

TREATMENT OF PARKINSON DISEASE SHOULD BE STARTED IN THE PRE-MOTOR STAGE- NO

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There is a lot of interest in identifying individuals who are in the pre-motor stages of Parkinson Disease (PD) and who maybe destined to get motor features sometime in the future. Because of its tremendous public health impact this area of research is of obvious importance not only to the Movement Disorders community but also the society at large. However, talking about treating pre-motor PD is premature for several reasons.

Before one initiates a therapy for a given disorder several basic questions needs to be answered. These are 'WHO TO TREAT, WHEN AND HOW LONG TO TREAT, and TREAT WITH WHAT.?'

Who to treat? Data from TEMPO, ELLDOPA and more recently the ADAGIO study is supportive of initiating symptomatic treatment of PD *as soon as the motor signs appear* and an unequivocal clinical diagnosis of PD can be made. However, in the absence of the cardinal motor manifestations of the disease, we are unable to precisely diagnose PD. There are multiple reports of non-motor symptoms such as constipation, depression, hyposmia or rapid eye movement sleep behavior disorder (RBD) antedating the occurrence of motor signs. However, there are plenty of individuals with some or all of the above features who never go on to develop PD. We are yet to fully understand the clinical significance of these findings. Studies like PARS may help identify individuals who are at a risk to develop PD.

When to treat and for how long to treat? Even if we know who is at risk the duration of the pre-motor stage is unknown. It is unclear if the duration it is years or decades? The long-term treatment is associated with a significant cost to the society and known and possibly unknown side effects. Without this knowledge it is irresponsible to subject individuals to a long term treatment.

Treat with What? There is no agent/s conclusively shown to be neuroprotective in PD. Drugs like rasagiline when used early in motor PD may be associated with an improved long-term outcome. However, it does not translate into neuroprotection. In individuals with non-motor risk factor an intervention may accelerate the onset of motor symptoms rather than delay it.

In conclusion, I believe that treating pre-motor PD, at the present time is premature and an impractical proposition.