Can tremor, depression and progression of the Parkinson's disease be suppressed simultaneously?

The short answer to this question is YES!

Parkinson's disease (PD) is the second most common age-related and progressive neurodegenerative disorder following Alzheimer's disease (AD). It is associated with motor deficits such as loss of ability to move the muscles voluntarily, rigidity, resting tremor and postural instability. In addition, non-motor symptoms such as depression, apathy, anxiety, mild to severe memory impairment, sleep perturbations (either insomnia or hypersomnia), bladder disturbances, orthostatic hypotension, sweating, pain, visual and olfactory deficits, constipation, nausea as well as inability to produce facial expression or recognize other's verbal and nonverbal cues, may accompany or precede the motor symptoms.

The exact cause of PD, which affects more than 10 million people worldwide and approximately 60,000 annually in US remains elusive. However, it is estimated that about 15% of cases are genetically related, although the interaction between the changes that occur in the genes (e.g., mutation) and the risk for developing PD is not fully understood. In addition, exposure to some toxic chemicals such as rotenone and paraquat that are used as agricultural pesticides, are considered risk factors for PD. Indeed, the interaction between genes and environment determines an individual's susceptibility to any disease including neurological and/or neuropsychiatric disorders. In latter case, 30-40% of patients with PD may also exhibit depression.

An intricate interaction between the brain, gut and the immune system maintains normalcy or "homeostasis." The brain even tries to generate some new neurons to compensate for the lost ones but unfortunately can never catch up! Nonetheless, the brain depends on what is referred to as brain-derived neurotrophic factor or BDNF to accomplish this. Curiously, an imbalance in the immune system resulting in neuroinflammation and an imbalance in BDNF, which may also be precipitated by neuroinflammation, may constitute a common denominator for both neuropsychiatric and neurodegenerative diseases including depression and PD.

Although available drugs for both depression and PD have potentially saved millions of lives they are still limited in their use and efficacy. In regard to PD specifically, none of the treatments addresses the progression of the disease as they all provide symptomatic relief. The gold-standard drug, L-dopa, which replaces the lost neurotransmitter dopamine in PD, not only loses its efficacy in few years but can also result in other debilitating involuntary movements referred to a L-dopa-induce dyskinesia or LID.

Extensive research in search of novel neuroprotectants, that is drugs that can prevent the degeneration of neurons including dopamine containing neurons have yielded promising results. Some of these drugs include nicotine, curcumin, resveratrol, ketamine and butyrate. In regard to

nicotine specifically, it is crucial to note that nicotine must be administered in pure form, and absolutely not through smoking, chewing tobacco or electric cigarettes, to provide the desired neuroprotection and help the mood. Moreover, the mode of nicotine administration is also critical. It is argued that *nicotine should be given in a pulsatile form, either through an inhaler or nasal spray,* as application of nicotine patch would not be expected to provide the desired effect. The suggestion that all mentioned drugs including nicotine may provide both neuroprotection and mood elevating effect, is supported by experimental data and jibes with the hypothesis that a neuroprotectant would have antidepressant effect and an antidepressant would exhibit at least some neuroprotection as the two conditions share overlapping neurochemical basis.

Thus, incorporation of the novel drugs, such as those mentioned above, into the current treatments for PD may not only enhance the therapeutic efficacy of the medication but also provide a brake on the progression of the disease. However, clinical trials are needed to verify the applicability of novel treatments.

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Publications

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