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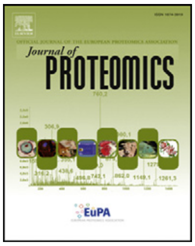

Review

Alzheimer's and Parkinson's diseases: An environmental proteomic point of view☆

Diogo Ribeiro Demartini[a],*, *Lucas Porcello Schilling*[b], *Jaderson Costa da Costa*[b],**, *Célia Regina Carlini*[a,b]

[a]*Center of Biotechnology, Federal University of Rio Grande do Sul, Av. Bento Gonçalves 9500, Prédio 43431, Sala 214, 91501-970 Porto Alegre, RS, Brazil*

[b]*Brain Institute of Rio Grande do Sul, Pontifical Catholic University of Rio Grande do Sul (PUCRS), Av. Ipiranga 6690, 90610-000 Porto Alegre, RS, Brazil*

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ABSTRACT

Alzheimer's and Parkinson's diseases are severe neurodegenerative conditions triggered by complex biochemical routes. Many groups are currently pursuing the search for valuable biomarkers to either perform early diagnostic or to follow the disease's progress. Several studies have reported relevant findings regarding environmental issues and the progression of such diseases. Here the etiology and mechanisms of these diseases are briefly reviewed. Approaches that might reveal candidate biomarkers and environmental stressors associated to the diseases were analyzed under a proteomic perspective.

This article is part of a Special Issue entitled: Environmental and structural proteomics.

Contents

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* *Correspondence to:* D.R. Demartini, Center of Biotechnology, Federal University of Rio Grande do Sul, Av. Bento Gonçalves 9500, Prédio 43431, Sala 214, 91501-970 Porto Alegre, RS, Brazil.

** *Correspondence to:* J.C. da Costa, Instituto do Cérebro (Inscer), Pontificia Universidade Católica do Rio Grande do Sul (PUCRS), Av. Ipiranga 6690, 90610-000 Porto Alegre, RS, Brazil.

E-mail addresses: diogord@terra.com.br, diogo.demartini@ufrgs.br (D.R. Demartini), jcc@pucrs.br (J.C. da Costa).

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1. Introduction

Proteomic approaches are widely used in biology, medicine, agriculture and many other areas. The main idea, regardless of the biological question behind, is to understand the expression, quantification, compartmentalization, mobilization, or modification of proteins under a specific condition. The types and numbers of these conditions vary extensively: development, biotic and abiotic stress, diseases, medical treatment, and so on. (See Figs. 1 and 2.)

Reports on environmental studies using proteomic approaches have increased in the past years. In these cases, "satellite" organisms aided to monitor different kinds of stresses caused by environmental conditions, such as water, air or soil pollution, intoxication by different poisons, heavy metals, organic solvents, ionizing radiation, and electromagnetic field [1–3].

Although there is a wide range of neurodegenerative diseases (NDs), in this review, the neurodegenerative disorders Parkinson's (PD) and Alzheimer's diseases (AD) were chosen to illustrate proteomic approaches and studies focusing on environmental proteomics.

2. Environmental proteomics

Environmental changes caused by different stressors can be studied applying proteomic approaches. These strategies can reflect the physiological response of living beings to changing conditions or stressful environmental states [4]. Minimal alterations on the environment may lead to important adaptations of organisms to this new condition. As pointed out by González-Fernándes and collaborators, environmental proteomics encompasses studies on toxic and defense mechanisms triggered by different pollutants, without previous knowledge about the biological systems themselves, which is one of the advantages of this approach [5]. Although proteomic studies can compare dynamic responses in several conditions, only in recent years has this strategy gained space in environmental issues, particularly biomarker searches for intoxication/contamination, or environmental risk factors [6].

Examples of studies performed in which the "environmental problem" was addressed using proteomics, include terrestrial ecosystems [2], semimetal intoxication [7], and exposure to tobacco smoke [8]. In a work performed by Montes-Nieto and collaborators using *Mus pretus* as a bioindicator, the protein expression profile of animals from Domingo Rubio stream was compared to that of animals from Doñana Biological Reserve (both in Spain), using 2-DE (two-dimensional electrophoresis) and peptide mass fingerprinting by MALDI-TOF (matrix-assisted laser-desorption ionization-time-of-flight). Relevant differences in the animal's proteome were identified, including proteins with a defensive role against the toxic and polluted environment as well as proteins that could make them more susceptible [9].

In a more recent publication also employing 2-DE as protein fractionation method, Company and co-workers compared subproteomes of the mussel *Bathymodiolus azoricus*. This animal lives in a gradient zone at the bottom of the oceans, in which water from the hydrothermal vents mixes with sea water, characterized by extreme variable conditions of pH, high metals and salt contents, and wide oscillations in temperature. Besides these extreme conditions, several reducing chemical species are present in this environment, which can cause severe oxidative damages through generation of reactive oxygen species (ROS). The authors selected mussels from different locations, and performed an enrichment of thiol-containing proteins, by using an activated thiol Sepharose matrix. Proteomic analysis was performed by 2-DE only, without protein identification by mass spectrometry. The authors found a correlation between thiol direct oxidation by ROS and the site of collection [10].

Dieldrin, a powerful organochloride pesticide which blocks gamma-amino-butyric acid (GABA) receptors in the CNS, was widely used in the 1960–1980s. This pesticide is very lipophilic, and accumulates in fish fat and muscle. In a study by Martyniuk and colleagues, gene expression analysis by microarray and iTRAQ were combined to quantitatively evaluate proteins differentially expressed in largemouth bass fishes fed on subchronic dieldrin-containing diets. The applied proteomic approach revealed decrease in the levels of seven proteins and increase of eleven other proteins in the dieldrin-fed group. Several of the identified proteins are known to be involved in human NDs, such as microtubule-associated tau protein, myelin basic protein, enolase 1, stathmin 1a, apolipoprotein E, and parvalbumin. Martyniuk's study has shown that dieldrin affected "pathological pathways" shared by both AD and PD, overlapping with proteomic signatures known for these neurological diseases [11], which are related to energy production, protection from oxidative damage, and synapse integrity. The authors suggested that "common pathways could be activated by stress or injury of the CNS and may be the result of apoptosis, inflammation, and oxidative damage that may precede neurotoxicity and neural damage" [12].

The effects of another important toxic agent, arsenic, was evaluated using SELDI-TOF (surface-enhanced laser desorption/ionization). This semimetal has high affinity to sulfhydryl groups in keratin, and can be detected in high amounts in the skin, hair and nails of intoxicated individuals [7]. In the study by Harezlak and coauthors, plasma samples from a population in Bangladesh known to be exposed to As were analyzed and an extensive questionnaire was applied to the subjects in order to understand their lifestyle. Authors used a