showed to be more effective than the older antidepressants (MAOIs and TCAs) for the treatment of depression [7]. This has become a serious problem in the treatment of depression. Only one third of the patients achieve remission of the symptoms in the first regimen of treatment [8], and approximately 30% of the patients do not respond to any treatment [9]. Therefore, it has become urgent to find more effective treatment. From the 1950s until the end of the 1990s, the drugs discovered by researchers and which were approved for the treatment of depression were those that act on the monoamine system. There are several researches being conducted on other mechanisms underlying depression and various drugs have been tested recently for the treatment of the disorder. One alternative to the catecholaminergic model is the study of substances that act on the glutamatergic system. The glutamate is related to memory, learning and cognition. A study has shown that the drugs aiming at a specific type of glutamate receptor in the brain-called NMDA receptor—could have antidepressant effects [10]. Some studies have explored ketamine, an NMDA receptor antagonist, for the treatment of treatment-resistant depression and acute suicidal ideation. Ketamine is a fast-acting antidepressant, and may help patients at risk of suicide [11]. Several controlled studies have shown a fast antidepressant effect to a single intravenous infusion of ketamine, although a relapse was observed shortly after the drug had been suspended [12]. Another option is the use of melatonin since they have a relevant role in the regulation of sleep and the circadian rhythms,

which are usually altered in depressed patients [13]. Agomelatine has been developed as an antidepressant. It acts as a melatonin receptor agonist [14]. Researches are being conducted in several fields (neuroendocrinology, inflammatory processes, neurogenesis or neuroplasticity) in search of alternatives to the current treatment. However, up to now, the only drugs approved for the treatment of depression are those which act on the neurotransmitters and/or monoamine receptors. Considering the complex biological processes involved in depression, it is mandatory to discover and develop new forms of treatment. It has become urgent to search for new strategies and discover new ways of treating depression in a more effective way.

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