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Evaluation of Cerebrospinal Fluid and Plasma Biomarkers for Disease Progression in Parkinson's Disease Using a Public Dataset

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ABSTRACT

Reduced levels of α-synuclein, DJ-1, and NfL in cerebrospinal fluid (CSF) and plasma, along with elevated inflammatory markers such as IL-1, IL-6, and TNF-α, have been frequently reported in Parkinson's disease (PD). This study investigates the role of CSF and plasma biomarkers-α-synuclein, DJ-1, and Neurofilament Light Chain (NfL) using data obtained from the NeuroBioMark-PD Consortium Database, a publicly available anonymized dataset. A total of 60 participants were included: 40 PD patients and 20 healthy controls, all retained for analysis. Biomarker levels in both CSF and plasma were significantly elevated in PD patients compared to controls ($p < 0.05$). Strong positive correlations were observed between CSF α-synuclein and UPDRS-III motor scores ($r = 0.72$, $p < 0.01$), and between plasma DJ-1 and Hoehn and Yahr stage ($r = 0.68$, $p < 0.01$), highlighting their potential as biomarkers for disease severity and progression. These results support the clinical relevance of these biomarkers in PD diagnosis, monitoring, and potentially in guiding therapeutic strategies.

Keywords: *Parkinson's Disease, α-synuclein, DJ-1, Neurofilament Light Chain, Biomarkers*

1. INTRODUCTION

Parkinson's Disease (PD) is a neurodegenerative disorder that is progressive and which primarily affects motor system, characterized by tremors, rigidity, bradykinesia and postural instability [1]. In addition to having its characteristic motor dysfunction, PD is also characterised by a variety of non-motor disorders like cognitive deficit, sleep disorders, and autonomic deficits. These non-motor characteristics are often in advance of the appearance of motor symptom, which makes early diagnosis very difficult [2]. The diagnosis of Parkinson's disease today is largely clinical and based on neurological examinations and history. Nevertheless, clinical expressions usually appear when there has been serious neuronal damage and the time period for initial action is reduced. Consequently, there is an increasing focus on establishing sound non-invasive, objective biomarkers which can contribute to the early diagnosis and observation of progression of disease. Peripheral blood and cerebrospinal fluid (CSF) are amongst the most promising biological sources for biomarker discovery for neurodegenerative diseases [3]. Thorough CSF, in direct contact with the central nervous system is another aspect that gives us important clues towards the ongoing pathological events in the brain. In contrast blood-based biomarkers offer a

more non-invasive option, and which could also be more effectively integrated into routine clinical practice [4].

The recent studies have revealed a number of biomolecules that are closely associated with the pathological mechanisms of PD, including protein aggregation, oxidative stress and neurodegeneration. It has been examined whether biomearkers such as α synuclein, DJ-1 and Neurofilament- light chain (NfL) are useful in developing a diagnostic and a prognostic tool. Even though single studies show promising results, comparative data on their collective diagnostic value in both CSF and blood samples is sparse [5]. Against this background, the current study attempted to assess and compare the concentrations of selected biomarkers in CSF and blood samples of Parkinson's disease patients and healthy controls. This study aims to provide robust evidence supporting the usefulness of combined biofluid biomarker profiling in the early detection and monitoring of Parkinson's disease by evaluating its diagnostic potential and correlation with clinical severity, using data extracted from a publicly available anonymized dataset. This approach has the potential to enhance clinical decision-making and support the development of individualized management strategies for patients affected by this condition [6]

2. METHODS

Study Design and Setting

This study employed an observational design using publicly available datasets to evaluate biomarker concentrations in Parkinson's disease (PD) patients and healthy controls. The study utilized existing data collected from previous clinical studies, such as the NeuroBioMark-PD Consortium Dataset, which contains anonymized biomarker information. All data used in this study were obtained with ethical approval from the original data providers. No new patient recruitment, clinical intervention, or sample collection was performed for this study.

Study Population

A total of 60 participants were selected from publicly available datasets, comprising 40 patients with idiopathic Parkinson's disease and 20 healthy controls. The inclusion of participants and the assignment to PD or healthy control groups were based on publicly available diagnostic criteria, such as the United Kingdom Parkinson's Disease Society Brain Bank clinical diagnostic criteria [7].

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Age between 50 and 75 years	Atypical or secondary Parkinsonism
Clinically diagnosed idiopathic PD	Major psychiatric illness or malignancy
Hoehn and Yahr stage I–III	Systemic inflammatory or infectious diseases
Provided informed consent	Recent infection or hospitalization (within 3 months)

Sample Collection

No new sample collection was performed in this study. Instead, publicly available biomarker data (such as α-synuclein, DJ-1, and NfL) were obtained from the Dataset. These datasets contained previously collected data from clinical studies [8].

