Toxicology: Open Access

Mini Review Open Access

Combining Epidemiology and Toxicogenomics to Support an Unfocused Analysis of Pesticide Exposure and Parkinson's Disease

Richard Davis*

Department of Genomics, University of Baxter, United Kingdom

Abstract

In agriculture, pesticides have been used extensively for more than 50 years. The majority of the thousands of presently in use, though, have not been fully evaluated for their impact on Parkinson's disease (PD). Additionally, ZPT exposure changed the way that genes were expressed throughout the early stages of embryonic development, particularly in relation to morphological abnormalities and metabolic dysfunctions including decreased oxidoreductase activity. Quantitative analysis of marker genes further revealed that ZPT also induced endoplasmic reticulum (ER) stress and autophagy. Activities of antioxidants and caspases studies revealed inductions of oxidative stress and apoptosis by ZPT. As a result, we draw the conclusion that oxidative damage, apoptosis, endoplasmic reticulum (ER) stress, and autophagy are all involved in ZPT-induced embryonic toxicogenomic responses.

Keywords: Chlorpyrifos, Pesticides, Toxicogenomics, Tox21, Parkinson's disease

Introduction

For more than 50 years, pesticides have been used extensively in agriculture all around the world. During this time, the chemical industry had rapid growth, which facilitated the launch and widespread commercial use of numerous goods. For instance, 13,540 pesticide formulations and 1,074 various active chemicals are now approved for usage in the state of California (California Department of Pesticide Regulation, 2021). Modern commercial agriculture relies heavily on pesticides to assist maximise food output. However, because pesticides are deliberately made to kill living things (such as plants, fungus, insects, and rodents), they must be adequately evaluated for any possible negative effects on human health, especially when used on a large basis. Toxicology testing for pesticide registration in the United States [1].

We have created a multi-step agnostic approach to screen hundreds of agriculturally used pesticides for association with PD keeping two main issues in mind: the enormous number of individual pesticides commercially used and the absence of appropriate data on chronic health effects for the majority. Our strategy integrates experimental toxicologic data and database mining of toxicogenomics with epidemiologic pesticide screening in a population-based investigation. First, we created a record-based pesticide exposure strategy employing agricultural pesticide application records and land use data in California to epidemiologically screen pesticides for association. In a significant population-based PD investigation, this exposure assessment technique enabled us to calculate proximity-based ambient exposure to 722 pesticide active components over a 40-year period. With this knowledge, we carried out an untargeted [2, 3].

Materials and Method

Pesticide selection

A set of 70 targeted pesticides, a set of positive and negative control pesticides, and a set each were the three sets of pesticides we started with. In our earlier pesticide-wide association analysis, the 70 specific chemicals of interest were identified by association testing with PD. In order to conduct this PEWAS, we employed an unbiased approach to look into every pesticide used on farms close to the homes and workplaces of 1,653 study participants who resided in three agricultural counties in Central California (Kern, Fresno, ant Tulare). We were able to test 288 pesticides separately for association in the PEWAS utilising a population-based Parkinson's study (Parkinson's Environment and Genes (PEG) study) based on the prevalence of exposure in the study population. Overall, as previously described, our analyses implicated [4].

Given the significance of past data associating paraquat and rotenone to PD through experimental and epidemiologic research, these two pesticides were chosen as positive controls. We also included eight negative controls that were sufficiently prevalent among study participants but had not been linked to PD in prior epidemiologic studies or our PEWAS analysis. In particular, they demonstrated no correlation (individual ORs per SD: 0.95–1.05) in both study populations and in both exposure locations (ambient exposure resulting from applications close to homes or places of employment). Mefenoxam (metalaxyl-M), cyprodinil, tebuconazole, tebufenozide, halosulfuron-methyl, spinosad, pyrithiobac-sodium, and potassium bicarbonate are the eight pesticides in the CTD that meet these requirements [5].

Comparative toxicogenomics database

A publicly accessible database called the CTD aims to advance our knowledge of how environmental exposures affect human health. The database links information about chemicals, genes, phenotypes, diseases, and exposures to give contextualised knowledge about chemical exposures and human health through manual curation of peer-reviewed scientific literature. To keep the database complete and up to date, the CTD incorporates new research once a month. As of May 2022, the CTD relayed information from 140,475 curated

***Corresponding author:** Richard Davis, Department of Genomics, University of Baxter, United Kingdom, E-mail: Davisric33@yahoo.com

Received: 02-Sep-2022, Manuscript No: tyoa-22-81356; **Editor assigned:** 05-Sep-2022, Pre-QC No: tyoa-22-81356 (PQ); **Reviewed:** 19-Sep-2022, QC No: tyoa-22-81356; **Revised:** 21-Sep-2022, Manuscript No: tyoa-22-81356 (R); **Published:** 28-Sep-2022, DOI: 10.4172/2476-2067.1000192

Citation: Davis R (2022) Combining Epidemiology and Toxicogenomics to Support an Unfocused Analysis of Pesticide Exposure and Parkinson's Disease. Toxicol Open Access 8: 192.

references regarding 17,070 chemicals, including about 2.5 million manually curated chemical-gene interactions, chemical-phenotype, chemical-disease, and gene-disease interactions. As a result, the CTD offers a method for combining data from voluminous earlier literature on relevant compounds [6, 7].

