The Selective Serotonin Reuptake Inhibitors: Antidepressants with Anticonvulsant Effects?

Because of the extensive interconnections of the serotonergic neurons with other neurotransmission systems in the brain; it is reasonable to expect that chronic ingestion of SSRIs could have long-term effects, not only on its primary target but on other non-serotonergic systems. Recently, the effects of chronic paroxetine intake on synaptic components of different neurotransmitters systems in the brain have been reviewed. According to this review, chronic paroxetine triggers changes in the levels of different neurotransmitters such as GABA, glutamate, dopamine, noradrenaline, galanine and substance P. Moreover, paroxetine also modifies the expression of several components including AMPA, orexine, histamine and opioid receptors as well as GABA and glutamate transporters [2]. These changes, especially those on the GABAergic and glutamatergic systems, could be related with the anticonvulsant properties showed by some SSRIs. Along with the changes observed on inhibitory and excitatory neurotransmission, it has been proposed that serotonin could directly modulate the abnormal neuronal firing that occur in seizures, through the hyper polarization of hippocampal neurons due to changes in the conductance of some ions.

As mentioned, several studies have demonstrated that administration of SSRIs inhibit the seizures induced by different experimental models. Recent evidence indicates that citalopram raise seizure threshold and decrease seizure-related mortality in mice exposed to maximal electroschok or pilocarpine [3]. High frequency activity is a common feature that is present in the electroencephalographic recording of some epileptic patients; this activity is reproducible in some animal models and has been postulated as a sign of epileptogenesis. Hence, it has been reported that citalopram has the ability to reduce the occurrence of high frequency activity in the hippocampus of rats administered with pilocarpine [4]. Sertraline and paroxetine also have been evaluated in animal models of seizures and the results were similar. Whereas sevtaline inhibited the seizures induced by pentylentetrazole and 4-aminopiridine [5], paroxetine delayed the onset and reduced the severity of seizures induced by picrotoxin [6].

Although, there are only few clinical studies about the effects of SSRIs in patients with epilepsy, it is noteworthy that some authors have reported that the treatment with citalopram reduced the frequency of seizures inducing a clear improvement in patients. Similarly, it has been reported that fluoxetine decreased the frequency of seizures and surprisingly in some patients the seizures practically disappeared. Extraordinarily, one study carried out a wide analysis about the seizure incidence in psychopharmacological clinical trials. Thus, this study described that in patients under SSRIs treatment the incidence of seizures is lower compared to patients under placebo treatment. Therefore, the main conclusion indicates that SSRIs have a seeming anticonvulsant effect [7]. Gradually, evidence has been adding to the yet unexplored relationship antidepressant-anticonvulsant. Furthermore, a recent case report indicated that a patient with severe
myoclonic epilepsy of the infancy, or also called Dravet syndrome, experienced a remarkable reduction of the seizures after treatment with fluoxetine [8].

The available preclinical and clinical data provides us with a promising perspective of the SSRIs for epilepsy treatment; however, we cannot forget that more clinical trials are needed to evaluate this growing hypothesis. Although the SSRIs are drugs with remarkable characteristics that allow its safety prescription over several months, forthcoming studies are necessary to analyze the long-term effects of SSRIs on the neurobiology of seizures. Despite the existent holes in the theory, I propose that SSRIs should be explored as an alternate therapeutic treatment against epilepsy.

References
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