## <u>SSRIs --- The Good, The Bad, and The Ugly ---</u> <u>The Brief, The Nasty, and The Devastating</u>

Why do many people feel better when they take SSRIs?

SSRIs do not only inhibit the reuptake of serotonin, they also inhibit the reuptake of catecholamines. By far the majority of people with depression are suffering from low catecholamines as much or more than low serotonin. But since the SSRIs at least at first increase the dopamine and norepinephrine almost as much as the serotonin activity, people feel better, and some even drop some weight, which makes them feel even better. (This symptomatic improvement from increasing catecholamines typically applies to your Parasympathetic and Anaerobic patients, and to a certain extent your Ketogenic patients.)

The problem is that within a few months, the elevated serotonin to catecholamine ratio switches to a low serotonin to catecholamine ratio. (For an explanation of why/how, read the Article, *"Neurotransmitters and Amino Acids."*) The medical name for this condition is Antidepressant Discontinuation Syndrome. The cause is not known for certain, but the mechanism proposed is that use of SSRIs for even a few weeks increases synaptic levels of serotonin, but results in down-regulation of post synaptic receptors. It can take two weeks or more of agony after stopping the drug for the natural serotonin metabolic pathway to right itself.

The second mechanism proposed is that stopping the SSRI causes a deficiency of synaptic serotonin. The abrupt withdrawal of even the pitiful amount of serotonin in the synapse still produced after the few weeks required to deplete the catecholamine and serotonin systems (as described above) exacerbates the downstream effects on other neurotransmitter systems (such as norepinephrine, dopamine and even gamma amino butyric acid). The results can be a wild combination of both depression and anxiety.

The accepted medical Standards of Care for Antidepressant Discontinuation Syndrome? --- Get back on the SSRI, of course! By that time, catecholamines are depleted and the person is running a deficiency of <u>both</u> sets of neurotransmitters. Ironically, when an individual is ready to give up on SSRIs, it can often be impossible to get off them. Why? The symptoms experienced when trying to get off are the very symptoms for which the patient was prescribed the drug. So, the person automatically assumes that the withdrawal symptoms prove just how much the drug is "needed". Tragic.

Why do some people have a terrible time getting off SSRIs after all their catecholamines and serotonin are depleted? My guess is because once all systems are down, the action of the drug to get the most out of what little neurotransmitters are being produced by keeping them in the synapse for a

long period of time is all those patients have to hold on to. Take that little crutch away and they collapse completely.

Rather than devastate the whole neurotransmitter system balance with SSRIs, the right approach is to achieve Sympathetic/Parasympathetic and Anaerobic/Dysaerobic balance with proper diet and supplements. Also essential for those patients who are truly low in serotonin is to address the <u>cause</u> of the low serotonin. Low serotonin comes from excess inflammatory Prostaglandins and cytokines that up-regulate the enzyme IDO. IDO then diverts the serotonin metabolic pathway away from serotonin production and into the production of other pro-inflammatory metabolites --- particularly quinolinic acid.

[This IDO dominance of the serotonin production pathway is illustrated in the tryptophan metabolic pathway you will find on the next page. In that pathway you will find tryptophan in the upper left hand corner, and across the top of the flow chart you see how tryptophan is converted to 5HTP, then to 5HT (serotonin) then to melatonin. --- But vertically down the left hand side of the pathway flow chart you find a path from tryptophan that leads to the production of kynurenine, then quinolinic acid. Note that IDO is the critical enzyme pushing the tryptophan pathway toward pro-inflammatory metabolites such as quinolinic acid, and away from serotonin production.

Note the Vicious Cycle. It is excess inflammation associated with Prostaglandin Imbalance that creates the excess of IDO --- then the excess of IDO creates quinolinic acid which is itself pro-inflammatory --- then that additional inflammation creates the production of more prostaglandins and thus more IDO --- and around the Vicious Cycle you go.]

The solution here is to reduce the ImmunoNeuroEndocrine Stress that caused the excess IDO --- which means supplementing with IMMUNO-SYNBIOTIC, TAURINE, ADAPTO-MAX, OXY-MAX, and OXY TONIC and/or ELECTRO TONIC and/or OXY D+ --- the most powerful way to reduce INFLAM-AGING, and thus control excess IDO production. ----- Vitamin D insufficiency is one other mechanism by which excess IDO is produced. So in some patients additional vitamin D as an adjunct to NUTRI-SPEC may be essential.

[If necessary, you can put the person on a temporary regimen of TYROSINE or PHENYLALANINE along with 5HTP to minimize the anguish while withdrawing from the SSRI.]



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