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Data Article

Differential gene expression data from the human central nervous system across Alzheimer's disease, Lewy body diseases, and the amyotrophic lateral sclerosis and frontotemporal dementia spectrum



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ABSTRACT

In Noori et al. [1], we hypothesized that there is a shared gene expression signature underlying neurodegenerative proteinopathies including Alzheimer's disease (AD), Lewy body diseases (LBD), and the amyotrophic lateral sclerosis and frontotemporal dementia (ALS-FTD) spectrum. To test this hypothesis, we performed a systematic review and metaanalysis of 60 human central nervous system transcriptomic datasets in the public Gene Expression Omnibus and Array-Express repositories, comprising a total of 2,600 AD, LBD, and ALS-FTD patients and age-matched controls which passed our stringent quality control pipeline. Here, we provide the results of differential expression analyses with data quality reports for each of these 60 datasets. This atlas of differential expression across AD, LBD, and ALS-FTD may guide future work to elucidate the pathophysiological drivers of these

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individual diseases as well as the common substrate of neurodegeneration.

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Specifications Table

SubjectMedical Sciences, BioinformaticsSpecific subject areaNeurodegeneration, TranscriptomicsType of dataDifferential expression analyses, data quality reports, and visualizations.How data were acquiredSystematic review of human central nervous system (CNS) transcriptomicsdatasets from patients with neurodegenerative diseases and healthy controls.Data formatAnalyzedParameters for data collectionDatasets were selected based on prespecified inclusion and exclusion criteria.Description of data collectionSystematic review of publicly available human gene expression datasets from puropatically relevant CNS regions of patients with Alzheimer's disease (AD), Lewy body diseases (LBD), and the amyotrophic lateral sclerosis and frontotemporal dementia (ALS-FTD) spectrum, as well as healthy controls. Datasets were retrieved from the NCBI Gene Expression Onnibus (EGD) and EBI ArrayExpress repositories, followed by rigorous data pre-processing and differential expression analysis.Data source locationMassachusetts United States Primary data sources: GEO: GSE109887, GSE139384, GSE118553, GSE132903, GSE13203, GSE131617, GSE122063, GSE106241, GSE84422, GSE3300, GSE43350, GSE13297, GSE20378, GSE15222, GSE16379, GSE15222, GSE16344, GSE52816, GSE23297, GSE20397, GSE20393, GSE1324, GSE54282, GSE34516, GSE23297, GSE20329, GSE13243, GSE139384, GSE13453, GSE132063, GSE13647, GSE20392, GSE13243, GSE132033, GSE20146, GSE20159, GSE132938, GSE15222, GSE163442, GSE34300, GSE54282, GSE3436, GSE23297, GSE20329, GSE16329, GSE15322, GSE16329, GSE132938, GSE15327, GSE20393, GSE13161, GSE23290, GSE132938, GSE13214, GSE56907, GSE20333, GSE20159, GSE19378, GSE1932, GSE16329, GSE20159, GSE16322, GSE20292, GSE20292, GSE20333, GSE20146, GSE20151,<		
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Value of the Data

• This dataset is a comprehensive atlas of differential gene expression data from Alzheimer's disease (AD), Lewy body diseases (LBD), and the amyotrophic lateral sclerosis and frontotemporal dementia (ALS-FTD) spectrum, providing insight into the genes and functional pathways which may drive pathogenesis uniquely in each disease, as well as collectively across all three neurodegenerative proteinopathies.

- Researchers may leverage this dataset to identify specific genes and pathways underlying neurodegeneration for future research endeavors such as pathophysiological studies and biomarker and therapeutic development.
- Future directions of this work may include comparison with single-cell and single-nuclei RNA-seq studies in postmortem specimens from patients with various neurodegenerative diseases as well as healthy subjects across the lifespan.

1. Data Description

Each gene expression dataset from the NCBI Gene Expression Omnibus (GEO) or EMBL-EBI ArrayExpress database, contained within individual directories in our Mendeley Data repository, was categorized by both disease and brain region and studied individually, entailing 89 separate analyses. For each analysis, the following data files are provided:

- 1. Data quality report generated via the *arrayQualityMetrics* package [2,3]. Data quality reports include dataset metadata from GEO or ArrayExpress, inter-array distance comparisons, principal component analyses, array intensity distributions, variance mean dependence, and MA plots for individual array quality. Each report can be examined by opening the index.html file included within the appropriate subdirectory.
- Boxplot of normalized expression data. Boxplots indicate sample label, disease label, and outlier detection from the data quality report, as well as the 20th percentile of expression.
- 3. Differential gene expression analysis. Each table lists differentially expressed genes (DEGs) along with their statistical significance, effect size, and accompanying metadata.
- 4. Volcano plot of DEGs. Volcano plots represent the statistical significance $(-\log_{10} \text{ of } p\text{-value})$ against the effect size $(\log_2 \text{ of fold-change})$.

2. Experimental design, Materials and Methods

All data analyses were performed in the R programming language and statistical computing environment (version 4.0.2).

2.1. Systematic review

The methodology of our systematic review of publicly available human central nervous system (CNS) gene expression datasets from AD, LBD, and ALS-FTD patients in the GEO and Array-Express repositories (following PRISMA guidelines [4]) is described in detail in Noori et al. [1]. Datasets were selected based on prespecified eligibility criteria. Briefly, inclusion criteria were: (1) original datasets, and (2) human microarray datasets from neuropathologically relevant CNS regions in AD, LBD, and ALS-FTD patients as well as healthy controls. This systematic review yielded 1648 control and 1586 disease samples from 60 datasets: 26 AD, 21 LBD, and 13 ALS-FTD. After the data pre-processing and quality control steps described below, a total of 2600 samples were analyzed.

2.2. Data pre-processing and analysis

Data were pre-processed and analyzed as described in Noori et al. [1]. Briefly, for each analysis, we used the Robust Multichip Average approach from the *oligo* package [5,6] followed by the *arrayQualityMetrics* package [2,3] to normalize expression data as needed, generate data quality reports, and detect outliers. Outliers were identified via boxplots, MA plots, and inter-array distance comparison. Samples which failed to pass any of these three outlier detection steps were discarded. The full data quality reports along with boxplots of the normalized expression data [7] are available in our Mendeley Data repository [8]. Outliers were represented by dashed lines in the boxplots. Next, probes were capped to filter for low signal, followed by surrogate variable analysis [9–11]. Finally, we performed differential expression analysis using the *limma* package [12–16] and created volcano plots of the DEGs [17]. The results of our differential expression analyses and the accompanying volcano plots are also available within our Mendeley Data repository [8].

2.3. Code availability

Source code is available on GitHub (https://github.com/ayushnoori/nd-diff-expr) and Zenodo [18].

Ethics Statement

Transcriptomics datasets included in our study were obtained from public repositories and there was no interaction with living human subjects. The downloaded transcriptomics datasets were generated from deidentified postmortem CNS tissue samples.

CRediT Author Statement

Ayush Noori: Conceptualization, Methodology, Software, Formal analysis, Writing - original draft; **Aziz M. Mezlini:** Methodology, Writing - review & editing; **Bradley T. Hyman:** Writing - review & editing, Funding acquisition; **Alberto Serrano-Pozo:** Conceptualization, Writing - original draft, Funding acquisition; **Sudeshna Das:** Supervision, Methodology, Writing - review & editing, Funding acquisition.

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Declaration of Competing Interest

The authors declare no competing financial interests.

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