Gamma-aminobutyric acid (GABA) for Schizophrenia?

New drug discoveries are often touted as yielding tremendous benefits, having fewer side effects than drugs previously approved. A great case in point is the atypical antipsychotic medications that were positioned as being "superior" to the older, typical antipsychotics. We now know this to be completely untrue. Atypical antipsychotics are no better than their predecessors[1,2] and produce an assortment of objectionable, life altering side-effects, such as weight gain, glucose dysregulation and dyslipidemia.[3]

There is an emerging amount of literature focusing on GABA-agonist drugs (either alone or in combination with antipsychotic medications) as means to symptomatically manage the cognitive problems that are associated with schizophrenia, particularly in executive function and working memory. Researchers and pharmaceutical companies are intensely studying this issue and are working on new agents that mitigate disturbances in GABA neuron transmission.[4,5]

Once again, there are reports indicating lots of enthusiasm and promise.[6,7] What will the studies show years from now? The skeptic in me is concerned, especially when a less expensive, naturally-occurring orthomolecule, already exists and can be readily tried as a treatment option for schizophrenic patients. In this issue, we have a paper from our orthomolecular colleague, Dr. Phyllis Bronson, in which she discusses the merits of supplemental GABA for anxiety. She presents two cases where GABA produced a benefit and recommends that it be considered for patients (especially, females) who need help in managing their anxiety.

While there are numerous studies that have evaluated the therapeutic effects of synthetic GABA-agonist drugs, there are only a handful of studies that have tested supplemental GABA.[8] Supplemental GABA might help the schizophrenic patients that we treat; probably having fewer side effects than derivative drugs mimicking its actions on the central nervous system. Several reasons suggest that supplemental GABA ought to be a valuable component of a comprehensive orthomolecular treatment plan.

Comorbid anxiety is a usual finding among schizophrenic patients. Symptoms of anxiety occur in some 60% of schizophrenic patients, and this adversely affects their outcome.[9] Further research has shown that social anxiety represents a significant problem for patients with psychosis and that it is not a rare phenomenon.[10,11] GABA has good anxiolytic properties and is well tolerated. When prescribed at 2-3 grams per day it can aid with sleep, induce relaxation, and control symptoms of anxiety.[12] Even though side effects are rare, there is one report of panic, neurologic tingling, flushing, and transient hypertension and tachycardia in a subject who ingested 10 grams orally on an empty stomach.[12] Smaller oral doses (1-3 grams daily) were reported to cause neurologic tingling and flushing in several volunteer subjects.[12]

Decades ago Hoffer reported that adrenochrome inhibits the decarboxylase enzyme that produces GABA, thus decreasing its formation in the brain.[13] He noted that, "the decrease in the convulsive threshold and the non-specific EEG abnormalities reported by authors for schizophrenia may be due to increased quantities of adrenochrome in the brain." Current research has demonstrated an abnormality in the expression of the gene for glutamic acid decarboxylase-67 (GAD67), which synthesizes GABA, in postmortem studies of schizophrenia.[14] While the cause of the GAD67 abnormalities is unknown, it has a negative effect upon GABA neuron transmission leading to cognitive impairments among schizophrenic patients.[15]

Even though the active form of vitamin B_6 (i.e., pyridoxal-5'-phosphate) is a cofactor for GAD, it may be more prudent to simply try supplemental GABA. While researchers and pharmaceutical companies are busy studying and promoting GABA-

agonist drugs, we might do less harm and therefore more good by prescribing this safe, naturally-occurring orthomolecule, to our schizophrenic patients.

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