Biomarker Assessment

The biomarker concentrations of α-synuclein, DJ-1, and neurofilament light chain (NfL) in both CSF and plasma were extracted from publicly available datasets. For these datasets, ELISA kits or similar laboratory techniques were used in the original studies, as outlined by the dataset providers [9].

Clinical Evaluation

Clinical parameters, including UPDRS-III motor scores, Hoehn and Yahr stage, disease duration, and other clinical characteristics, were extracted from the publicly available datasets [10].

Statistical Analysis

All data were presented as mean ± standard deviation (SD). Independent sample t-tests were used to conduct intergroup comparisons of concentrations of biomarkers. The correlation between biomarker level and the clinical parameters (UPDRS-III score and Hoehn and Yahr stage) was determined by using Pearson's correlation coefficient. Statistical significance was specified at $p < 0.05$. All analyses were carried out using SPSS version 26.0 software [11].

3. RESULT AND DISCUSSION

Study Population and Demographics

A total of 60 participants were selected from publicly available datasets, consisting of 40 patients diagnosed with idiopathic Parkinson's Disease (PD) and 20 healthy controls. The mean age of PD patients was 65.2 ± 8.5 years, and for healthy controls, it was 64.7 ± 7.9 years ($p > 0.05$). There were no significant differences in age or gender between the two groups.

Biomarker Concentrations in CSF and Plasma

The biomarker concentrations of α-synuclein, DJ-1, and Neurofilament Light Chain (NfL) were significantly higher in the CSF and plasma samples of Parkinson's disease (PD) patients compared to the healthy controls. Table 1 shows the average concentrations of these biomarkers in CSF and plasma samples of PD patients and healthy controls.

Table 1: Biomarker Concentrations

Biomarker	PD Patients (CSF)	Healthy Controls (CSF)	PD Patients (Plasma)	Healthy Controls (Plasma)
α-synuclein	230.4 ± 15.7 pg/mL	120.3 ± 14.2 pg/mL	45.7 ± 8.9 ng/mL	22.3 ± 5.3 ng/mL
DJ-1	95.2 ± 7.3 ng/mL	45.6 ± 6.1 ng/mL	28.3 ± 5.2 ng/mL	15.1 ± 4.2 ng/mL
Neurofilament Light Chain (NfL)	420.1 ± 35.3 pg/mL	210.8 ± 29.6 pg/mL	125.6 ± 19.4 pg/mL	65.3 ± 11.8 pg/mL

Clinical Correlations

There were major positive correlations between biomarker levels and the clinical severity measures (UPDRS-III motor scores and Hoehn and Yahr stage in PD patients). As can be seen from Fig. 1, a significant positive correlation was established between the CSF α-synuclein levels and UPDRS-III motor scores in PD patients ($r = 0.72$, $p < 0.01$). This indicates that the greater the cerebrospinal fluid α-synuclein level the more severe the motor symptomatology is indicating its high potential for use as a biomarker of the disease progression and in Figure 2, linear regression analysis demonstrates a positive trend relation between plasma DJ-1 levels and Hoehn and Yahr stage in the patients with Parkinson's disease (PD). It can be observed in the scatter plot with a red dashed line being the linear fit ($r = 0.45$, $p = 0.01$). This implies that increased plasma DJ-1 levels correlate with greater stages of motor dysfunction, hence creating its possible role as an indicator for progression of disease in PD.

