

## AUTORECEPTORS

I think it was Will Rogers, or perhaps his younger brother Roy, who said, "I never met an autoreceptor I didn't like." Autoreceptors are likeable, at least to me, in that when I grasped the concept, another light went on.

Basically autoreceptors on neurons serve to regulate neurotransmitter synthesis and release. If the autoreceptor signals that it is "full" of the neurotransmitter (NT), then the message is sent to slow the production of that NT. Clonidine is the poster child for understanding autoreceptors. It is an alpha-2 agonist. It tells the neuron to slow the synthesis and release of norepinephrine because the alpha-2 autoreceptors "think" clonidine is norepinephrine. Clonidine is, of course, a blood pressure medication but has found usefulness in psychiatry too.

On the other hand, an autoreceptor antagonist "tells" the neuron to synthesize and release more of the neurotransmitter. Such is the mechanism of SSRIs. We all know they block the reuptake of serotonin (5-HT) back into the neuron from whence it came, but they do much more to increase the synaptic availability of 5-HT. SSRIs are antagonists at two different 5-HT autoreceptors- one type at the cell body and one type at the axonal ending of the 5-HT neuron. The 5-HT<sub>1D</sub> autoreceptors are said to be somatodendritic because they are found on the cell body and the dendrites in the brainstem raphe nuclei. Not only do the SSRIs cause the signal to be sent to slow down, they overwhelm these autoreceptors to the point they are said to be desensitized, i.e. they stop working. On the other end of the neuron, or the axonal end, 5-HT<sub>1A</sub> autoreceptors are also antagonized thus signaling the need for more serotonin to be released. Thus both "ends" of the neuron are affected by SSRIs, leading to increased synthesis and release of 5-HT.

Of course, what is more interesting is that this increase in serotonin occurs long before an antidepressant effect is experienced by many patients. This brings to mind the fact that there are really only a few hundred thousand serotonin neurons in the central nervous system and as Dr. Alan Gelenberg wrote a few years ago, "There's really no evidence that depression is a serotonin-deficiency syndrome. It's like saying that a headache is an aspirin-deficiency syndrome."

And, just when I thought was beginning to understand something!