Disease course modification in Parkinson’s disease

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Personalized medicine is an emerging field that encompasses the use of risk algorithms, molecular diagnostics, targeted therapies and pharmacogenomics in order to improve health care. It is expected to impact the way drugs are developed and patients are treated in many fields, including neurodegenerative diseases in the near future. Parkinson’s disease (PD) is the second most common neurodegenerative disease in man and its clinical hallmark is the motor parkinsonian features, namely rest tremor, bradykinesia, rigidity and loss of postural reflexes; these symptoms, resulting from the loss of dopaminergic neurons in the substantianigra pars compacta, respond well to dopamine replacement therapy; The limitation of dopaminergic therapy is that patients soon develop motor fluctuations, shortening and loss of stability and predictability of the response as well as drug-induced involuntary movements termed dyskinesias; additionally they do not provide benefit for the multiple nonmotor symptoms affecting most patients’ lives and decreasing patients’ quality of life. Moreover they do not slow down disease progression with evolution of cumulative widespread neurological disability. In this review we will outline the applications of personalized medicine for the several stages from at risk populations to full-blown advanced PD. We expect to change the way we currently define PD with molecular diagnostics, the use of DNA-, protein- or mRNA-based biological markers to predict the risk for developing PD as well as the molecular phenotype of ongoing PD through its various stages. Genomic analysis of diseases with homogeneous clinical phenotypes will unveil distinct molecular entities that require different treatment strategies for optimal outcomes. Furthermore molecular-targeted therapies that slow degeneration of both dopaminergic and non-dopaminergic neurons will replace those that simply treat PD symptoms, providing long-term disease course modification. Finally, pharmacogentomic data that predicts therapy response and limitations in the individual patient based on his genomic profile will accompany many drugs.

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