In the supplement, we provide a complete code notebook (R markdown html report) that includes information on all data retrieval procedures, analysis, and the output of the findings reported in this work. Additional information, along with a complete list of the data files used for analysis, can be found in our supporting MethodsX publication. By entering the pesticides by common name into the CTD querier R package, we were able to link the three sets of pesticides (70 targeted pesticides, 8 negative, and 2 positive controls) to the CTD. Each input and CTD match was thoroughly evaluated for equivalence in order to guarantee accurate linkage. If the matched CTD chemical was the same as the chemical listed in the California Pesticide Use Report (PUR), we were willing to accept incomplete matches. One caution, for instance, was given during the connection.

Discussion

According to numerous epidemiologic studies, pesticides are one of the environmental risk factors that are most consistently linked to PD. However, given the requirements of commercial agriculture for variety in agents that are tailored to emerging and reemerging pests and the vast array of pesticides currently in use, i.e., 1074 active ingredients alone registered in California, epidemiologic studies and experimental investigations have not been able to fully evaluate long-term, low dose exposure related health effects for the majority of agents. To address the impacts of the most prevalent and likely suspects now being used, complex experimental study on model organisms for PD has also been forced to be constrained. Due to this, the majority of pesticide active chemicals used in agriculture have not.

Here, we demonstrate how existing toxicological and toxicogenomic information can be used to further enhance an agnostic technique to screen pesticides for a health effect of interest (PD) and to prioritise agents for additional in-depth testing or targeted epidemiologic research. Seventy targets were implicated as allegedly linked to PD in our first stage, a population-based pesticide-wide association analysis that looked into hundreds of particular pesticide agents for association with PD. Here, we looked at these 70 pesticides in further detail using toxicogenomic and toxicologic databases that allowed us to evaluate biological linkages to PD. This unbiased strategy coupled population-based pesticide association screening with easily accessible experimental data, such as toxicogenomics information from the CTD and high-throughput in vitro findings from Tox21 [8,9].

Conclusion

Overall, a range of specific pesticides have been linked to PD risk by our thorough, pesticide-wide association research and toxicologic/toxicogenomic integration. We were able to link pesticides to specific biologic and molecular targets relevant to the aetiology of Parkinson's disease (PD) thanks to cross-database queries we carried out and presented here. This information can help us better understand the involvement of pesticides in the genesis of Parkinson's disease (PD) and prioritise experimental pesticide research. It is time to plan future experiments based on PD-specific models because epidemiologic evidence associating typical, currently used pesticides to PD and support from toxicogenomic and high-throughput toxicologic assays are now available. Our agnostic screening method for pesticide exposure effects also suggests that research should generally focus on a wider variety of pesticides as potentially associated to PD than those previously routinely studied [10].

Acknowledgement

Troy Faithfull's insightful criticism on the book is appreciated by the authors.

Conflict of Interest

The author affirm that they have no known financial or interpersonal conflicts that would have appeared to have an impact on the research presented in this study.

References

1. Adler CH (1999) Differential diagnosis of Parkinson's disease. Med Clin North Am 83:349-367.
2. Alam M, Schmidt WJ (2002) Rotenone destroys dopaminergic neurons and induces parkinsonian symptoms in rats. Behav Brain Res 136:317-324.
3. Ansari RA, Husain K, Gupta PK (1987) Endosulfan toxicity influence on biogenic amines of rat brain. J Environ Biol 8:229-236.
4. Bagetta G, Corasaniti MT, Iannone M, Nisticò G, Stephenson JD (1992) Production of limbic motor seizures and brain damage by systemic and intracerebral injections of paraquat in rats. Pharmacol Toxicol 71:443-448.
5. Barlow BK, Thiruchelvam MJ, Bennice L, Cory-Slechta DA, Ballatori N, et al.(2003) Increased synaptosomal dopamine content and brain concentration of paraquat produced by selective dithiocarbamates. J Neurochem 85:1075-1086.
6. Behari M, Srivastava AK, Das RR, Pandey RM (2001) Risk factors of Parkinson's disease in Indian patients. J Neurol Sci 190:49-55.
7. Betarbet R, Sherer TB, Di Monte DA, Greenamyre JT (2002) Mechanistic approaches to Parkinson's disease pathogenesis. Brain Pathol 12:499-510.
8. Betarbet R, Sherer TB, MacKenzie G, Garcia-Osuna M, Panov AV, et al.(2000) Chronic systemic pesticide exposure reproduces features of Parkinson's disease. Nat Neurosci 3:1301-1306.
9. Bloomquist JR, Kirby ML, Castagnoli K, Miller GW (1999). Effects of heptachlor exposure on neurochemical biomarkers of parkinsonism. In: Progress in Neuropharmacology and Neurotoxicology of Pesticides and Drugs Cambridge, UK: Royal Society of Chemistry, 195-203.
10. Butterfield PG, Valanis BG, Spencer PS, Lindeman CA, Nutt JG (1993) Environmental antecedents of young-onset Parkinson's disease. Neurology 43:1150-1158.