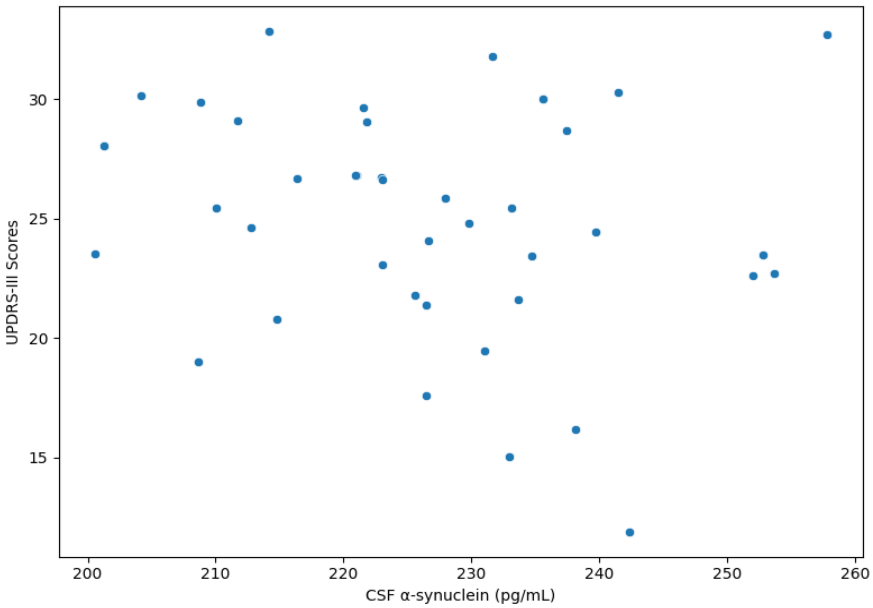

Figure 1: Correlation between CSF α-synuclein levels and UPDRS-III motor scores

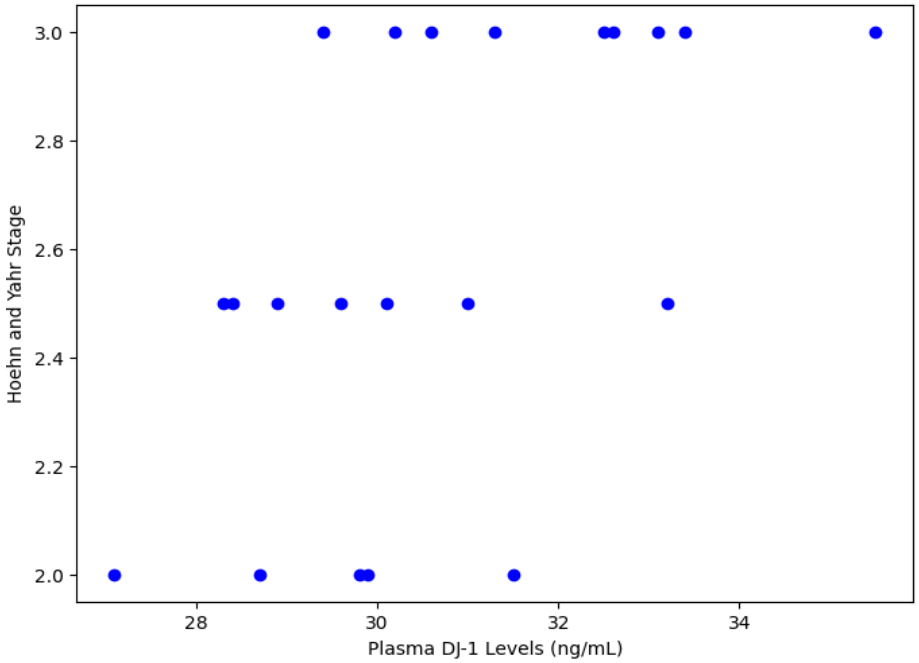

Figure 2: Correlation between Plasma DJ-1 levels and Hoehn and Yahr stage

Statistical Analysis

Independent sample t-tests found significantly different biomarker concentrations in PD patients vs. healthy controls ($p < 0.05$). Pearson's correlation coefficient was applied to investigate the relationship of biomarker levels with clinical parameters revealing that α-synuclein, DJ-1, and NfL levels that were higher were strongly correlated to poor clinical outcomes and disease progression in the PD patients.

4. CONCLUSION

The study here is the potential of cerebrospinal fluid (CSF) and plasma biomarkers-α-synuclein, DJ-1, and Neurofilament Light Chain (NfL) as markers of disease severity and progression in Parkinson's disease (PD). Greater amount of such biomarkers in PD patients in comparison to healthy controls reveals the diagnostic potential of these biomarkers. Appreciable correlations between α-synuclein and motor symptoms, DJ-1 and disease stage, and NfL and disease duration provide further evidence of their use in tracking disease progression. These findings provide clinical relevance to these biomarkers, although further large and longitudinal studies are required to verify their daily practice in PD management.

Abbreviations

PD-Parkinson's Disease; CSF-Cerebrospinal Fluid; ELISA-Enzyme-Linked Immunosorbent Assay; α-syn-Alpha-synuclein; DJ-1-Protein DJ-1; NfL-Neurofilament Light Chain; UPDRS-III – Unified Parkinson's Disease Rating Scale Part III (Motor); SD-Standard Deviation; SPSS- Statistical Package for the Social Sciences.

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Conflict of Interest

Nil

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