

**Title: Antidepressant Induced Delay of Motor Symptoms in Parkinson's Disease (AIDS-PD)**

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**Abstract.** Despite the fact that antidepressants have been tested for safety and efficacy regarding their classic clinical indication to relieve depression in Parkinson's disease (PD) clinical trials, the effects of these drugs on disease progression remain unknown. It has recently been demonstrated that administration of antidepressants such as tricyclics (TCAs) and selective serotonin reuptake inhibitors (SSRIs) modulate the signaling pathways involved in cell survival and plasticity. Additionally, preliminary data from our laboratory indicate that the TCA, amitriptyline (AMI) provides significant protection for DA neurons in a rat model of PD; and accordingly, may hold promise as both a treatment for PD-associated depression and the progression of the DA degeneration that occurs in PD. Therefore, the primary objective of this study is to assess whether *early* antidepressant treatment has disease modifying effects in PD patients. Utilizing an integrated database compiled from six completed clinical trials (from the Parkinson's Study Group (PSG) and the Neuroprotection Exploratory Trials in Parkinson's Disease Project (NET-PD)), we propose to examine the extent to which antidepressant treatment in PD patients may delay 'need for dopaminergic therapy' or slow decline in motor function. The aims of this proposal are twofold. First, we will assess whether there is an association between the initial use of antidepressants and time to dopaminergic therapy and degree of motor disability. Second, we will determine whether subjects treated with antidepressants that modify both serotonin and norepinephrine levels (such as TCAs and serotonin and norepinephrine reuptake inhibitors; SNRIs) will have a slower rate of progression than subjects treated with other classes of antidepressants. Our analysis will include patients from the placebo arm of the following trials: FS1, FS-TOO, ELLDOPA, QE2, TEMPO and PRECEPT. Results from this study will reveal whether antidepressants, in addition to improving depression, also retard the symptomatic progression of the disease.