

Impact of Pesticide Exposure on White Blood Cell Proteome in Parkinson's Disease: A Comparative Study

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Introduction: Epidemiological evidence suggests a link between pesticide exposure and Parkinson's disease (PD), while genetic and biochemical research has highlighted the role of the ubiquitin-proteasome system (UPS) in PD pathogenesis. It is hypothesized that pesticide exposure may increase PD risk by impairing the UPS. Proteomics provides a detailed protein expression profile in biological samples, offering insights into the signaling pathways present in different patient groups. In this work we identify and characterize the biological pathways and processes in white blood cell (WBC) samples from Parkinson's disease (PD) patients with and without pesticide exposure, and differentiate the protein profile between these groups using a proteomics approach. **Methods:** The study cohort comprised 77 PD patients, categorized into those exposed to pesticides (EP) and those not exposed to pesticides (NEP). Blood samples were collected in EDTA tubes, and processed to obtaining WBCs. Due to the high cost of individual analyses, samples were pooled for analysis. Peptides were extracted using the S-TRAP method, followed by shotgun proteomic analysis using LC-MS/MS (Q-Exactive Plus, EASY-nLCII-Thermo Scientific). The data-dependent acquisition (DDA) method was employed for the proteomic analysis, and the data were analyzed using bioinformatics tools. **Results:** A total of 861 proteins were identified and quantified. Among these, 98 proteins were unique to the EP group and 60 were unique to the NEP group. In total, 116 proteins were differentially expressed in EP patients and 78 in NEP patients. Notably, upregulated biological processes included responses to organic substances, while downregulated pathways involved detoxification of reactive oxygen species, cellular responses to chemical stress, and general stress responses. Prominent upregulated proteins included WNT5A-dependent internalization of FZD2, FZD5, and ROR2, amyloid fiber formation, and eNOS activation. **Conclusion:** This study identified several key biological pathways and processes altered in WBC of PD patients exposed to pesticides. Specifically, the analysis highlighted upregulation of pathways associated with WNT5A-dependent internalization of FZD2, FZD5, and ROR2, which are crucial for cellular signaling and possibly related to neuroinflammatory responses. Additionally, amyloid fiber formation and eNOS activation were prominent among the upregulated proteins, suggesting a link to oxidative stress and endothelial dysfunction. Conversely, downregulated pathways included detoxification of reactive oxygen species, cellular responses to chemical stress, and general stress responses. These findings emphasize the involvement of inflammatory mechanisms and oxidative stress in pesticide-exposed PD patients. The proteomic data provides novel insights into these pathways, contributing to a better understanding of how pesticide exposure may influence disease progression and highlighting potential targets for further research and intervention.

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