Depression as an early sign of parkinson's disease: involvement of serotonergic mechanisms

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Depression is one of the most common psychiatric syndromes in Parkinson's disease, with prevalence rates varying from 2.7% to 7.7% in population based studies to an average of 40% in patients attending outpatient clinics. A register study shows that depression antedates the diagnosis of PD in 9% of patients.
Two hypotheses for the pathophysiology of depression in PD exist, the serotonergic and the dopaminergic hypothesis. The serotonergic hypothesis is based on the fact that serotonergic tone is reduced in PD. Because serotonin inhibits striatal dopamine release, a lowering of serotonergic tone reduces this inhibition and thus facilitates dopamine release. However, at the same time a reduced serotonergic tone is a risk factor for the development of depression. The dopaminergic hypothesis considers affected mesolimbic dopaminergic pathways as the most important pathophysiological factor for depression, with resulting dysfunction in the self-reward systems. Neither of these hypotheses have been tested in an experimental setting.
We assessed the serotonergic hypothesis of depression in PD in an experimental way, using the tryptophan depletion paradigm. Where it is a known fact that other populations at risk for depression, such as subjects with a prior history of depression, or a family history of depression, react with lowering of mood during the ATD procedure, PD patients did not. Moreover, a pilot study with a 5HT2a SPECT ligand, did not reveal upregulation of frontal 5HT2a receptors in the brain, as is seen in major depression. Both studies do not support the serotonergic hypothesis. Alternative hypotheses, such as the dopaminergic hypothesis should be addressed in a similar experimental design.

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