

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease, affecting up to 10 million individuals worldwide [1]. Although symptomatic treatment ameliorates motor symptoms, currently there are no disease-modifying treatments.

A biomarker is defined by the National Institutes of Health as “a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacological responses to a therapeutic intervention” [2]. Thus, biomarkers include clinical data, measurements of biological samples (e.g., plasma, serum, cerebrospinal fluid) and application of brain imaging techniques to detect changes in brain structure and function.

As for PD, biomarkers represent tools potentially suitable for either clinical or research settings and useful in predicting onset, confirming diagnosis, detecting progression and evaluating the response to disease-modifying treatments. In addition, biomarkers' trends in different stages of disease may reflect the widespread neurochemical and neuroanatomical changes that occur throughout the course of PD and, thus, possibly suggest new insights in the pathophysiological mechanisms underlying disease progression [3,4] (Figure 1). The range of available biomarkers in PD is fast expanding and includes an increasing number of laboratory, clinical and imaging data [5]. Indeed, the latter two represent the cornerstones of the diagnostic criteria for PD recently proposed by the International Parkinson and Movement Disorders Society (MDS) task force on the definition of PD [5-7]. As for imaging biomarkers, the largest amount of evidence is available for SPECT DAT Scan which is currently used in both clinical and research settings [8,9]. On the contrary, scant of data are available for laboratory biomarkers. As such, although serum biomarkers would represent a

fascinating, cost-effective and easy to collect source of information in PD, no valid and reliable serum biomarkers have been identified so far.

References

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Scope of the thesis

The scope of this thesis is to explore the relationship between specific laboratory and imaging biomarkers and cognitive as well as behavioral features in de novo, drug-naïve PD patients.

In Part III of the thesis, we explored the role of serum Insulin-Growth Factor 1 (IGF-1) at diagnosis as a marker of worse cognitive performances.

In Part IV and V, we focused on the SPECT DAT Scan and aimed at demonstrating a direct relationship between nigro-striatal denervation and specific cognitive and behavioral features.

Indeed, we already reached such results in our small, single-center de novo PD population [1-4].

Thus, the main goal of the studies proposed in the present thesis were to replicate our previous findings in the largest cohort of de novo, drug-naïve PD patients existing worldwide, the Parkinson's Progression Markers Initiative (PPMI) study promoted by the Michael J Fox Foundation for Parkinson's research and following prospectively 424 de novo PD patients and 196 Healthy Controls (<http://www.ppmi-info.org>). Indeed, we took advantage of being an active part of the PPMI study and obtained the approval from the Steering Committee for dosing the IGF-1 serum levels of all the PPMI participants. The remaining data used for this thesis have been downloaded from the PPMI website (<http://www.ppmi-info.org/access-data-specimens/download-data>). The whole statistical design as well the execution for the three studies proposed have been performed entirely by the PhD candidate.

References

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